How common is chronic graft versus host disease (cGVHD)?

Chronic graft versus host disease (cGVHD) is a common complication following allogeneic transplant. It may affect 30-60% of patients transplanted from a related donor. The percentage may be higher (or lower) depending upon the age of the donor and/or recipient, stem cells vs. bone marrow vs. cord blood or haplo-identical as donor source, and type of transplant.

What is chronic graft versus host disease (cGVHD)?

When donor cells are transplanted into a recipient they contain donor T cells, which are a type of white blood cell. T cells are programmed to recognize what belongs in a patient’s body and what does not. Sometimes donor T Cells may see the recipient’s organs and tissues as foreign and attack them. This is how cGVHD develops.

When does cGVHD occur?

cGVHD usually occurs between 3-18 months after allogeneic transplant. It may occur as late as 5-10 years after transplant. cGVHD may last a few months to a few years, and may require lengthily treatment with topical therapy and/or oral/systemic therapies.

How is cGVHD treated?

Treatment of cGVHD is largely topical to affected organs, and may also require systemic (oral) immuno-therapies. It is very important to adhere to topical therapies as they are first line therapy for most cGVHD types. Topical therapies may help you avoid oral steroids or other systemic immunosuppressive agents, which may increase your infection risk and have more side effects.

What organs are affected by cGVHD?

cGVHD most commonly affects the skin and mouth in patients. It may also affect the eyes, lung, Gi tract, liver, genitalia, joints/muscles/fascia, nails and hair follicles. The symptoms may vary from mild to severe, and may affect one organ more than another.

What symptoms may I experience and how are they treated?

- **Oral cGVHD**: may appear as red ulcers, white spots, lacy changes, or ulcers. There may be dryness, sensitivity to cold & hot food/liquids, discomfort with citrus/spicy foods, and pain with eating. The dryness places you at risk for cavities and difficulty with swallowing certain foods. If severe it may lead to weight loss.

Oral cGVHD responds best to topical rinse treatments with steroids and/or tacrolimus. For the rinses to have MOST effect they must be used consistently 3-4 times per day and for long term. Steroid and tacrolimus rinses have the most potential for minimizing oral cGVHD symptoms. If you develop isolated sore areas or ulcers in the mouth, steroid gel can be directly applied to the area and covered with a gauze pad for 10 minutes to enhance absorption. If your lips are affected, tacrolimus ointment may help. At times you may need pain medication or other prescriptions to help with moisture/saliva production. Occasionally if these interventions are not successful oral steroids are considered.

Please talk to you BMT Team if you think you may have cGVHD symptoms.
• **Skin cGVHD:** may appear as a dry itchy red rash, pigment changes, thick skin, restrictions of joint or muscle movement, hair loss and brittle nails. Dryness and itchy skin are best managed with Hydrolatum skin cream, which is over the counter and very inexpensive. It is best to apply Hydrolatum after a shower or at bedtime (and to wear pajamas that are okay if they stain). Walking and range of motion (ROM) exercises will help thickening of the skin and restricted movements to joints. You may also apply moist heat 1-2 times per day prior to ROM exercises, with gentle massage and hydrolatum skin cream.

Topical steroid creams and/or tacrolimus ointment are often used alone to control skin cGVHD, they will need to be applied twice a day to affected areas. You will need to use these topical medications long term (months). Topical medications may control skin cGVHD, or they may be useful for problem areas like thick skin, joint restriction or ulcers, in combination with oral steroids. If you are asked by the BMT Care Team to apply hydrolatum over the steroid skin cream/ointment applications, this will allow for intensive skin penetration and more potent effect. Sometimes your BMT physician or Dermatologist will use topical steroids and/or tacrolimus to help you taper off systemic (oral) steroids for cGVHD of the skin.

**Please talk to your BMT Team if you think you may have cGVHD of the skin.**

One of the MOST IMPORTANT measures to prevent cGVHD is to avoid SUNBURN with a daily SPF 30+ UVA/UVB protection.

• **Ocular cGVHD:** may affect the eyes and cause them to feel dry, gritty and itchy. The cornea may appear red and inflamed, or there may be excessive tear production with dry eye. Some patients feel pain with eye opening or blinking, at times severe enough to impair ability to drive, work, or enjoy daily activities. If you have these symptoms, report them right away. Your BMT Team will refer you to a corneal specialist.

Ocular cGVHD impairs the eyes natural ability to lubricate itself due to lacrimal gland dysfunction. The result may cause corneal surface inflammation, corneal scarring and impaired vision. Treatment involves lubrication, reducing inflammation on surface of the eye and medications to improve tear production.

**All of these ocular medications are applied topically. Following prescribed topical prescriptions will help you feel better.**

First, you may use use preservative free artificial tears (Bion Tears, Systane, Optive) 3-6 times per day. If you have more severe dry eye, or wish to apply a more intense lubrication prior to sleep, a preservative free gel is very useful (Tears Again Liquid Gel or Genteal Gel) 1-3 times per day. Always wash hands prior to using eye drops. All of these are available over the counter at Retail Pharmacies like CVS/Walgreens or through Amazon.

Moisture chamber goggles or wrap-around sunglasses may also help maintain lubrication when you are outside in direct sunlight or windy environments.

Your corneal specialist may prescribe punctal occlusion (a small silicone plug inserted into tear duct) to help tears remain on surface of the eye. They may also prescribe special drops, called Autologous serum tears (an eye drop made from your own blood), to promote lubrication.
Your BMT Care Team or Corneal Specialist may prescribe steroid or tacrolimus eye drops to reduce corneal surface inflammation, these are cornerstone of treatment and should be used consistently for optimal effect. Often an antibiotic ointment is prescribed to prevent infection or slow evaporation of tears.

At times patients require systemic treatment with oral steroids or other immune-suppressive medications to treat ocular cGVHD; or a specialized referral for scleral lenses (contacts which help seal in moisture) to Boston Foundation for Sight.

Please talk to your BMT Team if you think you may have symptoms of ocular cGVHD.

- **Lung cGVHD:** may cause a dry cough, wheezing, progressive dyspnea (shortness of breath) with activities and fatigue. You may notice you develop these symptoms after a viral respiratory infection.

Lung cGVHD causes airflow obstruction across the small airways in your lungs. Your BMT Team will monitor by asking about your day to day breathing during your visits, they may obtain periodic pulmonary function tests to monitor your lung function.

If it is determined you have cGVHD of the lung, or bronchiolitis obliterans syndrome, your BMT Team may prescribe an inhaled topical steroid, in addition to other oral therapies. It is very important to adhere to the inhaled steroid and oral regimen to reduce airway inflammation and minimize long term fibrosis of small airways.

It is very important to avoid smoking and people with acute cough and cold symptoms. Your BMT Team may also recommend flu and pneumonia vaccines.

**If you think you may have lung cGVHD please talk to your BMT Team.**

- **Vaginal cGVHD:** may cause you to have vagina/vulvar dryness, burning, stinging, and tightening of vagina, pain with urination or with intercourse. It is very important to report these symptoms to your BMT Care Team.

Treatment involves topical therapy with steroid cream to vulva and/or vagina one to two times per day. Steroid ointments may be prescribed for a minimum of 3-4 weeks or continued until resolution (months+). Topical steroids may be applied externally in a thin layer to vulva, or with the use of an applicator for internal application into the vagina. Sometimes tacrolimus ointment is used in conjunction with steroid cream for more potent effect, or in place of steroid cream if there is concern for skin thinning (atrophy) or skin infection from steroids.

In addition, lubrication and moisture therapy are additional therapies for vaginal cGVHD.

Daily moisture with Replens, vitamin E oil, or olive oil is recommended. Prior to intercourse, dilator therapy or manual stimulation topical water based or silicone lubrication should be used liberally to avoid tissue trauma. We recommend KY Jelly or PJur Glide.
If topical steroid, tacrolimus and lubrication does not alleviate cGVHD of vulva or vagina, at times vaginal dilators, systemic oral steroids, ECP or other immune-suppressive medications may be considered.

Please talk to your BMT Care Team if you think you may have cGVHD of vulva/vagina.

- **Penile cGVHD**: may cause you to have penile skin erythema, lacy white changes, or skin irritation. It may cause pain with manual touch or with intercourse. It is very important to report these symptoms to your BMT Care Team.

  Treatment involves topical therapy with steroid cream to penile skin one to two times per day. Steroid ointments may be prescribed for a minimum of 3-4 weeks or continued until resolution (months+). Topical steroids may be applied externally in a thin layer to penile skin. Sometimes tacrolimus ointment is used in conjunction with steroid cream for more potent effect, or in place of steroid cream if there is concern for skin thinning (atrophy) or skin infection from steroids.

  Please talk to your BMT Care Team if you think you may have cGVHD of penile skin.

- **GI cGVHD**: may cause weight loss, difficulty swallowing, poor appetite, nausea, vomiting, chronic liquid stool and malabsorption syndromes (low iron, B12). Treatment may involve topical steroids with beclomethasone liquid or budesonide pills; they are swallowed but absorbed locally into gastric mucosa. They help reduce inflammation and reduce GI cGVHD symptoms.

**What Can I do to prevent cGVHD?**
- Adhere to transplant medications as best you can
- Avoid sunburn
- Avoid people with active cough and colds
- Report symptoms of cGVHD or infection early
- Remain hydrated
- Walk and remain as active as is comfortable

**What Can I do to manage cGVHD?**
- Adhere to topical medications and care plan
- Adhere to oral systemic medications
- cGVHD may change your physical appearance.
- Acknowledge that cGVHD can be emotionally and physically difficult
- Engage in Look Good Feel Good Programs or Support Groups if you are experiencing difficulty adjusting to effects from cGVHD
- Try to stay engaged in physical activity and exercise- it may help you express your anxiety, fear and stress
- It may help to engage in talk therapy, support groups, mindfulness and connect with other patients that are experiencing cGVHD.