

# Stemcell Transplantation- Types, Risks and Benefits

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## Abstract

Stem cells are the body's raw materials cells from which all other cells with specialized functions are generated. Under the right conditions in the body stem cells divide to form more cells, called daughter cells. These daughter cells either become new stem cells called self-renewal or become specialized cells i.e. differentiation with a more specific function, such as blood cells, brain cells, heart muscle or bone. Stem cells are unique and no other cell in the body has the natural ability to generate new cell types. Stem cell transplants, also known as bone marrow transplants, have been performed in the United States since the late 1960s. These transplants use adult stem cells. Adult stem cells are being tested in other applications, including a number of degenerative diseases, such as heart failure. Stem cells from umbilical cord blood have been successfully used in clinical trials to treat cancer and blood-related diseases.

**Keywords:** Stem cells; Transplantation; Hematopoietic stem cells; Pluripotent hemopoietic stem cell; Apheresis; cryopreservation; Autologous transplants; Allogeneic transplants; Syngeneic transplants; Graft-versus-cancer; Bone marrow; Engraftment

**Abbreviations:** HSCs: Hematopoietic stem cells; MSCs: Mesenchymal stem cells; PBSCs: Peripheral blood stem cells; BMT: Bone marrow transplantation; PBSCT: Peripheral blood stem cell transplantation; HSCT: Hematopoietic stem cell transplantation; HLA: Human leukocyte antigen typing; SLE: Systemic lupus erythematosus

## Introduction

Stem cells are cells with the potential to develop into many different types of cells in the body. They serve as a repair system for the body [1]. There are two main types of stem cells, embryonic stem cells and adult stem cells [2]. Stem cells are which have the remarkable potential to develop into many different cell types in the body during early life and growth and dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential [3] either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. Stem cells are distinguished from other cell types by two important characteristics [4]. First, they are unspecialized cells capable of renewing themselves through cell division, [5] sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues [6]. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions. Human embryonic stem cells [7] are embryos created for reproductive purposes through *in vitro* fertilization procedures [8]. Another breakthrough by identifying conditions that would allow some specialized adult cells to be "reprogrammed" genetically to assume a stem cell-like state [9].

Transplantation is a technique of replacing the recipient's damaged or absent organ from a donor [10]. A stem cell transplant is the infusion of healthy stem cells into your body. A stem cell transplant may be necessary if your bone marrow stops working and doesn't produce enough healthy stem cells. A stem cell transplant can help your body make enough healthy white blood cells, red blood cells or platelets [11] and reduce your risk of life-threatening infections, anemia [12] and bleeding. The procedure to replenish body's supply of healthy blood-

forming cells is generally called a stem cell transplant, it's also known as a bone marrow transplant or an umbilical cord blood transplant, [13] depending on the source of the stem cells. Stem cell transplantation is a very complex process that may span several months [14].

Bone marrow is the soft, sponge-like material found inside bones [15]. It contains immature cells known as hematopoietic or blood-forming stem cells [16]. Hematopoietic stem cells are different from embryonic stem cells [17]. Embryonic stem cells can develop into every type of cell in the body whereas 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 [18]; red blood cells, which carry oxygen; and platelets, which help the blood to clot [19]. Hematopoietic stem cells (HSCs) [20], bone marrow also contains mesenchymal stem [21-23] cells (MSCs). Most hematopoietic stem cells are found in the bone marrow, [24] but some cells, called peripheral blood stem cells (PBSCs), are found in the bloodstream. Hematopoietic stem cells can give rise to at least eight distinct blood cell lineages and can maintain lifelong blood production due to which they can exhibit a property of balancing self-renewal and differentiation [25]. Blood in the umbilical cord also contains hematopoietic stem cells. Cells from any of these sources can be used in transplants. Bone marrow [26] 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 [27].

## Hematopoietic Stem Cell Transplantation (HSCT)

Hematopoietic stem cell transplantation (HSCT) is the transplantation of Pluripotent hemopoietic stem cell or blood, often derived from bone marrow, umbilical cord blood or hematopoietic stem cells derived from a placenta [28-30]. Stem cell transplantation is a medical procedure in the fields of hematology and oncology, most

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often performed for people with diseases of the blood, bone marrow, or certain cancer [31]. With the availability of the stem cell growth factors GM-CSF and G-CSF [32,33], most hematopoietic stem cell transplantation procedures are performed using stem cells collected from the peripheral blood [34] such as cord blood or placenta derived stem cells, rather than from the bone marrow. Collecting peripheral blood stem cells [35] provides a bigger graft, [36] does not require that the donor be subjected to general anesthesia to collect the graft which results in a shorter time to engraftment, and may provide for a lower long-term relapse rate [37,38]. Depending upon the donor, the transplantation is called allogeneic, autologous or syngeneic. In each case, the source of these hematopoietic stem cells could be the bone marrow, peripheral blood or umbilical cord blood. Three different types of hematopoietic stem cells can be collected or harvested.

### Peripheral blood stem cells

Peripheral blood stem cells [39] are harvested from donated blood. The stem cells are separated and collected and the rest of the blood is returned to the donor. The stem cells used in PBSTC come from the bloodstream. A process called apheresis or leukapheresis is used to obtain PBSCs [40] 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 in which 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.

### Bone marrow stem cells

Bone marrow stem cells [41] are collected from the patient's hip bone through a surgical procedure. The stem cells used in BMT come from the liquid center of the bone, [42,43] 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 bone or, in rare cases, the breastbone and into the bone marrow to draw the marrow out of the bone [44]. 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 [45]. Stem cells can be cryopreserved for many years.

### Cord blood stem cells

Cord blood stem cells [46] are collected from a mother's placenta immediately after a child is born. Stem cells also may be retrieved from umbilical cord blood. 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.

## Types of Transplants

The three main types of stem cell transplants are autologous, syngeneic and allogeneic. The type of transplant needed will depend on the patient's specific medical condition and the availability of a matching donor.

### Autologous transplants

In autologous transplants, patients receive their own stem cells, with this type of transplant, patients act as their own donor i.e. a patient who is about to undergo cancer treatment will have his or her own stem cells removed and frozen for later use [47]. After the patient receives chemotherapy and/or radiation, the stem cells are thawed and put back into the patient's body [48]. This procedure may be done once or many times, depending on the need. Sometimes doctors will use extra-high doses of chemotherapy [49] during treatment to kill as many cancer cells [50] as possible if they know a patient will be getting a stem cell transplant soon after [51].

### Syngeneic transplants

In syngeneic transplants [52], patients receive stem cells from their identical twin. Since identical twins represent a small number of births, syngeneic transplantation is rare. Because identical twins have the same genes, they also have the same set of human leukocyte associated antigens. As a result, there is less chance of the transplant being rejected.

### Allogeneic transplants

In allogeneic transplants, patients receive stem cells from their brother, sister, or parent i.e. a person who is not related to the patient called an unrelated donor [53]. With an allogeneic transplant, the stem cells come from a donor often a sibling but sometimes another volunteer whose cells are considered a "match" for the patient. The process of finding a match is called tissue typing or human leukocyte antigen typing. HLA is a protein on the surface of blood cells [54]. Basically, the more "HLA markers" a patient and the potential donor have in common, the greater the chance that the transplant will be successful. Advantage of allogeneic stem cell transplant is that the donor stem cells make their own immune cells, which may help destroy any cancer cells [55] that may remain after high-dose treatment. This is called the *graft-versus-cancer* effect [56,57].

## Mechanism of Transplantation

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. 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 [58-60] usually occurs within about 2 to 4 weeks after transplantation. It can be observed by checking blood counts on a frequent basis [61].

## Risk Associated with Donation

In bone marrow donation only a small amount of bone marrow is removed, donating usually does not pose any significant problems for the donor [62]. The most serious risk involves the use of anesthesia [63,64] 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 [65]. 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. In peripheral blood stem cell donation [66], Apheresis usually causes minimal discomfort. During apheresis, the person may feel lightheadedness, chills, numbness around the lips, and cramping in the hands [67]. Unlike bone marrow donation, PBSC donation does not require anesthesia. The medication that is given to stimulate the mobilization of stem cells from the marrow into the bloodstream may cause bone and muscle aches, headaches, fatigue, nausea, vomiting, and/or difficulty sleeping [68,69]. These side effects generally stop within 2 to 3 days of the last dose of the medication. Unlike with an autologous transplant, there is a risk of rejection. Sometimes, though donor [70] being a good match, the transplant simply may not take. Other times, the donor cells can begin to make immune cells that attack the recipient's body. This condition is called graft-versus-host disease [71], and can be quite serious. Fortunately, most cases are successfully treated with steroids [72] and other medications. Sometimes, an upside of graft-versus-host disease is that the newly transplanted cells recognize the body's cancer cells [73] as different or foreign, and actually work to fight them. One advantage of autologous stem cell transplant is that you are getting your own cells back. This means there is no risk that your immune system [74] will reject the transplant or that the transplanted cells will attack or reject your body. Another common disease which is common is Graft-versus-host disease is a distinct syndrome which involves the development of skin rash, diarrhea, abdominal pain and hepatitis [75] jaundice within the first 100 days after an allogeneic bone marrow transplant. High-dose immunosuppressive therapy with autologous hematopoietic stem cell transplantation showed good results in the treatment of severe autoimmune diseases [76].

## Benefits

Advancements in stem cell therapies and tissue engineering hold great promise for regenerative medicine [77]. Stem cell transplants are used for treating patients whose stem cells have been damaged [78] by disease or for treating the disease. Stem cell transplants with kidney damage from pyelonephritis a type of urinary infection that has reached the kidney was found to improve kidney structure and function [79]. In various studies it's proved that the patients remained free from systemic lupus erythematosus (SLE) and improved continuously after high-dose chemotherapy [80] and hematopoietic stem-cell transplantation [81,82]. BMT and PBSCT are most commonly used in the treatment of leukemia [83] and lymphoma. They are most effective when the leukemia [84] or lymphoma is in remission i.e. the signs and symptoms of cancer have disappeared [85]. BMT and PBSCT are also used to treat other cancers such as neuroblastoma i.e. cancer that arises in immature nerve cells and affects mostly infants and children and multiple myeloma [86]. Donor stem cell transplantation may be an effective treatment for high risk myeloma patients with certain chromosomal abnormalities was proved recently. Autologous adult stem cell transplantation has been the latest tool in regenerative medical therapy and in cardiovascular diseases [87,88]. Autologous transplantation seems to be superior to both chemotherapy [89] and allogeneic transplantation for treatment of multiple myeloma but Syngeneic transplantation appears to be as good as autologous transplantation and therefore it is used to perform in patients with the disease whenever there is an identical twin donor available [90].

## Conclusion

Stem cell transplantation is a kind of medicine for cancer; here very high doses of chemo are used, often along with radiation therapy, to try to destroy all of the cancer. This treatment also kills the stem cells in the bone marrow. Advantage of autologous stem cell transplant is that the patient will be getting his/her own cells back. Advantage of allogeneic stem cell transplant is that the donor stem cells make their own immune cells, which may help destroy any cancer cells that may remain after high-dose treatment. Another possible advantage is that the donor can often be asked to donate more stem cells or even white blood cells if needed. Stem cells from healthy donors are also free of cancer cells. Soon after treatment, stem cells are given to replace those that were destroyed. These stem cells are given into a vein, much like a blood transfusion. Syngeneic transplants won't help destroy any remaining cancer cells because the new immune system is so much like yours. Every effort must be made to destroy all the cancer cells before the transplant is done to help keep the cancer from coming back. The Food and Drug Administration has approved an initial safety study using an embryonic stem cell therapy for the treatment of serious spinal cord injuries. Researchers are evaluating BMT and PBSCT in clinical trials for the treatment of various types of cancer.

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