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## Stem Cell or Bone Marrow Transplant

A stem cell transplant, also called a bone marrow transplant, can be used to treat certain types of cancer. This procedure might be called peripheral stem cell transplant or cord blood transplant, depending on where the stem cells come from. Here we'll explain stem cells and stem cell transplant, cover some of the issues that come with transplants, and describe what it's like to donate stem cells.

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## How Stem Cell and Bone Marrow Transplants Are Used to Treat Cancer

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## What are stem cells?

All of the blood cells in your body - white blood cells, red blood cells, and platelets - start out as young (immature) cells called **hematopoietic stem cells**. Hematopoietic means blood-forming. These are very young cells that are not fully developed. Even though they start out the same, these stem cells can mature into any type of blood cell, depending on what the body needs when each stem cell is developing.

Stem cells mostly live in the bone marrow (the spongy center of certain bones). This is 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 the immature stem cells also get into the bloodstream. These are called **peripheral blood stem cells**.

## Why stem cells are so important

Stem cells make red blood cells, white blood cells, and platelets. We need all of these types of blood cells to keep us alive. For these blood cells to do their jobs, you need to have enough of each of them in your blood.

### Red blood cells (RBCs)

Red blood cells carry oxygen away from the lungs to all of the cells in the body. They bring carbon dioxide from the cells back 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](#)<sup>1</sup>. This can make them look pale and feel weak, tired, and short of breath.

### White blood cells (WBCs)

White blood cells help fight infections caused by bacteria, viruses, and fungi. There are different types of WBCs.

**Neutrophils** are the most important type in fighting infections. They are the first cells to respond to an injury or when germs enter the body. When they are low, you have a higher risk of [infection](#)<sup>2</sup>. The absolute neutrophil count (ANC) is a measure of the number of neutrophils in your blood. When your ANC drops below a certain level, you have **neutropenia**. The lower the ANC, the greater the risk for infection.

**Lymphocytes** are another type of white blood cell. 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 in 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 to 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/mm<sup>3</sup>. This can be dangerous if bleeding occurs in the brain, or if blood begins to leak into the intestines or stomach.

You can get more information on blood counts and what the numbers mean in [Understanding Your Lab Test Results](#)<sup>3</sup>.

### **Where stem cells for transplants come from**

Depending on the type of transplant that's being done, 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 liquid tissue in the center of some bones. It has a rich supply of stem cells, and its main job is to make blood cells that circulate in your body. The bones of the pelvis (hip) have the most marrow and contain large numbers of stem cells. 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.

The bone marrow is harvested (removed) while the donor is under 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 on the lower back and into the back of the hip bone. The thick liquid marrow is pulled out through the needle. This is repeated until enough marrow has been taken out. (For more on this, see [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 put into the patient's blood through a vein, just like a blood transfusion. The stem cells travel to the bone marrow, where they engraft or "take" and start to make blood cells. Signs of the new blood cells usually can be measured in the patient's blood tests in a few weeks.

### Peripheral blood

Normally, not many stem cells are found in the blood. But giving stem cell donors shots of hormone-like substances called **growth factors** a few days before the harvest makes their stem cells 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 returned 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 [What's It Like to Donate Stem Cells?](#))

When they're given to the patient, the stem cells are put into a 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 in about 4 weeks.

### Umbilical cord blood

The blood of newborn babies normally has large numbers of stem cells. After birth, the blood that's 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. Cord blood can be frozen until needed. A cord blood transplant uses blood that normally is thrown out after a baby is born. After the baby is born, specially trained members of the health care team make sure the cord blood is carefully collected. The baby is not harmed in any way. More information on donating cord blood can be found in [What's It Like to Donate Stem Cells?](#)

Even though the blood of newborns has large numbers of stem cells, cord blood is only a small part of that number. So, a possible drawback of cord blood is the smaller number of stem cells in it. 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. Cord blood is given into the patient's blood just like a blood transfusion.

## Cancers that affect the bone marrow

Some cancers start in the bone marrow and others can spread to it. Cancer attacks the bone marrow, causing it to make too many of some cells that crowd out others, or causing it to make cells that aren't healthy and don't work like they should. For these cancers to stop growing, they need bone marrow cells to work properly and start making new, healthy cells.

Most of the cancers that affect bone marrow function are [leukemias](#)<sup>4</sup>, [multiple myeloma](#)<sup>5</sup>, and [lymphomas](#)<sup>6</sup>. All of these cancers start in blood cells. Other cancers can spread to the bone marrow, which can affect how blood cells function, too.

For certain types of leukemia, lymphoma, and multiple myeloma, a stem cell transplant can be an important part of treatment. The goal of the transplant is to wipe out the cancer cells and the damaged or non-healthy cells that aren't working right, and give the patient new, healthy stem cells to "start over."

## How a stem cell transplant works to treat cancer

Stem cell transplants are used to replace bone marrow cells that have been destroyed by cancer or destroyed by the [chemo](#)<sup>7</sup> and/or [radiation](#)<sup>8</sup> used to treat the cancer.

There are [different kinds of stem cell transplants](#). They all use very high doses of chemo (sometimes along with radiation) to kill cancer cells. But the high doses can also kill all the stem cells a person has and can cause the bone marrow to completely stop making blood cells for a period of time. In other words, all of a person's original stem cells are destroyed on purpose. But since our bodies need blood cells to function, this is where stem cell transplants come in. The transplanted stem cells help to "rescue" the bone marrow by replacing the body's stem cells that have been destroyed by treatment. So, transplanting the healthy cells lets doctors use much higher doses of chemo to try to kill all of the cancer cells, and the transplanted stem cells can grow into healthy, mature blood cells that work normally and reproduce cells that are free of cancer.

There's another way a stem cell transplant can work, if it's a transplant that uses stem

cells from another person (not the cancer patient). In these cases, the transplant can 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. The "graft" is the donated cells. The effect means that certain kinds of transplants actually help kill off the cancer cells, along with rescuing bone marrow and allowing normal blood cells to develop from the stem cells.

## Deciding to have a stem cell transplant

Although a stem cell transplant can help some patients, even giving some people a chance for a cure, the decision to have a transplant isn't easy. Like everything in your medical care, you need to be the one who makes the final choice about whether or not you'll have a stem cell transplant. Transplant has been used to cure thousands of people with otherwise deadly cancers. Still, there are possible risks and complications that can threaten life, too. People have died from complications of stem cell transplant. The expected risks and benefits must be weighed carefully before transplant.

Your cancer care team will compare the risks linked with the cancer itself to the [risks of the transplant](#). They may also talk to you about other treatment options or [clinical trials](#)<sup>9</sup>. The stage of the cancer, 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 this decision.

Here are some questions you might want to ask. For some of these, you may need to talk to the transplant team or the 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? What's the goal?
- How many transplants do you do for my kind of cancer every year? What is the success rate?
- Are there [clinical trials](#)<sup>10</sup> I should look into?
- Are there other treatment options I should think about?
- What type of stem cell transplant will I have? Why?
- What's the chance of finding a good match?
- What are the chances that the transplant will work?
- What's 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 treatment will I need before the transplant?
- How much will a transplant cost?
- What costs, if any, will my insurance cover? How much will I have to pay?
- Will it cover the costs of finding a donor?
- Will I be able to have children after the transplant? What are my options if I want to have children later?
- What [side effects](#) might I expect? How bad will they be? How long will they last?
- What types of medicine or self-care will be used to control side effects?
- How long might I have to be in the hospital?
- Will I be able to have visitors?
- What type of follow-up will be needed? How often?
- What vaccines will I need to get after transplant and when will I get them?
- What are the chances that the cancer will [come back](#)<sup>11</sup> after transplant?
- When will I be able to return to work?

Be sure to express all your concerns and get answers you understand. Make sure the team knows what's important to you, too. Transplant is a complicated process. Find out as much as you can and plan ahead before you start.

It's important to know the success rate of the planned transplant based on [your diagnosis](#)<sup>12</sup> and stage in treatment, along with any other conditions that might affect you and your transplant. In general, transplants tend to work better if they're done in early stages of disease or when you're 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.

Many people get a [second opinion](#)<sup>13</sup> before they decide to have a stem cell transplant. You may want to talk to your doctor about this, too. Also, call your health insurance company to ask if they will pay 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 by your insurance.

## Cost of transplant

Stem cell transplants cost a lot, and some types cost more than others. For example, getting a donor's cells costs more than collecting your own cells. And, different drug and radiation treatments used to destroy bone marrow can have high costs. Some transplants require more time in the hospital than others, and this can affect cost. Even though there are differences, stem cell transplants can cost hundreds of thousands of

dollars.

A transplant (or certain types of transplants) is still considered experimental for some types of cancer, especially some 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 your 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 in co-pays and/or co-insurance.

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/anemia.html](http://www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/anemia.html)
2. [www.cancer.org/cancer/managing-cancer/side-effects/infections.html](http://www.cancer.org/cancer/managing-cancer/side-effects/infections.html)
3. [www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html](http://www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html)
4. [www.cancer.org/cancer/types/leukemia.html](http://www.cancer.org/cancer/types/leukemia.html)
5. [www.cancer.org/cancer/types/multiple-myeloma.html](http://www.cancer.org/cancer/types/multiple-myeloma.html)
6. [www.cancer.org/cancer/types/lymphoma.html](http://www.cancer.org/cancer/types/lymphoma.html)
7. [www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html)
8. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html)
9. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html)
10. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html)
11. [www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html](http://www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html)
12. [www.cancer.org/cancer/understanding-cancer.html](http://www.cancer.org/cancer/understanding-cancer.html)
13. [www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html](http://www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html)

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American Society of Clinical Oncology (ASCO). What is a stem cell transplant (bone marrow transplant)? 2018. Accessed at <https://www.cancer.net/navigating-cancer-care/how-cancer-treated/bone-marrowstem-cell-transplantation/what-bone-marrow-transplant-stem-cell-transplant> on March 17, 2020.

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National Institutes of Health (NIH). Stem cell basics. 2016. Access at <https://stemcells.nih.gov/info/basics.htm> on March 17, 2020.

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## Types of Stem Cell and Bone Marrow Transplants

Stem cell transplants are used to put blood stem cells back into the body after the bone marrow has been destroyed by disease, chemotherapy (chemo), or radiation. Depending on where the stem cells come from, the transplant procedure may go by different names:

- **Bone marrow transplant (BMT)**
- **Peripheral blood stem cell transplant (PBSCT)**
- **Umbilical cord blood (UCB) transplant**

All of these can also be called **hematopoietic stem cell transplants**.

- [Autologous stem cell transplants](#)
- [Tandem \(double autologous\) transplants](#)
- [Allogeneic stem cell transplants \(including cord blood transplants\)](#)
- [Mini-transplants \(non-myeloablative transplants\)](#)
- [Syngeneic stem cell transplants \(for those with an identical sibling\)](#)
- [Half-matched transplants](#)
- [The importance of matching patients and donors](#)

In a typical stem cell transplant for cancer, a person first gets very high doses of [chemo](#)<sup>1</sup>, sometimes along with [radiation therapy](#)<sup>2</sup>, to try to kill all the cancer cells. This treatment also kills the stem cells in the bone marrow. This is called **myeloablation** or **myeloablative therapy**.

Soon after treatment, blood stem cells are given (transplanted) to replace those that were destroyed. The replacement stem cells are given into a vein, much like a blood transfusion. The goal is that over time, the transplanted cells will settle in the bone marrow, where they will begin to grow and make healthy new blood cells. This process is called **engraftment**.

There are 2 main types of transplants. They are named based on who donates the stem cells.

- **Autologous:** 'Auto' means **self**. The stem cells in autologous transplants come from the same person who will get the transplant, so the patient is their own donor.
- **Allogeneic:** 'Allo' means **other**. The stem cells in allogeneic transplants are from a person other than the patient, either a matched related or unrelated donor.

## Autologous stem cell transplants

In this type of transplant, the first step is to remove or **harvest** your own stem cells. Your stem cells are removed from either your bone marrow or your blood, and then frozen. (You can learn more about this process at [What's It Like to Donate Stem Cells?](#)) After you get high doses of chemo and/or radiation as your myeloablative therapy, the stem cells are thawed and given back to you.

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 can use autologous transplants for other diseases, too, like systemic sclerosis, multiple sclerosis (MS), Crohn's disease, and systemic lupus erythematosus (lupus).

## Benefits of autologous stem cell transplant

An advantage of an autologous stem cell transplant is that you're getting your own cells back. When you get your own stem cells back, you don't have to worry about them (called the engrafted cells or the "graft") being rejected by your body. You also don't

have to worry about immune cells from the transplant attacking healthy cells in your body (known as **graft-versus-host disease**), which is a concern with allogeneic transplants.

### **Risks of autologous stem cell transplant**

An autologous transplant graft might still fail, which means the transplanted stem cells don't go into the bone marrow and make blood cells like they should.

Also, autologous transplants can't produce the "graft-versus-cancer" effect, in which the donor immune cells from the transplant help kill any cancer cells that remain.

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

### **Getting rid of cancer cells in stem cells saved for autologous transplants**

To help prevent any remaining cancer cells from being transplanted along with stem cells, some centers treat the stem cells before they're given back to the patient. This may be called **purging**. While this might work for some patients, there haven't been enough studies yet to know if this is really a benefit. A possible downside of purging is that some normal stem cells can be lost during this process. This may cause your body to take longer to start making normal blood cells, and you might have very low and unsafe levels of white blood cells or platelets for a longer time. This could increase the risk of [infections](#)<sup>3</sup> or bleeding problems.

Another treatment to help kill cancer cells that might be in the returned stem cells involves giving anti-cancer drugs after the transplant. The stem cells are not treated. After transplant, the patient gets anti-cancer drugs to get rid of any cancer cells that may be in the body. This is called ***in vivo purging***. For instance, lenalidomide (Revlimid) may be used in this way for multiple myeloma. The need to remove cancer cells from transplanted stem cells or transplant patients and the best way to do it continues to be researched.

### **Tandem (double autologous) 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 as myeloablative therapy, 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. Usually, the 2 courses of

chemo are given within 6 months. The second one is given after the patient recovers from the first one.

Tandem transplants have become the standard of care for certain cancers. High-risk types of the childhood cancer neuroblastoma and adult multiple myeloma are cancers where tandem transplants seem to show good results. But doctors don't always agree that these are really better than a single transplant for certain cancers. Because this treatment involves 2 transplants, the risk of serious outcomes is higher than for a single transplant.

Sometimes an autologous transplant followed by an allogeneic transplant might also be called a tandem transplant. (See Mini-transplants below.)

### **Allogeneic stem cell transplants (including cord blood transplants)**

Allogeneic stem cell transplants use donor stem cells. In the most common type of allogeneic transplant, the stem cells come from a donor whose tissue type closely matches yours. (This is discussed in "Matching patients and donors.") The best donor is a close family member, usually a brother or sister. If you don't 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.

An allogeneic transplant works about the same way as an autologous transplant. Stem cells are collected from the donor and stored or frozen. After you get high doses of chemo and/or radiation as your myeloablative therapy, the donor's stem cells are thawed and given to you.

Allogeneic transplants are most often used to treat certain types of leukemia, lymphomas, multiple myeloma, myelodysplastic syndromes, and other bone marrow disorders such as aplastic anemia.

#### **Umbilical cord blood transplant**

Blood taken from the placenta and umbilical cord after a baby is born can also be used for an allogeneic transplant. This small volume of **cord blood** has a high number of stem cells in it.

Cord blood transplants can have some advantages. For example, there are already a large number of donated units in cord blood banks, so finding a donor match might be easier. These units have already been donated, so they don't need to be collected once

a match is found. A cord blood transplant is also less likely to be rejected by your body than is a transplant from an adult donor.

But cord blood transplants can have some downsides as well. There aren't as many stem cells in a cord blood unit as there are in a typical transplant from an adult donor. Because of this, cord blood transplants are used more often for children, who have smaller body sizes. These transplants can be used for adults as well, although sometimes a person might need to get more than one cord blood unit to help ensure there are enough stem cells for the transplant.

Cord blood transplants can also take longer to begin making new blood cells, during which time a person is vulnerable to infections and other problems caused by having low blood cell counts. For a newer cord blood product, known as omidubicel (Omisirge), the cord blood cells are treated in a lab with a special chemical, which helps them get to the bone marrow and start making new blood cells quicker once they're in the body.

### **Benefits of allogeneic stem cell transplant**

A major benefit of allogeneic transplants is that the donor stem cells make their own immune cells, which could help kill any cancer cells that remain after high-dose treatment. This is called the **graft-versus-cancer** or **graft-versus-tumor** effect.

Other advantages are that the donor can often be asked to donate more stem cells or even white blood cells if needed (although this isn't true for a cord blood transplant), and stem cells from healthy donors are free of cancer cells.

### **Risks of allogeneic stem cell transplants**

As with any type of transplant, there is a risk that the transplant, or graft, might not take – that is, the transplanted donor stem 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 could attack healthy cells in the patient's body. This is called **graft-versus-host disease**, and it can range from mild to life-threatening.

There is also a very small risk of certain infections from the donor cells, even though donors are tested before they donate.

Another risk is that some types of infections you had previously and which your immune system has had under control may resurface after an allogeneic transplant. This can

happen when your immune system is weakened (suppressed) by medicines called **immunosuppressive** drugs. Such infections can cause serious problems and can even be life-threatening.

### **Mini-transplants (non-myeloablative transplants)**

For some people, age or certain health conditions make it more risky to do myeloablative therapy that wipes 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. Your doctor might refer to it as a **non-myeloablative transplant** or mention **reduced-intensity conditioning (RIC)**. Patients getting a mini transplant typically get lower doses of chemo and/or radiation than if they were getting a standard myeloablative transplant. The goal in the mini-transplant is to kill some of the cancer cells (which will also kill 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 that it uses lower doses of chemo and/or radiation. And because the stem cells aren't all killed, blood cell counts don't drop as low while waiting for the new stem cells to start making normal blood cells. This makes it especially useful for older patients and those with other health problems. 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 people with fast-growing cancers. Also, although there might be fewer side effects from chemo and radiation than those from a standard allogeneic transplant, the risk of graft-versus-host disease is the same. Some studies have shown that for some cancers and some other blood conditions, both adults and children can have the same kinds of results with a mini-transplant as compared to a standard 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 patient has an identical sibling (twin or triplet) – someone who has the exact same tissue type. An advantage of syngeneic stem cell transplant is that graft-versus-host disease will not

be a problem. Also, there are no cancer cells in the transplanted stem cells, as there might be in an autologous transplant.

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

## Half-matched transplants

Improvements have been made in the use of family members as donors. This kind of transplant is called a half-match (**haploidentical**) transplant for people who don't have fully matching or identical family member. This can be another option to consider, along with cord blood transplant and matched unrelated donor (MUD) transplant.

## The importance of matching patients and donors

If possible, it is very important that the donor and recipient are a close tissue match to avoid graft rejection. Graft rejection happens when the recipient's immune system recognizes the donor cells as foreign and tries to destroy them as it would a bacteria or virus. Graft rejection can lead to graft failure, but it's 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 attack their new "home." This is called **graft-versus-host disease**. (See [Stem Cell Transplant Side Effects](#) for more on this). The new, 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.

## What makes a stem cell donor a match? What does being an HLA match mean?

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 them from both of our parents and, in turn, pass them on to 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 best 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 important, and even a sample with a couple of mismatched antigens 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 to reduce the risks of mismatched types between unrelated donors, more than the basic 6 HLA antigens may be tested. For example, sometimes doctors try and get a 10 out of 10 match. Certain transplant centers now require high-resolution matching, which looks more deeply into tissue types and allow more specific HLA matching.

### **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, like those listed here. 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.

**Be the Match** (formerly the **National Marrow Donor Program**) Toll-free number: 1-800-MARROW-2 (1-800-627-7692) Website: [www.bethematch.org](http://www.bethematch.org)<sup>4</sup>

**Blood & Marrow Transplant Information Network** Toll-free number: 1-888-597-7674 Website: [www.bmtinfonet.org](http://www.bmtinfonet.org)<sup>5</sup>



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. When compared to other ethnic groups, white people have a better chance of finding a perfect match for stem cell transplant among unrelated donors. This is because ethnic groups have differing HLA types, and in the past there was less diversity in donor registries, or fewer non-White donors. However, the chances of finding an unrelated donor match improve each year, as more volunteers become aware of registries and sign up for them.

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. Also, 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 can be tolerated in which particular situations – that is, which mismatched antigens 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.

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html)
2. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html)
3. [www.cancer.org/cancer/managing-cancer/side-effects/infections.html](http://www.cancer.org/cancer/managing-cancer/side-effects/infections.html)
4. [www.bethematch.org/](http://www.bethematch.org/)
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## Donating Stem Cells and Bone Marrow

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 if they need an autologous transplant.

- [If you want to donate stem cells for someone else](#)
- [Before the donation: Informed consent and further testing](#)
- [How stem cells are collected](#)

### If you want to donate stem cells for someone else

Medical guidelines are in place to protect the health of potential donors, as well as the health of bone marrow and stem cell transplant patients. Many factors can affect if a person is eligible to register as a donor.

People, including cancer survivors, who want to donate stem cells or join a volunteer registry can check the eligibility list available through the registry. They can also speak

with a health care provider 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 Be the Match or the donor center in your area.

**Be the Match** (formerly the **National Marrow Donor Program**) Toll-free number: 1-800-MARROW-2 (1-800-627-7692) Website: [www.bethematch.org](http://www.bethematch.org)<sup>1</sup>

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.

## **Before the donation: Informed consent and further testing**

If a possible stem cell donor is found to be a good match for a recipient, steps are taken to teach the donor about the transplant process and make sure they are 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 they are in good health.

## **How stem cells are collected**

Stem cells may be collected from these 3 different sources:

- Bone marrow
- Peripheral stem cells
- Umbilical cord blood

Each method of collection is explained here.

### **Collecting bone marrow stem cells**

This process is often called **bone marrow harvest**. It's done in an operating room, while the donor is under general anesthesia (given medicine to put them into a deep sleep so they don't feel pain). The marrow cells are taken from the back of the pelvic (hip) bone. The donor lies face down, and 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 able 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 pain medications or nonsteroidal anti-inflammatory drugs 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 get back to their usual activities in 2 to 3 days. But it could take 2 or 3 weeks before they feel completely back to normal.

There aren't many risks for donors and serious complications are rare. But bone marrow donation is a surgical procedure. Rare complications could include anesthesia reactions, infection, nerve or muscle damage, 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. Even so, be sure to ask about insurance coverage before you decide to have the bone marrow harvest done.

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're frozen, for example, if the donor lives far away from the recipient.

## Collecting peripheral blood stem cells

For several days before starting the donation process, the donor is given a daily injection (shot) of a drug that causes the bone marrow to make and release a lot of 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 pain medications or nonsteroidal anti-inflammatory drugs. [Nausea](#)<sup>2</sup>, [sleeping problems](#)<sup>3</sup>, low-grade (mild) fevers, and tiredness are other possible effects. These go away once the injections are finished and collection is completed.

After the shots, blood is removed through a catheter (a thin, flexible plastic tube) that's put in a large vein in the arm. 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, often through the same catheter. (In some cases, a catheter may be put in each arm – one takes out blood and the other puts it back.) This process is called **apheresis**. 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, blockage of the catheter, or [infection](#)<sup>4</sup> of the catheter or at the area where it enters the vein. [Blood clots](#)<sup>5</sup> 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 tingly, 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 their own use later on. For some people, there are a few differences. For instance, sometimes chemotherapy (chemo) is given before the growth factor drug 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.

## Collecting umbilical cord blood

Cord blood is the blood that's left in the placenta and umbilical cord after a baby is born. Collecting it does not pose any health risk to the infant or the mother. 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.

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. Many hospitals collect cord blood for donation, which makes it easier for parents to donate. Parents can donate their newborn's cord blood to volunteer or public cord blood banks at no cost. For more about donating your newborn's cord blood, call 1-800-MARROW2 (1-800-627-7692) or visit [Be the Match](#)<sup>6</sup>.

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. If you want to donate or bank (save) your child's cord blood, you'll 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'll be asked to answer health questions and sign a consent form.

Parents may want to bank their child's cord blood if the family has a history of diseases that may benefit from stem cell transplant. There are several private companies offer this service. 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.
- Some diseases that can be treated with transplant require stem cells that come from another donor (allogeneic). Infusing autologous cord blood stem cells that contain the same disease or condition would not cure the disease.
- The shelf life of cord blood is not known. Because cord blood storage is a recent development, scientists don't know whether blood taken at birth will be useful if a family member develops a disease treatable by stem cell transplant 50 years later.
- The private collection fee can be a few thousand dollars, with another couple hundred dollars per year to store the cord blood. You'll want to check on costs because they'll probably increase over time, and they may vary from one part of the country to another.

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](http://www.parentsguidecordblood.org)<sup>7</sup>.

## Hyperlinks

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2. [www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html](http://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html)
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# Getting a Stem Cell or Bone Marrow Transplant

When the decision is made to have a stem cell or bone marrow transplant, there are several steps in the process. The steps are much the same, no matter what type of transplant you're going to have.

- [Evaluation and preparation for a transplant](#)
- [Hospital admission or outpatient treatment for transplants](#)
- [Conditioning treatment \(chemo and/or radiation therapy\)](#)
- [Infusion of stem cells](#)
- [Recovery after infusion](#)
- [Discharge from the hospital after transplant](#)
- [Rehabilitation after stem cell transplant](#)

## 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 for some people, problems can lead to severe complications or even death. You'll want to weigh the [benefits and risks](#) before you start.

Transplants can also be hard emotionally. They often require being in the hospital, being isolated, and there's 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. Some of the side effects are really unpleasant and can be serious. Your cancer care team will do everything they can to make you comfortable, but some of the side effects may not be completely controlled or relieved.

Before you have a transplant, you need to discuss the transplant process and all its effects with your doctors. It also helps to talk with others who have already had transplants.

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. For example, you'll need a responsible adult who will be with you to give you medicines, help watch for problems, and stay in touch with your transplant 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 will 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 (this is a blood test)
- 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 (this is a medical procedure that happens in the hospital or clinic)
- 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)
- Appointments 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 \(CVC\)](#)<sup>1</sup> 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're getting an autologous transplant, a special catheter can be placed that can also be used when your stem cells are being removed or harvested.

The CVC 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, people 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. 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 [Types of Stem Cell Transplants for Cancer Treatment](#) may be an option for some of these people.

## Hospital admission or outpatient treatment for transplants

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 pre-transplant chemo or radiation treatment begins (see the next section), 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'll need to be very near the transplant center during the early stages. You'll need a family member or loved one to be a caregiver who can stay with you all the time. You and the caregiver will also need reliable transportation 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 in the hospital if your situation changes or if you start having complications.

To reduce the chance of [infection](#)<sup>2</sup> 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're going to be treated as an outpatient, you will get instructions on avoiding infection. Usually, people who have transplants are in a separate, special part of the hospital to keep as many germs away as possible.

The transplant experience can be overwhelming. Your transplant team will be there to help you prepare for the process physically and emotionally and to 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's no going back – there can be serious problems if treatment is stopped at any time during transplant.

Having a transplant takes a serious commitment from you and your caregiver and family, so it is important to know exactly what to expect.

## Conditioning treatment (chemo and/or radiation therapy)

Conditioning, also known as **pre-transplant treatment**, **bone marrow preparation**, or **myeloablation**, is usually treatment with high-dose [chemo](#)<sup>3</sup> and/or [radiation therapy](#)<sup>4</sup>. 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 any remaining cancer cells in the patient's body

The conditioning treatment is different for every transplant. Your treatment will be planned based on the type of cancer you have, the type of transplant, and any chemo or radiation therapy you've had in the past.

If chemo is part of your treatment plan, it will be given in your central venous catheter and/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 very 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](#)<sup>5</sup> that will need to be treated with strong pain medicines. You may also have [nausea, vomiting](#),<sup>6</sup> be unable to eat, [lose your hair](#)<sup>7</sup>, and have lung or [breathing problems](#)<sup>8</sup>.

Conditioning can also cause premature menopause in women and often makes people sterile ([unable to have children](#)<sup>9</sup>). (See [Stem Cell Transplant Side Effects](#).)

## Infusion of stem cells

After the conditioning treatment, you'll be given a couple of days to rest before getting the stem cells. They will be given through your central venous catheter, much like a blood transfusion. If the stem cells were frozen, you might get some drugs before the stem cells are given. These drugs are used to help reduce your risk of reacting to the preservatives that are used when freezing the cells.

If the stem cells were frozen, they are thawed in warm water then given right away. There may be more than 1 bag of stem cells. For allogeneic or syngeneic transplants, the donor cells may be harvested (removed) in an operating room, and then processed

in the lab right away. Once they are ready, the cells are brought in and given to you – they're not frozen. 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 patients 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

[Side effects from the infusion](#)<sup>10</sup> are rare and usually mild. The preserving agent used when freezing the stem cells causes many of the side effects. For instance, 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 [side effects](#)<sup>11</sup> you might have during and right after the stem cell infusion 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 start 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 a number of weeks.

During the first couple of weeks you'll 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. 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](#)<sup>12</sup>), or bleeding from too few platelets ([thrombocytopenia](#)<sup>13</sup>). Many patients have high fevers and need IV antibiotics to treat serious infections. [Transfusions](#)<sup>14</sup> of red blood cells and platelets are often needed until the bone marrow starts working 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 stomach, heart, lung, liver, or kidney problems. ([Stem Cell Transplant Side Effects](#) goes into the details.) 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.

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 after transplant.

## **Discharge from the hospital after transplant**

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'll need to take
- 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
- 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 providers

## 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:

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

([Why Are Stem Cell Transplants Used as Cancer Treatment?](#) has more information about neutrophils, platelets, and hematocrit).

If you do not meet all of these requirements, but still don't need the intensive care of the transplant unit, you might be moved to another oncology unit. When you do go home, you might need to stay near the transplant center for some time, depending on your condition.

## Rehabilitation after stem cell transplant

The process of stem cell transplant doesn't end when you go home. You'll feel tired, and some people have physical or mental health problems in the rehabilitation period. You might still be taking a lot of medicines. These ongoing needs must now be managed at home, so caregiver and friend/family support is very important.

Transplant patients are followed closely during rehab. You might need daily or weekly exams along with things like [blood tests](#)<sup>15</sup>, and maybe other tests, too. During early rehab, you also might need blood and platelet transfusions, antibiotics, or other treatments. At first you'll need to see your transplant team often, maybe even every day, but you'll progress to less frequent visits 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. During this time, your team will still be closely watching you.

Some problems might show up as much as a year or more after the stem cells were infused. They 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
- 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
- New cancers caused by the transplant

Other problems can also come up, such as:

- 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 concerns

Your transplant team is still there to help you, even though the transplant happened months ago. It's important that you tell 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. They can also help you know if problems are serious, or a normal part of recovery. The National Bone Marrow Transplant Link helps patients, caregivers, and families by providing information and support services before, during, and after transplant. They can be reached at 1-800-LINK-BMT (1-800-546-5268) or online at [www.nbmtlink.org](http://www.nbmtlink.org)<sup>16</sup>.

## Hyperlinks



1. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html)
2. [www.cancer.org/cancer/managing-cancer/side-effects/infections.html](http://www.cancer.org/cancer/managing-cancer/side-effects/infections.html)
3. [www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html)
4. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html)
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9. [www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/how-cancer-treatment-affects-fertility.html](http://www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/how-cancer-treatment-affects-fertility.html)
10. [www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-reactions.html](http://www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-reactions.html)
11. [www.cancer.org/cancer/managing-cancer/side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects.html)
12. [www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/neutropenia.html](http://www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/neutropenia.html)
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15. [www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html](http://www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html)
16. [www.nbmtlink.org/](http://www.nbmtlink.org/)

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## Stem Cell or Bone Marrow Transplant Side Effects

- [Problems soon after transplant](#)
- [Transplant problems that may show up later](#)
- [Stem cell transplants and fertility](#)

## Problems soon after transplant

Many of the problems that can happen shortly after the transplant come from having the bone marrow wiped out by medicines or radiation just before the transplant. Others may be side effects of the conditioning treatments themselves.

Your transplant team can help you cope with side effects. Some can be prevented, and most can be treated to help you feel better. 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. Ask for their after hours contact numbers to make sure you will be able to do this.

### Mouth and throat pain

**Mucositis** (inflammation or [sores in the mouth](#)<sup>1</sup>) is a short-term side effect that can happen with chemo and radiation. It usually gets better within a few weeks after treatment, but it can make it very painful to eat and drink.

Good nutrition is important for people with cancer. If mouth pain or sores make it hard to eat or swallow, your transplant team can help you develop a plan to manage your symptoms.

### Nausea and vomiting

Because chemotherapy drugs can cause severe [nausea and vomiting](#)<sup>2</sup>, doctors often give anti-nausea medicines at the same time as chemo to try to prevent it. 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 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.

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

## Infection

For at least the first 6 weeks after transplant, until the new stem cells start making white blood cells (engraftment), you can easily get serious [infections](#)<sup>3</sup>. 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. This is because right after the transplant you don't have many white blood cells that are working well, and they are the primary immune cells that fight off infections.

You may be given antibiotics to try to prevent infections until your blood counts reach a certain level. For instance, pneumocystis pneumonia (often called PCP) is a common infection that's 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. Antibiotics are often used to keep transplant patients from getting this.

Your doctor may check you before the 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 infection that many adults have or had in the past. Adults with healthy immune systems may not have any symptoms because their immune system can keep the virus under control. But, CMV can be a cause of serious pneumonia in people who have had transplants, because the transplant lowers the amount of white blood cells they have. Pneumonia from CMV 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 this infection while you are in the hospital.

After engraftment, the risk of infection is lower, but it still can happen. It can take 6 months to a year after transplant for the immune system to work as well as it should. It can take even longer for patients with graft-versus-host disease (GVHD, see below). It's important to talk to your cancer care team about your risk for infection during this time.

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 keep you from being exposed 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're 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. You might need to avoid certain foods 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](#)<sup>4</sup>. Your family may need to move the cat's litter box away from places you eat or spend your time. Also, you should not clean pet cages or litter boxes during this time. Instead, give this task to a family member or friend.

Your transplant team will tell you and your family in detail about the [precautions](#)<sup>5</sup> you need to follow. There are many viruses, bacteria, and fungi that can cause infection after your transplant. You may be at risk for some more than others.

Despite all these precautions, patients often develop fevers, one of the first signs of infection. In fact, sometimes fever is the only sign of infection, so it's very important to contact your cancer care team if you have one or if you have any other signs of infection. You'll probably be asked to take your temperature by mouth every day or twice a day for a while. And your cancer care team will let you know when you should call in your temperature to them. If you get a fever, tests will be done to look for possible causes of the infection (chest x-rays, urine tests, and blood cultures) and antibiotics will be started.

## **Bleeding and transfusions**

After transplant, you're 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 several 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, a platelet transfusion may be needed. You'll need to follow precautions until your platelet counts stay at safe levels.

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

For more information on the transfusion process, see [Blood Transfusion and Donation](#)<sup>6</sup>.

## **Interstitial pneumonitis and other lung problems**

**Pneumonitis** is a type of inflammation (swelling) in lung tissue that's most common in the first 100 days after 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).

Pneumonitis can be severe, especially if total body irradiation was given with chemo as part of the pre-transplant (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 your body as foreign. (Remember: The recipient's immune system has mostly been destroyed by conditioning treatment and cannot fight back, so 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 could 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 will develop acute GVHD. It's less common in younger patients and in those with closer HLA matches between donor and the patient.

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 can 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

Doctors try to prevent acute GVHD by giving drugs that suppress the immune system, such as steroids (glucocorticoids), methotrexate, cyclosporine, tacrolimus, or certain monoclonal antibodies. These drugs are given before acute GVHD starts and can help prevent serious GVHD. Still, mild GVHD will almost always happen in allogeneic transplant patients. Other drugs are being tested in different combinations for GVHD prevention.

The risk of acute GVHD can also be lowered by removing 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.

If acute GVHD does occur, it is most often mild, mainly affecting the skin. But sometimes it can be more serious, or even life-threatening.

Mild cases can often be treated with a steroid drug applied to the skin (topically) as an ointment, cream, or lotion, or with other skin treatments. More serious cases of GVHD might need to be treated with a steroid drug taken as a pill or injected into a vein. If steroids aren't effective, other drugs that affect the immune system can be used.

## Chronic GVHD

Chronic GVHD can start anywhere from about 90 to 600 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
- Bloating abdomen (belly)
- Pain in the upper right part of the abdomen (belly)
- Increased levels of liver enzymes in the blood (seen on blood tests)
- Skin that 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. Most patients with chronic GVHD can stop the immunosuppressive drugs after their symptoms improve.

### **Hepatic veno-occlusive disease (VOD)**

Hepatic veno-occlusive disease (VOD) is a serious problem in which tiny veins and other blood vessels inside the liver become blocked. It's not common, and it only happens in people with allogeneic transplants, and mainly in those who got the drugs busulfan or melphalan as part of conditioning, or treatment that was given before the transplant.

VOD usually happens within about 3 weeks after transplant. 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 (this is where the liver is), and quick weight gain (mostly from fluid that bloats the belly). It is life-threatening, so early diagnosis of VOD is very important. Researchers continue to find ways to try to measure a person's chances of getting VOD so that treatment can start as soon as possible.

### **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. Still, it's not very common.

Graft failure can lead to serious bleeding and/or infection. Graft failure is 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.

Although it can be very upsetting to have this happen, these people can get treated with a second dose of stem cells, if they are 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 pre-transplant chemo or radiation 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
- 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)

The medicines used in transplants can harm the body's organs, such as the heart, lungs, kidneys, liver, bones/joints, 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 before the transplant, 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 tests, lung/breathing studies, and other tests will help look for and keep tabs on organ problems.

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 that comes back**

The goal of a stem cell transplant in cancer is to prolong life and, in many cases, even cure the cancer. But in some cases, the cancer comes back (sometimes called relapse or recurrence depending on when it might occur after a transplant). Relapse or recurrence can happen a few months to a few years after transplant. It happens much more rarely 5 or more years after transplant.

If cancer comes back, 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](#)<sup>7</sup> or [targeted therapy](#)<sup>8</sup>. 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 have them.

Other options may include [palliative \(comfort\) care](#)<sup>9</sup>, or a [clinical trial](#)<sup>10</sup> 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 benefits and risks before you decide.

### **Second 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](#)<sup>11</sup> after transplant. 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.

A cancer called post-transplant lymphoproliferative disease (PTLD), if it occurs, usually develops within the first year after the transplant. Other conditions and cancers that can happen are solid tumor cancers in different organs, leukemia, and myelodysplastic syndromes. These other conditions, if they occur, tend to develop a few years or longer after the transplant.

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; the younger a person is when radiation is given, the more that person is at risk for certain types of cancer.
- Immune system problems (such as graft-versus-host disease, HLA-mismatched allogeneic transplant, and immunosuppressant therapy)
- Infection with viruses such as Epstein-Barr (EBV), cytomegalovirus (CMV), hepatitis B (HBV), or hepatitis C (HCV)
- The type of cancer you received the transplant for: for people who had their transplant when younger than 30 years old, those who had certain leukemias had a higher risk of having another cancer than people who did not have these leukemias.

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.

### **Post-transplant lymphoproliferative disorder**

Post-transplant lymphoproliferative 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 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 pre-transplant treatment given weakens the immune system, allowing the EBV infection to get out of control, which can lead to a PTLD.

Still, PTLD after allogeneic stem cell transplant is fairly rare. It most often develops within 1 to 6 months after allogeneic stem cell transplant, when the immune system is

still very weak.

PTLD is life-threatening. It may show up as lymph node swelling, fever, and chills. There's 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 rituximab to kill the B cells, and giving anti-viral drugs to treat the EBV.

Even though PTLD doesn't often happen after transplant, it's more likely to occur with less well-matched donors and when strong suppression of the immune system is needed. Studies are being done to identify risk factors for PTLD and look for ways to prevent it in transplant patients who are at risk.

## **Stem cell transplants and fertility**

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 about ways to protect your fertility before treatment. Your doctor may be able to tell you if a particular treatment will be likely to cause infertility.

After chemo or radiation, some 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. Fertility returns in some men, but the timing is unpredictable. Men might consider storing their sperm before having a transplant.

For more information on having children after being treated for cancer or sexual problems related to cancer treatment, see [Fertility and Sexual Side Effects](#)<sup>12</sup>.

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/mouth-sores.html](http://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/mouth-sores.html)
2. [www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html](http://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html)
3. [www.cancer.org/cancer/managing-cancer/side-effects/infections.html](http://www.cancer.org/cancer/managing-cancer/side-effects/infections.html)
4. [www.cancer.org/cancer/survivorship/coping/caring-for-pets-during-cancer-treatment.html](http://www.cancer.org/cancer/survivorship/coping/caring-for-pets-during-cancer-treatment.html)
5. [www.cancer.org/cancer/survivorship/coping/nutrition/weak-immune-system.html](http://www.cancer.org/cancer/survivorship/coping/nutrition/weak-immune-system.html)
6. [www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/blood-transfusion-and-donation.html)
7. [www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html)
8. [www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html)
9. [www.cancer.org/cancer/managing-cancer/palliative-care.html](http://www.cancer.org/cancer/managing-cancer/palliative-care.html)
10. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html)
11. [www.cancer.org/cancer/survivorship/long-term-health-concerns/second-cancers-in-adults.html](http://www.cancer.org/cancer/survivorship/long-term-health-concerns/second-cancers-in-adults.html)
12. [www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects.html)

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