BONE MARROW AND STEM CELL TRANSPLANTS

Hematopoietic stem cells are immature cells that can grow and change into any type of blood cell - red blood cells, white blood cells or platelets. Hematopoietic stem cells can be found in the bone marrow, circulating blood (also called peripheral blood) and umbilical cords.

Stem cells, because they divide rapidly, are sensitive to chemotherapy and radiation therapy. Patients with lymphoma that is difficult to treat or resistant to standard therapy may benefit from chemotherapy or radiation therapy given in very high doses (myeloablative therapy). However, this can potentially destroy all stem cells and leave the patient at very high risk for infection.

To combat this problem, they will receive stem cells to replenish those destroyed by high dose chemotherapy. If the patient receives their own previously stored stem cells, it is called an autologous transplant. An allogeneic stem cell transplant is when stem cells are taken from another person (donor) and given to the patient (recipient). Typically, the donor is a family member; however, an allogeneic transplant can also be done with an unrelated donor.

There are three main types of lymphocytes: B lymphocytes, T lymphocytes, and Natural killer cells. Lymphocytes are a type of white blood cell and are a major part of the lymphatic system. Together with other cells of the immune system, they work to fight infection and prevent disease.

LYMPHOMA CANADA

INFORMATION. HELP. HOPE.

GRAFT VERSUS HOST DISEASE

REACH US

BY PHONE

TOLL FREE | 1.866.659.5556
NATIONAL OFFICE | 905.858.5967

ONLINE

www.lymphoma.ca
info@lymphoma.ca

BY MAIL

Lymphoma Canada
6860 Century Avenue, Suite 202
Mississauga, ON L5N 2W5

LYMPHOMA CANADA

WHAT IS GRAFT-VERSUS-HOST DISEASE?

Graft-versus-host disease (GVHD) is a serious complication that can occur after allogeneic stem cell transplantation – the transfer of stem cells from a healthy person (the donor) to a patient to restore the patient's immune system. GVHD occurs when the healthy stem cells from the donor (called the graft) attack the patient's cells (called the host), causing damage to tissues and organs.

Donated stem cells also contain some lymphocytes. Lymphocytes are white blood cells that help protect the body from infection. To defend itself, the body must be able to distinguish between what belongs in the body ("self") and what is foreign to it ("non-self"). One of the benefits of an allogeneic transplant is that the donor lymphocytes may recognize any remaining cancer cells in the patient as foreign and coordinate an attack to eliminate them. This is called the "graft-versus-tumor effect."

The same ability of lymphocytes to recognize "self" from "non-self" can create a severe complication. Lymphocytes recognize "self" from "non-self" by a system of proteins called human leukocyte antigens (HLA). HLAs are found on the surface of many cells in the body. The donor's lymphocytes may recognize HLAs on the patient's cells as "non-self", leading the donor lymphocytes to attack the patient's healthy cells. This condition is called "graft-versus-host disease" (GVHD).

WHAT ARE LYMPHOCYTES?

TYPES OF GRAFT-VERSUS-HOST DISEASE

ACUTE GVHD

Acute GVHD starts within the first 100 days after the transplant. Approximately one in three patients who are transplanted with cells from a related donor develop acute GVHD. Approximately half of patients who are transplanted with cells from an unrelated donor develop acute GVHD. This condition can be mild to very severe and even life-threatening, if not controlled and treated. It can cause different symptoms, depending on the organs affected.

GRADE	DESCRIPTION
1 (mild)	• skin rash covering < 25% of the body • no liver or intestinal problems
2 (moderate)	• skin rash covering < 25% of the body • mild liver and intestinal problems
3 (severe)	• generalized skin redness • moderate liver and intestinal problems
4 (life-threatening)	• blisters and peeling skin • severe liver and intestinal problems

SYMPTOMS INCLUDE:
Rashes, which include burning and redness, that erupt on the palms or soles and may spread to the trunk and eventually the entire body.
Blistering, causing the exposed skin surface to flake off in severe cases.
Nausea, vomiting, abdominal cramps, diarrhea and loss of appetite, which can indicate the digestive tract is affected.
Jaundice, or a yellowing of the skin, which can indicate that the liver is damaged.

CHRONIC GVHD

Chronic GVHD usually occurs three to four months post-transplant, but in some cases may not develop for a year or more after the transplant. It is more likely to occur in patients who had acute GVHD, but may still appear without prior acute GVHD. Chronic GVHD occurs in about half of allogeneic transplants.

Chronic GVHD may involve a single organ or several organs and symptoms range from mild to life-threatening. It most often affects the mouth, skin, gut and liver. It can also affect other areas, such as the eyes, joints and lungs. Patients are regularly assessed for chronic GVHD during routine follow-up appointments with their transplant doctor.

SYMPTOMS INCLUDE:
Patches of skin may be lost, skin colour may deepen, and texture may become hard.
Scarring may occur, causing the motion of nearby joints to become restricted.
Hair loss may accompany skin injury.
Mouth and throat ulcers (sores).
Dry eyes can lead to loss of tear formation, general eye redness and irritation. Dryness of the vagina and other surfaces may also occur.
The lungs may also show effects of drying and scarring.
Liver injury can result in liver failure and diminished bile flow. Bile may back up into the blood and cause jaundice (yellowing of the skin and eyes).

PREVENTION AND TREATMENT OF GRAFT-VERSUS-HOST DISEASE

PREVENTION

Several advances in transplantation techniques have helped to reduce the risk of developing GVHD:

More precise HLA tissue matching: GVHD can develop when the donor and patient have different tissue types. The patient's transplant team will try to find a donor who closely matches the patient. The closer the match between the tissue type of the donor and the recipient, the lower the risk of developing GVHD.

Immunosuppressive drugs: A combination of medications is often given to the patient before and after transplantation to prevent GVHD. Some common immunosuppressive drugs that are given to patients include methotrexate, cyclosporine, tacrolimus, sirolimus, and corticosteroids (e.g. prednisone). If a patient develops GVHD while taking preventative drugs, management will be switched to GVHD treatment.

Depletion of T lymphocytes from the donor graft: Selective T cell depletion is a technique used to remove the specific T cells that can cause GVHD. This process can cause other issues however, such as increased rates of relapse, graft rejection, and post-transplant infections. Researchers are currently working on refining this technique.

The use of umbilical cord blood as the source of donor cells: For patients without perfectly matched donors, umbilical cord blood stored in public banks can be used as an alternative source of stem cells. Cord blood has fewer lymphocytes and they are less mature, so there is a lower chance of severe GVHD.

TREATMENT

Treatment decisions are made based on an individual patient's circumstances, e.g. what parts of the body are affected. As treatments for GVHD suppress the immune system, they can make patients more likely to develop infections. Controlling GVHD often involves getting the right balance of medication.

Corticosteroids, like prednisone, are the main treatment for acute and chronic GVHD. These medicines weaken the new immune system so it doesn't attack the body. Starting GVHD treatment as early as possible can lead to better results.

For patients whose GVHD does not improve with steroid treatment (steroid-refractory GVHD), other treatments are available.

Ibrutinib is approved in Canada for chronic GVHD that does not respond to, or has stopped responding to, steroids.

Other treatments for GVHD commonly used in Canada include: cyclosporine, tacrolimus, extracoporeal photopheresis (ECT), mycophenolate mofetil, rituximab, and imatinib mesylate.