DANA-FARBER/BRIGHAM AND WOMEN'S
CANCER CENTER

Oral Chronic Graft-Versus-Host Disease

What is oral chronic graft-versus-host disease?

Chronic graft-versus-host disease (cGVHD) is a frequent complication following allogeneic hematopoietic cell transplantation. cGVHD develops in greater than 70% of patients, usually within 6-12 months of transplantation. The skin and mouth are the most frequently involved sites, and in some cases, the mouth may be the first or only area affected. Similar to cGVHD in other parts of the body, oral cGVHD is variable and may range from not being painful at all to being so painful as to make it difficult to eat and speak.

How may oral cGVHD present in the mouth?

1. It may present very similar to a condition called oral lichen planus, which varies from white lacey patches to open sores, frequently involving the tongue and inner cheeks. These lesions may cause discomfort, particularly when in contact with spicy, acidic, or crunchy foods.
2. It may affect the salivary glands, resulting in xerostomia (dry mouth) and an increased risk for developing dental decay. Inflammation of minor salivary glands may result in the presence of small blisters (superficial mucoceles) on the palate and inside of the lips, which usually resolve spontaneously within hours or days but may cause discomfort during eating.
3. Rarely, some patients with advanced cGVHD of the skin may develop tightening of the skin around the mouth, leading to limited mouth opening.

What causes oral cGVHD?

Depending on how well "matched" your donor was (even if he/she was a family member), there are many ways in which the donor immune system recognizes aspects of your body as "foreign" and attacks it. While oral cGVHD is seen to a greater degree in less well matched transplants, it can still develop even in ideally matched situations. Oral cGVHD is NOT infectious in nature and you cannot spread it to family members or friends.

How do we know it is oral cGVHD?

Usually your oncologist or oral medicine specialist can diagnose oral cGVHD just by taking a good history and doing a good clinical examination. However, a biopsy may be necessary in some cases.

How do we treat oral cGVHD?

Despite already being on systemic immunosuppressive medications such as prednisone, tacrolimus (Prograf™), sirolimus (Rapamune™) and mycophenolate (Cellcept™), many patients with oral cGVHD often still require intensive topical therapy for the mouth. The goal is to control the disease by reducing the amount of inflammation, thereby reducing pain and sensitivity.

You will likely be treated with topical steroids 3-4 times a day for a few weeks. Sometimes, if there is a large ulcer, your doctor may recommend treating the area "intralesionally" (with a steroid injection directly into the involved area), to speed the healing process. In severe cases, steroid tablets such as prednisone may need to be taken for several weeks to help heal the lesions.

The most commonly prescribed topical steroids are fluocinonide or clobetasol gel (or compounded clobsetasol rinse), and dexamethasone rinse. You may also be prescribed a topical non-steroid medication called tacrolimus, either as an ointment or as a compounded rinse. You may notice what is known as a "black box warning" on the tacrolimus packaging because animal studies showed an increased cancer risk from using this medication. We believe this risk to be minimal compared to the benefits you will experience. In spite of this warning, it is also widely prescribed by dermatologists because it successfully treats many skin conditions.

After symptoms have been brought under control, you may reduce the frequency of therapy to the lowest amount needed to maintain comfort, increasing the frequency during flare-ups as needed. It is a good idea to stop treatment completely if you have no discomfort to let your mouth rest rather than use the topical therapy continuously.

Instructions for applying a gel or ointment: After rinsing your mouth with water, gently pat the affected area(s) dry with cotton gauze. Place a small amount of gel on a clean finger, dab it onto the area that hurts and do not eat or drink for 15 minutes for the steroid to be absorbed. It will not hurt you to swallow some of this gel. You may also apply the gel to gauze and place the gauze against the affected area that you are treating. If the gums are involved, a custom tray, like those used for teeth bleaching but covering the affected gums, may be worn with the steroid in it for 30 minutes once or twice a day.

You may notice that the packaging of the steroid may have the following warning: "Not for internal use" or "For external use only." Such topical steroids have been used for decades to treat inflammatory conditions in the mouth effectively. The warning is there because these steroids are not FDA-approved for this use although there are many studies that demonstrate their effectiveness and safety for treating oral diseases.

Instructions for using a mouth rinse/solution: If you have extensive or difficult to reach oral lesions, you may be prescribed a topical steroid solution (typically dexamethasone) that is used as a mouthwash. A teaspoon (5 ml) of solution should be rinsed for 5 minutes then spat out, and you should not eat or drink for 15 minutes afterwards. It is very important to hold the solution in your mouth for the full five minutes to ensure it works effectively. You may also be prescribed tacrolimus or clobetasol compounded into a rinse by a special compounding pharmacy. You would use it the same way as the dexamethasone.

Any of these topical gels or rinses may cause slight stinging when applied or rinsed. Your doctor may ask you to combine the gel or rinse you are using with topical numbing medicine called viscous lidocaine to ease this burning or stinging sensation. These treatments may cause you to develop a yeast infection ("thrush") in your mouth. Your doctor may prescribe an anti-yeast (anti-fungal) rinse such as nystatin, clotrimazole troches, or fluconazole tablets to prevent and/or treat the yeast infection.

What can I expect?

Oral cGVHD tends to come and go. Some days it will feel better, and other days it may feel worse. It tends to get worse if your body is stressed, either physically (such as having a cold) or emotionally. During flares, it is best to avoid crunchy, spicy and acidic foods, as well as strong toothpastes as they may worsen your symptoms. As far as we know, oral cGVHD can persist for many years although it tends to "burn out" after the first couple of years. If you have a dry mouth, this may further exacerbate the symptoms.

If your mouth feels dry, try to avoid caffeinated and alcoholic beverages and be sure to drink plenty of water throughout the day. There are specific "dry mouth" products that are available over the counter that may help relieve the symptoms to some degree. Many patients find that the Biotene™ line of products are helpful, and these can be used as often as you like. A children's toothpaste may also be more comfortable to use. In more severe cases, medications such as pilocarpine (Salagen™) and cevimeline (Evoxac™) may be prescribed to stimulate the salivary glands to produce more saliva. Some patients develop cavities from the dry mouth and the use of a prescription fluoride gel (Prevident™) and remineralizing paste (MI Paste™) is very important to control this in those at high risk. You should continue to see your dentist at least every 6 months for check-ups.

Oral cGVHD and oral cancer

Patients with cGVHD are at an increased risk for developing oral cancer and should be checked for this at least once a year. Oral cGVHD can look similar to early oral cancer lesions so it is best to be seen by a specialist who is familiar with oral cGVHD, such as the dental specialists here at Brigham and Women's Hospital. Periodic biopsies of suspicious lesions may be necessary.