Graft-versus-Host-Disease (GvHD)

Graft-versus-disease is a common complication after a bone marrow, stem cell or cord blood transplant using cells from a donor.

**Graft-versus-Host Disease (GVHD) is a common complication following a transplant using donor cells. GVHD is not an issue for patients who had a transplant using their own stem cells.**

What Is GVHD?

GVHD occurs when the donor's immune system (the graft) perceives the patient's organs and tissues (the host) as unfamiliar cells that should be destroyed. The cells that trigger this reaction are a type of white blood cell called T-cells.

Between 20 and 50 percent of patients transplanted with donor cells develop graft-versus-host disease after transplant. The percentage is higher in:

- older patients
- patients who were transplanted with cells from an unrelated donor
- patients transplanted with peripheral blood stem cells, rather than bone marrow or cord blood.

Most cases of GVHD are mild or moderate and resolve over time. However, GVHD can be more severe and, in some cases, life-threatening.

Types of GVHD

There are two forms of GVHD: acute GVHD and chronic GVHD. Patients may develop one, both or neither.
Each has a different effect on organs and tissues. Although acute and chronic GVHD usually occur during different time periods after transplant, it is possible to have both at the same time.

**Acute Graft-versus-Host Disease (aGVHD)**

Approximately 30-40 percent of patients who are transplanted with cells from a related donor develop acute GVHD. Approximately fifty percent of patients who are transplanted with cells from an unrelated donor develop acute GVHD.

Acute GVHD typically occurs during the first three months after transplant. The disease usually begins as a mild or faint rash on the patient's back or abdomen; it can also appear on the hands or feet. The rash may spread and eventually may resemble sunburn with peeling or blistering.

Acute GVHD can also cause:

- stomach and intestinal pain
- vomiting
- cramping
- nausea
- watery or bloody diarrhea
- elevated liver enzymes

**Reducing the Risk of Acute GVHD.**

To reduce the risk of developing acute GVHD, patients are typically given one of these drug combinations:

- cyclosporine and methotrexate
- tacrolimus and methotrexate
- cyclosporine and mycophenolate mofetil

If you develop acute GVHD, prednisone or methylprednisolone may be added. Eventually you will
be weaned off these drugs when your condition improves.

At some transplant centers, the T-cells that cause graft-versus-host disease are removed from the donor cells prior to transplant. This procedure is called T-cell depletion.

Although T-cell depletion reduces the risk of acute GVHD, it can increase the risk of relapse in some patients. Researchers are exploring whether removing a certain type of T-cell from the donor's cells will protect against GVHD without an increased risk of relapse.

**Chronic Graft-versus-Host Disease (cGVHD)**

Chronic graft-versus-host disease is a complication that develops in approximately 50 percent of patients who are transplanted with stem cells from a donor. Chronic GVHD is not a complication for patients who were transplanted with their own stem cells.

Chronic GVHD is different than acute GVHD. It usually develops later than acute GVHD and can affect more organs and tissues.

**Risk Factors for Developing Chronic GVHD**

Chronic GVHD occurs most often in patients who:

- previously had acute GVHD
- are older
- had a mismatched or unrelated donor
- were transplanted with stem cells collected from the bloodstream, rather than bone marrow

**Which Organs are Affected by Chronic GVHD?**
Chronic GVHD typically affects:

- skin and nails
- mouth
- eyes
- liver

Less frequently, chronic GVHD affects the:

- lungs
- intestines
- joints
- genitals

How is Chronic GVHD Treated?

Drugs that suppress the immune system, such as prednisone, cyclosporine, tacrolimus, mycophenolate mofetil and rapamycin, are used to control chronic GVHD. While your immune system is suppressed, you will be at a higher risk of developing infections.

*Patients with chronic GVHD usually require treatment for one to three years.*

Approximately 15 percent require treatment for seven or more years.

Watch a Video about Chronic GVHD.
Skin GVHD

Chronic GVHD often affects the skin. Symptoms include:

- dry, itchy rash
- a change in skin color
- thickening of the skin that can restrict joint movement
- taut skin

Skin GVHD may also cause:

- brittle or splitting fingernails and toenails
- hair loss or thinning hair
- an inability to sweat

Corticosteroids or tacrolimus ointment applied directly on the skin may relieve the symptoms. If tight skin is restricting joint movement, physical therapy is often recommended.

Extracorporeal photopheresis (ECP) is another treatment for skin GVHD. This procedure, which is not available at all transplant centers, removes some white blood cells from the patient, mixes them with psoralen, and exposes them to ultraviolet light. The cells are then reinfused into the patient. Find a hospital that offers ECP [1].

If you have, or have had, skin GVHD, it is important to protect your skin from exposure to the sun.
Skin GVHD can increase your risk of developing skin cancer.

When outside, wear a hat, long sleeves and pants. Use a strong sunscreen (SPF30 or higher) on any exposed skin. Keep in mind that the sun's rays can be just as damaging on a cool, cloudy day as they are on a hot, sunny day.

Companies like Sun Precautions® [2] and Coolibar® [3] offer sun protective clothing that can help shield your skin from the sun's harmful ultraviolet rays. The makers of RIT Dye make SunGuard™ [4], a laundry detergent additive that will add sun block to your everyday clothing.

Watch a Video about GVHD of the Skin and Connective Tissues

Your Mouth and Chronic GVHD

Chronic GVHD often affects the mouth and salivary glands. It can cause painful red ulcers which may extend down the throat, and sensitivity to toothpaste or certain foods.

Patients with chronic GVHD in their mouth often have a very dry mouth. Since a lack of saliva can lead to cavities, it is important to see a dentist once or twice a year for a thorough cleaning and check-up.
Oral chronic GVHD is usually treated with a topical steroid applied to your mouth. Medication such as lidocaine may be prescribed to control the pain.

Oral GVHD can make eating difficult. Get tips for managing eating problems after transplant. [5]

Watch a Video about GVHD of the Mouth and Salivary Glands. [6]

Your Eyes and Chronic GVHD

Chronic GVHD can affect your eyes, making them dry and itchy. In severe cases, chronic GVHD can affect your vision.

Dry eyes can be managed with artificial tears, ointments or tear duct plugs that help retain moisture in your eyes. Oral medications like Salagen® and Evoxac® can stimulate tears that moisturize the eyes. Special goggles called chamber glasses can also help keep your eyes moist.

If the problem is more severe, eye drops made from your blood serum may help.

A special type of contact lens called PROSE, offered by BostonSight® [7], has improved vision for some patients with ocular GVHD.

If you GVHD is affecting your eyes, be sure to wear sunglasses with UV protection when in the sun to
protect your eyes from further damage.

Watch a Video about Your Eyes and Chronic GVHD

Your Lungs and Chronic GVHD

Chronic GVHD can affect the lungs and lead to problems such as bronchiolitis obliterans syndrome (BOS). If you are having breathing difficulties, be sure to let your doctor know right away.

Watch a Video about Your Lungs and GVHD
Chronic GVHD of the Liver

Abnormal liver function tests may signal chronic GVHD in the liver, although other issues can cause liver test abnormalities as well. An ultrasound of the liver and a liver biopsy can confirm the diagnosis of liver GVHD.

Patients with liver GVHD may be treated with prednisone or ursodeoxicolic acid. If these treatments fail, your doctor may try extracorporeal photopheresis to manage the problem.

Chronic GVHD of the Gastrointestinal Tract

Chronic GVHD can affect the esophagus, stomach and colon. Symptoms may include:

- difficult or painful swallowing
- weight loss
- nausea and vomiting
- diarrhea

Prednisone and topical steroids such as budesonide or beclomethasone may be used to manage the problem. Other drugs such as infliximab, etanercept as well as extracorporeal photopheresis may also help.

Watch a Video about Chronic GVHD of the Gastrointestinal Tract and Liver.
Chronic GVHD of the Genitals

In women, chronic GVHD can affect the vagina and vulva causing dryness, itching, pain, ulcers and scarring. In men, chronic GVHD may cause itching or scarring on the penis and scrotum.

A gynecologist or urologist familiar with GVHD should be consulted as soon as symptoms appear. Water based lubricants, topical steroids, and dilators may help relieve genital GVHD.

Monitor Yourself for Symptoms of GVHD

Like many conditions, chronic GVHD is easier to treat if detected early.

Contact your doctor if you develop any of the following symptoms:

- rash
- skin discoloration,
- tightness or changes in texture of your skin
- thinning hair
- changes in texture of your nails
- dry eyes
- blurred vision
• persistent dry mouth
• mouth sensitivity to foods or toothpaste
• vaginal dryness, irritation or tightening
• penis irritation
• nausea, vomiting, diarrhea, loss of appetite, unexplained weight loss
• chronic cough, wheezing, shortness of breath
• difficulty fully extending fingers, wrists, elbows, knees or ankles
• fatigue
• low grade fever

These symptoms may be caused by something other than chronic GVHD, but you should report them to your doctor immediately so that you can be evaluated.

Many primary care physicians and hematologists are not familiar with the signs and symptoms of chronic GVHD. Ask your doctor to contact your transplant team, or call them yourself, if you suspect you may be developing chronic GVHD, since prompt treatment is important.

If you are diagnosed with chronic GVHD, it is important that you take your medication even when you start to feel better. Stopping your medication too early can cause your GVHD to flare up again or worsen and may cause permanent damage.

Side Effects of Treatments for GVHD

The drugs used to treat chronic GVHD have side effects. Most are temporary and end when the drug is discontinued.

Prednisone can cause:

• osteoporosis (weak and brittle bones)
• joint deterioration, which may require joint replacement
• increased risk of infection
• cataracts
• weight gain
• moon face
- mood swings
- depression

**Cyclosporine** and **tacrolimus** can cause:

- kidney problems
- headaches
- tremors
- seizures
- nausea
- high blood pressure
- loss of magnesium

**Mycophenolate mofetil** can cause:

- Nausea and vomiting
- Diarrhea
- Bleeding
- Increased risk of infection
- Anemia

**Rapamycin** (*sirolimus*) can cause:

- increased risk of infection
- increase risk of bleeding
- elevated levels of glucose (sugar) in the blood
- swelling

While you are taking these drugs, which weaken your immune system, it is very important that you take steps to prevent an infection. Infection is the leading cause of death among patients with chronic GVHD. Most patients are either put on antibiotics to prevent bacterial infections, or are given antibiotics to have on hand in case they develop a fever.

Read about other steps you can take to reduce your risk of developing a serious infection. [8]

**National Cancer Institute Chronic GVHD Program**

An important resource for people living with chronic GVHD is the National Cancer Institute's chronic GVHD program. Patients between the ages of one and 75 can schedule an appointment
for a comprehensive evaluation of their GVHD. Specialists familiar with how chronic GVHD affects every part of a patient's body conduct the four-day physical examination, and make recommendations on how best to manage your disease.

The medical evaluation is free of charge and takes place in Bethesda, Maryland. The program is part of a clinical trial designed to gather a national database of information about chronic GVHD so that better treatments can be developed. For details email the NCI Study Team [9] or phone 301-594-9336.

Coping with the Stress of GVHD

GVHD can be a trying experience emotionally as well as physically. The side effects of drugs used to treat GVHD can cause:

- depression
- confusion
- anxiety
- mood swings
- exaggerated feelings of anger, excitement or sadness

This can make living with GVHD difficult both for you and your family.

It helps to remember that these side effects are temporary and will end when you are taken off the drugs. Some patients are prescribed medications to stabilize mood swings and reduce anxiety while they have GVHD.

It can help to talk with others who are experiencing GVHD to get support and insights into managing this challenging side effect. BMT InfoNet's Caring Connections Program [10] can put you in touch with others who have experienced GVHD.

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