

Bone Marrow and Hematopoietic Stem Cells—Fact Sheet and Frequently Asked Questions (FAQs)

What are bone marrow and hematopoietic stem cells?

Bone marrow is the soft, sponge-like material found inside bones. It contains immature cells known as hematopoietic or blood-forming stem cells. (Hematopoietic stem cells are different from embryonic stem cells. Embryonic stem cells can develop into every type of cell in the body.) Hematopoietic stem cells divide to form more blood-forming stem cells, or they mature into one of three types of blood cells: white blood cells, which fight infection; red blood cells, which carry oxygen; and platelets, which help the blood to clot. Most hematopoietic stem cells are found in the bone marrow, but some cells, called peripheral blood stem cells (PBSCs), are found in the bloodstream. Blood in the umbilical cord also contains hematopoietic stem cells. Cells from any of these sources can be used in transplants.

What are bone marrow transplantation and peripheral blood stem cell transplantation?

Bone marrow transplantation (BMT) and peripheral blood stem cell transplantation (PBSCT) are procedures that restore stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy. There are three types of transplants:

- In autologous transplants, patients receive their own stem cells.
- In syngeneic transplants, patients receive stem cells from their identical twin.

In allogeneic transplants, patients receive stem cells from their brother, sister, or parent. A person who is not related to the patient (an unrelated donor) also may be used.

Why are BMT and PBSCT used in cancer treatment?

One reason BMT and PBSCT are used in cancer treatment is to make it possible for patients to receive very high doses of chemotherapy and/or radiation therapy. To understand more about why BMT and PBSCT are used, it is helpful to understand how chemotherapy and radiation therapy work.

Chemotherapy and radiation therapy generally affect cells that divide rapidly. They are used to treat cancer because cancer cells divide more often than most healthy cells. However, because bone marrow cells also divide frequently, high-dose treatments can severely damage or destroy the patient's bone marrow. Without healthy bone marrow, the patient is no longer able to make the blood cells needed to carry oxygen, fight infection, and prevent bleeding. BMT and PBSCT replace stem cells that were destroyed by treatment. The healthy, transplanted stem cells can restore the bone marrow's ability to produce the blood cells the patient needs.

In some types of leukemia, the graft-versus-tumor (GVT) effect that occurs after allogeneic BMT and PBSCT is crucial to the effectiveness of the treatment. GVT occurs when white blood cells from the donor (the graft) identify the cancer cells that

remain in the patient's body after the chemotherapy and/or radiation therapy (the tumor) as foreign and attack them.

What types of cancer use BMT and PBSCT?

BMT and PBSCT are most commonly used in the treatment of leukemia and lymphoma. They are most effective when the leukemia or lymphoma is in remission (the signs and symptoms of cancer have disappeared). BMT and PBSCT are also used to treat other cancers such as neuroblastoma (cancer that arises in immature nerve cells and affects mostly infants and children) and multiple myeloma. Researchers are evaluating BMT and PBSCT in clinical trials (research studies) for the treatment of various types of cancer.

How are the donor's stem cells matched to the patient's stem cells in allogeneic or syngeneic transplantation?

To minimize potential side effects, doctors most often use transplanted stem cells that match the patient's own stem cells as closely as possible. People have different sets of proteins, called human leukocyte-associated (HLA) antigens, on the surface of their cells. The set of proteins, called the HLA type, is identified by a special blood test.

In most cases, the success of allogeneic transplantation depends in part on how well the HLA antigens of the donor's stem cells match those of the recipient's stem cells. The higher the number of matching HLA antigens, the greater the chance that the patient's body will accept the donor's stem cells. In general, patients are less likely to develop a complication known as graft-versus-host disease (GVHD) if the stem cells of the donor and patient are closely matched.

Close relatives, especially brothers and sisters, are more likely than unrelated people to be HLA-matched. However, only 25 to 35 percent of patients have an HLA-matched sibling. The chances of obtaining HLA-matched stem cells from an unrelated donor are slightly better, approximately 50 percent. Among unrelated donors, HLA-matching is greatly improved when the donor and recipient have the same ethnic and racial background. Although the number of donors is increasing overall, individuals from certain ethnic and racial groups still have a lower chance of finding a matching donor. Large volunteer donor registries can assist in finding an appropriate unrelated donor (see Question 18).

Because identical twins have the same genes, they have the same set of HLA antigens. As a result, the patient's body will accept a transplant from an identical twin. However, identical twins represent a small number of all births, so syngeneic transplantation is rare.

How is bone marrow obtained for transplantation?

The stem cells used in BMT come from the liquid center of the bone, called the marrow. In general, the procedure for obtaining bone marrow, which is called "harvesting," is similar for all three types of BMTs (autologous, syngeneic, and allogeneic). The donor is given either general anesthesia, which puts the person to

sleep during the procedure, or regional anesthesia, which causes loss of feeling below the waist. Needles are inserted through the skin over the pelvic (hip) bone or, in rare cases, the sternum (breastbone), and into the bone marrow to draw the marrow out of the bone. Harvesting the marrow takes about an hour.

The harvested bone marrow is then processed to remove blood and bone fragments. Harvested bone marrow can be combined with a preservative and frozen to keep the stem cells alive until they are needed. This technique is known as cryopreservation. Stem cells can be cryopreserved for many years.

How are PBSCs obtained for transplantation?

The stem cells used in PBSCT come from the bloodstream. A process called apheresis or leukapheresis is used to obtain PBSCs for transplantation. For 4 or 5 days before apheresis, the donor may be given a medication to increase the number of stem cells released into the bloodstream. In apheresis, blood is removed through a large vein in the arm or a central venous catheter (a flexible tube that is placed in a large vein in the neck, chest, or groin area). The blood goes through a machine that removes the stem cells. The blood is then returned to the donor and the collected cells are stored. Apheresis typically takes 4 to 6 hours. The stem cells are then frozen until they are given to the recipient.

How are umbilical cord stem cells obtained for transplantation?

Stem cells also may be retrieved from umbilical cord blood. For this to occur, the mother must contact a cord blood bank before the baby's birth. The cord blood bank may request that she complete a questionnaire and give a small blood sample.

Cord blood banks may be public or commercial. Public cord blood banks accept donations of cord blood and may provide the donated stem cells to another matched individual in their network. In contrast, commercial cord blood banks will store the cord blood for the family, in case it is needed later for the child or another family member.

After the baby is born and the umbilical cord has been cut, blood is retrieved from the umbilical cord and placenta. This process poses minimal health risk to the mother or the child. If the mother agrees, the umbilical cord blood is processed and frozen for storage by the cord blood bank. Only a small amount of blood can be retrieved from the umbilical cord and placenta, so the collected stem cells are typically used for children or small adults.

Are any risks associated with donating bone marrow?

Because only a small amount of bone marrow is removed, donating usually does not pose any significant problems for the donor. The most serious risk associated with donating bone marrow involves the use of anesthesia during the procedure.

The area where the bone marrow was taken out may feel stiff or sore for a few days, and the donor may feel tired. Within a few weeks, the donor's body replaces the donated marrow; however, the time required for a donor to recover varies. Some

people are back to their usual routine within 2 or 3 days, while others may take up to 3 to 4 weeks to fully recover their strength.

Are any risks associated with donating PBSCs?

Apheresis usually causes minimal discomfort. During apheresis, the person may feel lightheadedness, chills, numbness around the lips, and cramping in the hands. Unlike bone marrow donation, PBSC donation does not require anesthesia. The medication that is given to stimulate the release of stem cells from the marrow into the bloodstream may cause bone and muscle aches, headaches, fatigue, nausea, vomiting, and/or difficulty sleeping. These side effects generally stop within 2 to 3 days of the last dose of the medication.

How does the patient receive the stem cells during the transplant?

After being treated with high-dose anticancer drugs and/or radiation, the patient receives the stem cells through an intravenous (IV) line just like a blood transfusion. This part of the transplant takes 1 to 5 hours.

Are any special measures taken when the cancer patient is also the donor (autologous transplant)?

The stem cells used for autologous transplantation must be relatively free of cancer cells. The harvested cells can sometimes be treated before transplantation in a process known as “purging” to get rid of cancer cells. This process can remove some cancer cells from the harvested cells and minimize the chance that cancer will come back. Because purging may damage some healthy stem cells, more cells are obtained from the patient before the transplant so that enough healthy stem cells will remain after purging.

What happens after the stem cells have been transplanted to the patient?

After entering the bloodstream, the stem cells travel to the bone marrow, where they begin to produce new white blood cells, red blood cells, and platelets in a process known as “engraftment.” Engraftment usually occurs within about 2 to 4 weeks after transplantation. Doctors monitor it by checking blood counts on a frequent basis. Complete recovery of immune function takes much longer, however—up to several months for autologous transplant recipients and 1 to 2 years for patients receiving allogeneic or syngeneic transplants. Doctors evaluate the results of various blood tests to confirm that new blood cells are being produced and that the cancer has not returned. Bone marrow aspiration (the removal of a small sample of bone marrow through a needle for examination under a microscope) can also help doctors determine how well the new marrow is working.

What are the possible side effects of BMT and PBSCT?

The major risk of both treatments is an increased susceptibility to infection and bleeding as a result of the high-dose cancer treatment. Doctors may give the patient

antibiotics to prevent or treat infection. They may also give the patient transfusions of platelets to prevent bleeding and red blood cells to treat anemia. Patients who undergo BMT and PBSCT may experience short-term side effects such as nausea, vomiting, fatigue, loss of appetite, mouth sores, hair loss, and skin reactions.

Potential long-term risks include complications of the pretransplant chemotherapy and radiation therapy, such as infertility (the inability to produce children); cataracts (clouding of the lens of the eye, which causes loss of vision); secondary (new) cancers; and damage to the liver, kidneys, lungs, and/or heart.

With allogeneic transplants, a complication known as graft-versus-host disease (GVHD) sometimes develops. GVHD occurs when white blood cells from the donor (the graft) identify cells in the patient's body (the host) as foreign and attack them. The most commonly damaged organs are the skin, liver, and intestines. This complication can develop within a few weeks of the transplant (acute GVHD) or much later (chronic GVHD). To prevent this complication, the patient may receive medications that suppress the immune system. Additionally, the donated stem cells can be treated to remove the white blood cells that cause GVHD in a process called "T-cell depletion." If GVHD develops, it can be very serious and is treated with steroids or other immunosuppressive agents. GVHD can be difficult to treat, but some studies suggest that patients with leukemia who develop GVHD are less likely to have the cancer come back. Clinical trials are being conducted to find ways to prevent and treat GVHD.

The likelihood and severity of complications are specific to the patient's treatment and should be discussed with the patient's doctor.

What is a "mini-transplant"?

A "mini-transplant" (also called a non-myeloablative or reduced-intensity transplant) is a type of allogeneic transplant. This approach is being studied in clinical trials for the treatment of several types of cancer, including leukemia, lymphoma, multiple myeloma, and other cancers of the blood.

A mini-transplant uses lower, less toxic doses of chemotherapy and/or radiation to prepare the patient for an allogeneic transplant. The use of lower doses of anticancer drugs and radiation eliminates some, but not all, of the patient's bone marrow. It also reduces the number of cancer cells and suppresses the patient's immune system to prevent rejection of the transplant.

Unlike traditional BMT or PBSCT, cells from both the donor and the patient may exist in the patient's body for some time after a mini-transplant. Once the cells from the donor begin to engraft, they may cause the graft-versus-tumor (GVT) effect and work to destroy the cancer cells that were not eliminated by the anticancer drugs and/or radiation. To boost the GVT effect, the patient may be given an injection of their donor's white blood cells. This procedure is called a "donor lymphocyte infusion.

What is a "tandem transplant"?

A "tandem transplant" is a type of autologous transplant. This method is being studied in clinical trials for the treatment of several types of cancer, including

multiple myeloma and germ cell cancer. During a tandem transplant, a patient receives two sequential courses of high-dose chemotherapy with stem cell transplant. Typically, the two courses are given several weeks to several months apart. Researchers hope that this method can prevent the cancer from recurring (coming back) at a later time.