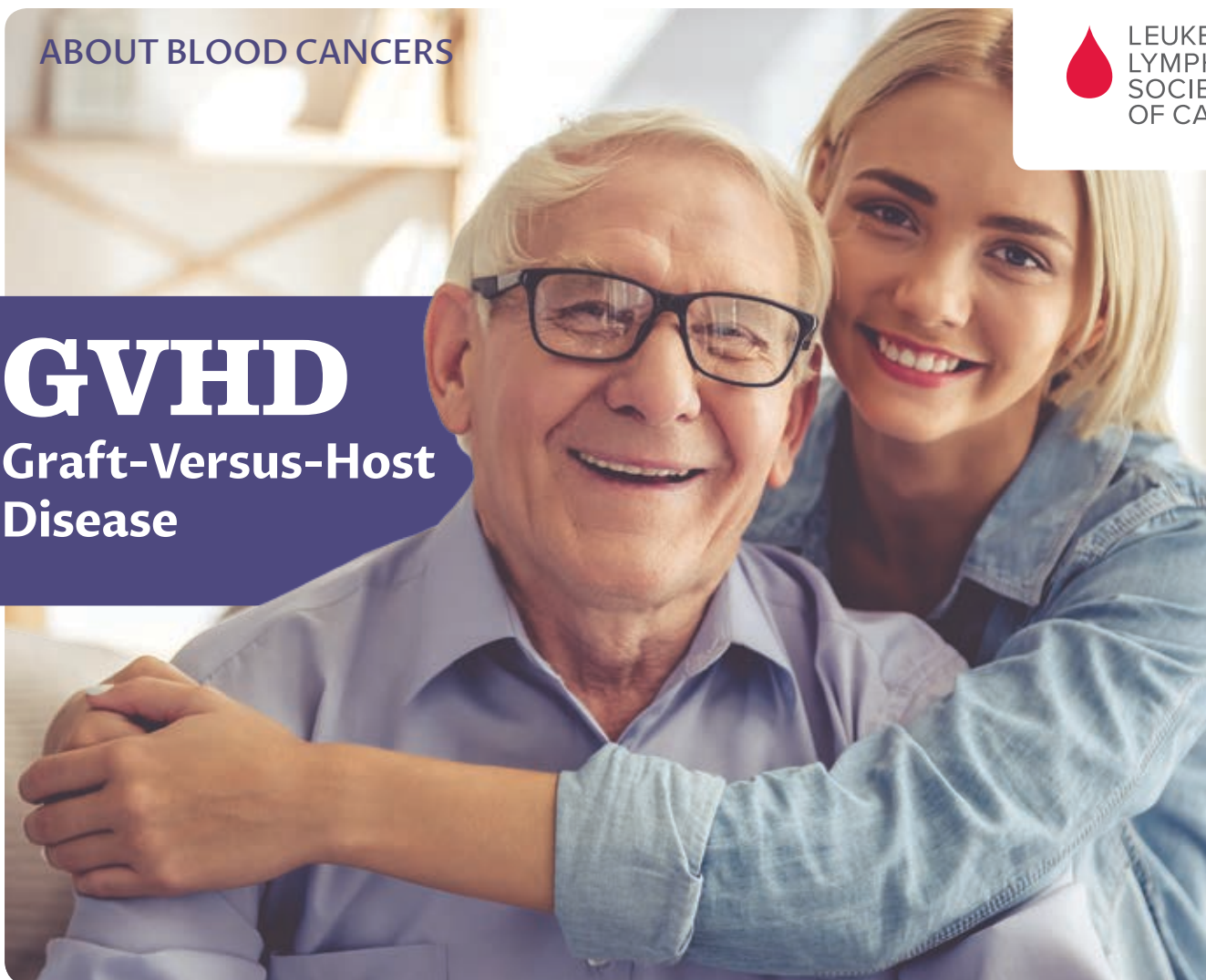


GVHD

Graft-Versus-Host Disease



WHAT YOU NEED TO KNOW

You or your loved one has been diagnosed with a type of blood cancer. One of the treatments your doctor may offer is a stem cell transplant. A serious complication of a stem cell transplant from a donor is graft-versus-host disease (GVHD). What does it mean and how might it affect you?

This fact sheet will help you:

- Get an overview of stem cell transplants
- Understand the two different types of stem cell transplants
- Learn about GVHD
- Understand the symptoms and types of GVHD
- Learn about ways to prevent GVHD
- Get an overview of treatment options



What is a stem cell transplant?

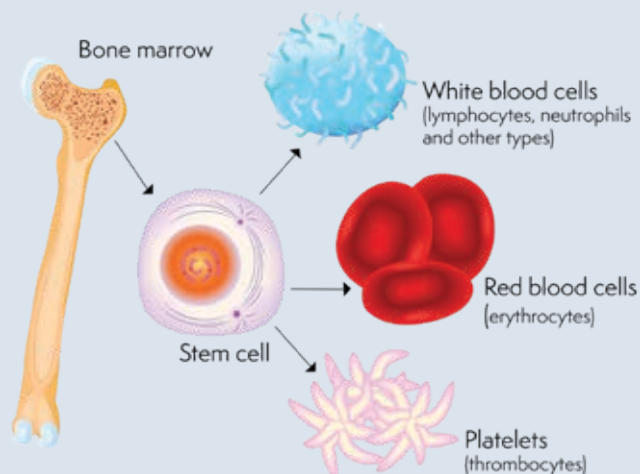
Your body depends on stem cells to produce blood cells. With a stem cell transplant, you receive healthy cells to replace the ones that have been destroyed by cancer or by high doses of chemotherapy and/or radiation therapy.

The two main types of stem cell transplants used for blood cancers are:

Autologous: Stem cells come from your body, so you can receive high doses of chemotherapy, with or without radiation. The stem cells then restore your bone marrow's ability to make new blood cells and reset your immune system.

Allogeneic: Stem cells from a healthy person (the donor) or donated umbilical cord blood replace stem cells in your bone marrow. This type of transplant is an effective treatment for many blood cancers and can provide a long-term cure. These new stem cells replace your stem cells that have been damaged by cancer or by the treatment.

With an allogeneic stem cell transplant, you will first go through a conditioning regimen that includes chemotherapy and often radiation therapy. This weakens your immune system and allows the new stem cells from the donor to start making new blood cells and generate a new immune system.



What is graft-versus-host disease (GVHD)?

GVHD is a serious complication that may occur after an allogeneic stem cell transplant if the donor cells (the graft) attack the cells of the recipient (the host). Donated stem cells contain T-cells, a type of white blood cell that helps protect your body from infection.

About T-cells and GVHD

- Graft-versus-host disease happens when donor cells (graft) mistakenly attack the recipient's (host) tissue and cells after an allogeneic stem cell transplant
 - T-cells are part of your immune system; they help to recognize what belongs in your body versus what is foreign and possibly dangerous
 - T-cells recognize and destroy harmful invaders like infections and bacteria
 - Donor T-cells may attack harmful cancer cells, known as graft-versus-tumour effect, and can help prevent the cancer from coming back (relapsing)
 - Donor T-cells can also recognize your healthy cells as foreign and attack your healthy tissues and organs
 - The attack can damage your organs and may cause them to stop working
- Graft-versus-tumour effect and graft-versus-host disease take time to develop. GVHD can be mild, moderate, or severe.

Types of GVHD

There are two main types of GVHD: acute and chronic. People can develop one or both types. Some people may not develop either type. Each type affects different organs and tissues and has different signs and symptoms.

The National Institutes of Health has classified GVHD into four categories, based on the signs and when it starts:

- **Classic acute GVHD:** Signs appear within 100 days of the stem cell transplant and are acute
- **Persistent, recurrent, or late-onset acute GVHD:** Signs appear more than 100 days after the transplant and are acute
- **Classic chronic GVHD:** Signs appear at any time after the transplant and are chronic
- **Overlap syndrome:** Signs appear at any time after the transplant and are both acute and chronic

Acute graft-versus-host disease

About acute GVHD

- Major cause of medical problems and death after an allogeneic stem cell transplant
- Between 30% and 70% of transplant recipients develop acute GVHD
- May be mild (grade 1), moderate, or severe (grade 4)
- Classified according to the number of organs involved and how much they are affected

Risk factors

Certain factors can increase your risk of getting chronic GVHD:

- Human leukocyte antigen mismatch (unrelated donor)
- Your age
- Female donor giving to a male recipient
- Intensity of the pre-transplant conditioning regimen (chemotherapy and sometimes radiation to destroy cancer cells)
- Donor lymphocyte infusion, a procedure done after the transplant

Signs and symptoms

Acute GVHD most commonly affects the skin, liver, and GI tract (stomach, intestines, and colon).

You may experience:

- Skin rash (most common symptom)
 - Often starts as a faint rash that can spread to your entire body
 - Mild forms may be uncomfortable and look like a sunburn
 - More severe rash includes blisters and peeling skin
- Gastrointestinal (GI) tract changes
 - Diarrhea is the most classic sign when your colon is inflamed
 - Other symptoms include stomach pain, bleeding, and/or nausea with vomiting
- Liver changes without symptoms
 - Often shows up as jaundice (skin or eyes look yellowish)
 - Can result in bleeding and confusion or extra fluid in the stomach
- Low blood counts
 - When your body responds to the attack on your organs

Following an allogeneic stem cell transplant, watch for the warning signs of acute GVHD. Contact your doctor right away if you have any of these symptoms. Early detection and treatment may help limit the severity of symptoms.

Chronic graft-versus-host disease

About chronic GVHD

- A leading cause of medical problems and death after an allogeneic stem cell transplant
- Between 30% and 70% of transplant recipients develop chronic GVHD
- Can involve a single organ or several organs
- Can last for years or for the rest of your life

Risk factors

Certain factors can increase your risk of getting chronic GVHD:

- Human leukocyte antigen mismatch (unrelated donor)
- Your age
- Your donor's age
- A female donor giving to a male recipient (and the number of children the female donor has had)
- Source of the stem cell:
 - Higher risk if it's not from bone marrow
 - Lowest risk if it's from umbilical cord blood
- Prior acute GVHD

Signs and symptoms

Symptoms of chronic GVHD can be moderate or life-threatening. They can affect a single organ or area of your body or be widespread. It most commonly affects the skin, mouth, eyes, liver, GI tract, lungs, and joints.

You may experience:

- Dry, painful, and itchy eyes
 - Difficulty tolerating bright lights, blurred vision, and blindness
- Dry mouth and difficulty eating
 - Painful ulcers in your throat, gum disease and tooth decay, and sensitivity to hot, cold, spicy, and acidic foods and carbonated drinks
- Skin rash
 - Dry, itchy, and tight skin, with a change in colour; restricted joint movements; sensitivity to changes in temperature
- Changes to hair and nails
 - Hard, brittle nails
 - Loss of hair on your body and scalp, and/or premature grey hair
- Loss of appetite and unexplained weight loss
 - Nausea, vomiting, diarrhea, stomach pain
- Shortness of breath, difficulty breathing, wheezing, and persistent cough
- Liver changes
 - Abdominal swelling, jaundice (yellowish colouring of the skin or eyes)
- Muscle and joint weakness, including cramping and stiffness
- Physical changes to genitals
 - For females: The vagina may become dry, itchy, and painful due to narrowing, ulcers, and scarring, and intercourse can be painful
 - For males: Urethra (tube that carries urine out of the body) may become narrower and scarred, and irritation can cause itching and scarring of the penis and scrotum

Contact your doctor right away if any of these symptoms appear. Early detection and treatment may help limit the severity of symptoms.



Preventing GVHD

Moderate and severe GVHD can cause significant illness and decrease your chances of survival. Once it develops, it can be difficult to treat. Doctors use various methods before and after a stem cell transplant to prevent GVHD and reduce how severe it gets.

Method	Description
HLA typing and matching	<p>GVHD can develop when the donor and the recipient have different tissue types. Human leukocyte antigen (HLA) typing is a blood test used to find out how closely your tissue type matches another person's.</p> <p>HLA matching is based on HLA markers. The more markers two people share, the less likely it is that their immune systems will attack each other.</p> <p>For most people, possible matches include:</p> <ul style="list-style-type: none">• Siblings: often the ideal donor, as they share some HLA markers• Registered donors: from a volunteer donor registry• Cord blood donors: stem cells are collected from a healthy newborn's umbilical cord and stored in a public bank (often available more quickly than other donors)
Haploidentical transplant	<p>A transplant from a family member who is a half match. The risks can be reduced using the medication cyclophosphamide after the transplant. This type of donor is often available more quickly than a full match.</p>
Immuno-suppressive drugs	<p>You will be given immunosuppressive drugs before and after your stem cell transplant. These drugs lower the function of the donor's T-cells.</p>
T-cell depletion	<p>Donor T-cells can be removed (depleted) so they do not affect you. This can be done by taking medication just before or after the treatment, or by using a machine to remove the T-cells before you receive the stem cells.</p>



GVHD treatment

Your treatment will focus on immunosuppression (lowering your immune response and its ability to fight infections and diseases) using corticosteroids. The type of treatment depends on how severe the symptoms are and if there are concerns about complications.

Types of treatment

- **Corticosteroids** are used for acute and chronic GVHD to suppress (weaken) the immune system; these are often combined with other immunosuppression medications (like cyclosporine, tacrolimus, or sirolimus)
- **Topical steroid cream** is used for mild skin-only acute GVHD and mild chronic GVHD
- **Steroid eye drops** are used for chronic GVHD of the eye
- **Photopheresis** for acute GVHD removes some lymphocytes from your blood, exposes them to light, then returns them to your body

Supportive treatments

Supportive therapies can also help, depending on the type of GVHD you have and the organs involved. These are some common therapies:

- **Total parenteral nutrition (TPN)** or intravenous feeding is used for acute GVHD of the bowel to help you from getting weaker when you can't get enough nutrients by mouth
- **Antimicrobials** are medicines used to fight bacteria, viruses, and fungi given your higher risk of infection
- **Bone-strengthening agents** prevent bone loss from taking steroids

Treatment side effects

Immunosuppressant medications weaken your immune system. A common side effect is a higher risk of infection. Most side effects from medication improve or go away after treatment ends. Speak to your doctor if you are having side effects. They will try to find the lowest dose to control GVHD while limiting side effects.

Other side effects

Other possible side effects of GVHD therapy are:

- Weight gain, insomnia, bone loss (osteoporosis), high blood sugar, high blood pressure, cataracts, mood swings, and depression from long-term use of corticosteroids
- Kidney problems, more hair growth on your body, and (in rare cases) neurological problems (seizure, tremor, confusion, anxiety) from cyclosporine or tacrolimus
- Liver problems, nausea, vomiting, stomach pain, and mouth sores from methotrexate
- Mouth sores, liver function issues, high fat levels in your blood, lung toxicity, and diarrhea from sirolimus

Taking care of yourself

You can help limit the complications of GVHD by:

- Taking your prescribed medications, even when you feel healthy
- Trying to prevent infections by washing your hands often and asking friends and family to visit only if they are healthy
- Avoiding the sun by wearing a hat, long-sleeved shirt, and long pants, and use a high-SPF sunscreen
- Keeping your skin moist by having short showers, using a mild soap and moisturizing lotion, avoiding scratching, and taking prescribed steroid creams
- Wearing sunglasses with UV protection
- Maintaining good dental hygiene and go for frequent dental check-ups
- Following the diet prescribed by your doctor and avoid spicy foods
- Exercising and stretch regularly
- Getting any vaccinations recommended by your transplant team, unless you have an allergy or a severe contraindication (reason not to get the vaccine)



Living with GVHD can be overwhelming. Seek medical help if you are feeling “down” or “blue” or don’t want to do anything – and your mood does not improve over time. These could be signs of depression, an illness that should be treated even when you’re undergoing treatment for GVHD. Treatment for depression has important benefits for people living with cancer.

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This publication was made possible thanks to the support of:



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