Bone Marrow Transplantation & Peripheral Blood Stem Cell Transplantation: Q & A

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:
  - Patients receive their own stem cells (*autologous transplants*).
  - Patients receive stem cells from their identical twin (*syngeneic transplants*).
  - Patients receive stem cells from someone other than themselves or an identical twin. The patient's brother, sister, parent or a person not related to the patient may be used (*allogeneic transplants*).

KEY POINTS

- 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.
- After being treated with high-dose anticancer drugs and/or radiation, the patient receives the harvested stem cells. They travel to the bone marrow and begin to produce new blood cells.
- A “mini-transplant” uses lower, less toxic doses of chemotherapy and/or radiation to prepare the patient for transplant.
- A “tandem transplant” involves two sequential courses of high-dose chemotherapy and stem cell transplant.
- The National Marrow Donor Program® (NMDP) maintains an international registry of volunteer stem cell donors.

WHAT ARE BONE MARROW AND HEMATOPOIETIC STEM CELLS?

- Bone marrow is the soft, sponge-like material found inside bones. Bone marrow contains a specific king of cell that creates blood-forming stem cells (*hematopoietic*). 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.
  - 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.

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. But, 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.
  - 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

identify the cancer cells that remain in the patient's body after the chemotherapy and/or radiation therapy (the tumor) as foreign. They then 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. This means that the signs and symptoms of cancer have disappeared. BMT and PBSCT are also used to treat other cancers such as:

- Cancer that arises in immature nerve cells and affects mostly infants and children (*neuroblastoma*).
- Cancer of the plasma cells (*multiple myeloma*).

Researchers are evaluating BMT and PBSCT 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 on the surface of their cells. They are called human leukocyte-associated (HLA) antigens. 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. But 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. It is approximately 50 percent. Among unrelated donors, HLA-matching is greatly improved when the donor and recipient have the same ethnic and racial background. The number of donors is increasing. But individuals from certain ethnic and racial groups still have a lower chance of finding a matching donor. Large volunteer donor registries can help in finding an appropriate unrelated donor.
- Identical twins have the same genes. So they have the same set of HLA antigens. As a result, the patient's body will accept a transplant from an identical twin. But 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. This is called the marrow. In general, the procedure for obtaining bone marrow, which is called *harvesting*, is similar for all three types of BMT's (autologous, syngeneic, and allogeneic). The donor is given either general or regional anesthesia. General anesthesia puts the person to sleep during the procedure. Regional anesthesia causes loss of feeling below the waist. Needles are inserted through the skin over the hip (*pelvic*) bone or, in rare cases, the breastbone (*sternum*). Then they go 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 preserved this way for many years.

HOW ARE PBSC'S OBTAINED FOR TRANSPLANTATION?

The stem cells used in PBSCT come from the bloodstream. A process called apheresis is used to obtain PBSC's 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. This is 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. The collected cells are then stored. Apheresis typically takes 4 to 6 hours. The stem cells are then frozen until they are given to the recipient. Apheresis may also be called leukapheresis.

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. They 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. This is 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 does not cause health risks 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?

- Only a small amount of bone marrow is removed. So donating usually does not pose any significant problems for the donor. The most serious risk 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. But the time required for a donor to recover varies. Some people are back to their usual routine within 2 or 3 days. Others may take up to 3 to 4 weeks to fully recover their strength.

ARE ANY RISKS ASSOCIATED WITH DONATING PBSC'S?

Apheresis usually causes little discomfort. During apheresis, the patient may feel:

- Lightheadedness.
- Chills.
- Numbness around the lips.
- 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.
- 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. A process known as *purging* is used 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. Purging may damage some healthy stem cells. So more cells are obtained from the patient before the transplant. This is to ensure 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. There 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. Your caregivers monitor it by checking blood counts on a frequent basis. Complete recovery of immune function takes much longer. It can take up to several months for autologous transplant recipients and 1 to 2 years for patients receiving allogeneic or syngeneic transplants.

Caregivers evaluate the results of various blood tests to confirm that new blood cells are being produced and that the cancer has not returned. The removal of a small sample of bone marrow through a needle for examination under a microscope (*bone marrow aspiration*) can also help caregivers 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. Caregivers 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. These include:
  - Nausea.
  - Vomiting.
  - Fatigue.
  - Loss of appetite.
  - Mouth sores.
  - Hair loss.
  - Skin reactions.
- Potential long-term risks include complications of the pre-transplant chemotherapy and radiation therapy, such as:
  - Inability to produce children (*infertility*).
  - Clouding of the lens of the eye (*cataracts*). This causes loss of vision.
  - New (*secondary*) cancers.
  - 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 identify cells in the patient's body 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. Also, the donated stem cells can be treated to remove the white blood cells that cause GVHD. This is a process called *T-cell depletion*. If GVHD develops, it can be very serious. It 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. They should be discussed with your caregiver.

WHAT IS A “MINI-TRANSPLANT”?

- A “mini-transplant” is also called a non-myeloablative or reduced-intensity transplant. It is a type of allogeneic transplant. This approach is being studied in clinical trials for the treatment of several types of cancer. These include:
  - Leukemia.
  - Lymphoma.
  - Multiple myeloma.
  - 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 anti-cancer drugs and radiation eliminates some, but not all, of the patient's bone marrow. It also reduces the number of cancer cells. It also 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 courses of high-dose chemotherapy, one after another (*sequential*), 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 coming back at a later time.

HOW DO PATIENTS COVER THE COST OF BMT OR PBSCT?

- Advances in treatment methods, including the use of PBSCT, have reduced the amount of time many patients must spend in the hospital by speeding recovery. This shorter recovery time has brought about a reduction in cost. But BMT and PBSCT are complicated technical procedures. So they are very expensive. Many health insurance companies cover some of the costs of transplantation for certain types of cancer. Insurers may also cover a portion of the costs if special care is required when the patient returns home.
- There are options for relieving the financial burden associated with BMT and PBSCT. A hospital social worker is a valuable resource in planning for these financial needs. Federal Government programs and local service organizations may also be able to help.
  - The National Cancer Institute's (NCI) Cancer Information Service (CIS) can provide patients and their families with additional information about sources of financial assistance (see below).

WHAT ARE THE COSTS OF DONATING BONE MARROW, PBSC'S, OR UMBILICAL CORD BLOOD?

- Persons willing to donate bone marrow or PBSC's must have a sample of blood drawn to determine their HLA type. This blood test usually costs $65 to $100. The donor may be asked to pay for this blood test. Or the donor center may cover part of the cost. Community groups and other organizations may also provide financial assistance. Once a donor is identified as a match for a patient, all of the costs pertaining to the retrieval of bone marrow or PBSC's is covered by the patient or the patient's medical insurance.
- A woman can donate her baby's umbilical cord blood to public cord blood banks at no charge. But commercial blood banks do charge varying fees to store umbilical cord blood for the private use of the patient or his/her family.

WHERE CAN PEOPLE GET MORE INFORMATION ABOUT POTENTIAL DONORS AND TRANSPLANT CENTERS?

The National Marrow Donor Program® (NMDP) is a federally funded nonprofit organization. It was created to improve the effectiveness of the search for donors. The NMDP maintains an international registry of volunteers willing to be donors for all sources of blood stem cells used in transplantation:

- Bone marrow.
- Peripheral blood.
- Umbilical cord blood.

The NMDP Web site contains a list of participating transplant centers at http://www.marrow.org on the Internet. The list includes descriptions of the centers as well as their transplant experience, survival statistics, research interests, pre-transplant costs, and contact information.

Organization: National Marrow Donor Program
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E-mail: Available through the Web site
Internet Web site: http://www.marrow.org

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