GUIDE FOR HEALTHCARE PROFESSIONALS

LEUKEMIA & LYMPHOMA SOCIETY OF CANADA®

Managing Graft-Versus-Host Disease GvHD

Graft-versus-host disease (GvHD) is a serious health complication that can result from an allogeneic stem cell transplant. It can happen when donor T-cells mistakenly attack the transplant recipient's host tissue and cells, leading to an immune response that affects healthy tissues and organs.

This fact sheet provides an overview of GvHD for healthcare professionals. It reviews presenting symptoms, treatment options and side effects to effectively support your patients.

Highlights

- GvHD is a common, potentially life-threatening side effect for people who have had an allogeneic stem cell transplant, impacting up to 70% of recipients
- GvHD can be mild, moderate, or severe and worsens quickly when not treated
- There are two main types of GvHD: acute and chronic
- A key risk factor for GvHD is when there is a donor–recipient mismatch
- GvHD is diagnosed through a physical exam, lab tests, and/or biopsy results
- Clinical trials are underway to investigate new treatments; discuss the options with your patients

Acute GvHD

Acute GvHD usually develops within 100 days after the stem cell transplant and is often intense. Acute GvHD can involve a single organ or multiple organs. It is a leading cause of medical problems and potential death after an allogeneic stem cell transplant, affecting 30% to 50% of people who receive a donor transplant.

Risk factors for acute GvHD:

- Mismatch between donor and recipient tissue types
- Mismatch between donor and recipient ages
- Advanced age of either the donor or recipient
- A donor who has been pregnant in the past
- A donor giving stem cells to a recipient of the opposite sex
- The intensity and duration of chemotherapy and radiation before the transplant
- Donor lymphocyte infusion, a procedure done after the transplant

Presenting symptoms

Although acute GvHD can affect any part of the body, including lungs, kidneys, thymus and lymph nodes, bone marrow, and the central nervous system, the most common areas affected are the skin, gastrointestinal (GI) tract, and the liver.

The patient may experience these symptoms:

Area affected	Symptoms of acute GvHD
Skin	• Faint rash that can spread to the entire body • Mild rash that may look like a sunburn • Severe rash that includes blisters and peeling skin
GI tract	• Diarrhea • Stomach pain • Bleeding • Nausea and vomiting
Liver	• Jaundice (yellowish skin or eyes) • Bleeding • Confusion • Extra fluid in the abdomen

Acute GvHD is classified according to the number of organs involved, how they are affected, and the severity of symptoms:

- **Grade 1:** mild symptoms
- **Grade 2:** moderate symptoms
- **Grade 3:** severe symptoms
- **Grade 4:** very severe symptoms

People with grades 3 and 4 acute GvHD tend to have worse outcomes and a lower chance of survival.

Chronic GvHD

Chronic GvHD (cGvHD) usually develops more than 80 days after a stem cell transplant. cGvHD means the condition is ongoing and worsens over a long period. It is a leading cause of medical problems and potential death after a donor stem cell transplant, affecting 30% to 70% of transplant recipients. In some cases, it can cause permanent damage to an organ.

cGvHD may last for years or the rest of a person's life and can negatively impact a patient's quality of life.

Risk factors for chronic GvHD:

- Mismatch between donor and recipient tissue types
- Mismatch between donor and recipient ages
- Source of the stem cell:
  - Higher risk if it is from peripheral blood rather than bone marrow
  - Lowest risk if it is from umbilical cord blood
- Patient previously experiencing acute GvHD

Presenting symptoms

Symptoms of cGvHD can be mild or life-threatening, affecting a single organ or area of the body. It may be widespread and affect multiple organs. cGvHD most commonly affects the skin, eyes, mouth, genitals, GI tract, lungs, liver, and muscles and joints.

The patient may experience these symptoms:

Area affected	Symptoms of chronic GvHD
Skin	• Skin rash • Dry, itchy, and/or tight skin, with a change in colour • Ulcerations
Eyes	• Dry, painful, and itchy eyes • Difficulty tolerating bright lights • Blurred vision • Blindness (only in severe cases)
Mouth	• Dry mouth • Difficulty eating • Painful ulcers in the throat • Gum disease and tooth decay • Sensitivity to hot, cold, spicy, and acidic foods and carbonated drinks
Genitals	• Women: vaginal dryness, ulcerations, scarring, difficult or painful intercourse • Men: narrowing of the urethra, itching, or scarring of the penis and scrotum
GI tract	• Loss of appetite • Unexplained weight loss • Diarrhea and stomach pain • Nausea and vomiting
Lungs	• Shortness of breath • Difficulty breathing • Wheezing • Persistent cough
Liver	• Abdominal swelling • Jaundice (yellowish skin or eyes)
Muscles and joints	• Muscle and joint weakness • Cramping and stiffness • Restricted joint movements
Body temperature	• Sensitivity to changes in temperature
Hair and nails	• Hard, brittle nails • Hair loss (body and scalp) and/or premature grey hair

Treatment options and side effects

Treatment for GvHD depends on several factors, including whether a patient has acute or chronic GvHD. Common GvHD treatments and side effects include:

Steroids

Corticosteroids are commonly used as a first line of treatment for both acute GvHD and cGvHD in an effort to reduce inflammation and the severity of symptoms.

- **Systemic steroids** may be administered orally, intravenously, or by muscle injection. Most people with severe GvHD (acute or chronic) will receive systemic steroids.
- **Topical steroid cream** is used for mild cGvHD and for acute GvHD that features only a skin rash as a symptom.
- **Steroid eye drops** are used for cGvHD of the eye.

Potential side effects: Depending on the treatment, the patient may experience weight gain, insomnia, osteoporosis, high blood sugar, high blood pressure, cataracts, infection, mood swings, and depression from long-term use of corticosteroids.

Immuno-therapies

If steroids do not improve or resolve the patient's GvHD, they may be given immunotherapies, such as:

- JAK inhibitors (orally or by IV) to target T cells and lower the immune response
- Photopheresis (cellular immunotherapy) to remove lymphocytes from the blood, expose them to light, and return them to the body
- ROCK2 inhibitors (belumosudil)
- CSF1R inhibitors (axatilimab)
- BTK inhibitors (ibrutinib)
- mTOR inhibitors (sirolimus)
- Calcineurin inhibitors (tacrolimus or cyclosporine)
- B-cell depleting therapies (rituximab)

Other therapies, such as methotrexate, hydroxychloroquine, and imatinib, have also shown some effectiveness in treating GvHD.

Potential side effects: Each type of immunotherapy has different potential side effects. Common side effects include rashes, diarrhea, fatigue, nausea, vomiting, and decreased thyroid hormone levels.

Supportive therapies

Supportive therapies may also be used to treat GvHD, including:

- **Total parenteral nutrition (TPN)** or intravenous feeding is used for acute GvHD of the bowel to help patients who are unable to get sufficient nutrients by mouth.
  - **Potential side effects:** infection, blood clots, GI atrophy, glucose imbalance, liver reactions or disease, gallbladder problems, fluid overload, hunger pangs, and bone demineralization
- **Antimicrobials,** which may be used to fight bacteria, viruses, and fungi.
  - **Potential side effects:** diarrhea, nausea, vomiting, rash, yeast infection, and dizziness
- **Bone-strengthening agents** may be used to prevent bone loss from steroid use.
  - **Potential side effects:** upset stomach, heartburn, bone and muscle or joint pain

Patient education

There are ways to help your patients reduce the complications associated with GvHD and manage their symptoms. While GvHD can be resolved in many cases, it affects quality of life for people experiencing symptoms. When you are working with patients, encourage them to:

- ☐ Take their medications even if they start to feel better
- ☐ Monitor their symptoms and make an appointment with their medical team if new symptoms appear
- ☐ Get vaccinations offered by the transplant team
- ☐ Reduce the risk of infection with handwashing and limit visits to healthy family and friends
- ☐ Avoid the sun and prevent skin exposure
- ☐ Keep skin moist using mild soap-free body cleanser, moisturizing lotion, and prescribed steroid creams
- ☐ Go for frequent dental check-ups
- ☐ Follow the diet prescribed by the doctor and avoid spicy foods
- ☐ Exercise and stretch regularly

PATIENT RESOURCES

The LLSC has developed fact sheets for people living with GvHD and their loved ones:

- Understanding Graft-versus-Host Disease
- Treating Graft-versus-Host Disease

Emerging therapies

Researchers are examining new methods to prevent GvHD in clinical trials; these include immunosuppressive drugs and new prophylaxis medications.

Call us to learn more about the Clinical Trial Service

Clinical Trial Nurse Navigators are registered nurses with expertise in blood cancers. They can provide potential clinical trial options, guide you in your efforts to enroll your patient in a clinical trial, and be available for support throughout the clinical trial experience.

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1 833 222-4884 • info@bloodcancers.ca • bloodcancers.ca