LEUKEMIA & LYMPHOMA SOCIETY®

# Graft-Versus-Host Disease

**No. 32** in a series providing the latest information for patients, caregivers and healthcare professionals

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## Highlights

- Graft-versus-host disease (GVHD) is a potentially serious complication of allogeneic stem cell transplantation.
  - Allogeneic stem cell transplantation is a procedure in which a person receives stem cells from an adult donor or from donated umbilical cord blood. These stem cells replace the cells in the bone marrow that generate the blood cells and include the white blood cells that form the immune system.
  - Allogeneic stem cell transplantation is an effective treatment for many genetic diseases and blood cancers such as leukemia and lymphoma.
- Donated stem cells, containing donor T-cells, are infused into a patient's body.
  - T-cells are a type of white blood cell that help protect the body by recognizing foreign invaders (like infections and bacteria) and destroying them.
  - The T-cells' ability to not harm healthy cells relies on T-cells being able to tell the difference between what belongs in the body ("self") and what is foreign ("non-self").
  - This recognition may help donor T-cells attack residual cancer cells, and in this way allogeneic transplant helps cure blood cancers.
  - But donor T-cells may also recognize the patient's healthy cells as "non-self," and unleash an attack on the patient's healthy tissues and organs.
  - The "attack" may impair an organ's function or may cause it to fail altogether.
- When the donor cells ("the graft") attack the cells of the patient ("the host"), the condition is called "graft-versus-host disease" or GVHD.
- There are two main categories of GVHD: acute GVHD and chronic GVHD.
  - Each type of GVHD affects different organs and tissues and has different signs and symptoms.
  - Patients may get one type or both types of acute and chronic GVHD, one following the other (sequentially) or both at the same time (concurrently). Some patients may not develop GVHD at all.
- GVHD can be mild, moderate or severe. There are treatments for GVHD, but in some patients GVHD may not respond to treatment.

## Introduction

Graft-versus-host disease (GVHD) is a serious complication that may occur after allogeneic stem cell transplantation. An allogeneic stem cell transplantation is a treatment for many genetic diseases and blood cancers such as leukemia and lymphoma. During allogeneic stem cell transplantation, a person receives stem cells from a donor or from donated umbilical cord blood. These "new" stem cells replace the patient's stem cells that have been damaged by disease or by treatments for the disease.

These are the stages of an allogeneic stem cell transplant:

- Before an allogeneic stem cell transplantation, patients receive a conditioning regimen, consisting of chemotherapy and sometimes radiation therapy. The conditioning regimen is given to destroy cancer cells in the body (in patients having transplants for cancer). The conditioning regimen also suppresses the recipient's immune system, which allows the new stem cells from the donor to start making new blood cells and ultimately generate a new immune system in the recipient's body.
  - There is a lag between when the previous (the patient's) immune system stops functioning and the new (the donor's) immune system takes over.
  - During this period without healthy bone marrow, patients' bodies are unable to make blood cells, including white blood cells.
  - Without adequate white blood cells, patients are unable to fight infections properly, leading to a period of increased risk of infection.
- After the conditioning regimen, patients receive an infusion of donor stem cells to replace the patient's blood-making system and immune system. The transplanted 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."
- Donated stem cells that are transplanted also contain some T-cells from the donor.
  - T-cells are a type of white blood cell that help protect the body from infection. They recognize what belongs in the body and what is foreign and potentially dangerous. T-cells know that bacteria, viruses and fungi are harmful.
  - To defend itself from infection, the body must be able to distinguish between what belongs in the body ("self") and what is foreign to it ("non-self").

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- One of the benefits of an allogeneic transplant is that the donor T-cells may recognize as foreign any of the patient's cancer cells that survived the conditioning regimen. The donor T-cells are much more likely than the patient's own T-cells to identify the cancer cells as "non-self," and they coordinate an attack to eliminate them. This helps prevent the cancer from relapsing. This is called the "graft-versus-tumor effect."
- But the same ability of T-cells to recognize self from non-self can create a severe complication. T-cells recognize "self" from "non-self" by a system of proteins called human leukocyte antigen (HLA) that marks many cells. Human leukocyte-associated antigens are proteins found on the surface of most cells in the body. They make up a unique person's tissue type.

  – The donor's T-cells may regard HLA or other markers on the patient's cells as "non-self" and may attack the patient's healthy cells in organs, impairing their ability to function and potentially causing organ failure.

  – When donor cells (the graft) attack the tissue and the cells of the patient (the host), this condition is called "graft-versus-host disease" (GVHD).

At first, the donor cells (the graft) are partially weakened and controlled by the patient's own immune system. Graft-versus-tumor and graft-versus-host effects do not tend to reach full strength until the patient's immune system has been fully suppressed. This tends to happen early within the first 30 days with a myeloablative (full strength) transplant but may occur later with a reduced intensity or a non-myeloablative (mini) transplant.

GVHD can be mild, moderate or severe. Successful treatments for GVHD have been developed, but in some patients, GVHD may not respond. In addition, treating GVHD often weakens T-cells and can leave patients more vulnerable to infections or other complications.

## Classification/Types of GVHD

There are two main categories of GVHD: acute graft-versus-host disease and chronic graft-versus-host disease. Each type affects different organs and tissues and has different signs and symptoms. Patients may develop one type or both types, or may not develop either type.

The National Institutes of Health consensus criteria has classified GVHD based on the timing of presentation and the signs present:

- **Classic Acute GVHD** – Signs of the disease occur within 100 days of stem cell transplantation and display features of acute GVHD. Diagnostic and distinctive features of chronic GVHD are absent.
- **Persistent, recurrent or late-onset Acute GVHD** – Cases present more than 100 days after transplantation, with features of acute GVHD. Diagnostic and distinctive features of chronic GVHD are absent.
- **Classic Chronic GVHD** – Cases may present at any time after transplantation. Diagnostic and distinctive features of chronic GVHD are present. There are no features of acute GVHD.
- **Overlap syndrome** – Cases may present at any time after transplantation with features of both chronic GVHD and acute GVHD.

## Acute GVHD

Acute GVHD is a significant cause of medical problems and death following an allogeneic stem cell transplantation. The frequency of acute GVHD varies significantly among populations, making it impossible to specify how common it is. Somewhere between 30 and 70 percent of transplant recipients develop acute GVHD, depending on donor type, transplant technique, and other features. Acute GVHD primarily affects the skin, the liver and the gastrointestinal tract (stomach, intestines and colon).

**Risk Factors.** The following risk factors are usually associated with an increased risk of moderate to severe acute GVHD:

- HLA "mismatch," or unrelated donor
- Older patient age
- Female donor to male recipient
- Intensity of the conditioning regimen or total body irradiation during conditioning regimen
- Donor lymphocyte infusion: a procedure after a stem cell transplantation that infuses more lymphocytes, including T-cells, from the stem cell donor

**Symptoms.** The following are some symptoms of acute GVHD.

- Skin rash
  - Rash is the most common symptom of acute GVHD
  - Often starts as a faint rash that may appear anywhere, including the palms of the hands and soles of the feet
  - Rash may spread to cover the entire body
  - Mild forms may be minimally uncomfortable and look like a mild sunburn
  - More severe rash features blistering and peeling skin
- Gastrointestinal (GI) tract disorders
  - The most classic sign of GI GVHD is diarrhea, caused by an inflammation of the colon, and it can be as severe as several liters of stool each day.
  - Other symptoms include abdominal pain, bleeding and/or nausea with vomiting.
- Liver: acute GVHD of the liver
  - Acute GVHD of the liver is most commonly asymptomatic and can only be identified by blood tests
  - Can appear as jaundice (yellowing of skin or eyes) from liver toxicity and inability to excrete a substance called

bilirubin (bilirubin is produced when the liver breaks down old red blood cells)

- Sometimes patients develop bleeding, confusion, or ascites (excess fluid in the abdomen) due to liver failure

Low blood counts are not necessarily classic signs of acute GVHD, but it is extremely common for patients with GVHD to develop low blood counts. This is the body's response to the immune system's attack on organs.

**Diagnosis and Grading.** Patients with signs and symptoms of acute GVHD may need to have tests to confirm the diagnosis and rule out other conditions that may mimic acute GVHD, such as drug reactions and infections.

Acute GVHD may be mild, moderate or severe. Doctors classify the severity of acute GVHD according to the number of organs involved and the degree to which they are affected. Acute GVHD is staged and graded from I (mildest) to IV (most severe). Patients with grade III/IV acute GVHD tend to have poorer outcomes and decreased survival.

Patients must be aware of the warning signs of acute GVHD and should call their doctors immediately if they have any symptoms. Early detection and treatment may help limit the severity of the disease.

## Chronic GVHD

Chronic GVHD is a syndrome that may involve a single organ or several organs. It is one of the leading causes of medical problems and death after allogeneic stem cell transplantation. Approximately 30-70 percent of patients receiving an allogeneic stem cell transplantation develop chronic GVHD. Since it is a chronic condition, it can last for years or even a lifetime. Chronic GVHD symptoms range from mild to life-threatening. Today, doctors are making every effort to prevent GVHD. See page 4.

**Risk Factors.** The following risk factors are associated with chronic GVHD:

- HLA mismatch or unrelated donor
- Older patient age
- Older donor age
- Female donor for male recipient and number of children the female donor has had
- Stem cell source
  - Stem cells retrieved from peripheral blood have a higher risk of causing chronic GVHD than stem cells retrieved from bone marrow.
  - Stem cells retrieved from cord blood have the lowest risk of causing chronic GVHD.
- Prior acute GVHD

**Symptoms.** Symptoms of chronic GVHD may be restricted to a single organ or site in the body, or they may be widespread. Among the most commonly affected parts of the body are the skin, mouth, eyes, liver, gastrointestinal (GI) tract, lungs and joints. Symptoms of chronic GVHD may include any of the following:

- Eyes
  - Dry, painful, itchy eyes
  - Difficulty tolerating bright lights
  - Blurred vision
  - Blindness
- Mouth
  - Very dry mouth
  - Sensitivity to hot, cold, spicy and acidic foods, mint (often in toothpaste), and carbonated drinks
  - Painful mouth ulcers that may extend down the throat
  - Difficulty eating
  - Gum disease and tooth decay
- Skin
  - Rash
  - Dry, tight, itchy skin
  - Thickening of the skin which may result in restriction of joint movement
  - Change in skin color
  - Intolerance to temperature changes caused by damaged sweat glands
- Nails
  - Changes in nail texture
  - Hard, brittle nails
  - Nail loss
- Scalp and body hair
  - Loss of hair on the head
  - Premature gray hair
  - Loss of body hair
- Gastrointestinal (GI) tract
  - Loss of appetite
  - Unexplained weight loss
  - Nausea
  - Vomiting
  - Diarrhea
  - Stomach pain
- Lungs
  - Shortness of breath and difficulty breathing
  - Persistent cough that does not go away
  - Wheezing

- Liver
  - Abdominal swelling
  - Jaundice (yellow discoloration of the skin and/or eyes)
- Muscles and joints
  - Muscle weakness and cramps
  - Joint stiffness or difficulty fully extending fingers, wrists, elbows, knees and ankles
- Genitals and sex organs
  - Female
    - Vaginal dryness, itching and pain
    - Vaginal ulcerations and scarring
    - Narrowing of the vagina
    - Difficult or painful intercourse
  - Male
    - Narrowing or scarring of the urethra
    - Itching or scarring on the penis and scrotum
    - Irritation of the penis

Patients should contact their doctors immediately if any of these symptoms occur. While a symptom may be caused by something other than chronic GVHD, it needs to be evaluated by the doctor. Early detection and treatment may help limit the severity of the disease.

## Preventing GVHD

The development of moderate and severe GVHD is associated with significant illness and a decrease in survival. Once it is established, it is difficult to treat. Because of this, doctors try to reduce the occurrence and severity of GVHD before and after transplantation and take every precaution to prevent GVHD.

**HLA Typing and Finding a Match.** GVHD can develop when the donor and the recipient have different tissue types. The patient's transplant team will try to find a donor who closely matches the patient. This helps reduce the risk of GVHD in a transplant using standard techniques. Human leukocyte antigen (HLA) typing is a blood test used to determine how closely the tissue type of one person matches the tissue type of another.

There are many HLA markers. HLA matching, however, is usually based on either eight or ten HLA markers. The more markers two people share, the greater the chance that their immune systems will not view each other as foreign and are less likely to attack each other. Identical twins match exactly because they have the same genes. But for most people, possible matches include:

### Siblings

- People inherit half their HLA markers from their mothers and half from their fathers
- Often the ideal donor is a patient's sibling who has inherited the same HLA markers
- Each child of a set of the same parents has four possible combinations of HLA types which are inherited randomly. Therefore, each full sibling has a 25 percent chance of being a perfectly matched donor
- Smaller families mean only about 30 percent of patients have a matched sibling

### Matching registered donors

- Finding a perfectly matched donor may depend on volunteer donor registries
- Finding a perfectly matched unrelated donor may depend on a patient's ethnic origin
- People of white European origin have a 75 percent chance of finding a perfectly matched related donor based on a narrow range of HLA types in populations that settled in Europe and prevalence of these populations in countries with large unrelated donor registries
- People of African origin have a very poor chance of having a perfectly matched unrelated donor (<20 percent)

### Cord blood donors

For patients without perfectly matched donors, cord blood stored in public banks can be used as an alternative source of stem cells. In cord blood transplantation, the stem cells have been collected from the umbilical cord of healthy newborns.

- Cord blood units have fewer T-cells and they are less mature, so there is a lower chance of severe GVHD
- Cord blood units do not have to match as closely as stem cell donations from adult donors
- Cord blood may be a viable alternative source of stem cells for patients without a well-matched related or unrelated donor
- But because cord blood units contain fewer stem cells
  - It may be difficult to use in people with larger body sizes
  - Smaller cell dose and a more immature immune system tends to be linked to longer times to engraftment and higher risks of infection, which may make these transplants more dangerous for some patients

**Haploidentical Transplant.** Over the last several years, investigators around the world have discovered methods to transplant from family members who are only half-matched. This is called a haploidentical transplant. When

comparing haploidentical transplants using post-transplant cyclophosphamide to typical matched transplants, the risk of acute GVHD does not seem to be any worse and the rate of chronic GVHD appears to be lower related to the use of post-transplant cyclophosphamide.

Cord blood and haploidentical transplants have a major advantage over matched unrelated donors because they are available much more quickly (potentially in 2-4 weeks), while matched unrelated donor cells may take a month or more to obtain. This is extremely important in high-risk blood cancers for patients who may relapse while waiting for a transplant. The donor type (matched unrelated, cord blood, or half-matched) that ultimately leads to the best outcomes is unclear, and is under active investigation.

**Medication.** Doctors try to prevent GVHD by treating patients with immunosuppressive drugs to suppress donor T-cell function. These drugs are given before and after the stem cell infusion.

There is no standard regimen for the prevention of GVHD, and different combinations of medications are given in different institutions. Some common medications that are given to prevent GVHD include:

- Methotrexate (Trexall®)
- Cyclosporine
- Tacrolimus (Prograf®)
- Mycophenolate mofetil (CellCept®)
- Sirolimus (Rapamune®)
- Corticosteroids (methylprednisolone or prednisone)
- Antithymocyte globulin (ATG)
- Alemtuzumab (Campath®)
- Cyclophosphamide (Cytoxan®)

In the United States, two main drug regimens are used for preventing GVHD:

- Calcineurin inhibitor-based immunosuppression. This is currently the most commonly used regimen in the United States and Europe. It combines a calcineurin inhibitor (tacrolimus or cyclosporine) with another medicine (usually methotrexate, mycophenolate mofetil, or sirolimus). Typically, both medications are started right around the time of stem cell infusion. The second drug is usually tapered within the first month or so after the transplant while the calcineurin inhibitor is continued for 60-120 days after the transplant.
- High dose post-transplant cyclophosphamide. This type of regimen involves a high dose of the chemotherapy drug cyclophosphamide in the first few days after the transplant. This drug selectively targets a population of recovering cells that may be particularly inclined to cause GVHD. Patients who receive matched stem cells may only be prescribed cyclophosphamide, while those who have haploidentical donors usually receive additional oral medicines such as calcineurin inhibitors, sirolimus and/or mycophenolate mofetil.

**T-Cell Depletion.** Because there is a connection between donor T-cells and GVHD, one option to reduce the incidence of GVHD is to remove (deplete) donor T-cells to prevent them from negatively affecting patients. There are two major ways to do this:

- In vivo (within the body) T-cell depletion consists of giving medications like ATG or alemtuzumab to the recipient just before or just after transplant. In vivo T-cell depletion is typically added to another immune suppressant regimen to reduce the risks of GVHD.
- Ex vivo (outside the body) T-cell depletion uses a machine to remove T-cells from the stem cells before the stem cells are given to the patient.This procedure is more efficient in completing the removal of T-cells, allowing patients to avoid taking medications for GVHD prophylaxis.

T-cell depletion, however, leads to increased injury to the immune system post-transplant, and is therefore associated with more infections. Also, T-cells help prevent cancer relapse, so there are concerns that such depletion may increase relapse risk. For these reasons, T-cell depletion may be used in different populations at different transplant centers, or may not be used at all. Large randomized clinical trials are currently looking at the impact of different approaches in preventing GVHD.

## Treatment

Immunosuppression (suppression of the body's immune system and its ability to fight infections and other diseases) with corticosteroids forms the basis of therapy in both acute and chronic GVHD. Other medications that lower the immune response are also used. Treatment may be either outpatient or inpatient. Treatment decisions are determined by the severity of the patient's symptoms and concerns about complications.

**Treatment for Acute GVHD.** After transplantation, patients usually continue to take the immunosuppressive drugs (such as cyclosporine, tacrolimus, and methotrexate) that they were given prior to transplantation. Many patients who develop acute GVHD are successfully treated with increased immunosuppression in the form of corticosteroids (medicines such as prednisone, methylprednisolone, dexamethasone and beclomethasone).

Patients with mild skin-only acute GVHD will usually continue with their original medications such as cyclosporine or tacrolimus and add a topical steroid cream (topical means applied directly to a part of the body) to their treatment plan.

Treatment for patients with systemic or "whole-system" manifestations and/or more severe acute GVHD usually consists of continuing the original immunosuppressive prevention and adding a corticosteroid such as methylprednisolone or prednisone.

There is no clear best treatment to use in patients with acute GVHD who do not respond to steroids. Patients who fail to respond to steroid therapy are labeled "steroid-refractory." Please see the section *Options for Steroid Refractory GVHD* below for more information.

**Treatment for Chronic GVHD.** Patients with mild symptoms limited to a single organ or site can often be managed with close observation or with local therapies. For example, patients with mild chronic GVHD of the skin may be treated with topical steroid ointments, and others with chronic GVHD of the eye (ocular GVHD) may be treated with steroid eye drops.

Patients with more severe symptoms or multi-organ involvement typically require systemic or "whole-system" treatment, which travels in the bloodstream and reaches cells throughout the entire body. Prednisone is the standard first-line systemic therapy for chronic GVHD. For patients who do not respond to steroid treatment, second line treatments are available. Please see the section *Options for Steroid-Refractory GVHD* below for information on other options.

It is important for patients to continue taking their medication, even if they are starting to feel better. Stopping medication too soon may cause chronic GVHD to flare up or worsen, which may result in permanent damage. Once chronic GVHD begins to stabilize and improve, doctors may consider tapering the medications over time, and eventually the drugs may be discontinued.

**Options for Steroid-Refractory GVHD.** For patients whose acute or chronic GVHD does not improve with corticosteroids, doctors will try second-line therapies. Patients are encouraged to participate in clinical trials, which may offer access to new drugs or better administration of current drugs. Widely used drugs include:

- Ruxolitinib (Jakafi®). This drug is FDA-approved for the treatment of adult and pediatric patients 12 years and older with steroid-refractory acute graft-versus-host disease.
- Ibrutinib (Imbruvica®). This drug is FDA-approved for the treatment of adult patients with chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy
- Belumosudil (Rezurock™). This drugs is FDA approved for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (cGVHD) after failure of at least two prior lines of systemic therapy.
- Mycophenolate mofetil
- Sirolimus
- Tacrolimus or cyclosporine
- Monoclonal antibodies such as infliximab (Remicade®), tocilizumab (Actemra®), alemtuzumab (Campath®), basiliximab (Simulect®), daclizumab (Zinbryta®), and denileukin diftitox (Ontak®)
- Antithymocyte globulin (ATG)
- Pentostatin (Nipent®)

Photopheresis: doctors may also recommend this extracorporeal (outside the body) treatment that uses light to treat acute GVHD. In this procedure, blood is removed from the patient's body and enters a machine that separates the lymphocytes from the blood. The blood is returned to the patient without the lymphocytes. The lymphocytes are exposed to a photosensitizing agent, 8-methoxypsoralen, and then treated with ultraviolet light. The treatment of lymphocytes alters their function and the altered lymphocytes are returned to the body. One theory suggests that when these altered lymphocytes go back into the body, they die or are killed by residual portions of the patient's immune system. This may help slow or stop the progression of GVHD.

New drugs and strategies to treat acute GVHD are currently being tested in clinical trials. Patients are encouraged to explore clinical trials as a treatment option. See *Treatments Under Investigation* on page 7.

**Supportive Treatments for GVHD.** In addition to medications, it is critically important that patients receive appropriate supportive therapies. These depend on the patient's type of GVHD and organs involved. Common supportive therapies include:

- TPN (total parenteral nutrition), also called intravenous feeding, for acute GVHD of the bowel, to prevent malnutrition and keep people from getting weaker
- Antimicrobials (medicines against bacteria, viruses, and fungi) to prevent additional risks of infection from the added immunosuppressants used to prevent and treat GVHD.
- Bone-strengthening agents to prevent bone loss from steroids

Taking these medications as prescribed may be as important as the medicines for GVHD in assuring function and survival.

## Side Effects of Treatment

Many medications used to treat GVHD are immunosuppressants. They work by weakening the immune system, so these drugs can all increase a patient's risk of getting an infection. In addition to infection, each of them can cause other side effects:

- Corticosteroids (prednisone, methylprednisolone, dexamethasone, beclomethasone, clobetasol)—prolonged systemic use may cause weight gain, insomnia, bone loss (osteoporosis), high blood sugar, high blood pressure,

cataract formation, mood swings, depression

- Cyclosporine/Tacrolimus—kidney problems, increased hair growth on the body, and rarely neurologic problems such as seizures, tremors, confusion, anxiety
- Methotrexate—liver problems, nausea, vomiting, abdominal pain, mouth sores
- Sirolimus—mouth sores, liver function abnormalities, very high fat levels in the blood, lung toxicity, diarrhea; may affect levels of other drugs in the body, requiring dose adjustments

Patients should discuss any side effects they experience with their doctors. Doctors will try to find the lowest dose of medicine to control GVHD while limiting side effects. Most medication side effects improve or go away once treatment is completed.

## Treatments Under Investigation

Patients are encouraged to look for, see if they are eligible, and enter ongoing clinical trials. Clinical trials test new drugs and treatments before they are approved by the FDA as standard treatments.

Clinical trials are carefully controlled research studies, conducted under guidelines, to help researchers determine the beneficial effects and possible adverse side effects of new treatments. Clinical trials are designed to be accurate and safe. Patient participation in clinical trials is important in the development of new and more effective treatments for GVHD, and may provide patients with additional treatment options.

Patients interested in participating in clinical trials are encouraged to talk to their doctors about whether a clinical trial would be appropriate for them. LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct individualized clinical-trial searches for patients, family members and healthcare professionals. When appropriate, personalized clinical-trial navigation by trained nurses is also available.

Successful treatments for both acute GVHD and chronic GVHD have been developed, but GVHD does not always respond to treatment. Two drugs currently being tested in clinical trials include ruxolitinib (Jakafi®) and ibrutinib (Imbruvica®). All patients are encouraged to participate in clinical trials. These studies may allow patients access to new agents and help doctors and researchers understand the optimal treatment for GVHD.

## Take Care of Yourself

There are some steps patients can take to help minimize the risk of developing GVHD. In some cases, however, GVHD will occur despite all efforts to prevent it. The following are some suggestions to help limit the occurrence and complications of GVHD:

- If a doctor prescribes medications to help prevent GVHD, it is important to take these medications, even when patients are feeling healthy. If the patient is unable to take medications for any reason, or if any symptoms of GVHD are noticed, the doctor should be called immediately. Early detection and treatment may help limit the severity of the disease.
- It is important for patients to try to prevent infections. Patients should wash their hands often and ask family members and friends who are sick not to visit until they are healthy.
- Exposure to the sun's ultraviolet rays may increase a patient's risk of developing GVHD. It is important to avoid the sun as much as possible. When outside, wear a hat, long sleeves and pants. Some companies offer sun-protective clothing that can help shield skin from the sun's harmful ultraviolet rays. Apply SPF30 sunscreen or higher on any exposed skin.
- Keeping skin moist will help prevent it from becoming overly dry and flaky. Avoid long showers, and use a gentle, mild soap and a good moisturizing lotion every day. Try to avoid scratching. The doctor will prescribe steroid creams to ease itching and burning and to treat GVHD of the skin.
- If chronic GVHD is affecting the eyes, be sure to wear sunglasses with UV protection when outside to protect eyes from further damage. Patients may also want to find an ophthalmologist who specializes in the management of dry eyes and diseases of the cornea.
- Patients with chronic GVHD of the mouth may have a very dry mouth, which can lead to cavities. Patients should maintain good oral (dental) hygiene. It is important to see a dentist for routine dental cleanings and checkups. Dental check-ups may need to increase from the usual twice per year to four or more times per year for good prevention and maintenance.
- Patients with diarrhea should follow the diet prescribed by the doctor and dietitian to prevent worsening diarrhea. Avoid spicy foods. It is also important to avoid skin problems caused by diarrhea, such as irritation around the rectal area. Clean this area well after each occurrence of diarrhea. Tell the doctor if this area gets red, cracked, painful or infected.
- Consider regular exercise and stretching. These activities can help preserve bone health, increase muscle strength, decrease pain and fatigue, and improve mobility. Physical therapy to maintain strength and joint mobility can prevent disability that may occur from chronic GVHD and the side effects of immunosuppressive treatments.

- Unless they have allergies or severe contraindications, patients should receive vaccinations offered by their transplant team. The immunities to disease that patients acquired prior to their transplantation are generally lost after stem cell transplantation. Most transplant centers will start vaccinations six to twelve months after transplantation. These often include the inactivated flu vaccine, pneumococcal vaccine, and "childhood" vaccines such as DTaP and hepatitis B. Patients with chronic GVHD or T-cell depleted transplants are usually advised to avoid vaccinations with live viruses such as varicella (chicken pox) until the GVHD is resolved and the use of immunosuppressive drugs has ended.

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## We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the United States and in Canada. To find the chapter nearest to you, visit our Web site at www.LLS.org/chapterfind or contact

**The Leukemia & Lymphoma Society**
3 International Drive, Suite 200
Rye Brook, NY 10573
Contact an Information Specialist at (800) 955-4572
Email: infocenter@LLS.org

LLS offers free information and services for patients and families touched by blood cancers. The following entries list various resources available to you. Use this information to learn more, to ask questions and to make the most of your healthcare team.

**Consult with an Information Specialist.** Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease and treatment information. Language services are available. For more information, please:

- Call: (800) 955-4572 (M-F, from 9 am to 9 pm EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/informationspecialists
- Visit: www.LLS.org/informationspecialists

**Free Information Booklets.** LLS offers free education and support booklets that can either be read online or ordered. For more information, please visit www.LLS.org/booklets.

**Información en Español (LLS Information in Spanish).** For more information, please visit www.LLS.org/espanol.

**Telephone/Web Education Programs.** LLS offers free telephone/Web education programs for patients, caregivers and healthcare professionals. For more information, please visit www.LLS.org/programs.

**LLS Community.** The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. To join, visit www.LLS.org/community.

**Weekly Online Chats.** Moderated online chats can provide support and help cancer patients reach out and share information. For more information, please visit www.LLS.org/chat.

**LLS Chapters.** LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups, and other great resources. For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: www.LLS.org/chapterfind

**Clinical Trials (Research Studies).** New treatments for patients are ongoing. Patients can learn about clinical trials and how to access them. For more information, please call (800) 955-4572 to speak with our LLS Information Specialists who can help conduct clinical trial searches. When appropriate, personalized clinical trial navigation by trained nurses is also available.

**Advocacy.** The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

## Other Resources

**Be The Match®**
**(888) 999-6743**
**www.BeTheMatch.org**
Be The Match® is a global leader in bone marrow transplantation. Be The Match,® operated by the National Marrow Donor Program,® manages the largest and most diverse marrow registry in the world. Be The Match® also conducts research to improve transplant outcomes and provides support and resources for patients.

**Blood & Marrow Transplant Information Network (BMT InfoNet)**
**(888) 597-7674**
**www.bmtinfonet.org**

The Blood & Marrow Transplant Information Network (BMT InfoNet) is dedicated to providing transplant patients, survivors and their loved ones with emotional support and high quality, easy-to-understand information about bone marrow, peripheral blood stem cell and cord blood transplants.

**National Bone Marrow Transplant Link (nbmtLINK)**
**(800) 546-5268**
**www.nbmtlink.org**

The mission of the National Bone Marrow Transplant Link (nbmtLink) is to help patients as well as their caregivers, families, and the health care community meet the many challenges of bone marrow/stem cell transplant by providing vital information and support services.

**PearlPoint Cancer Support**
**(877) 467-1936**
**www.pearlpoint.org**

PearlPoint Cancer Support offers free one-on-one nutrition consultations. A registered dietitian with experience in oncology nutrition can assist patients with healthy eating strategies, side effect management, and survivorship nutrition as well as provide additional nutrition resources.

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