



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

What we'll cover here

This document reviews bone marrow transplants and different types of stem cell transplants used to treat cancer. We'll outline what stem cells do, why people need transplants, and what a transplant is like for most people. We'll also cover some of the issues that come with transplants, and 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, and is pronounced **he**-muh-toe-poi-**ET**-ick.) Even though they are called *stem cells*, they are **not** the same as the embryos' stem cells that are studied in cloning and other types of research. Here, the words stem cells refer to blood-forming 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 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*. They can all be called *hematopoietic stem cell transplants*.

Today hundreds of thousands of patients have had stem cell transplants. Transplant teams are better able to care for transplant patients and 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 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 a *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 weak, tired, and short of breath.

White blood cells (leukocytes)

White blood cells (WBCs) are a crucial part of the immune system. They help fight infections caused by bacteria, viruses, and fungi.

There are different types of WBCs. Neutrophils are the most important type in fighting bacterial infections. The absolute neutrophil count (ANC) is a measure of the neutrophils in your blood. When your ANC drops below 1,000 per cubic millimeter (1,000/mm³) you have *neutropenia*, and you have a higher risk of serious infection. The danger is greatest when levels are below 500/mm³.

Stem cells make another type of white blood cell called *lymphocytes*. There are different kinds of lymphocytes, such as T lymphocytes (T cells), B lymphocytes (B cells), and natural killer (NK) cells. Some lymphocytes make antibodies to help fight infections. The body depends on lymphocytes to recognize its own cells and reject cells that don't belong to the body, such as invading germs or cells that are transplanted from someone else.

Platelets (thrombocytes)

Platelets are pieces of cells that seal damaged blood vessels and help blood clot, both of which are important in stopping bleeding. A normal platelet count is usually between 150,000/cubic mm and 450,000/cubic mm, depending on the lab that does the test. A person whose platelet count drops below normal 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/mm³. This can be dangerous if bleeding occurs in the brain, or if blood begins to leak into the intestine or stomach.

More information on blood counts and what the numbers mean is available in our document called *Understanding Your Lab Test Results*.

Why would someone need a stem cell transplant?

Stem cell transplants are used to replace bone marrow that isn't working or 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.

Damaged or diseased 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, which is sometimes given with 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. The transplanted cells replace the body's source of blood cells after the bone marrow and its stem cells have been destroyed by the treatment. This transplant lets doctors use much higher doses of chemo 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 way other than just replacing stem cells. 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.

Thinking about a stem cell transplant

It's a tough decision. Although a stem cell transplant can help some patients, even giving some cancer patients a chance for a cure, making up your mind to have a transplant isn't easy. Like everything in medicine, you make the final choice as to whether or not you'll have a stem cell transplant. Your cancer care team compares the risks linked with the cancer itself versus the risks of the transplant procedure, and will discuss the expected risks and benefits with you. They may also talk with you about other options like chemotherapy, radiation, or clinical trials for your disease. Transplants have serious risks, and patients can die 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.

You'll want to ask a lot of questions to be sure you understand what's likely to happen. Some people bring a friend or family member to help them remember what the doctor or transplant team says, remind them of questions they had, and take notes. Some people prefer to record these conversations, if the doctor or nurse is OK with that and agrees to it.

Be sure to express your concerns and ask for clarification if you aren't sure how something will affect you. Make sure the doctor knows what's important to you, too. This is a complicated process, and you'll want to find out as much as you can and plan ahead before you start.

Many people ask for a second opinion before they decide to have a stem cell transplant. It's important to know about the success rate of the planned transplant based on your diagnosis and your stage in treatment. In general, transplants tend to work better if they're done in early stages of disease or when you are in remission, when your overall health is good. Ask about these factors and how they affect the expected outcomes of your transplant or other treatment.

Also, call your health insurance company to ask about reimbursement for a second opinion before you go. You might also want to talk with them about your possible transplant, and ask which transplant centers are covered under your insurance. See also “Cost of transplant” in the section “Other transplant issues.”

Weigh the risks before transplant

Despite the possible short-term problems and those that can crop up after a while, 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. The expected risks and benefits 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 risks.

Types of stem cell transplants for treating cancer

In a typical stem cell transplant for cancer very high doses of chemo are used, often along with radiation therapy, to try to destroy all the cancer cells. 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 named based on who gives the stem cells.

- *Autologous* (aw-**tahl**-uh-gus)—the cells come from you
- *Allogeneic* (**al**-o-jen-**NEE**-ick or **al**-o-jen-**NAY**-ick)—the cells come from a matched related or unrelated donor
- *Syngeneic* (**sin**-jen-**NEE**-ick or **sin**-jen-**NAY**-ick)—the cells come from your identical twin or triplet

Autologous stem cell transplants

These stem cells come from you alone. In this type of transplant, your 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. To find out more about that process, please see the section “What’s it like to donate stem cells?” 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. When you donate your own stem cells you don’t have to worry about the graft attacking your body (graft-versus-host disease) or about getting a new infection from another person. But there can still be graft failure, and autologous transplants can’t produce the “graft-versus-cancer” effect.

This kind of transplant is mainly used to treat certain leukemias, lymphomas, and multiple myeloma. It’s sometimes used for other cancers, like testicular cancer and neuroblastoma, and certain cancers in children. Doctors are looking at how autologous transplants might be used to treat other diseases, too, like systemic sclerosis, multiple sclerosis, Crohn disease, and systemic lupus erythematosus.

Getting rid of cancer cells in autologous transplants

A possible disadvantage of an autologous transplant is that cancer cells may be picked up along with the stem cells and then put back into your body later. Another disadvantage is that your

immune system is still the same as before when your stem cells engraft. The cancer cells were able to grow despite your immune cells before, and may be able to do so again.

To prevent this, doctors may give you anti-cancer drugs or treat your stem cells in other ways to reduce the number of cancer cells that may be present. Some centers treat the stem cells to try to remove any cancer cells before they are given back to the patient. This is sometimes called “*purging*.” It isn’t clear that this really helps, as it has not yet been proven to reduce the risk of cancer coming back (recurrence).

A possible downside of purging is that some normal stem cells can be lost during this process, causing the patient to take longer to begin making normal blood cells, and have unsafe levels of white blood cells or platelets for a longer time. This could increase the risk of infections or bleeding problems.

One popular method now is to give the stem cells without treating them. Then, after transplant, the patient gets a medicine to get rid of cancer cells that may be in the body. This is called *in vivo purging*. Rituximab (Rituxan®), a monoclonal antibody drug, may be used for this in certain lymphomas and leukemias, and other drugs are being tested. The need to remove cancer cells from transplants or transplant patients and the best way to do it is being researched.

Tandem transplants

Doing 2 autologous transplants in a row is known as a *tandem transplant* or a *double autologous transplant*. In this type of transplant, the 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 transplant. Most often both courses of chemo are given within 6 months, with the second one given after the patient recovers from the first one.

Tandem transplants are most often used to treat multiple myeloma and advanced testicular cancer, but doctors do not always agree that these are really better than a single transplant for certain cancers. Because this involves 2 transplants, the risk of serious outcomes is higher than for a single transplant. Tandem transplants are still being studied to find out when they might be best used.

Sometimes an autologous transplant followed by an allogeneic transplant might also be called a tandem transplant (see “Mini-transplants” in the section “Allogeneic stem cell transplants”).

Allogeneic stem cell transplants

In the most common type of allogeneic transplant, the stem cells come from a donor whose tissue type closely matches the patient’s. (This is discussed later under “HLA matching” in the section called “Donor matching for allogeneic transplant.”) The best donor is a close family member, usually a brother or sister. If you do not have a good match in your family, a donor might be found in the general public through a national registry. This is sometimes called a *MUD (matched unrelated donor) transplant*. Transplants with a MUD are usually riskier than those with a relative who is a good match.

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 volume of blood has a high number of stem cells that tend to multiply quickly. 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 is limited to small adults and children. Doctors are

now looking at different ways to use cord blood for transplant in larger adults, such as using cord blood from 2 donors.

Pros of allogeneic stem cell transplant: The donor stem cells make their own immune cells, which could help destroy any cancer cells that remain after high-dose treatment. This is called the *graft-versus-cancer* effect. Other advantages are that the donor can often be asked to donate more stem cells or even white blood cells if needed, and stem cells from healthy donors are free of cancer cells.

Cons to allogeneic stem cell transplants: The transplant, also known as the *graft*, might not take — that is, the donor cells could 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 may not just attack the cancer cells — they could attack healthy cells in the patient’s body. This is called *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. A 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, multiple myeloma, myelodysplastic syndrome, and other bone marrow disorders such as aplastic anemia.

Mini transplants (non-myeloablative transplants)

For some people, age or certain health conditions make it more risky to wipe out all of their bone marrow before a transplant. For those people, doctors can use a type of allogeneic transplant that’s 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 might 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 along with 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 chemotherapy (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 normal blood cells. 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. Rarely, it may be used in patients who have already had a transplant.

Mini-transplants treat some diseases better than others. They may not work well for patients with a lot of cancer in their body or those with fast-growing cancers. Also, although side effects from chemo and radiation may be less than those from a standard allogeneic transplant, the risk of *graft-versus-host disease* is not.

This procedure has only been used since the late 1990s and long-term patient outcomes are not yet clear. There are lower risks of some complications, but the cancer may be more likely to relapse (come back). Ways to improve outcomes are still being studied.

Studies have looked at using an allogeneic mini-transplant after an autologous transplant. This is another type of tandem transplant (see “Tandem transplants” under “Autologous transplant”) 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 transplants – for those with an identical sibling

This is a special kind of allogeneic transplant that can only be used when the recipient has an identical sibling (twin or triplet) who can donate — someone who will 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 in an autologous transplant.

A disadvantage is that because the new immune system is so much like the recipient’s immune system, there is no graft-versus-cancer effect, either. Every effort must be made to destroy all the cancer cells before the transplant is done to help keep the cancer from relapsing (coming back).

Half-matched transplants

Some centers are doing half-match (*haploidentical*) transplants for people who don’t have closely matching family members. This technique is most often used in children, usually with a parent as the donor, though a child can also donate to a parent. Half of the HLA factors will match perfectly, and the other half typically don’t match at all, so the procedure requires a special way to get rid of a certain white blood cells that can cause graft-versus-host disease. It’s still rarely done, but it’s being studied in a few centers in the United States. Researchers are continuing to learn new ways to make haploidentical transplants more successful.

Sources of stem cells for transplant

There are 3 possible sources of stem cells to use for transplants:

- Bone marrow (from you or someone else)
- The bloodstream (peripheral blood – from you or someone else)
- Umbilical cord blood from newborns

Bone marrow

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

Bone marrow 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.

When the bone marrow is removed (harvested), the donor gets general anesthesia (drugs are used to put the patient into a deep sleep so they don't feel pain). A large needle is put through the skin and into the back of the hip bone. The thick liquid marrow is pulled out through the needle. This is repeated several times until enough marrow has been taken out or harvested. (For more on this, see the section called "What's it like to donate stem cells?")

The harvested marrow is filtered, stored in a special solution in bags, and then frozen. When the marrow is to be used, it's thawed and then given into the vein just like a blood transfusion. The stem cells travel to the recipient's bone marrow. Over time, they engraft or "take" 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 blood. A special thin flexible tube (called a *catheter*) is put into a large vein in the donor and attached to tubing that carries the blood to a special machine. The machine separates the stem cells from the rest of the blood, which is given back to the donor during the same procedure. 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 "What's it like to donate stem cells?")

After the patient is treated with chemotherapy and/or radiation, the stem cells are infused into the vein, much like a blood transfusion. The stem cells travel to the bone marrow, engraft, and then start making 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 family members or among the people who have signed up to donate. For these patients, umbilical cord blood may be a source of stem cells. About 1 in 3 unrelated hematopoietic stem cell transplants are done with 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. A cord blood transplant uses blood that normally is thrown out after a baby is born.

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 "What's it like to donate stem cells?"

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, cord blood transplants can take longer to take hold 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 *dual-cord-blood transplant*. A third way cord blood is being used is in 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 are 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).

When stem cell transplants were first used, they were all bone marrow transplants. But today peripheral blood stem cell transplants are much more common. Often, doctors are able to harvest more stem cells from peripheral blood than from bone marrow. It's also easier for donors to give peripheral blood stem cells than bone marrow, although it takes longer. Another plus for peripheral blood stem cell transplants is that the recipient's blood count often recovers faster than with a bone marrow transplant. But the risk of chronic 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 doesn't 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 risk and severity of graft-versus-host disease (described in the section called "Problems that may come up shortly after transplant"). But cord blood cells usually take longer to engraft. This leaves the patient at 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 for more after the cord blood stem cells are used.

Donor matching for allogeneic 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 from other people as foreign, too. This becomes very important in an allogeneic stem cell transplant.

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*, and it can lead to graft failure. This is rare when the donor and recipient are well matched.

A more common problem 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" for details). The grafted stem cells attack the body of the person who got the transplant. This is another reason it's so important 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. We inherit one of each of these pairs 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 6 of the known major HLA antigens are the same — a 6 out of 6 match. People with these matches have a lower chance of graft-versus-host disease, graft rejection, having a weak immune system, and getting serious infections. 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, for siblings since their cells vary less than an unrelated donor. But more than the basic 6 HLA antigens are often tested on unrelated donors to reduce the risks of mismatched types. Sometimes doctors will want to look at 5 pairs of antigens, for example, to try and get a 10 out of 10 match. Certain transplant centers now require high-resolution matching, which looks more deeply into tissue types. Other centers are doing clinical trials with related half-matched donors and different chemotherapy schedules. This is an active area of research because it's often hard 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 from both parents. If possible, the search for a donor usually starts with the patient's brothers and sisters (siblings), who have the same parents as the patient. The chance that any one sibling would be a perfect match (that is, that you both received the same set of HLA antigens from each of your parents) is 1 out of 4.

If a sibling is not a good match, the search could 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 transplant team will widen the search to the general public.

As unlikely as it seems, it's possible to find a good match with a stranger. To help with this process, the team will use transplant registries (see the "To learn more" section). Registries serve as matchmakers between patients and volunteer donors. They can search for and access millions of possible donors and hundreds of thousands of cord blood units. The largest registry in the United States is *Be the Match* (formerly called the National Marrow Donor Program) which has recently merged with another agency, the Caitlin Raymond International Registry. They have access to millions of international records, and have successfully matched thousands of donors and recipients.

The chances of finding an unrelated donor match 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 seem to be less likely to take part in donor registries. Depending on a person's tissue typing, several other international registries also are available. Sometimes the best matches are found in people with a similar racial or ethnic background. Finding an unrelated donor can take months, though cord blood may be a little faster. A single match can require going through millions of records.

Now that transplant centers are more often using high-resolution tests, matching is becoming more complex. Perfect 10 out of 10 matches at that level are much harder to find. But transplant teams are also getting better at figuring out what kinds of mismatches they can get away with in which situations – that is, which mismatched sites are less likely to affect transplant success and survival.

Keep in mind that there are stages to this process – there may be several matches that look promising but don't work out as hoped. The team and registry will keep looking for the best possible match for you. If your team finds an adult donor through a transplant registry, the registry will contact the donor to set up the final testing and donation. If your team finds matching cord blood, the registry will have the cord blood sent to your transplant center.

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.

Evaluation and preparation for a transplant

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's 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's 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 will 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, including high-resolution 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)
- Consultations 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 (thin tube) 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, a special catheter can be placed that can also be used for apheresis (**a**-fur-**REE**-sis) to harvest your stem cells. The catheter will stay in 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.

Transplant 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 or outpatient treatment

The hospital’s transplant team will decide if you need to be in the hospital to have your transplant, if it will be done in an outpatient center, or if you will be in the hospital just for parts of it. If you

have to be in the hospital, you will probably go in the day before the transplant procedure is scheduled to start. Before conditioning treatment begins (see section below), the transplant team makes sure you and your family understand the process and want to go forward with it.

If you will be having all or part of your transplant as an outpatient, you will need to be very near the transplant center during the early stages. You'll need a family member or loved one as a caregiver who can stay with you all the time. You and the caregiver will also need reliable transportation to get you to and from the clinic. The transplant team will be watching you closely for complications, so expect to be at the clinic every day for a few weeks. You may still need to be admitted to the hospital if your situation changes or if you start having complications.

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 an air pressure system that makes sure no unclean outside air gets into the room. If you are going to be treated as an outpatient or at home, you will get instructions on avoiding infection.

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.

It's important for you and your family to know what to expect, because once conditioning treatment begins (see the next section), there is no going back — there can be serious problems if treatment is stopped at any time during transplant.

Conditioning treatment

Conditioning, also known as *bone marrow preparation* or *myeloablation*, is treatment with high-dose chemo and/or radiation therapy. It's the first step in the transplant process and typically takes a week or two. It's done for one or more of these 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

The conditioning treatment is different for every transplant. Your individual treatment will be planned 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's given to the entire body (called *total body irradiation* or TBI). TBI may be given in a single treatment session or in divided doses over a few days.

This phase of the transplant can be very uncomfortable because high treatment doses are used. Chemo and radiation side effects can make you sick, and it may take you 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 them in our Guide to Cancer Drugs, or call us for more information.

Conditioning can also cause premature menopause in women and often makes both men and women sterile (unable to have children). (See “Stem cell transplant and having children” in the section called “Transplant problems that may show up later.”) 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.

The big day: infusion of stem cells

After the conditioning treatment, you will be given a couple of days to rest before getting the stem cells. They will be given through your IV catheter, much like a blood transfusion. If the stem cells were frozen, you might get some drugs before the stem cells are given. This is done to reduce your risk of reacting to the preservatives that are used in 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 (removed) in an operating room, and then processed in the lab. Once they are ready, the cells are brought in and infused (given to you). 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 a 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 used when freezing the cells (called *dimethylsulfoxide* or *DMSO*) causes many of the side effects. You might have a strong taste of garlic or creamed corn in your mouth. Sucking on candy or sipping flavored drinks during and after the infusion can help with the taste. Your body will also smell like this. The smell may bother those around you, but you might not even notice it. The smell, along with the taste, may last for a few days, but slowly fades away. Often having cut up 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 or immediate side effects of the stem cell infusion might 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 after infusion

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 it’s usually about 2 to 6 weeks. You’ll be in the hospital or visit the transplant center daily for at least a few 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 help keep you from getting infections (this is called *prophylactic* antibiotics). You may get a combination of 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 from too few white blood cells (*neutropenia*), or bleeding from too few platelets (*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 feelings 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 might feel as if 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 from the hospital

Planning to go home

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 be your primary caregiver and what the job will be like, and who will be the back-up caregiver in case your main caregiver gets sick and can't be near you

What has to happen before you can go home?

For the most part, transplant centers don't send patients home 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/mm³
- They have a hematocrit of at least 25% to 30%
- They have a platelet count of at least 15,000 to 20,000/mm³
- 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. When you do go home, you may need to stay near the transplant center for some time, depending on your condition.

Rehabilitation

The roller coaster ride typically continues after you go home. Plus, you will be feeling pretty tired after going through the transplant process. After discharge, some people have physical or mental health problems in the rehabilitation period. These ongoing needs must now be managed at home and caregiver and friend/family support is very important.

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 might need blood and platelet transfusions, antibiotics, or other treatments. The exams 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 might show up as much as 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, early menopause, pain or discomfort during sex, or loss of interest in sex (see “Stem cell transplant and having children” in the section “Transplant problems that may show up later”)
- New cancers caused by the transplant

Your transplant team is still available to help you. It’s 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 soon after transplant

Here are 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 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 or transplant team about any problems you have or changes you notice. Some of these problems can be life-threatening, so it’s important to be able to reach your doctor or transplant team at night, on weekends, and during holidays. Be sure you know how to do this.

Mouth and throat pain

Mucositis (inflammation or sores in the mouth) is a short-term side effect that can happen with chemo and radiation. It usually gets better within a few weeks after chemo, but it can make it very painful to eat and drink. It can be a challenge to eat and avoid dehydration. If your mouth hurts, you may be given medicine to numb your mouth or help the pain. You may need to take the medicine before meals so that it's easier to eat. Be sure to tell your doctor about any pain and if the medicines to help it are working.

Good nutrition is important for people with cancer. If mouth pain or sores make it hard to eat or swallow, your health care team will help you develop a plan to manage your symptoms. For more suggestions, see our document, *Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families*.

Nausea and vomiting

Because chemotherapy drugs can cause severe nausea and vomiting, doctors often give anti-nausea medicines at the same time as chemo to try and prevent it. This is still true when you're getting chemo as part of a bone marrow transplant.

Anti-nausea medicines are often given on a regular schedule around the clock. This means you take them even if you don't have any problems. Sometimes you may be asked to take a medicine on an "as needed" schedule. This means you take the medicine at the first sign of nausea to keep it from getting worse. In many cases, 2 or more medicines are used.

No one drug can prevent or control chemo-related nausea and vomiting 100% of the time. You'll need to tell the doctor and nurses how well your medicines are controlling your nausea and vomiting. If they aren't working, they will need to be changed.

As much as possible, the goal is to prevent nausea and vomiting, because it's easier to prevent it than it is to stop it once it starts. Preventive treatment should start before the chemo is given and should continue for as long as the chemo is likely to cause vomiting, which can be up to 7 to 10 days after the last dose.

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. While your white blood cell counts are low, you are said to be *neutropenic*. (See "White blood cells" in the section called "What are stem cells and why are they used in transplants?" 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. Fungal infections can also be an issue. 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 called "The transplant process," you may be given antibiotics to try to prevent infections until your blood counts reach a certain level. For instance, pneumocystis pneumonia (pronounced **new-mo-SIST**-is new-**moan**-ee-uh, often called PCP) is a common infection that is easy to catch. Even though the germ doesn't harm people with normal immune systems, for others it can cause fever, cough, and serious breathing problems. Doctors often give patients antibiotics to keep them 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 systems of most patients to work as well as they should. It can take even longer for patients with graft-versus-host disease (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 will be needed to avoid exposure to germs. While in the hospital, everyone who enters your room must wash their hands well. They may 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 may be told not to eat certain 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 for a while.

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 antibiotics will be started right away. Be sure to ask which symptoms you should call the doctor about at nights and on weekends (also ask how to contact your doctor in an emergency).

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. Platelet counts are low for 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 a certain level (such as 20,000/mm³ or even lower), a platelet transfusion may be needed. (A low platelet count is called *thrombocytopenia*.) You will need to follow precautions until your platelet counts stay at safe levels. (See "Platelets" in the section called "What are stem cells and why are they transplanted?" for more information.)

It also takes time for your 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 (**new-muh-NY-tus**) is a type of lung inflammation that's most common in the first 100 days after a stem cell transplant. But some lung problems can happen much later — even 2 or more years after transplant.

Pneumonia caused by infection happens more often, but pneumonitis may be caused by radiation, graft-versus-host disease, or chemo rather than germs. It's caused by damage to the areas between the cells of the lungs (called *interstitial spaces*, pronounced **in-ter-STIH-shul**). 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 will do breathing tests every few months if you have graft-versus-host disease (see next section).

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

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. (Remember: 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 after transplant.) 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 range from barely noticeable to life-threatening. Doctors 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. A person may have one, both, or neither type of GVHD.

Acute GVHD

Acute GVHD can happen 10 to 90 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's 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 (watery and sometimes bloody)
- Loss of appetite

- Yellowing of the skin and eyes (jaundice)
- Abdominal (belly) pain
- Weight loss

Most cases are mild, and those who recover from 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, such as steroids, certain monoclonal antibodies, methotrexate, cyclosporine, and tacrolimus to lessen the immune response. These drugs are given before acute GVHD starts and can help prevent serious GVHD, but mild GVHD will almost always happen in allogeneic transplant patients. New and old drugs in different combinations are being tested for GVHD prevention.

The risk of acute GVHD can also be decreased by removing a certain kind immune cells (called T-cells) from the donor stem cells before the transplant. But this can also increase the risk of viral infection, leukemia relapse, and graft failure (which is discussed later). 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 let the donor T-cells destroy any cancer cells left. Preventing and managing GVHD are major priorities for research.

Chronic GVHD

Chronic GVHD can start anywhere from about 100 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 a bad sunburn. A fever may also develop. Other symptoms of chronic GVHD can include:

- Decreased appetite
- Diarrhea
- Abdominal (belly) cramps
- Weight loss
- Yellowing of the skin and eyes (jaundice)
- Enlarged liver
- Bloated abdomen (belly)
- Pain in the upper right part of the abdomen (belly)
- Increased levels of liver enzymes in the blood (seen on blood tests)
- The skin feels tight
- Dry, burning eyes
- Dryness or painful sores in the mouth
- Burning sensations when eating acidic foods

- Bacterial infections
- Blockages in the smaller 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 the “Infection” section).

Hepatic veno-occlusive disease

Hepatic veno-occlusive (heh-**pat**-ick **vee**-no - uh-**kloo**-siv) disease (VOD) is a serious problem in which tiny veins and other blood vessels inside the liver become blocked. It only happens in people with allogeneic transplants, and mainly in those who got the drugs busulfan or melphalan as part of conditioning.

VOD usually happens within 3 weeks of conditioning. It’s 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 fluid that bloats the belly). Sometimes it can result in liver failure and death.

Doctors have found that giving busulfan in the vein (IV) rather than by mouth may reduce the risk of VOD. New ways to treat this problem are being tested.

Graft failure

Grafts fail when the body does not accept the new stem cells (the graft). The stem cells that were given do not go into the bone marrow and multiply like they should. Graft failure is more common when the patient and donor are not well matched and when patients get stem cells that have had the T-cells removed. It can also happen in patients who get a low number of stem cells, such as a single umbilical cord unit.

Graft failure can lead to serious bleeding and/or infection. It’s suspected in patients whose counts do not start going up within 3 to 4 weeks of a bone marrow or peripheral blood transplant, or within 7 weeks of a cord blood transplant.

It may be treated by a second dose of stem cells, if available. Grafts rarely fail, but if they do it can result in death.

Transplant problems that may show up later

The type of problems that can happen after a 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 when the transplant was done, the length and degree of immune system suppression, and whether chronic graft-versus-host-disease (GVHD) is present and how bad it is. The problems can be caused by the conditioning treatment (the pre-transplant chemotherapy 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). Possible long-term risks of transplant include:

- Organ damage (to the liver, kidneys, lungs, heart and/or bones and joints)

- Relapse (the cancer comes back)
- Secondary (new) cancers
- Abnormal growth of lymph tissues
- Infertility (the inability to produce children)
- Hormone changes, such as changes in the thyroid or pituitary gland
- Cataracts (clouding of the lens of the eye, which causes vision loss)

Organ damage

The medicines used in transplants can harm the body's organs, such as the heart, lungs, kidneys, liver, and nervous system. You may need careful follow-up with close monitoring and treatment of the long-term organ problems that the transplant can cause. Some of these, like infertility, should be discussed early in the transplant process, so you can prepare for them.

It's important to find and quickly treat any long-term problems. Tell your doctor right away if you notice any changes or problems. Physical exams by your doctor, blood work, imaging studies and other tests will help look for and keep tabs on organ problems. 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 give them the best possible quality of life.

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 or targeted therapy. Some patients who have had allogeneic transplants may be helped by getting white blood cells from the same donor (this is called *donor lymphocyte infusion*) to boost the graft-versus-cancer effect. 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's 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.

Secondary cancers(new cancers caused by treatment)

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 getting another cancer after a transplant 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* (**my**-uh-lo-dis-**PLAY**-zhuh) or myelodysplastic syndrome (**my**-uh-lo-dis-**PLAS** tick), 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, brain, liver, cervix, thyroid, breast, and bone.

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 graft-versus-host disease, 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*.

Post-transplant lymphoproliferative disorder

Post-transplant lymphoproliferative (**lim**-fo-pruh-LIH-fer-uh-tiv) disorder (PTLD) is an out-of-control growth of lymph cells, actually a type of lymphoma, that can develop after an allogeneic

stem cell transplant. It's 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, 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 PTLT.

Still, PTLT after allogeneic stem cell transplant is fairly rare. It most often happens in recipients of T-cell-depleted stem cells. It can occur in patients who got stem cells from mismatched or unrelated donors. 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 PTLT.

PTLTs most often occur within 1 to 6 months after allogeneic stem cell transplant, when the immune system is still very weak.

PTLT is life-threatening. It may show up as lymph node swelling, fever, and chills. There is no one standard treatment, but it's 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 PTLT doesn't happen a lot after transplant, it's 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 PTLT and look for ways to prevent it in transplant patients who are at risk.

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 cells that are transplanted, 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.

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 protect 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.

The drugs used during transplant can also damage sperm, so men should use birth control to avoid starting a pregnancy during and for some time after the transplant process. Transplants may cause temporary or permanent infertility for men as well. Men might consider storing their sperm before having a transplant. This process can take several days. Sperm samples are collected, then frozen and stored in a sperm bank. The stored sperm can later be thawed and used to fertilize a partner's egg using artificial insemination. Fertility returns in some men, but the timing is unpredictable.

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 on having children after being treated for cancer, see our document called *Fertility and Women With Cancer* or *Fertility and Men With Cancer*. For more information on sexual problems, see our documents called *Sexuality for the Man With Cancer* and *Sexuality for the Woman With Cancer*.

Other transplant issues

Cost of transplant

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

A transplant (or certain types of transplants) is still considered experimental for many types of cancer, especially many solid tumor cancers, so insurers might not cover the cost. No matter what illness you have, it's important to find out what your insurer will cover before deciding on a transplant, including donor match testing, cell collection, drug treatments, hospital stay, and follow-up care. Go over the transplant plan with them to find out what's covered. Ask if the doctors and transplant team you plan to use are in their network, and how reimbursement will work. Some larger insurance companies have transplant case managers. If not, you might ask to speak with a patient advocate. You can also talk with financial or insurance specialists at your doctor's office, transplant center, and hospital about what expenses you are likely to have. This will help you get an idea of what you might have to pay.

Saving your newborn's umbilical cord blood for later private use

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. Other parents store their newborn's cord blood in private cord blood banks just in case the child or a close relative needs it someday. Several private companies offer this service as a form of "biological insurance."

The collection fee can be \$1,500 to \$2,400, with around another \$150 per year to store the cord blood. You will want to check on costs because they will probably increase over time, 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 things to think about:

- A single cord blood unit might not have enough stem cells for most adults, so personal cord blood use could 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 What’s it like to donate stem cells? More information on private family cord blood banking can be found at the Parent’s Guide to Cord Blood Foundation. You can visit their website at www.parentsguidecordblood.org.

What questions should I ask my doctor before transplant?

BEFORE you agree to a transplant, you might 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?
- What is the plan if the transplant doesn’t work?
- What are the risks of waiting or trying other treatments first?
- 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 are my options 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?

What's it like to donate stem cells?

People usually volunteer to donate stem cells for an allogeneic transplant either because they have a loved one or friend who needs a match or because they want to help people. Some people give their stem cells so they can get them back later for an autologous transplant.

If you want to donate stem cells for someone else

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 "To learn more" section for contact information).

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 cord blood should make arrangements for it early in the pregnancy, at least 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 possible stem cell donor is 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. If a person decides to donate, a consent form must be signed after the risks of donating are fully discussed. The donor is not pressured to take part. It's always a choice.

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

How bone marrow stem cells are collected

This process is often called *bone marrow harvest*, and it's done in an operating room. 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. The marrow cells are taken from the back of the pelvic (hip) bone. A large needle is put through the skin and into the back of the hip bone. It's pushed through the bone to the center and the thick, liquid marrow is pulled out through the needle. This is repeated several

times until enough marrow has been taken out (harvested). 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 blood was taken from the donor before the marrow donation, it's often given back to the donor at this time.

After the bone marrow is harvested, the donor is taken to the recovery room while the anesthesia wears off. The donor may then be taken to a hospital room and 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®) or non-steroidal anti-inflammatory drugs (such as aspirin, ibuprofen, or naproxen) are 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 could take 2 or 3 weeks before they feel completely back to normal.

There are few risks for donors 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®). This is a growth-factor drug that causes the bone marrow to make and release stem cells into the blood. Filgrastim can cause some side effects, the most common being bone pain and headaches. These may be helped by over-the-counter acetaminophen (Tylenol) or nonsteroidal 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.

Blood is removed through a catheter (a thin, flexible plastic tube) that is put in a large vein in the arm or chest. It's then 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 through the same catheter. This process is called *apheresis* (**a-fur-REE-sis**). It takes about 2 to 4 hours and is done as an outpatient procedure. Often the process needs to be repeated daily for a few days, until enough stem cells have been collected.

Possible side effects of the catheter can include trouble placing the catheter in the vein, a collapsed lung from catheter placement, blockage of the catheter, or infection of the catheter or at the area where it enters the vein. Blood clots are another possible side effect. During the apheresis

procedure donors may have problems caused by low calcium levels from the anti-coagulant drug used to keep the blood from clotting in the machine. These can include feeling lightheaded or tingling, and having chills or muscle cramps. These go away after donation is complete, but may be treated by giving the donor calcium supplements.

The process of donating cells for yourself (autologous stem cell donation) is pretty much the same as when someone donates them for someone else (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 chemotherapy (chemo) is given before the filgrastim is used to tell the body to make stem cells. Also, sometimes it can be hard to get enough stem cells from a person with cancer. Even after several days of apheresis, there may not be enough for the transplant. This is more likely to be a problem if the patient has had certain kinds of chemo in the past, or if they have an illness that affects their bone marrow.

Sometimes a second drug called plerixafor (Mozobil[®]) is used along with filgrastim in people with non-Hodgkin lymphoma or multiple myeloma. This boosts the stem cell numbers in the blood, and helps reduce the number of apheresis sessions needed to get enough stem cells. It may cause nausea, diarrhea, and sometimes, vomiting. There are medicines to help if these symptoms become a problem. Rarely the spleen can enlarge and even rupture. This can cause severe internal bleeding and requires emergency medical care. The patient should tell the doctor right away if they have any pain in their left shoulder or under their left rib cage which can be symptoms of this emergency.

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 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 Be the Match.

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

To learn more

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org.

Dealing with cancer

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

Coping With Cancer in Everyday Life (also in Spanish)

Talking With Your Doctor (also in Spanish)

Understanding Your Lab Test Results

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

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

Distress in People With Cancer

Cancer treatment and side effects

A Guide to Chemotherapy (also in Spanish)

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

Infections in People With Cancer

Blood Product Transfusion and Donation

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

Fertility and Women With Cancer

Fertility and Men With Cancer

Sexuality for the Man With Cancer (also in Spanish)

Sexuality for the Woman With Cancer (also in Spanish)

Second Cancers Caused by Cancer Treatment

For caregivers

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

What It Takes to Be a Caregiver

What You Need to Know as a Cancer Caregiver

When Someone You Know Has Cancer (also in Spanish)

Books

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

National organizations and websites*

Be the Match (formerly the National Marrow Donor Program)

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

Website: www.bethematch.org

Free booklets, webcasts, and online information for potential donors and patients, including kids and teens. Helps patients find stem cell and cord blood matches, supports them throughout the transplant process, from planning to life after transplant (see Patients and Families, Support and Resources section). Offers financial help to eligible under-insured patients through the Patient Assistance Program. Also offers an online application and mail-order kit to join the Be the Match donor registry. Interpreters available for people who call and can say (in English) what language they speak, though it may take a few minutes.

Blood & Marrow Transplant Information Network

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

Website: www.bmtinfonet.org

Provides information and support services to bone marrow, stem cell, and cord blood transplant patients, caregivers, and survivors. “Caring Connection” matches you to a transplant survivor to get support and guidance from someone who has had real experience with the process; also can help with understanding insurance issues and has a transplant center directory.

National Bone Marrow Transplant Link (nbmtLink)

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

Website: www.nbmtlink.org

Helps patients, caregivers, and families by providing information and support services before, during, and after transplant. Offers one-on-one conversations with trained peer support volunteers who are transplant survivors, caregivers, and donors; telephone support groups, facilitated by nurses, that link patients and families together to offer mutual support; and videos and publications for patients and caregivers.

National Foundation for Transplants (NFT)

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

Website: www.transplants.org

Provides fund raising guidance, which helps patients, their families, and friends to raise money for all types of transplants, including stem cell or bone marrow, in the US.

**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.

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Last Medical Review: 10/2/2013

Last Revised: 10/2/2013

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