



# Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)

## What we'll cover here

Here we will give you a review of bone marrow transplants and different types of stem cell transplants that are used to treat cancer. We will outline what transplant is like for most people, and discuss some of the issues that come with it. We will also briefly cover what it's like to donate stem cells.

## What are stem cells and why are they transplanted?

All of the blood cells in your body start out as young (immature) cells called *hematopoietic stem cells*. (*Hematopoietic* means blood-forming.) Even though they may be called “stem cells” for short, these cells are **not** the same as stem cells from embryos that are studied in cloning and other types of research. Here, we will use “stem cells” to mean hematopoietic stem cells.

Stem cells mostly live in the bone marrow (the spongy center of certain bones), where they divide to make new blood cells. Once blood cells are mature they leave the bone marrow and enter the bloodstream. A small number of stem cells also get into the bloodstream. These are called *peripheral blood stem cells*.

Stem cell transplants are used to restore the stem cells when the bone marrow has been destroyed by disease, chemotherapy (chemo), or radiation. Depending on the source of the stem cells, this procedure may be called a *bone marrow transplant*, a *peripheral blood stem cell transplant*, or a *cord blood transplant*. We will give you more detail on each of these later. Any of these types may be called a *hematopoietic stem cell transplant*.

The first successful bone marrow transplant was done in 1968. It was not until nearly 20 years later that stem cells taken from circulating (peripheral) blood were transplanted with success. More recently, doctors have begun using cord blood from the placenta and umbilical cords of newborn babies as another source of stem cells.

Today hundreds of thousands of patients have had stem cell transplants, and up to 50,000 new transplants are done each year. This has led to better care for transplant patients and helped doctors know more about which patients are likely to have better results after transplant.

## What makes stem cells so important?

Stem cells make the 3 main types of blood cells: red blood cells, white blood cells, and platelets.

We need all of these types of blood cells to keep us alive. And in order for these blood cells to do their jobs, you need to have enough of each type in your blood.

### **Red blood cells (erythrocytes)**

Red blood cells (RBCs) carry oxygen from the lungs to all of the cells in the body, and then bring carbon dioxide back from the cells to the lungs to be exhaled. A blood test called the *hematocrit* shows how much of your blood is made up of RBCs. The normal range is about 35% to 50% for adults. People whose hematocrit is below this level have *anemia*. This can make them look pale and feel cold, tired, and short of breath.

### **White blood cells (leukocytes)**

White blood cells (WBCs) fight infections caused by bacteria, viruses, and fungi. There are different types of WBCs. The most important in fighting infections are called *neutrophils*. When your *absolute neutrophil count (ANC)* drops below 1,000 per cubic millimeter ( $1,000/\text{mm}^3$ ) you have *neutropenia*, and your risk of infection increases. The danger is greatest at levels below  $500/\text{mm}^3$ .

Another type of white blood cell the stem cells make are called *lymphocytes*. These are immune cells that can make antibodies and help fight infections, and includes the highly specialized T-lymphocytes (T cells), B-lymphocytes (B cells), and natural killer (NK) cells. Certain of these lymphocytes are responsible for the body's ability to recognize its own cells and reject cells that are transplanted from someone else. This can play out differently after stem cells are transplanted from another donor. Then, it becomes the donor immune cells that decide what is "self" and what isn't. The donor immune cells can attack the recipient's body (see "Graft-versus-host disease" in the section called "Problems that may come up shortly after transplant.")

## Platelets (thrombocytes)

Platelets are pieces of cells that seal damaged blood vessels and help blood to clot, both of which are important in stopping bleeding. A normal platelet count is usually between 150,000/mm<sup>3</sup> and 450,000/mm<sup>3</sup>. A person whose platelet count drops below 150,000/mm<sup>3</sup> is said to have *thrombocytopenia*, and may bruise more easily, bleed longer, and have nosebleeds or bleeding gums. Spontaneous bleeding (bleeding with no known injury) can happen if a person's platelet count drops lower than 20,000/mm<sup>3</sup>. This can be dangerous if bleeding occurs in the brain, or if blood begins to leak from the intestine or stomach.

More information on blood counts and what the numbers on your test results mean is available in our document called *Understanding Your Lab Test Results* which you can read on our Web site, [www.cancer.org](http://www.cancer.org), or get by calling 1-800-227-2345.

## When do people need stem cell transplants?

Stem cell transplants are used to replace bone marrow that has been destroyed by disease, chemo, or radiation. In some diseases, like leukemia, aplastic anemia, certain inherited blood diseases, and some diseases of the immune system, the stem cells in the bone marrow don't work the way they should. The stem cells can make too few blood cells, too few immune cells, or too many abnormal cells. Any of these problems can cause the body to not have enough normal red blood cells, white blood cells, or platelets. A stem cell transplant may help correct these problems.

In some cancers, such as certain leukemias, multiple myeloma, and some lymphomas, a stem cell transplant can be an important part of treatment. It works like this: high doses of chemo or radiation work better than standard doses to kill cancer cells. But high doses can also cause the bone marrow to completely stop making blood cells, which we need to live. This is where stem cell transplants come in. They can be used to replace the body's source of blood cells after the bone marrow and its stem cells have been destroyed by the treatment. The rescue transplant allows doctors to use much higher doses of chemo or radiation to try to kill all of the cancer cells.

A stem cell transplant from another person can also help treat certain types of cancer in a different way other than just replacing stem cells. The donated cells can often find and kill cancer cells better than the immune cells of the person who had the cancer ever could. This is called the "graft-versus-cancer" or "graft-versus-leukemia" effect. It means that certain kinds of transplants actually help fight the cancer cells, rather than simply replacing the blood cells.

Making the decision to have a transplant is not easy. The cancer care team must compare the risks linked with the cancer itself versus the risks of the transplant procedure. Transplant risks are serious, and death can result from complications. The stage of the disease, patient's age, time from diagnosis to transplant, donor type, and the patient's overall health are all part of weighing the pros and cons before making the decision.

# Types of stem cell transplants for treating cancer

In a typical stem cell transplant very high doses of chemo are used, often along with radiation therapy, to try to destroy all of the cancer. This treatment also kills the stem cells in the bone marrow. Soon after treatment, stem cells are given to replace those that were destroyed. These stem cells are given into a vein, much like a blood transfusion. Over time they settle in the bone marrow and begin to grow and make healthy blood cells. This process is called *engraftment*.

There are 3 basic types of transplants. They are called *autologous* (cells come from you), *allogeneic* (cells come from a matched related or unrelated donor), and *syngeneic* (cells come from your identical twin). The type of transplant depends on where the stem cells come from.

## Autologous stem cell transplant

In this type of transplant, your own stem cells are taken before you get cancer treatment that destroys them. Your stem cells are removed, or *harvested*, from either your bone marrow or your blood and then frozen. After you get high doses of chemo and/or radiation the stem cells are thawed and given back to you.

One advantage of autologous stem cell transplant is that you are getting your own cells back. This means there is no risk that your immune system will reject the transplant or that the transplanted cells will attack or reject your body.

A possible disadvantage is that cancer cells may be harvested along with the stem cells and then put back into your body. To prevent this, doctors may give you anti-cancer drugs or use other methods to treat your stem cells and reduce the number of cancer cells that may be present. (See the section, “Getting rid of cancer cells in autologous transplants.”) Another disadvantage is that you have the same immune system when your stem cells engraft. The cancer cells were able to grow in the presence of your immune cells before, and may be able to do so again.

This kind of transplant is mainly used to treat some leukemias and lymphomas, and multiple myeloma. It is sometimes used for other cancers, especially in children.

## Tandem transplants

In a tandem transplant, a patient gets 2 courses of high-dose chemo, each followed by a transplant of their own stem cells. All of the stem cells needed are collected before the first high-dose chemo treatment, and half of them are used for each procedure. Most often both courses of chemo are given within 6 months, with the second one done after the patient recovers from the first one. A tandem transplant is also called a *double autologous transplant*.

Tandem transplants are sometimes used to treat certain types of cancer, but doctors do not agree on when and how to use this type of transplant. For many people, the risk of serious outcomes is quite high. Tandem transplants are still being studied to find out when they might be best used.

## Allogeneic stem cell transplant

Here, the stem cells do not come from the patient, but from a donor whose tissue type closely matches the patient. (This is discussed later under “HLA matching” in the section “Allogeneic transplant: The importance of a matched donor.”) The donor is often a family member, usually a brother or sister. If you do not have a good match in your family, a donor may be found from the general public through a national registry. This may be called a *MUD* (*matched unrelated donor*) transplant.

Blood taken from the placenta and umbilical cord of newborns is a newer source of stem cells for allogeneic transplant. Called *cord blood*, this small unit of blood has a high number of stem cells. But the number of stem cells in a unit of cord blood is often too low for large adults, so this source of stem cells has so far been used more in small adults and children. Doctors are now studying different ways to use cord blood for transplant.

An advantage of allogeneic stem cell transplant is that the donor stem cells make their own immune cells, which may help destroy any cancer cells that may remain after high-dose treatment. This is called the *graft-versus-cancer* effect. Another possible advantage is that the donor can often be asked to donate more stem cells or even white blood cells if needed. Stem cells from healthy donors are also free of cancer cells.

Still, there are many possible drawbacks to allogeneic stem cell transplants. The transplant, also known as the *graft*, may not “take” – that is, the donor cells may be more likely to die or be destroyed by the patient’s body before settling in the bone marrow. Another risk is that the immune cells from the donor can attack the patient’s body – a condition known as *graft-versus-host disease* (described in the section called “Problems that may come up shortly after transplant”). There is also a very small risk of certain infections from the donor cells, even though donors are tested before they donate. The higher risk comes from infections you have had, and which your immune system has under control. These infections often surface after allogeneic transplant because your immune system is held in check (suppressed) by medicines called *immunosuppressive* drugs. These infections can cause serious problems and even death.

Allogeneic transplant is most often used to treat certain types of leukemia, lymphomas, and other bone marrow disorders such as myelodysplasia.

### **Non-myeloablative or mini-transplants (allogeneic)**

Some people have health conditions that would make it more risky to wipe out all of the bone marrow before a transplant. For those people, doctors can use a type of allogeneic transplant that is sometimes called a “mini-transplant.” Compared with a standard allogeneic transplant, this one uses less chemo and/or radiation to get the patient ready for the transplant. Your doctor may refer to it as a *non-myeloablative transplant* or

mention *reduced-intensity conditioning (RIC)*. The idea here is to kill some of the cancer cells, some of the bone marrow, and suppress the immune system just enough to allow donor stem cells to settle in the bone marrow.

Unlike the standard allogeneic transplant, cells from both the donor and the patient exist together in the patient's body for some time after a mini-transplant. But slowly, over the course of months, the donor cells take over the bone marrow and replace the patient's own bone marrow cells. These new cells can then develop an immune response to the cancer and help kill off the patient's cancer cells – the graft-versus-cancer effect.

One advantage of a mini-transplant is the lower doses of chemo and/or radiation. And because the stem cells aren't all killed, blood cell counts don't drop as low while waiting for the new stem cells to start making blood. This makes it especially useful in older patients and those with other health problems who aren't strong enough for a standard allogeneic stem cell transplant. It may rarely be used in patients who have already had a transplant.

Mini-transplants have been found to treat some diseases better than others. They may not work well for patients with a lot of cancer in their body at the time of transplant or those with fast-growing cancer. Also, the lowered immune response can still lead to graft-versus-host disease.

This procedure is actively being studied, but it has only been in use since the late 1990s and long-term patient outcomes are not yet available. There are lower risks of complications, but the cancer may be more likely to return (relapse). Ways to improve the outcomes are still being studied.

Another future possibility is autologous transplant followed by an allogeneic mini-transplant. This is being tested in certain types of cancer, such as multiple myeloma. The autologous transplant can help decrease the amount of cancer present so that the lower doses of chemo given before the mini-transplant can work better. And the recipient still gets the benefit of the graft-versus-cancer effect of the allogeneic transplant.

## Syngeneic stem cell transplant

This is a special kind of allogeneic transplant that can only happen when the donor and recipient are identical twins or identical triplets – who always have the same tissue type. An advantage of syngeneic stem cell transplant is that graft-versus-host disease will not be a problem. There are no cancer cells in the transplant, either, as there would be from an autologous transplant. A disadvantage is that this type of transplant won't help destroy any remaining cancer cells because the new immune system is so much like yours. Every effort must be made to destroy all the cancer cells before the transplant is done to help keep the cancer from coming back (relapse).

## Sources of stem cells for transplant

There are 3 possible sources of stem cells to use for transplants: bone marrow, the bloodstream (peripheral blood), and umbilical cord blood from newborns. Although bone

marrow was the first source used in stem cell transplant, peripheral blood is used most often today.

## Bone marrow

Bone marrow is the spongy tissue in the center of bones. Its main job is to make blood cells that circulate in your body and immune cells that fight infection.

Bone marrow was the first source used for stem cell transplants because it has a rich supply of stem cells. The bones of the pelvis (hip) contain the most marrow and have large numbers of stem cells in them. For this reason, cells from the pelvic bone are used most often for a bone marrow transplant. Enough marrow must be removed to collect a large number of healthy stem cells.

For a bone marrow transplant, the donor gets general anesthesia (drugs are used to put the patient into a deep sleep). Several large needle sticks are made through the skin into the back of the pelvic bone to remove marrow. The thick, liquid marrow is pulled out through the needle. (For more on this, see the section called “The donor experience.”)

The harvested marrow is filtered, stored in a special solution in bags, and then frozen. When the marrow is to be used, it is thawed and then given just like a blood transfusion. The stem cells travel to the recipient’s bone marrow. There, they engraft or “take” over time and begin to make blood cells. Signs of the new blood cells usually can be measured in the patient’s blood tests in about 2 to 4 weeks.

## Peripheral blood

Normally, few stem cells are found in the blood. But giving hormone-like substances called *growth factors* to stem cell donors a few days before the harvest causes their stem cells to grow faster and move from the bone marrow into the blood.

For a peripheral blood stem cell transplant, the stem cells are taken from the blood. A very thin flexible tube (called a *catheter*) is put into one of the donor’s veins and attached to tubing that goes to a special machine. The machine separates the blood, and keeps only the stem cells. The rest of the blood goes back to the donor. This takes several hours, and may need to be repeated for a few days to get enough stem cells. The stem cells are filtered, stored in bags, and frozen until the patient is ready for them. For more on this, see the section called “The donor experience.”

After the patient is treated with chemo and/or radiation, the stem cells are given in an infusion much like a blood transfusion. The stem cells travel to the bone marrow, engraft, and then grow and make new, normal blood cells. The new cells are usually found in the patient’s blood a few days sooner than when bone marrow stem cells are used, usually in about 10 to 20 days.

## Umbilical cord blood

Not everyone who needs an allogeneic stem cell transplant can find a well-matched donor among the people who have signed up to donate. For these patients, umbilical cord blood may be a potential source of stem cells. Around 30% of unrelated hematopoietic stem cell transplants now come from cord blood.

A large number of stem cells are normally found in the blood of newborn babies. After birth, the blood that is left behind in the placenta and umbilical cord (known as *cord blood*) can be taken and stored for later use in a stem cell transplant. The cord blood is frozen until needed.

Cord blood transplant uses blood that is normally thrown out. The first cord blood transplant was done in 1988, and its use has been growing ever since. For more information on donating cord blood, see the section called “The donor experience.”

A possible drawback of cord blood is the smaller number of stem cells present. But this is partly balanced by the fact that each cord blood stem cell can form more blood cells than a stem cell from adult bone marrow. Still, it can take cord blood transplants longer to engraft and start working. To be safe, most cord blood transplants done so far have been in children and smaller adults. Researchers are now looking for ways to use cord blood for transplants in larger adults. One approach that is being taken is to find ways to increase the numbers of these cells in the lab before the transplant. Another approach is the use of the cord blood from 2 infants at the same time for one adult transplant, called a *double-unit cord blood transplant*. A third way cord blood is being used is in the setting of a “mini-transplant.” In this case, the bone marrow is not completely destroyed so there are some host stem cells left before and during the time that the cord blood stem cells engraft. Other strategies to better use cord blood transplants are being actively studied.

## Which stem cell source is best?

All 3 sources of stem cells can be used for the same goal: to give the patient healthy stem cells that will mature into healthy blood cells. There may be some pros and cons to each source, but all are usually able to provide the needed number of stem cells (with the exception noted above in umbilical cord blood).

At first, all stem cell transplants done were bone marrow transplants. But today peripheral blood stem cell transplants are far more common. Often, doctors are able to harvest more stem cells from peripheral blood than from bone marrow. It’s also easier for the donor to give peripheral blood stem cells than bone marrow. Another plus for peripheral blood stem cell transplant is that the recipient’s blood count often recovers faster than with a bone marrow transplant. But the risk of graft-versus-host disease is somewhat higher with peripheral blood stem cell transplants than with bone marrow transplants.

Cord blood transplant may be an option if a good match can’t be found among volunteer stem cell donors. Even though well-matched cord blood is generally best, studies suggest that cord blood does not have to be as closely matched as bone marrow or peripheral

blood. This may be an advantage for patients with rare tissue types. This type of transplant also does not require a separate donation procedure and may reduce the severity of graft-versus-host disease (described in the section called “Problems that may come up shortly after transplant”). Cord blood cells usually take longer to engraft. This leaves the patient at a high risk for infection and bleeding longer than is seen with transplanted marrow or peripheral blood stem cells. Another drawback is that, unlike bone marrow transplant or peripheral blood stem cell transplant, the donor cannot be called back to give more if needed after the cord blood stem cells are used.

## **Allogeneic transplant: The importance of a matched donor**

The immune system plays an important role in the success of any allogeneic stem cell transplant. The immune system normally keeps us healthy by destroying anything in the body it sees as foreign, such as bacteria or viruses. A working immune system recognizes cells coming from other people as foreign, too.

If the tissue type match between donor and recipient is not close, the patient’s immune system may see the new stem cells as foreign and destroy them. This is called *graft rejection*, which can lead to graft failure. This is rare, because the pre-transplant treatment (chemo and/or radiation) mostly destroys the immune system.

Another problem that can happen is that when the donor stem cells make their own immune cells, the new cells may see the patient’s cells as foreign and turn against their new home. This type of attack is called graft-versus-host disease (see “Graft-versus-host disease” in the section called “Problems that may come up shortly after transplant”). The grafted stem cells attack the body of the person who got the transplant. This is a common problem, and it’s the main reason why every effort is made to find the closest match possible.

### **HLA matching**

Many factors play a role in how the immune system knows the difference between “self” and “non-self,” but the most important for transplants is the *human leukocyte antigen (HLA)* system. Human leukocyte antigens are proteins found on the surface of most cells. They make up a person’s *tissue type*, which is different from a person’s blood type.

Each person has a number of pairs of HLA antigens (the best-known ones being A, B, C, DR, DQ, and DP). We inherit one of each of these antigens from each of our parents (and pass one of each pair on to each of our children). Doctors try to match these antigens when finding a donor for a person getting a stem cell transplant.

How well the donor’s and recipient’s HLA tissue types match plays a large part in whether the transplant will work. A match is better when all of the major HLA antigens are the same – a 6 out of 6 match. These have a lower chance of graft-versus-host disease, a common complication of donor transplants. For bone marrow and peripheral

blood stem cell transplants, sometimes a donor with a single mismatched antigen is used – a 5 out of 6 match. For cord blood transplants a perfect HLA match doesn't seem to be as crucial for success, and even a sample with a couple of mismatched proteins may be OK.

Doctors keep learning more about better ways to match donors. Today, fewer tests may be needed on siblings, since their cells vary less than an unrelated donor. But on unrelated donors, more than the basic 6 HLA antigens are often tested to reduce the risk of graft-versus-host disease. Sometimes doctors will want to look at 5 pairs of antigens, for example, to try and obtain a 10 out of 10 match. Certain transplant centers require higher levels of matching. Others are doing clinical trials with related half-matched donors and different chemotherapy schedules. This is an active area of research because it is often difficult to find a good HLA match.

## Finding a match

There are thousands of different combinations of possible HLA tissue types. This can make it hard to find an exact match. HLA antigens are inherited. The search for a donor usually starts with the patient's brothers and sisters (siblings), who have the same parents as the patient, if possible. The chance that a sibling would be a perfect match (that is, that you both received the same set of HLA antigens from each of your parents) is about 1 out of 4.

If a good match is not found in a sibling, the search may then move on to relatives who are less likely to be a good match – parents, half siblings, and extended family, such as aunts, uncles, or cousins. (Spouses are no more likely to be good matches than other people who are not related.) If no relatives are found to be a close match, the search then widens to the general public.

As unlikely as it seems, it is possible to find a good match with a stranger. To help with this process, bone marrow transplant registries are used (see the section called "To learn more"). Registries serve as matchmakers between patients and volunteer donors. The largest registry in the United States is the National Marrow Donor Program. It lists the tissue types of about 9 million possible donors and nearly 145,000 cord blood units. Another agency, the Caitlin Raymond International Registry, has access to millions of international records. These agencies have successfully matched thousands of donors and recipients. The chances of finding a matched unrelated donor improve each year, as more volunteers sign up. Today, about half of white people who need a stem cell transplant may find a perfect match among unrelated donors. This drops to about 1 out of 10 people in other ethnic groups, mostly because their HLA types are more diverse and they are less likely to take part in donor registries. Depending on a person's tissue typing, several other international registries also are available. Finding an unrelated donor can take months, though. A single match can require going through many, many records.

# The donor experience

People usually volunteer to become stem cell donors either because they have a loved one in need of a match or because they want to help people they don't know.

## If you want to donate stem cells

People who want to donate stem cells or join a volunteer registry can speak with their doctors or contact the National Marrow Donor Program to find the nearest donor center. Potential donors are asked questions to make sure they are healthy enough to donate and don't pose a risk of infection to the recipient. For more information about donor eligibility guidelines, contact the National Marrow Donor Program or the donor center in your area (see the section called "To learn more").

A simple blood test is done to learn the potential donor's HLA type. There may be a one-time, tax-deductible fee of about \$75 to \$100 for this test. People who join a volunteer donor registry will most likely have their tissue type kept on file until they reach age 60.

Pregnant women who want to donate their baby's umbilical cord blood should set it up before the third trimester. Donation is safe, free, and does not affect the birth process. For more, see the section called "How umbilical cord blood is collected."

## Informed consent and further testing: Before the donation

If a potential stem cell donor is found to be a good match for a recipient, steps are taken to teach the donor about the transplant process and make sure he or she is making an informed decision. A consent form must be signed after the risks of donating are fully discussed, if the person decides to donate. The donor is not pressured to take part. It is always a choice.

If a person decides to donate, a medical exam and blood tests are done to make sure the donor is in good health.

A donor might also give a couple of pints of blood, which is stored in a blood bank. The blood is given back to the donor when the stem cells are removed.

## How bone marrow stem cells are collected

The donor is put under general anesthesia (given medicine to put them into a deep sleep so they don't feel pain) while bone marrow is taken. This is often called *bone marrow harvest*, and is done in an operating room. The marrow cells are taken from the back of the pelvic (hip) bone. Enough cells must be collected for the transplant, but the amount taken depends on the donor's weight. Often, about 10% of the donor's marrow, or about 2 pints, are collected. This takes about 1 to 2 hours. The body will replace these cells within 4 to 6 weeks. If the donor gave blood before the marrow donation, it may be given back to the donor at this time.

After the bone marrow harvest is done, the donor is taken to the recovery room while the anesthesia wears off. The donor may then be taken to a hospital room, and be watched until fully alert and able to eat and drink. In most cases, the donor is free to leave the hospital within a few hours or by the next morning.

The donor may have soreness, bruising, and aching at the back of the hips and lower back for a few days. Over-the-counter acetaminophen (Tylenol<sup>®</sup>) or non-steroidal anti-inflammatory drugs (such as aspirin, ibuprofen, or naproxen) are often helpful. Some people may feel tired or weak, and have trouble walking for a few days. The donor might be told to take iron supplements until the number of red blood cells returns to normal. Most donors are back to their usual schedule in 2 to 3 days. But it may take 2 or 3 weeks before they feel completely back to normal.

Risks for donors are minimal and serious complications are rare. But bone marrow donation is a surgical procedure. Rare complications could include anesthesia reactions, infection, transfusion reactions (if a blood transfusion of someone else's blood is needed – this doesn't happen if you get your own blood), or injury at the needle insertion sites. Problems such as sore throat or nausea may be caused by anesthesia.

Allogeneic stem cell donors do not have to pay for the harvesting because the recipient's insurance company usually covers the cost.

Once the cells are collected, they are filtered through fine mesh screens. This prevents bone or fat particles from being given to the recipient. For an allogeneic or syngeneic transplant, the cells may be given to the recipient through a vein soon after they are harvested. Sometimes they are frozen, such as when the donor lives far away from the recipient.

## How peripheral blood stem cells are collected

For several days before starting the donation process, the donor is given a daily injection (shot) of *filgrastim* (*Neupogen*<sup>®</sup>). This is a growth-factor drug that causes the bone marrow to make and release stem cells into the blood. Neupogen can cause some side effects, the most common being bone pain and headaches. These may be helped by over-the-counter acetaminophen (Tylenol) or non-steroidal anti-inflammatory drugs (like aspirin or ibuprofen). Nausea, sleeping problems, low-grade (mild) fevers, and tiredness are other possible effects. These go away once the injections are finished and collection is completed.

Peripheral blood stem cells are taken through a catheter (a thin, flexible plastic tube) that is put in a large vein in the arm or chest. Blood is taken out and cycled through a machine that separates the stem cells from the other blood cells. The stem cells are kept while the rest of the blood is returned to the donor. This process is called *apheresis*. It takes about 2 to 4 hours and is done as an outpatient procedure. Sometimes the process needs to be repeated daily for a few days, until enough stem cells have been collected.

Possible side effects of the procedure can include trouble placing the catheter in the vein, blockage of the catheter, or infection from the catheter. Blood clots are another possible

side effect. During the apheresis procedure donors may feel lightheaded or tingling and/or chills from the anti-coagulant drug used to keep the blood from clotting in the machine. These effects go away after donation is complete.

The process of donating cells for yourself (autologous stem cell donation) is pretty much the same as when someone donates them for someone else to use (allogeneic donation). It's just that in autologous stem cell donation the donor is also the recipient, giving stem cells for his or her own use later on. For some people, there are a few differences. For instance, sometimes it can be hard to get enough stem cells from the person with cancer. Even after several days of apheresis, you may not have enough stem cells for the transplant. This is more likely to be a problem if you have had certain kinds of chemo in the past, or if your illness affects your bone marrow. Sometimes a second drug called plerixifor (Mozobil<sup>®</sup>) is used along with filgrastim (Neupogen) in people with non-Hodgkin lymphoma or multiple myeloma. This boosts the stem cell numbers in the blood, and helps to reduce the number of apheresis sessions needed to get enough stem cells. It may cause nausea, diarrhea, and sometimes, vomiting. Your doctor will be able to give you medicines to help if these symptoms become a problem for you. It's important to tell your doctor right away if you have any pain in your left shoulder or under your left rib cage; rarely the spleen can get enlarged and even rupture. This can cause severe internal bleeding and requires emergency medical care.

## How umbilical cord blood is collected

Parents can donate their newborn's cord blood to volunteer or public cord blood banks at no cost. This process does not pose any health risk to the infant. Cord blood transplants use blood that would otherwise be thrown away.

After the umbilical cord is clamped and cut, the placenta and umbilical cord are cleaned. The cord blood is put into a sterile container, mixed with a preservative, and frozen until needed.

Remember that if you do want to donate or bank (save) your child's cord blood, you will need to arrange it before the baby is born. Some banks require you to set it up before the 28th week of pregnancy, although others accept later setups. Among other things, you will be asked to answer health questions and sign a consent form.

Many hospitals collect cord blood for donation, which makes it easier for parents to donate. For more about donating your newborn's cord blood, call 1-800-MARROW2 (1-800-627-7692) or visit the National Marrow Donor Program at [www.marrow.org/HELP/Donate\\_Cord\\_Blood\\_Share\\_Life/index.html](http://www.marrow.org/HELP/Donate_Cord_Blood_Share_Life/index.html)

Privately storing a baby's cord blood for future use is not the same as donating. It is covered in the section called "Other issues related to stem cell transplants."

# Getting rid of cancer cells in autologous transplants

For autologous transplants, some centers clean or “purge” the stem cells before they are given back to the patient. This is done to remove any cancer cells that might be mixed in with them. It is unclear whether this helps, as it has not yet been proven to reduce the risk of cancer coming back (recurrence).

A possible downside is that some normal stem cells can be lost during this process. This may cause the patient to need more time to begin making normal blood cells and leave the patient without white blood cells or platelets for a longer time. This, in turn, may cause an increased risk of infection or bleeding problems.

One method that is popular now is to give the stem cells without treating them. After transplant, the patient gets a medicine to get rid of cancer cells left in the body. This is called *in vivo purging*. Rituximab (Rituxan<sup>®</sup>), a monoclonal antibody drug, may be used for this. Research is being done to look at the need to remove cancer cells from transplants and the best way to do it.

## The transplant process

There are several steps in the transplant process. The steps are much the same, no matter what type of transplant you are going to have.

### Patient evaluation and preparation

You will first be evaluated to find out if you are eligible for a transplant. A transplant is very hard on your body. For many people, transplants can mean a cure, but complications can lead to death in some cases. You will want to weigh the pros and cons before you start.

Transplants can be hard emotionally, too. They often require being in the hospital, being isolated, and there is a high risk of side effects. Many of the effects are short-term, but some problems can go on for years. This can mean changes in the way you live your life. For some people it's just for a while, but for others the changes may be lifelong.

It is also very hard going through weeks and months of not knowing how your transplant will turn out. This takes a lot of time and emotional energy from the patient, caregivers, and loved ones. It is very important to have the support of those close to you. You will need, for instance, a responsible adult who will be with you to give you medicines, help watch for problems, and stay in touch with the team after you go home. Your transplant team can help you and your caregiver learn what you need to know. The team can also help you and your loved ones work through the ups and downs as you prepare for and go through the transplant.

Many different medical tests may be done, and questions will be asked to try to find out how well you can handle the transplant process. These might include:

- HLA tissue typing
- A complete health history and physical exam
- Evaluation of your psychological and emotional strengths
- Identifying who will be your primary caregiver throughout the transplant process
- Bone marrow biopsy
- CT (computed tomography) scan or MRI (magnetic resonance imaging)
- Heart tests, such as an EKG (electrocardiogram) or echocardiogram
- Lung studies, such as a chest x-ray and PFTs (pulmonary function tests)
- Consults with other members of the transplant team, such as a dentist, dietitian, or social worker
- Blood tests, such as a complete blood count, blood chemistries, and screening for viruses like hepatitis B, CMV, and HIV

You will also talk about your health insurance coverage and related costs that you might have to pay.

You may have a central venous catheter put into a large vein in your chest. This is most often done as outpatient surgery, and usually only local anesthesia is needed (the place where the catheter goes in is made numb). Nurses will use the catheter to draw blood and give you medicines. If you are getting an autologous transplant, it can also be used for apheresis to harvest your stem cells. The catheter will stay in place during your treatment and for some time afterward, usually until your transplanted stem cells have engrafted and your blood counts are on a steady climb to normal.

## **Eligibility**

Younger people, those who are in the early stages of disease, or those who have not already had a lot of treatment, often do better with transplants. Some transplant centers set age limits. For instance, they may not allow regular allogeneic transplants for people over 50 or autologous transplants for people over 60 or 65. Some people also may not be eligible for transplant if they have other major health problems, such as serious heart, lung, liver, or kidney disease. A “mini-transplant,” described under “Allogeneic stem cell transplant” in the section called “Types of stem cell transplants for treating cancer” may be an option for some of these patients.

## **Hospital admission**

The hospital’s transplant team will decide if you need to be in the hospital to have your transplant, or if it will be done in an outpatient center. If you have to be in the hospital, you will likely go in the day before the transplant is scheduled. During this time, the

transplant team makes sure you and your family understand the process and want to go forward with it.

The transplant experience can be overwhelming. Your transplant team will be there to help you physically and emotionally prepare for the process and discuss your needs. Every effort will be made to answer questions so you and your family fully understand what will be happening to you as you go through transplant. This is important because once conditioning treatment begins (see below), there is no going back – serious problems can result if treatment is stopped at any time during transplant.

To reduce the chance of infection during treatment, patients who are in the hospital are put in private rooms that have special air filters. The room may also have a protective barrier to separate it from other rooms and hallways. Some have a positive air pressure system to make sure no unclean outside air gets into the room.

## Conditioning treatment

*Conditioning*, also known as *bone marrow preparation* or *myeloablation*, is treatment with high-dose chemo and/or radiation therapy. It is done for one or more of the following reasons:

- To make room in the bone marrow for the transplanted stem cells
- To suppress the patient's immune system to lessen the chance of graft rejection
- To destroy all of the cancer cells anywhere in the patient's body

No one conditioning treatment is used for every transplant. Your treatment will be planned just for you based on the type of cancer you have, the type of transplant, and any chemo or radiation therapy you have had in the past.

If chemo is part of your treatment plan, it will be given in an intravenous (IV) line or as pills. If radiation therapy is planned, it is given to the entire body (called *total body irradiation* or TBI). The TBI may be given all at once in a single treatment session or in divided doses over a few days.

This phase of the transplant can be very uncomfortable since high doses are used. Chemo and radiation side effects can make you sick, and it may take months to fully recover. A very common problem is mouth sores that will need to be treated with strong pain medicines. You may also have nausea, vomiting, be unable to eat, lose your hair, and have lung or breathing problems. If you know what medicines your doctors will be using for conditioning, you can find out more about each drug on our Web site at [www.cancer.org](http://www.cancer.org), or call us for more information.

Conditioning may also cause premature menopause in women and will likely make both men and women unable to have children. (See “Stem cell transplant and having children” in the section called “Long-term problems after transplant.”) Before you have a transplant, you need to discuss the transplant process and all its effects with your doctors. It also helps to talk to others who have already had transplants.

## Infusion of stem cells

After the conditioning treatment, you are given a couple of days to rest before getting the stem cells. They will be given through your IV catheter, much like a short blood transfusion. If the stem cells were frozen, you may get some medicines before the stem cells are given. This is done to reduce your risk of reacting to the preservatives that are used when freezing the cells.

If the stem cells were frozen, they are thawed in warm water then given right away. For allogeneic or syngeneic transplants, the donor cells may be harvested in an operating room, then processed in the lab. Once they are ready, the cells are brought in and infused. The length of time it takes to get all the stem cells depends on how much fluid the stem cells are in.

You will be awake for this process and it doesn't hurt. This is big step and often has great meaning for recipients and their families. Many people consider this their rebirth or chance at a second life. They may celebrate this day as they would their actual birthday.

Infusion side effects are rare and usually mild. The preserving agent that is used when freezing the cells (called *dimethylsulfoxide* or *DMSO*) causes many of the side effects. It can cause you to have a strong taste of garlic or creamed corn in your mouth. Sucking on candy or sipping flavored drinks after the infusion can help with the taste. Your body will also smell like this. The smell may bother those around you, but you may not even notice it. The smell, along with the taste, may last for a few days, but slowly fades away. Often having cut oranges in the room will offset the odor. Patients who have transplants from cells that were not frozen do not have this problem because the cells are not mixed with the preserving agent.

Other short-term side effects of the stem cell infusion may include:

- Fever or chills
- Shortness of breath
- Hives
- Tightness in the chest
- Low blood pressure
- Coughing
- Chest pain
- Less urine output
- Feeling weak

Again, side effects are rare and usually mild. If they do happen, they are treated as needed. The stem cell infusion must always be completed.

## Recovery

The recovery stage begins after the stem cell infusion. During this time, you and your family wait for the cells to engraft, or “take,” after which they begin to multiply and make new blood cells. The time it takes to start seeing a steady return to normal blood counts varies depending on the patient and the transplant type, but is usually about 2 to 6 weeks.

During the first couple of weeks you will have low numbers of red and white blood cells and platelets. Right after transplant, when your counts are the lowest, you may be given antibiotics to keep you from getting infections (called *prophylactic* antibiotics). You may get anti-bacterial, anti-fungal, and anti-viral drugs. These are usually given until your white blood cell count reaches a certain level. Still, you can have problems, such as infection due to low white blood cell counts (*neutropenia*), or bleeding due to low platelet levels (*thrombocytopenia*). Many patients have high fevers and need IV antibiotics to treat serious infections. Transfusions of red blood cells and platelets are given until the bone marrow is working again and new blood cells are being made by the infused stem cells.

Except for graft-versus-host disease, which only happens with allogeneic transplants, the side effects from autologous, allogeneic, and syngeneic stem cell transplants are much the same. Problems may include gastrointestinal (GI) or stomach problems, and heart, lung, liver or kidney problems. (We will talk more about these later, in the section called “Problems that may come up shortly after transplant.”) You might also go through times of distress, anxiety, depression, joy, or anger. Adjusting emotionally after the stem cells can be hard because of the length of time you feel ill and isolated from others.

Having a transplant is a big decision. Your life and your relationships will be disrupted. Your future becomes uncertain, the process makes you feel bad, and financially it can be overwhelming. You may feel like you are on an emotional roller coaster during this time. Support and encouragement from family, friends, and the transplant team are very important to get you through the challenges of transplant.

## Discharge

### Discharge planning

The discharge process actually begins weeks before your transplant. It starts with the transplant team teaching you and your primary (main) caregiver about:

- The precautions you will need to take
- How to prepare your home
- How to care for your central venous catheter
- How to take good care of your mouth and teeth

- What foods you should and shouldn't eat
- Activities you can and can't do
- When to call the transplant team or other health care professionals
- Who will take the role of primary caregiver and what the job will involve, and who will be the back-up caregiver in case your main caregiver gets sick and can't be near you

## Discharge criteria

For the most part, transplant centers don't discharge patients until they meet the following criteria (See the section called "What are stem cells and why are they transplanted?" for more information about neutrophils, platelets, and hematocrit):

- They have no fever for 48 hours
- They are able to take and keep down pills or other drugs for 48 hours
- Their nausea, vomiting, and diarrhea are controlled with medicine
- Their neutrophil count (absolute neutrophil count or ANC) is at least 500 to 1,000/mm<sup>3</sup>
- They have a hematocrit of at least 25% to 30%
- They have a platelet count of at least 15,000 to 20,000/mm<sup>3</sup>
- They have someone to help them at home and a safe and supportive home environment

If patients do not meet all of these requirements, but still don't need the intensive care of the transplant unit, they may be moved another oncology unit.

## Rehabilitation

The roller coaster ride often continues after you go home. Plus, you will be feeling pretty tired after going through the transplant process. After discharge, in the rehabilitation period, some people have physical or mental health problems. These ongoing needs must now be managed at home.

Transplant patients are still followed closely during rehab. You may need daily or weekly exams along with things like blood tests, chest x-rays, bone marrow tests, or spinal taps (lumbar punctures). During early rehab, you also may need blood and platelet transfusions, antibiotics, or other treatments. These visits are frequent at first, maybe even every day, but will be needed less often if things are going well. It can take 6 to 12 months, or even longer, for blood counts to get close to normal and your immune system to work well.

Some problems may show up even a year or more after the stem cells are infused. Physical problems are usually from the chemo and/or radiation treatment, but other issues may pop up too. Problems can include:

- Graft-versus-host disease (in allogeneic transplants)
- Infections
- Lung problems, such as pneumonia or inflammation that makes it hard to breathe
- Kidney, liver, or heart problems
- Low thyroid function
- Overwhelming tiredness (fatigue)
- Limited ability to exercise
- Memory loss, trouble concentrating
- Emotional distress, depression, body image changes, anxiety
- Social isolation
- Changes in relationships
- Changes in how you view the meaning of life
- Feeling indebted to others
- Job and insurance discrimination
- Slowed growth and development (in children)
- Cataracts
- Reproductive or sexual problems (like infertility and early menopause)
- Secondary cancers

Your transplant team is still available to help you. It is important that you talk to them about any problems you are having – they can help you get the support you need to manage the changes that you are going through.

## **Problems that may come up shortly after transplant**

This is a review of some of the more common problems that may happen shortly after transplant. Many of them come from having the bone marrow wiped out by medicines or radiation just before the transplant. Others may result from the specific medicines that are

used for the conditioning phase, or from the radiation. Some of these problems tend to happen less often and be less severe in people who get “mini-transplants.”

This is not a complete list and you should tell your doctor about any problems you have or changes you notice. Some of these problems can be life-threatening, so it is important to be able to reach your doctor or transplant team at night, on weekends, and during holidays.

## Infection

During the first 6 weeks after transplant, until the new bone marrow starts making white blood cells (engraftment), you can easily get serious infections. During this time of having low white blood cell counts you are said to be *neutropenic*. (See “White blood cells (leukocytes)” in the section called “What are stem cells and why are they transplanted?” for more information.) Bacterial infections are most common during this time, but viral infections that were controlled by your immune system can become active again. And even infections that cause only mild symptoms in people with normal immune systems can be quite dangerous for you.

As discussed in “Recovery” in the section, “The transplant process,” you may get antibiotics to try to prevent infections until your blood counts reach a certain level. For instance, pneumocystis pneumonia (PCP) is a common infection that is easy to catch. Even though it doesn’t harm people with normal immune systems, for others it can cause fever, cough, and serious breathing problems. Doctors often give antibiotics to keep patients from getting this.

Your doctor may check you before transplant for signs of certain infections that may become active after transplant, and give you special medicines to keep those germs under control. For example, the virus called CMV (cytomegalovirus) is a common cause of pneumonia in people who have had transplants. It mainly happens to people who were already infected with CMV, or whose donor had the virus. If neither you nor your donor had CMV, the transplant team might follow special precautions to prevent infection while you are in the hospital.

After engraftment, the risk of infection is lower, but it still can happen. It takes 6 months to a year after a transplant for the immune system of most patients to work as well as it should. It can take even longer for patients with GVHD.

Because of the increased risk, you will be watched closely for signs of infection, such as fever, cough, shortness of breath, or diarrhea. Your doctor may check your blood often, and extra precautions to avoid exposure to germs will be needed. While in the hospital, everyone who enters your room must wash their hands well. They probably will also wear gowns, shoe coverings, gloves, and masks.

Since flowers and plants can carry bacteria and fungi, they are not allowed in your room. For the same reason, you cannot eat fresh fruits and vegetables. All your food must be well cooked and handled very carefully by you and family members. Certain foods may need to be avoided.

You may also be told to avoid contact with soil, feces (stool, both human and animal), aquariums, reptiles, and exotic pets. Your team may tell you to avoid being near disturbed soil, bird droppings, or mold. You will need to wash your hands after touching pets. Your family may need to move the cat's litter box away from places you eat or spend your time. Some transplant teams recommend cleaning carpets, floors, furniture, and drapes before you go home. Your transplant team will tell you and your family in detail about the precautions you need to follow during this time. There are many viruses, bacteria, and fungi that can cause infection after your transplant.

Despite all these precautions, patients often develop fevers, one of the first signs of infection. If you do get a fever or other signs of infection, tests will be done to look for the cause of the infection (chest x-rays, urine tests, and blood cultures) and IV (intravenous) antibiotics will be started right away. Be sure to ask which symptoms you should call the doctor about at nights and on weekends.

## Bleeding and transfusions

After a transplant, you are at risk for bleeding because the conditioning treatment destroys your body's ability to make platelets. (Platelets are the blood cells that help blood to clot.) While you wait for your transplanted stem cells to start working, your transplant team may have you follow special precautions to avoid injury and bleeding. A low platelet count usually lasts at least 3 weeks after transplant. In the meantime, you might notice easy bruising and bleeding, such as nosebleeds and bleeding gums. If your platelet count drops below  $20,000/\text{mm}^3$  (thrombocytopenia), a platelet transfusion may be needed. Precautions will be needed until your platelet counts stay at safe levels. (See "Platelets (thrombocytes)" in the section called "What are stem cells and why are they transplanted?" for more information.)

It also takes time for the bone marrow to begin making red blood cells, and you might need red blood cell transfusions from time to time as you recover.

## Interstitial pneumonitis and other lung problems

Pneumonitis is a type of lung inflammation that is most common in the first 100 days after a stem cell transplant, but some lung problems can happen after 2 years or more. Pneumonia caused by infection happens more often, but pneumonitis may be caused by radiation, graft-versus-host disease, or chemo rather than germs. It is caused by damage to the areas between the cells of the lungs (called *interstitial spaces*). Pneumonitis can be severe, especially if total body irradiation was given with chemo as part of the conditioning treatment. Chest x-rays will be taken in the hospital to watch for pneumonitis as well as pneumonia. Some doctors do breathing tests every few months to find lung problems early.

There are many types of lung and breathing problems that also need to be handled quickly. You should report any shortness of breath or changes in your breathing to your doctor or transplant team right away.

## Graft-versus-host disease

Graft-versus-host disease (GVHD) can happen in allogeneic transplants when the immune cells from the donor see the recipient's body as foreign. (The recipient's immune system has mostly been destroyed by conditioning treatment and cannot fight back – the new stem cells make up most of the immune system.) The donor immune cells may attack certain organs, most often the skin, gastrointestinal (GI) tract, and liver. This can change the way the organs work and increase the chances of infection.

GVHD reactions are very common and can vary from barely noticeable to life-threatening. Doctors often think of GVHD as acute or chronic. Acute GVHD starts soon after transplant and lasts a short time. Chronic GVHD starts later and lasts a long time. The same person can have both acute and chronic GVHD.

Acute GVHD may happen 10 to 70 days after a transplant, though the average time is around 25 days. About one-third to one-half of allogeneic transplant recipients develops acute GVHD. It is less common in younger patients and in those with closer HLA matches between donor and recipient. The first signs are usually a rash, burning, and redness of the skin on the palms and soles. This can spread over the entire body. Other symptoms include nausea, vomiting, stomach cramps, diarrhea, loss of appetite, yellowing of the skin and eyes (jaundice), belly pain, and weight loss. Most cases are mild, and those who develop it usually have no long-term effects. How well a person does depends on how bad the GVHD is. Some cases of GVHD can lead to death.

Doctors try to prevent acute GVHD by giving drugs to lessen the immune response, such as steroids, monoclonal antibodies, methotrexate, cyclosporine, and tacrolimus. New and old drugs in different combinations are being tested for GVHD prevention. Although these can help prevent serious GVHD, mild GVHD will almost always happen in allogeneic transplant patients.

Chronic (ongoing) GVHD can occur anywhere from about 70 to 400 days after the stem cell transplant. A rash on the palms of the hands or the soles of the feet is often the earliest sign. The rash can spread and is usually itchy and dry. In severe cases, the skin may blister and peel, like after a bad sunburn. A fever may also develop. Other symptoms of chronic GVHD can include:

- Decreased appetite
- Diarrhea
- Abdominal (belly) cramps
- Weight loss
- Jaundice (yellow color of the skin and eyes)
- Enlarged liver
- Bloated abdomen (belly)

- Pain in the upper right part of the abdomen
- Increased levels of liver enzymes in the blood
- The skin feels tight
- Dry, burning eyes
- Dryness or sores in the mouth
- Burning sensations when eating acidic foods
- Bacterial infections
- Blockages in airways of the lungs

Chronic GVHD is treated with medicines that suppress the immune system, much like those used for acute GVHD. These drugs can increase your risk of infection for as long as you are treated for GVHD (see “Infection” above).

The risk of GVHD can be decreased by removing some immune cells (known as T-cells) from the donor stem cells before the transplant. But this can also increase the risk of graft failure (see below). Researchers are looking at new ways to remove only certain cells, called *alloactivated T-cells*, from donor grafts. This would reduce the severity of GVHD and still allow the donor T-cells to destroy any cancer cells that may be left. Prevention and management of GVHD are major priorities for research.

## Hepatic veno-occlusive disease

Hepatic veno-occlusive disease (VOD) is a serious problem in which blood flow inside the liver is blocked. It only happens in people with allogeneic transplants, and mainly in those who got the drugs busulfan or melphalan as part of conditioning. It usually happens within 3 weeks of conditioning. VOD is more common in older people who had liver problems before the transplant, and in those with acute GVHD. It starts with yellowing skin and eyes, dark urine, tenderness below the right ribs, and quick weight gain (mostly from bloating in the belly). Doctors have found that giving busulfan in the vein rather than by mouth may reduce the risk of VOD. New ways to treat this problem are being tested, but sometimes it can result in liver failure and death.

## Graft failure

Graft failure happens when the body does not accept the new stem cells (the graft). Graft failure is more common in patients whose donor is not well matched and in patients who get stem cells that have had the T-cells removed. It can also happen in people who get a low number of stem cells, such as a single umbilical cord unit. It may be treated by a second dose of stem cells, if one is available. Graft failure very rarely happens, but it can result in death.

# After-transplant problems that may show up later

The type of problems that can happen after transplant depend on many factors, such as the type of transplant done, the conditioning treatment used, the patient's overall health, the patient's age at the time of transplant, the length and degree of immune system suppression, and whether chronic GVHD is present and how bad it is. The problems can be caused by the conditioning treatment (the pre-transplant chemo and radiation therapy), especially total body irradiation, or by other drugs used during transplant (such as the drugs that may be needed to suppress the immune system after transplant). Potential long-term risks of transplant include:

- Infertility (the inability to produce children) (This is discussed in “Stem cell transplant and having children” in the section called “Long-term problems after transplant.”)
- Hormone changes, such as changes in the thyroid or pituitary gland
- Damage to the liver, kidneys, lungs, heart and/or bones and joints
- Cataracts (clouding of the lens of the eye, which causes vision loss)
- Abnormal growth of lymph tissues (see “Post-transplant lymphoproliferative disorders” in the section, “Long-term problems after transplant.”)
- Secondary (new) cancers
- Relapse (the cancer comes back)

## Organ problems

You may need careful follow-up with close monitoring and treatment of the long-term organ problems that the transplant process can cause. Some of these, like infertility, are discussed early in the transplant process, so you can be prepared for them.

It is important that any long-term problems are found and treated quickly. Physical exams by your doctor, blood work, imaging studies, and telling your doctor about any changes or problems you've noticed will help with this. Your breathing may also be tested regularly to see if your lungs are showing signs of GVHD. As transplant methods have improved, more people are living longer and doctors are learning more about the long-term results of stem cell transplant. Researchers continue to look for better ways to care for these survivors to ensure the best possible quality of life.

## Secondary (new) cancers

Along with the possibility of the original cancer coming back (relapse) after it was treated with a stem cell transplant, there is also a chance of having a second cancer after

transplant. The general risk of cancer is estimated to be 4 to 11 times that of people who have not had transplants.

Studies have shown that people who have had allogeneic transplants have a higher risk of second cancer than people who got a different type of stem cell transplant. Cancers that happen a few months after transplant are mainly lymphomas, especially the B-cell types. These seem to be caused by a common virus known as Epstein-Barr virus, or EBV. The immune system can normally keep the virus under control, but EBV can cause cancer – especially when the immune system is being suppressed with drugs, as it is after allogeneic transplant.

Acute leukemia is a type of cancer that can develop a few years after stem cell transplants. Another disorder of the bone marrow called myelodysplasia (or myelodysplastic syndrome), in which the bone marrow makes defective blood cells, can also happen a few years after transplant. Myelodysplasia is not really a cancer, but it can develop into cancer in some people. For more, see our document called *Myelodysplastic Syndromes*.

Secondary cancers that happen many years later may include solid tumor cancers, often of the skin, mouth, and lung.

Risk factors for developing a second cancer are being studied and may include:

- Radiation (such as total body irradiation) and high-dose chemo as part of the conditioning treatment
- Previous chemo or radiation treatment that was not part of the transplant process
- Immune system problems (such as GVHD, HLA-mismatched allogeneic transplant, and immunosuppressant therapy)
- Being older than age 40 at the time of transplant
- Infection with viruses such as Epstein-Barr (EBV), cytomegalovirus (CMV), hepatitis B (HBV), or hepatitis C (HCV)

Some second cancers can show up a few months or a few years after transplant. But second cancers can take many years to develop, so the best studies are in those who have lived a long time after treatment. Successfully treating a first cancer gives a second cancer time (and the chance) to develop. No matter what type of cancer is treated, and even without the high doses used for transplant, treatments like radiation and chemo can lead to a second cancer in the future. For more information on this, please see our document called *Second Cancers Caused by Cancer Treatment*. You can read it on our Web site, [www.cancer.org](http://www.cancer.org), or call us for a free copy.

## Post-transplant lymphoproliferative disorder

Post-transplant lymphoproliferative disorder (PTLD) is an out-of-control growth of lymph cells that can be seen after an allogeneic stem cell transplant. It is linked to a malfunction of T-cells (a type of white blood cell that is part of the immune system) and

the presence of Epstein-Barr virus (EBV). T-cells normally help rid the body of cells that contain viruses. When the T-cells aren't working well, EBV-infected B-lymphocytes (a type of white blood cell) can grow and multiply. Most people are infected with EBV at some time during their lives. In the United States, as many as 95% of adults between 35 and 40 years of age have been infected, but the infection is controlled by a healthy immune system. The conditioning treatment given before transplant weakens the immune system, allowing the EBV infection to get out of control, which can lead to a PTLD.

Still, PTLD after allogeneic stem cell transplant is rare. It most often happens in recipients of T-cell-depleted stem cells. It can happen in recipients of stem cells that came from a mismatched or unrelated donor. It also happens in people who need anti-thymocyte globulin (ATG) or anti-CD3 monoclonal antibody for treatment of acute graft-versus-host disease (GVHD). Recipients who got stem cells from older donors and recipients who had severe immune problems before transplant may also have a higher risk of developing a PTLD.

PTLDs after allogeneic stem cell transplant most often happen within 1 to 6 months after transplant, when the immune system is still very weak. PTLD is life-threatening. It may show up as lymph node swelling, fever, and chills. There is no one standard treatment, but it is often treated by cutting back on immunosuppressant drugs to let the patient's immune system fight back. Other treatments include white blood cell (lymphocyte) transfusions to boost the immune response, using drugs like Rituxan to kill the B cells, and giving anti-viral drugs to treat the EBV.

Even though PTLD doesn't happen a lot after transplant, it is likely to happen more as the use of less-matched donors and the need for strong suppression of the immune system goes up. Studies are being done to identify risk factors for PTLD and look for ways to watch for it in transplant patients who are at risk.

## Cancer relapse

The goal of a stem cell transplant in cancer is to prolong life and even cure the cancer. But in some cases, the cancer comes back (relapses). Relapse can happen a few months to a few years after transplant. It happens much more rarely 5 or more years after transplant.

After relapse, treatment options are often quite limited. A lot depends on your overall health at that point, and whether the type of cancer you have responds well to drug treatment. Treatment for those who are otherwise healthy and strong may include chemotherapy. A few with chronic myelocytic leukemia who have had allogeneic transplants may be helped by getting white blood cells from your donor (this is called donor lymphocyte infusion). Sometimes a second transplant is possible. But most of these treatments pose serious risks even to healthier patients, so those who are frail, older, or have chronic health problems are often unable to get them.

Other options may include palliative (comfort) care, or a clinical trial of an investigational treatment. It is important to know what the expected outcome of any further treatment might be, so talk with your doctor about the purpose of the treatment. Be sure you understand the pros and cons before you decide.

## Stem cell transplant and having children

Most people who have stem cell transplants become infertile (unable to have children). This is not caused by the transplant itself, but rather by the high doses of chemo and/or radiation therapy used. These treatments affect both normal and abnormal cells, and often damage reproductive organs. But not all stem cell transplant recipients become infertile. If having children is important to you, or if you think it might be important in the future, talk to your doctor before treatment about ways to save your fertility. Your doctor may be able to tell you if a particular treatment will be likely to cause infertility.

After chemo or radiation, women may find their menstrual periods become irregular or stop completely. This doesn't always mean they cannot get pregnant, so birth control should be used before and after a transplant. The drugs used in transplants can harm a growing fetus.

Men might consider storing their sperm before having a transplant. Sperm samples are collected, then frozen and stored in a sperm bank. This process can take several days. The stored sperm can later be thawed and used to fertilize a partner's egg using artificial insemination.

Other kinds of reproductive techniques, including cryogenic preservation (freezing) of embryos, sperm, and eggs are available for future donation. Adoption is another of the many possibilities for couples who want to have families after transplant.

For more information see our document called *Fertility and Cancer: What Are My Options?* You can read it on our Web site at [www.cancer.org](http://www.cancer.org) or get a free copy by calling 1-800-227-2345.

## Weigh the risks before transplant

Despite the possible long- and short-term problems, stem cell transplant has been used to cure thousands of people with otherwise deadly cancers. Still, the possible risks and complications can threaten life, too; and they must be weighed carefully before transplant. Research today is being done to not only to cure cancer, but also to improve transplant methods and reduce the chance of problems after transplant.

## Other issues related to transplants

### Cost of transplant

Stem cell transplants cost a lot. The total cost for the procedure can vary, but it can easily reach \$100,000 or more. Allogeneic transplants tend to cost even more and can get up to \$200,000 or higher.

A transplant is still considered experimental for many types of cancer, especially solid tumors, so insurers may not cover the cost. No matter what illness you have, it is

important to find out what your insurer will cover before deciding on a transplant. You need to have an idea of what you might have to pay.

## Saving your newborn's umbilical cord blood for later

Some parents choose to donate their infant's cord blood to a public blood bank, so that it may be used by anyone who needs it. Another option is that parents can store their newborn's cord blood in private cord blood banks for possible future use by the child or a close relative. Several private companies offer this service as a form of "biological insurance," just in case the child should need a stem cell transplant at some point later in life.

The collection fee can be \$1,500 to \$2,000 and the fee to store the cord blood is around \$150 per year. You will want to check on costs because they will probably increase, and they may vary from one part of the country to another.

Parents may want to think about banking their child's cord blood, especially in families that have a history of, or close relatives with, diseases that may benefit from stem cell transplant. But here are some important points to think about:

- A single cord blood unit would not have enough stem cells for most adults, so personal cord blood use would likely be limited to childhood or early adolescence.
- Most medical specialists feel that the chance that the average child or close relative will be helped by storing his or her own cord blood is very low. Estimates have ranged from 1 out of 1,000 to 1 out of 200,000. This means that most privately-collected cord blood will likely be wasted.
- Some diseases that are treatable by transplant require stem cells that come from another donor (allogeneic). Infusing autologous cord blood stem cells that contain the same defect would not cure the disease.
- The "shelf life" of cord blood is not known. Because cord blood storage is a recent development, scientists do not know whether blood taken at birth will be useful if a family member develops a disease treatable by stem cell transplant 50 years later. Some scientists suspect that advances in immunology and genetics will have substitutes for stored cord blood by that time.

If you would like to learn more about donating your newborn's cord blood, see the section called "The donor experience." More information on private family cord blood banking can be found at the Parent's Guide to Cord Blood Foundation. You can visit their Web site at [www.parentsguidecordblood.org](http://www.parentsguidecordblood.org).

# What questions should I ask my doctor before transplant?

**BEFORE** you agree to a transplant, you may want to ask your doctor the following questions. For some of these, your doctor may refer you to the transplant team or people who work with insurance and payments for the doctor's office and/or the hospital:

- Is a transplant the best option for me? Why? Are there other options I should consider?
- What type of stem cell transplant will I have? Why?
- What is the chance of finding a good match?
- What are the chances that the transplant will work?
- Is stem cell transplant considered experimental for my disease? Why?
- What are the risks to me?
- What type of conditioning treatment will I need?
- What is the estimated cost?
- What costs, if any, will be covered by my insurance? How much will I have to pay?
- What side effects might I expect? How bad will they be? How long will they last?
- Will I be able to have children after the transplant? What options do I have if I want to have children later?
- What types of medicine or self-care will be used to control side effects?
- Will I be able to have visitors?
- When will I be able to return to work?
- What vaccines will I need and when?
- What type of follow-up will be needed after I am discharged? How often?
- What are the chances that my cancer will come back after treatment?

# To learn more

## More information from your American Cancer Society

We have selected some related information that may also be helpful to you. These materials may be read on our Web site at [www.cancer.org](http://www.cancer.org) or ordered from our toll-free number, 1-800-227-2345.

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

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

Infections in People With Cancer

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

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

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

A Message of Hope: Coping With Cancer in Everyday Life (also available in Spanish)

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

Fertility and Cancer: What Are My Options?

Understanding Your Lab Test Results

Helping Children When a Family Member Has Cancer: Dealing With Treatment (also available in Spanish)

Sexuality for the Man With Cancer (also available in Spanish)

Sexuality for the Woman With Cancer (also available in Spanish)

Second Cancers Caused by Cancer Treatment

Blood Product Donation and Transfusion

When Someone You Know Has Cancer (also available in Spanish)

## Books

The following books are available from your American Cancer Society. Call us to ask about costs or to place your order.

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

*Couples Confronting Cancer: Keeping Your Relationship Strong*

*The American Cancer Society Complete Guide to Nutrition for Cancer Survivors: Eating Well, Staying Well During and After Cancer*

*What to Eat During Cancer Treatment* (cookbook)

*What Helped Get Me Through: Cancer Survivors Share Wisdom and Hope*

*Because... Someone I Love Has Cancer: Kids' Activity Book*

## National organizations and Web sites\*

### **National Marrow Donor Program**

Toll-free number: 1-800-MARROW-2 (1-800-627-7692)

Web site: [www.marrow.org](http://www.marrow.org)

Offers free educational materials for potential donors and patients, helps patients find matches through registries of stem cell donors and cord blood units; and offers financial help to eligible under-insured patients through the Patient Assistance Program. Interpreters are available for people who call and can say (in English) what language they speak, though it may take a few minutes.

### **Caitlin Raymond International Registry**

Toll-free number: 1-800-726-2824

Web site: [www.crir.org](http://www.crir.org)

Will perform a free international search for an unrelated bone marrow or cord blood donor, and provides resources and assistance to doctors and patients throughout every aspect of the search process.

### **Blood & Marrow Transplant Information Network**

Toll-free number: 1-888-597-7674

Web site: [www.bmtinfonet.org](http://www.bmtinfonet.org)

Provides information and support services to bone marrow, stem cell, and cord blood transplant patients and survivors.

### **National Bone Marrow Transplant Link (nbmtLink)**

Toll-free number: 1-800-LINK-BMT (1-800-546-5268)

Web site: [www.nbmtlink.org](http://www.nbmtlink.org)

Helps patients, their caregivers, families, and health care professionals meet the many challenges of bone marrow/stem cell transplant (BMT) by providing vital information and support services before, during, and after a BMT.

### **National Foundation for Transplants (NFT)**

Toll-free number: 1-800-489-3863

Web site: [www.transplants.org](http://www.transplants.org)

Provides fund raising guidance, which helps patients, their families, and friends to raise money for transplant care.

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

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

## References

American Academy of Pediatrics Section on Hematology/Oncology; American Academy of Pediatrics Section on Allergy/Immunology, Lubin BH, Shearer WT. Policy Statement: Cord blood banking for potential future transplantation. *Pediatrics*. 2007;119(1):165-170.

Arai S, Miklos DB. Rituximab in hematopoietic cell transplantation. *Expert Opin Biol Ther*. 2010 Apr 26.

Arfons LM, Tomblyn M, Rocha V, Lazarus HM. Second hematopoietic stem cell transplantation in myeloid malignancies. *Curr Opin Hematol*. 2009;16(2):112-23.

Bhatia S, Bhatia R. Transplantation-Related Malignancies. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology, 8th ed*. Philadelphia, Pa: Wolters Kluwer/Lippincott Williams & Wilkins; 2008: 2417-2426.

Bishop MR, Pavletic SZ. Hematopoietic stem cell transplantation. In: Abeloff MD, Armitage JO, Niederhuber JE, et al. *Abeloff's Clinical Oncology, 4th ed*. Philadelphia: Churchill Livingstone Elsevier; 2008: 501-512.

Brunstein CG, Weisdorf DJ. Future of cord blood for oncology uses. *Bone Marrow Transplant*. 2009;44(10):699-707.

Centers for Disease Control, National Center for Infectious Diseases. Epstein Barr Virus and Infectious Mononucleosis. Accessed at [www.cdc.gov/ncidod/diseases/ebv.htm](http://www.cdc.gov/ncidod/diseases/ebv.htm) on May 6, 2011.

Champlin R. Hematopoietic cellular transplantation. In: Kufe DW, Pollock RE, Weichselbaum RR, Bast RC, Gansler TS, Holland JF, Frei E, eds. *Cancer Medicine*. 6th ed. Hamilton, Ontario: BC, Decker Inc.; 2003:1019-1036.

Childs RW. Allogeneic hematopoietic stem cell transplantation. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:2548-2568.

Cutler C, Ballen K. Reduced-intensity conditioning and umbilical cord blood transplantation in adults. *Bone Marrow Transplant*. 2009;44(10):667-71.

Delaney C, Ratajczak MZ, Laughlin MJ. Strategies to enhance umbilical cord blood stem cell engraftment in adult patients. *Expert Rev Hematol*. 2010;3(3):273-283.

Druker BJ, Lee SJ. Chronic Myelogenous Leukemia. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:2267-2278.

Gallagher G, Forrest DL. Second Solid Cancers After Allogeneic Hematopoietic Stem Cell Transplantation. *Cancer*. 2007;109:84-92.

Gallardo D, de la Cámara R, Nieto JB, Espigado I, et al. Is mobilized peripheral blood comparable with bone marrow as a source of hematopoietic stem cells for allogeneic transplantation from HLA-identical sibling donors? A case-control study. *Haematologica*. 2009;94(9):1282-8.

Harper JL, Corbacioglu S. Venous-occlusive Hepatic Disease, 6/22/10. Accessed at <http://emedicine.medscape.com/article/989167-overview> on May 6, 2011.

Hede K. Half-Match Bone Marrow Transplants May Raise Odds for More Recipients. *J Natl Cancer Inst*. 2011;103(10):781-783.

Kumar A, Kharfan-Dabaja MA, Glasmacher A, Djulbegovic B. Tandem versus single autologous hematopoietic cell transplantation for the treatment of multiple myeloma: a systematic review and meta-analysis. *J Natl Cancer Inst*. 2009;101(2):100-6.

Ludajic K, Balavarca Y, Bickeböller H. Minor ABO-mismatches are risk factors for acute graft-versus-host disease in hematopoietic stem cell transplant patients. *Biol Blood Marrow Transplant*. 2009;15(11):1400-1406.

Mineishi S, Ferrara JLM. Autologous stem cell transplantation. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:2541-2548.

National Cancer Institute. *Bone Marrow Transplantation and Peripheral Blood Stem Cell Transplantation*. Accessed at [www.cancer.gov/cancertopics/factsheet/Therapy/bone-marrow-transplant](http://www.cancer.gov/cancertopics/factsheet/Therapy/bone-marrow-transplant) on May 6, 2011.

National Comprehensive Cancer Center Network. NCCN Guidelines for Cancer Care by Site. Accessed at [www.nccn.org/professionals/physician\\_gls/f\\_guidelines.asp](http://www.nccn.org/professionals/physician_gls/f_guidelines.asp) on May 5, 2011

National Marrow Donor Program. Accessed at [www.marrow.org/](http://www.marrow.org/) on May 6, 2011.

Samavedi V, Sacher RA. Hematopoietic Stem Cell Transplantation. December 2010. Accessed at <http://emedicine.medscape.com/article/208954-overview> on May 11, 2011,

Socie G, Salooja N, Cohen A, et al. Nonmalignant late effects after allogeneic stem cell transplantation. *Blood*. 2003;101:3373-3385.

Sundin M, Le Blanc K, Ringden O, et al. The role of HLA mismatch, splenectomy and recipient Epstein-Barr virus seronegativity as risk factors in post-transplant lymphoproliferative disorder following allogeneic hematopoietic stem cell transplantation. *Haematologica/The Hematology Journal*. 2006;91:1059-1067.

Vargo MM, Smith RG, Stubblefield MD. Rehabilitation of the Cancer Patient. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:2857-2883.

Weisdorf DJ, Nelson G, Lee SJ, et al; Chronic Leukemia Working Committee. Sibling versus unrelated donor allogeneic hematopoietic cell transplantation for chronic myelogenous leukemia: refined HLA matching reveals more graft-versus-host disease but not less relapse. *Biol Blood Marrow Transplant*. 2009;15(11):1475-8.

Williams KM, Chien JW, Gladwin MT, Pavletic SZ. Bronchiolitis obliterans after allogeneic hematopoietic stem cell transplantation. *JAMA*. 2009;302(3):306-14.

Zamkoff KW, Bergman S, Beaty MW, et. al. Fatal EBV-related post-transplant lymphoproliferative disorder (LPD) after matched related donor nonmyeloablative peripheral blood progenitor cell transplant. *Bone Marrow Transplantation*. 2003;31:219-222.

Last Medical Review: 5/19/2011

Last Revised: 5/19/2011

2011 Copyright American Cancer Society

For additional assistance please contact your American Cancer Society  
1 · 800 · ACS-2345 or [www.cancer.org](http://www.cancer.org)