Oral Graft-versus-Host Disease: From Surviving to Thriving

Celebrating a Second Chance at Life Survivorship Symposium

May 3-9, 2025

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Oral GVHD: From Surviving to Thriving

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Learning Objectives

- Normal anatomy and function of components of the oral and facial complex
- How chronic GVHD may affect teeth, gums, and the lining in the mouth and throat
- Safe and effective approaches to manage oral chronic GVHD and its complications
- The importance of long-term follow-up and preventive care for oral GVHD
- How to find and work with local oral healthcare professionals or oral medicine specialists who have expertise in oral GVHD

Oral Medicine:
Integrating Medicine & Dentistry

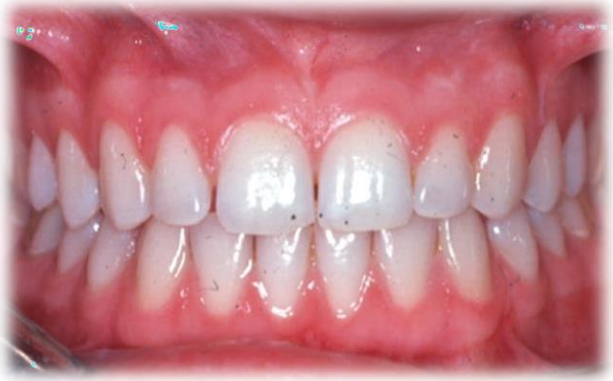
Oral Medicine is the specialty concerned with the oral health of **medically complex patients** and with the diagnosis and non-surgical management of **medically- related disorders or conditions affecting the oral and maxillofacial region**.

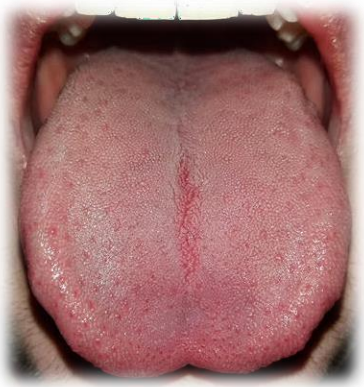
Oral Medicine:
Integrating Medicine & Dentistry

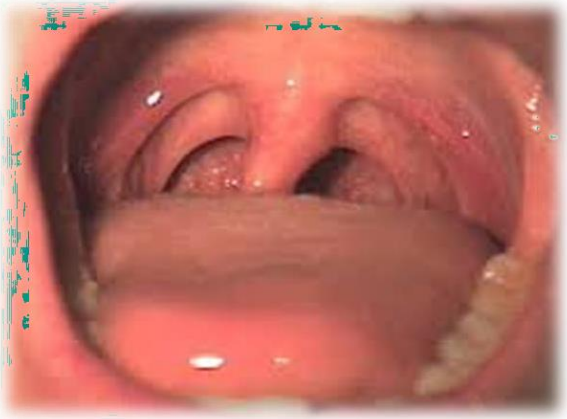
- Diagnosis and treatment of diseases in orofacial complex
- Management of oral complications of systemic disease and its treatment

Duke Oral Medicine

- **Oral lesions** due to medical illness or treatment, such as herpes, candida, anemia, aphthous stomatitis, zoster
- **Oral mucosal diseases** such as lichen planus, pemphigus, pemphigoid, intraoral contact allergy, leukoplakia
- **Oral ramifications of cancer and its treatment** (mucositis, GVHD, xerostomia, osteoradionecrosis, medication-related osteonecrosis of the jaw, trismus)
- **Autoimmune or rheumatologic diseases that affect the orofacial region** (Sjögren's, rheumatoid arthritis, lupus, scleroderma)
- **Dry mouth (xerostomia) & salivary gland disease** related to medical illness or treatment
- **Oral evaluation/clearance prior to cancer treatment or surgery**







The Orofacial Complex

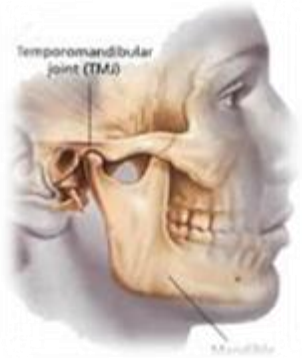
Mucosa (soft tissue lining)

Salivary Glands & Saliva (spit)

Dentition (teeth)

Periodontium (gums and bone)

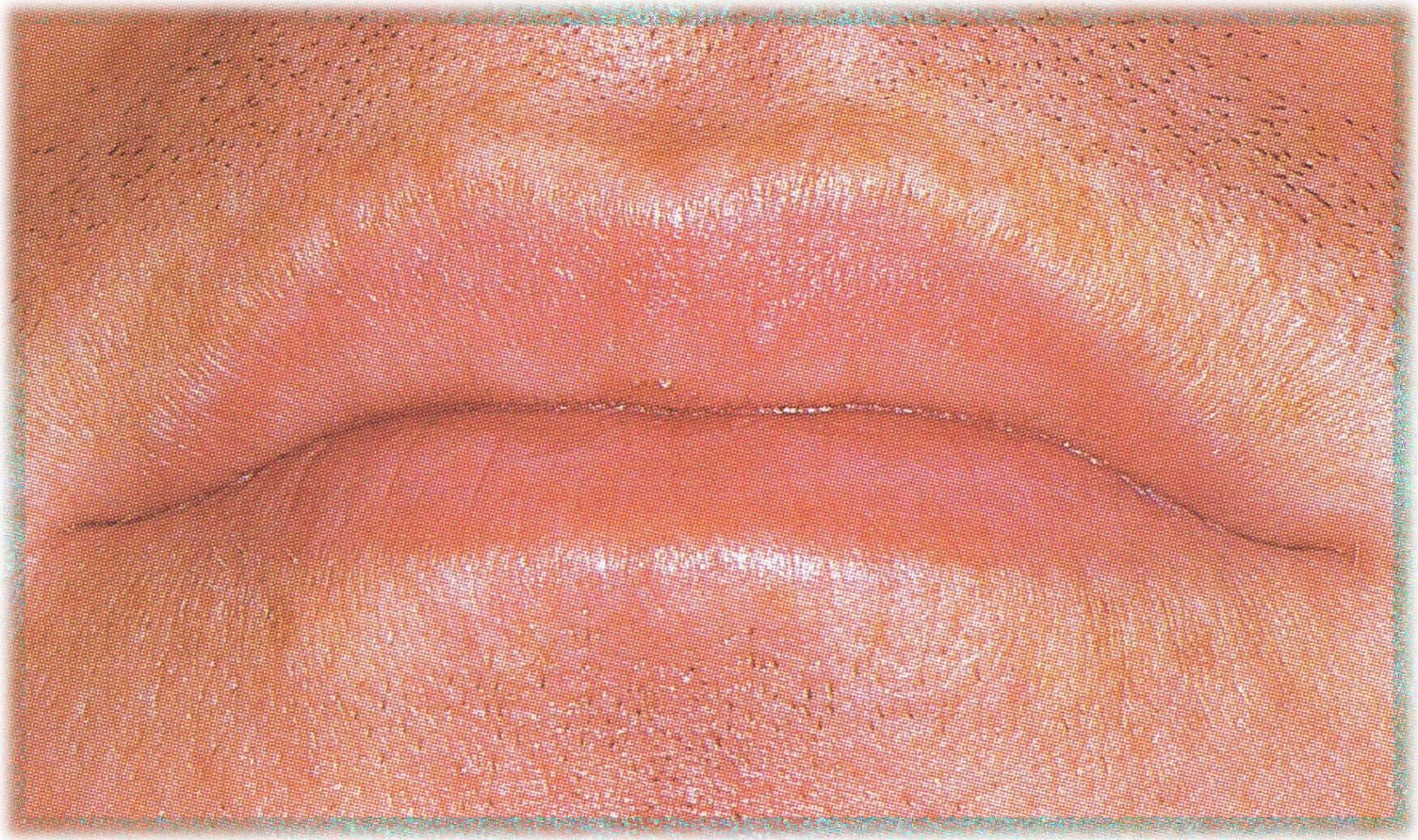
TMJ & Masticatory System (joint and chewing)



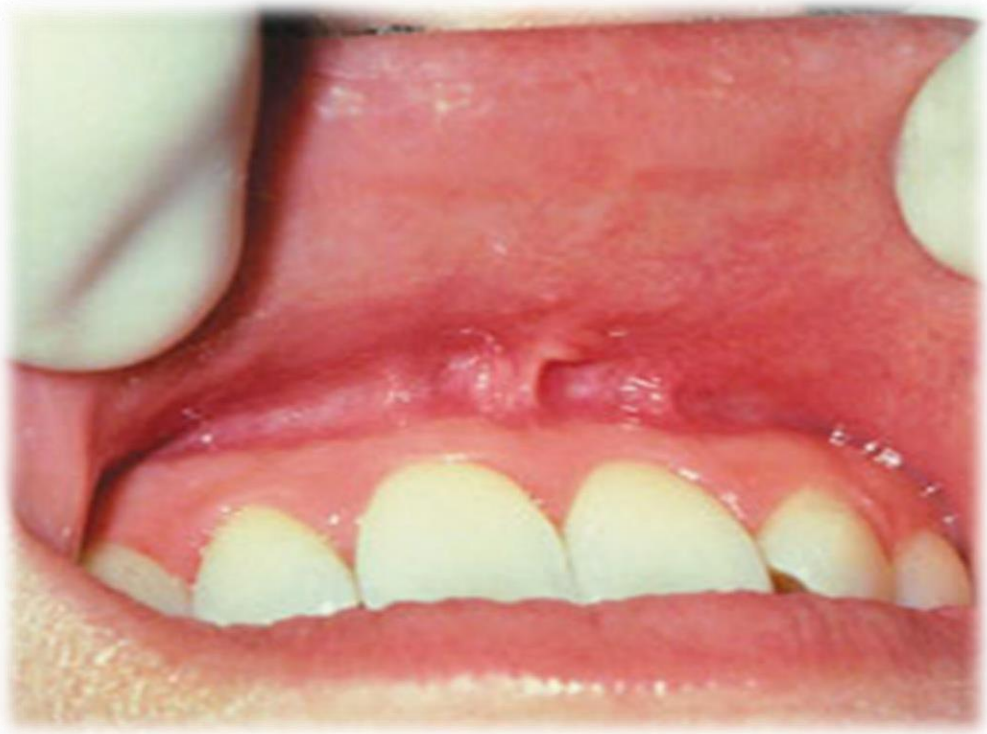
Oral Exam

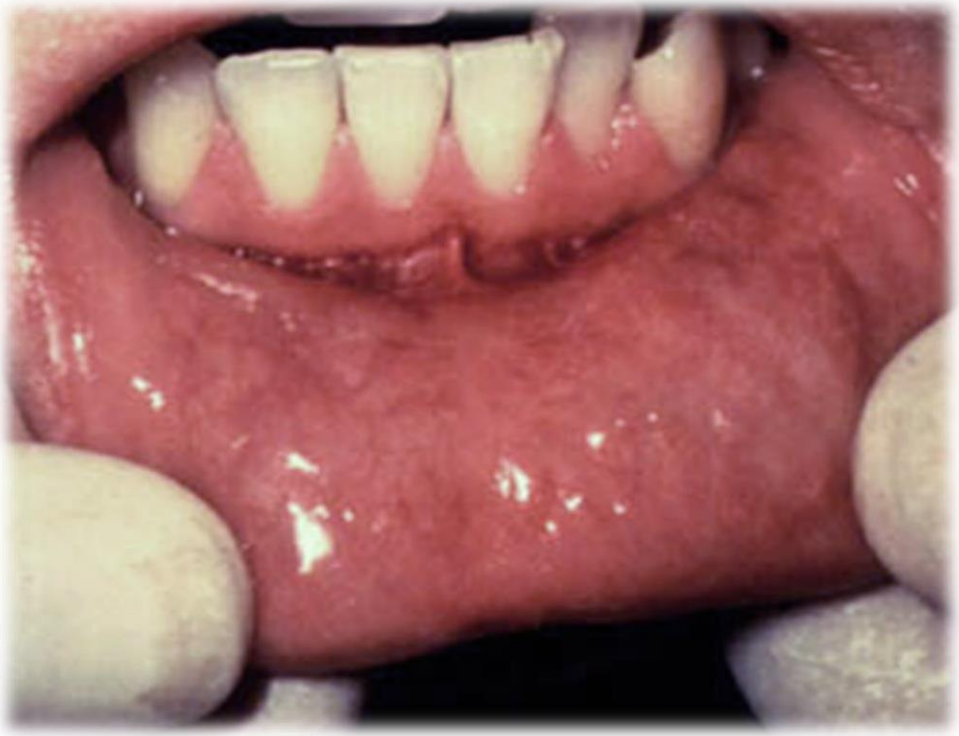
Normal Oral Tissues

Lips

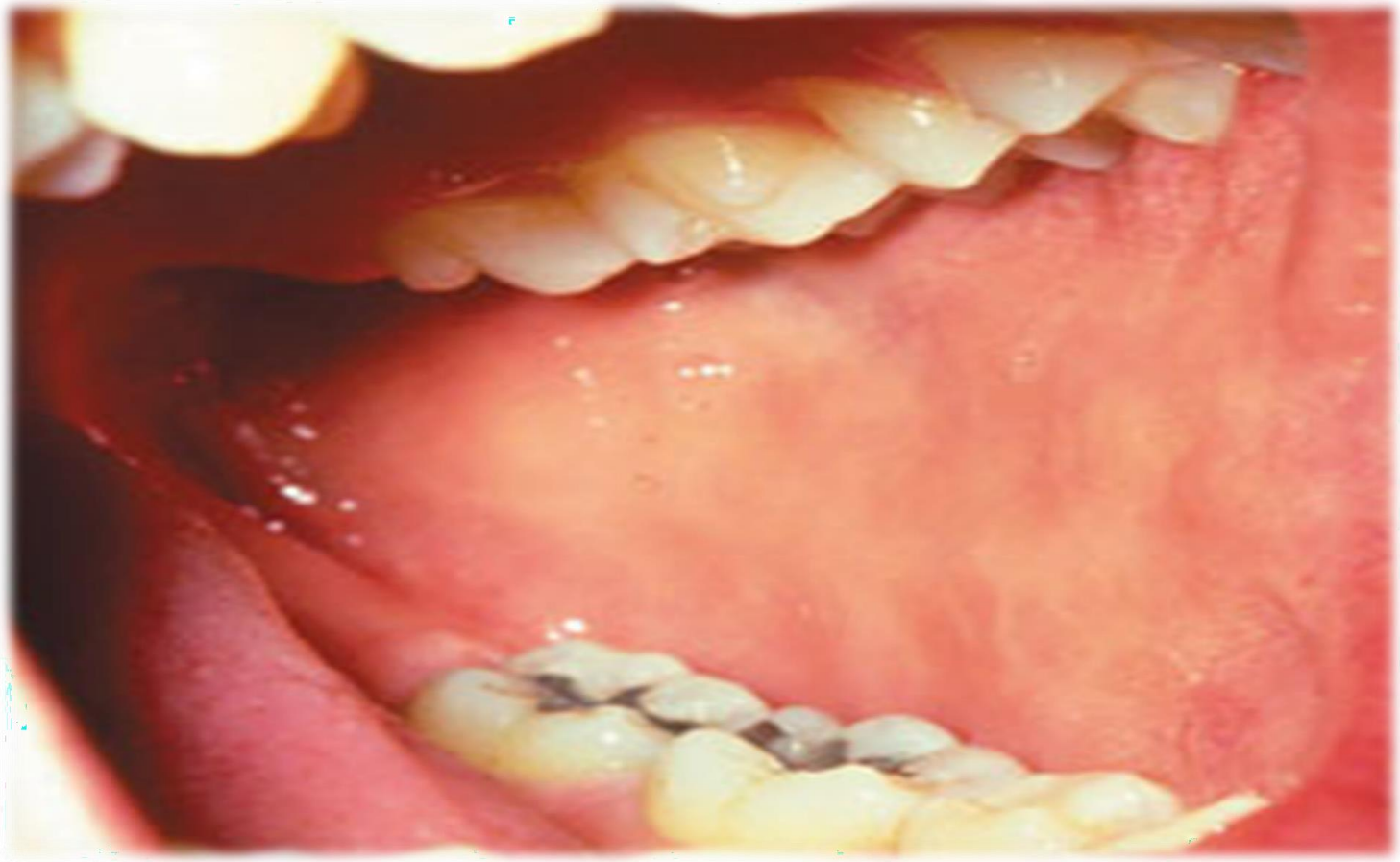


Labial Mucosa (Lining of Lips)

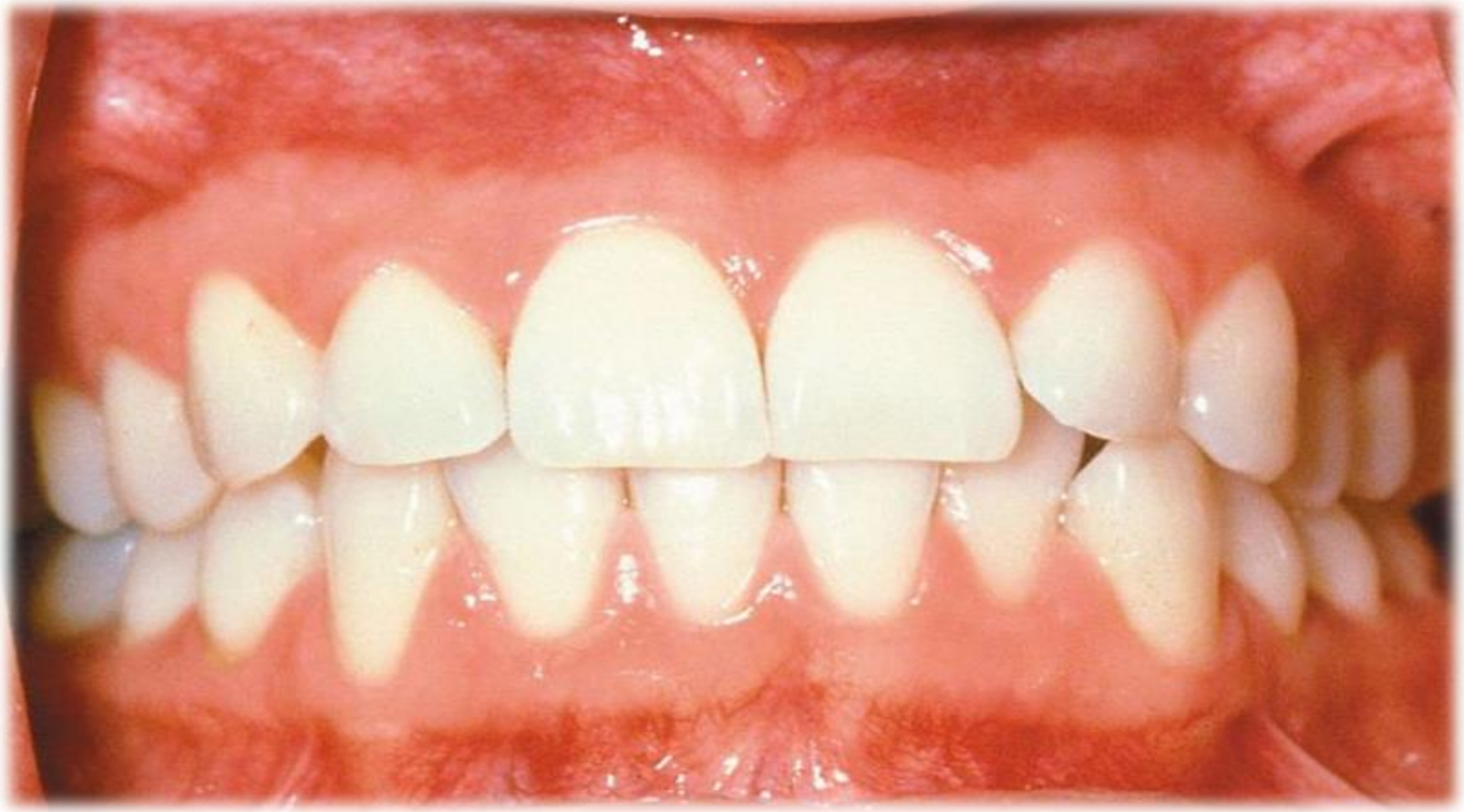




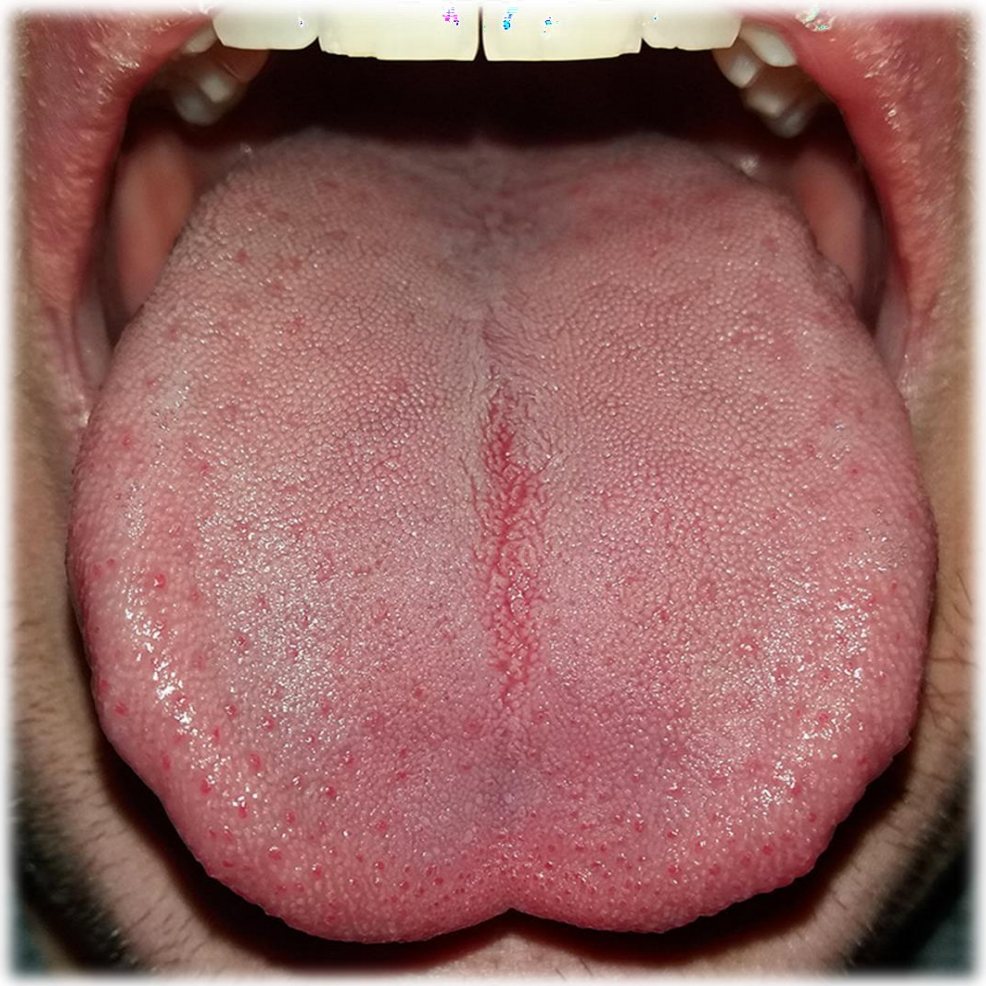
Buccal Mucosa (inside of cheeks)

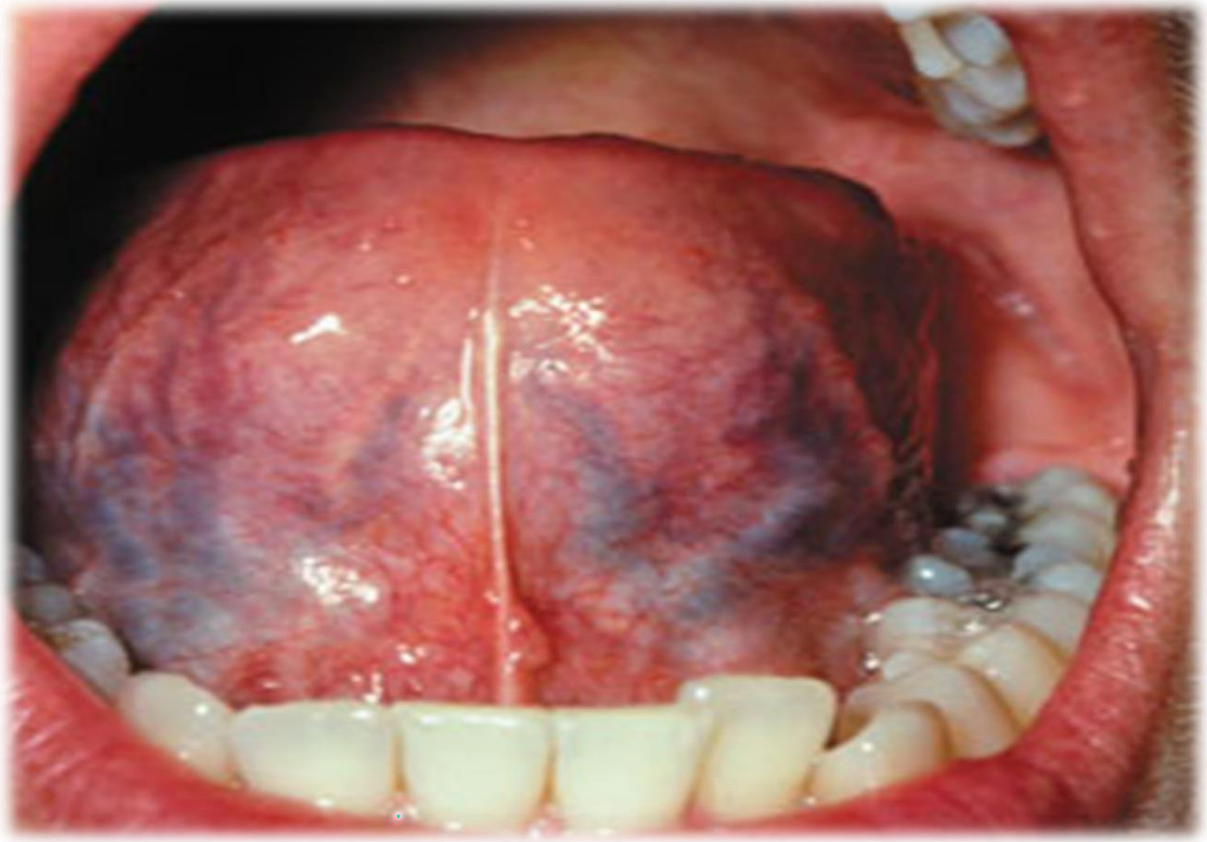


Gingiva (Gums)

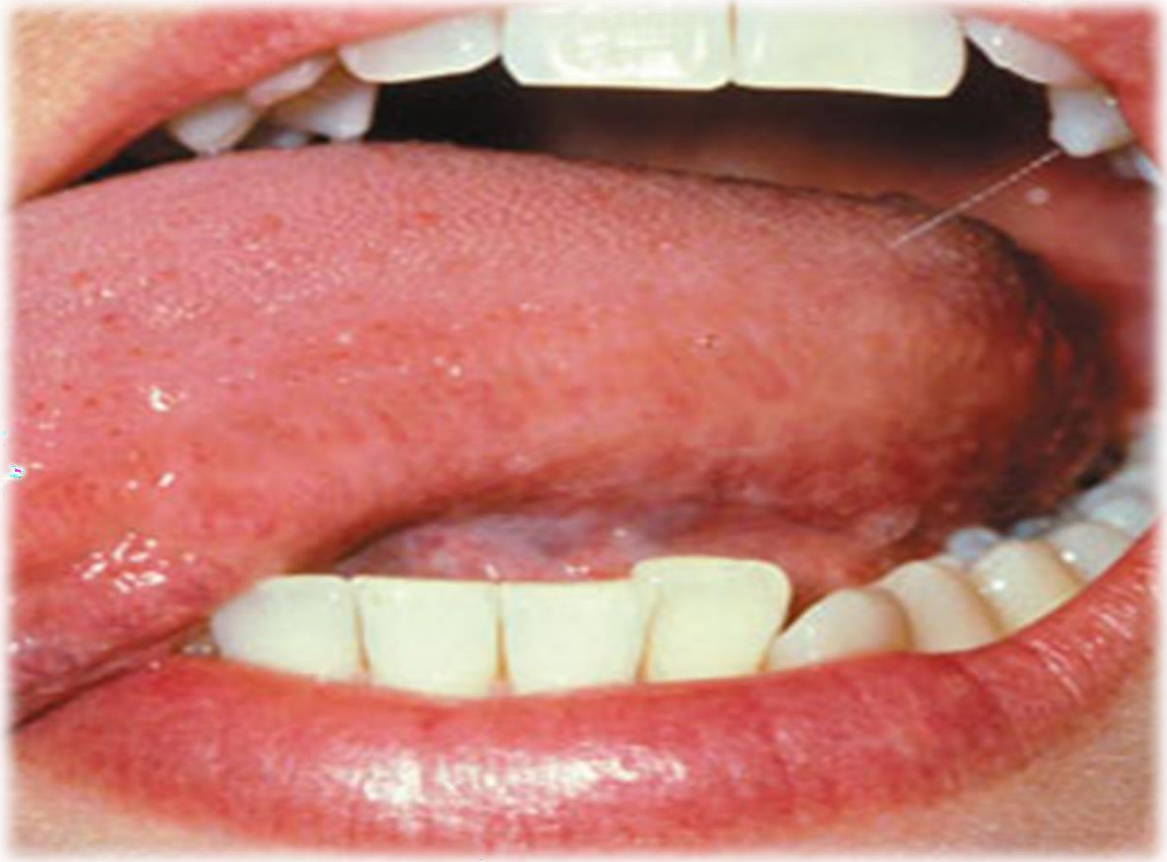


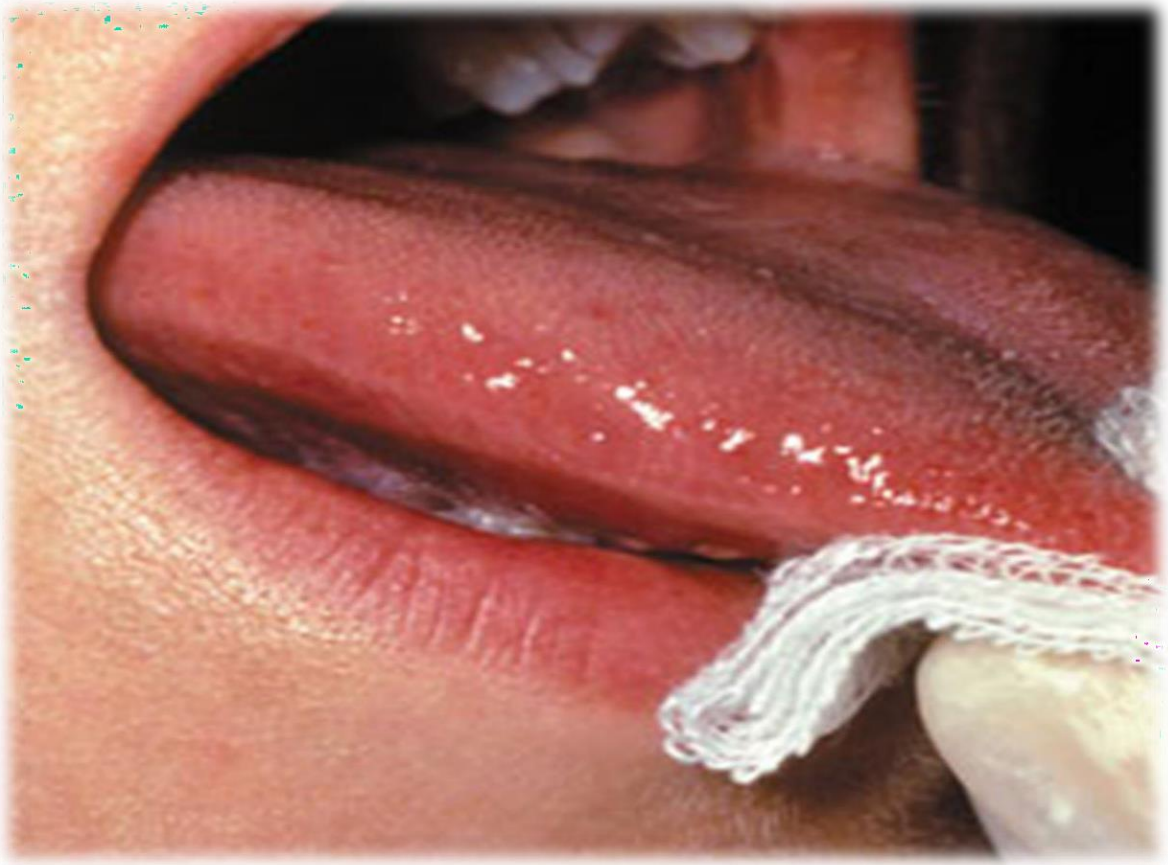
Tongue: Dorsal (top) & Ventral (under)



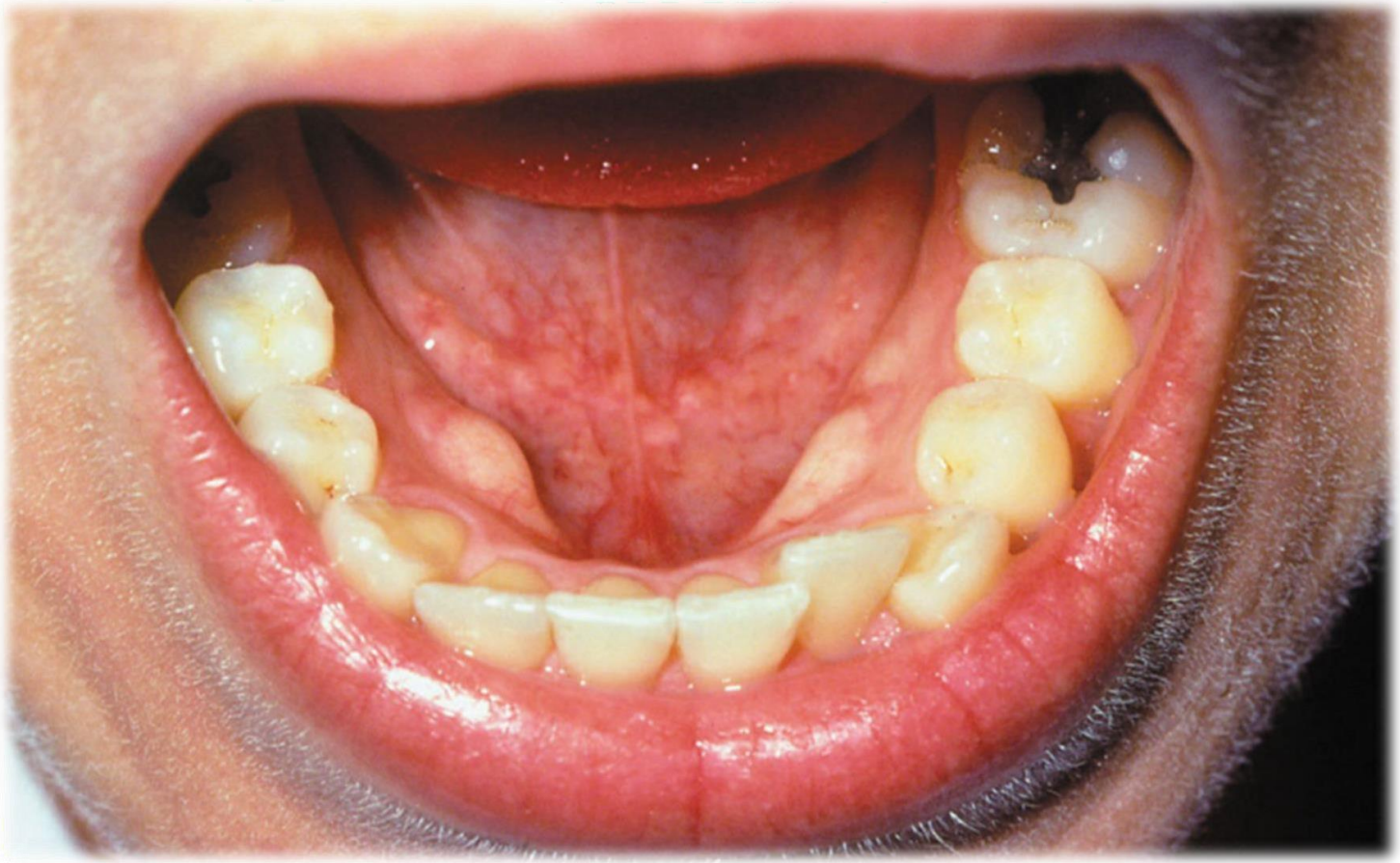


Tongue: Lateral Borders (Sides)

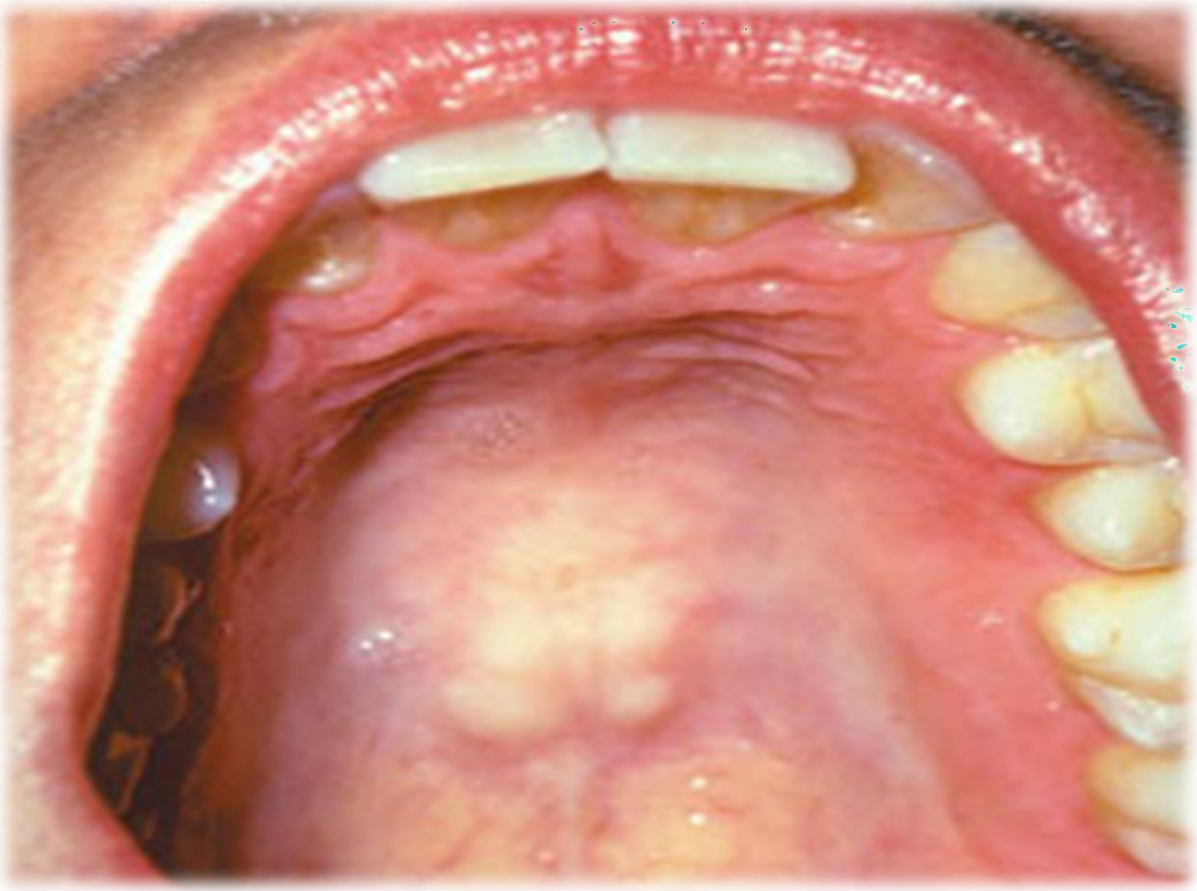




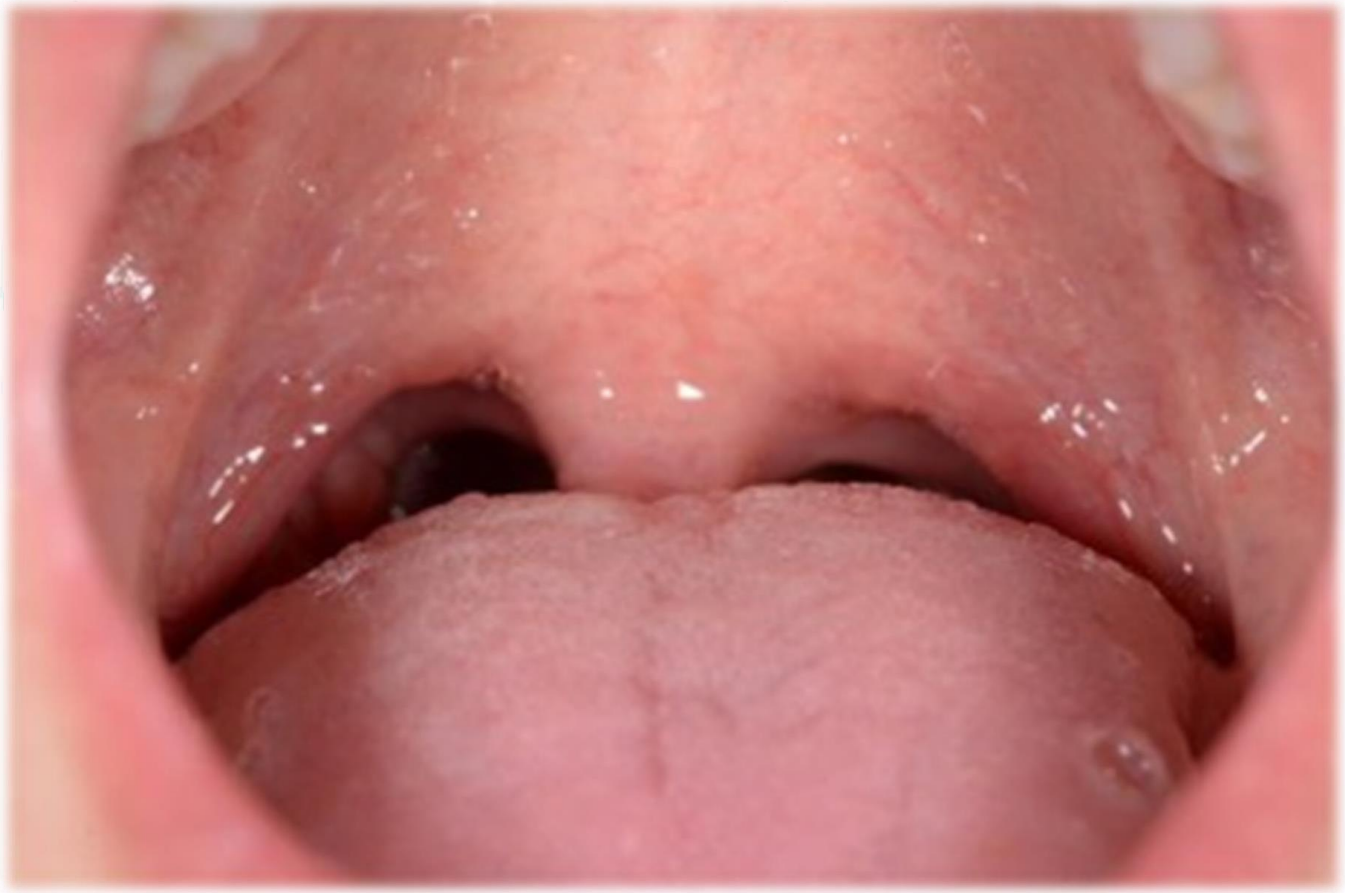
Floor of Mouth

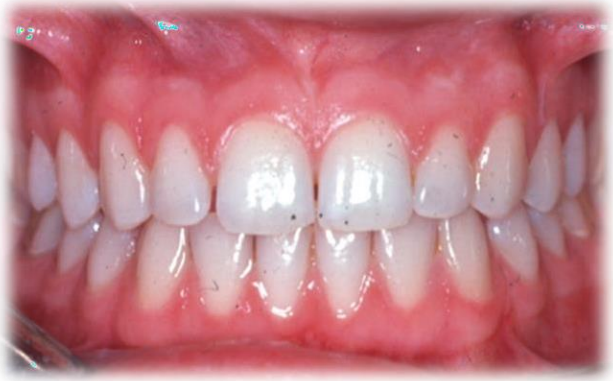


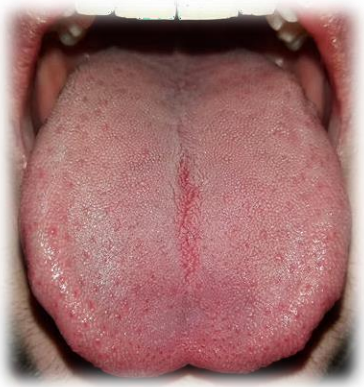
Hard Palate (Roof of Mouth)

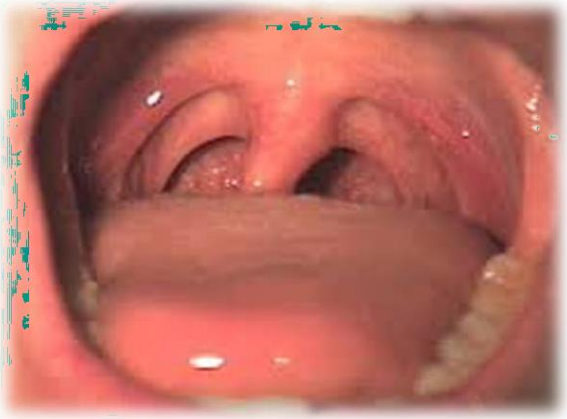


Soft Palate









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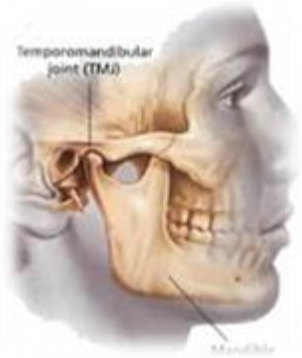


Oral GVHD

What is Oral GVHD?

- Chronic graft-versus-host disease (cGVHD) is a frequent and serious complication following allogeneic hematopoietic stem cell transplantation (HSCT).
- Oral cGVHD is very common; in some cases, the mouth may be the only affected area of the body.
- Symptoms associated with oral cGVHD include:
  - mouth pain
  - sensitivity to normally tolerated foods and drinks
  - reduced mouth opening
  - dry mouth

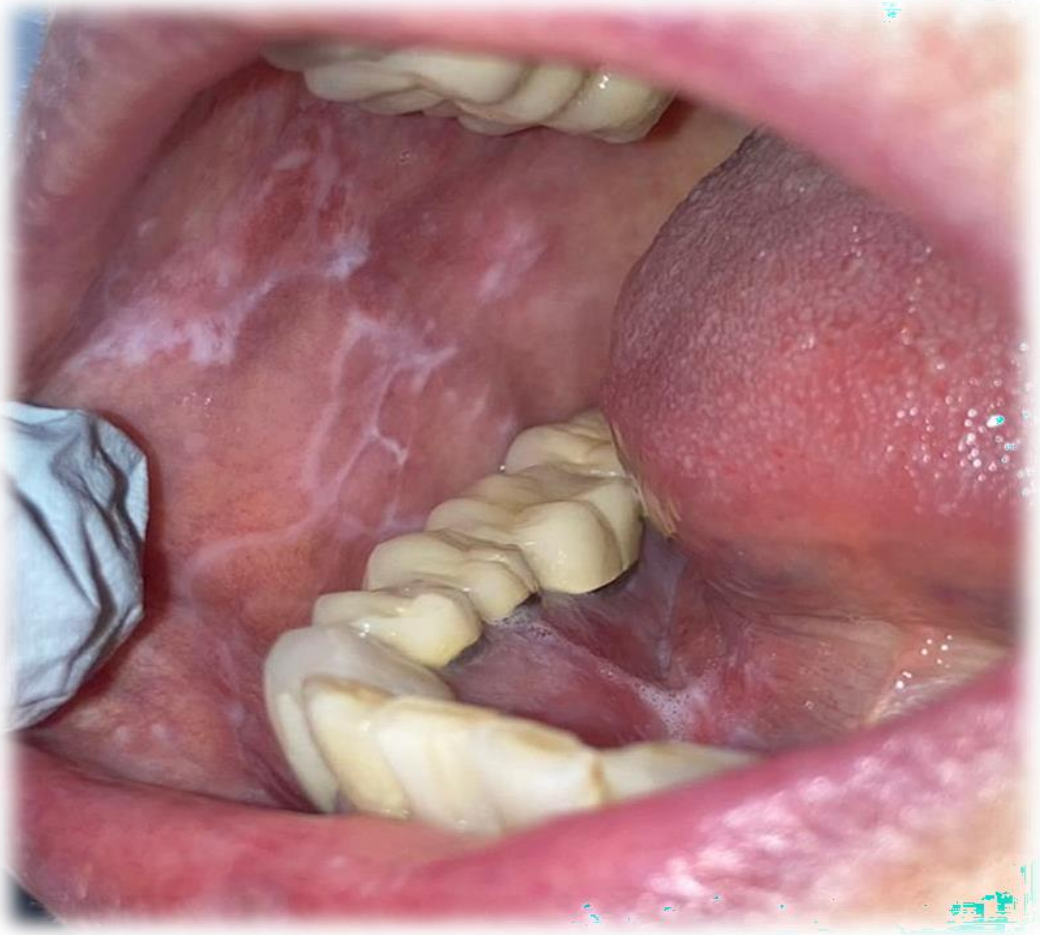
What Causes Oral Chronic GVHD?

- Donor immune cells recognize parts of the patient's body as "foreign" and mount an immune attack
- The risk of developing cGVHD is greatly dependent on how well "matched" the donor was to the recipient

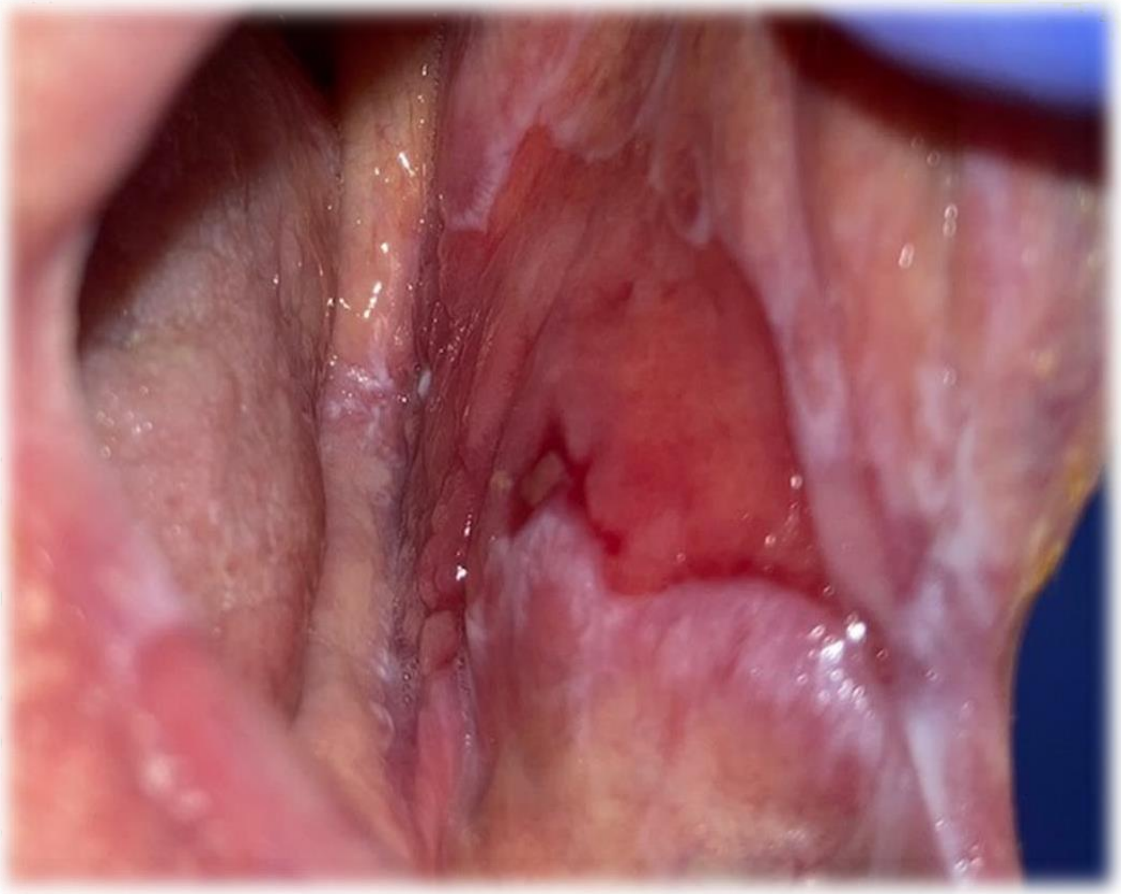
How Does Oral GVHD Appear in the Mouth?

RETICULAR GVHD

- most common form
- looks like lacy white lines
- often on the inner cheek or the sides or top of the tongue
- not typically painful



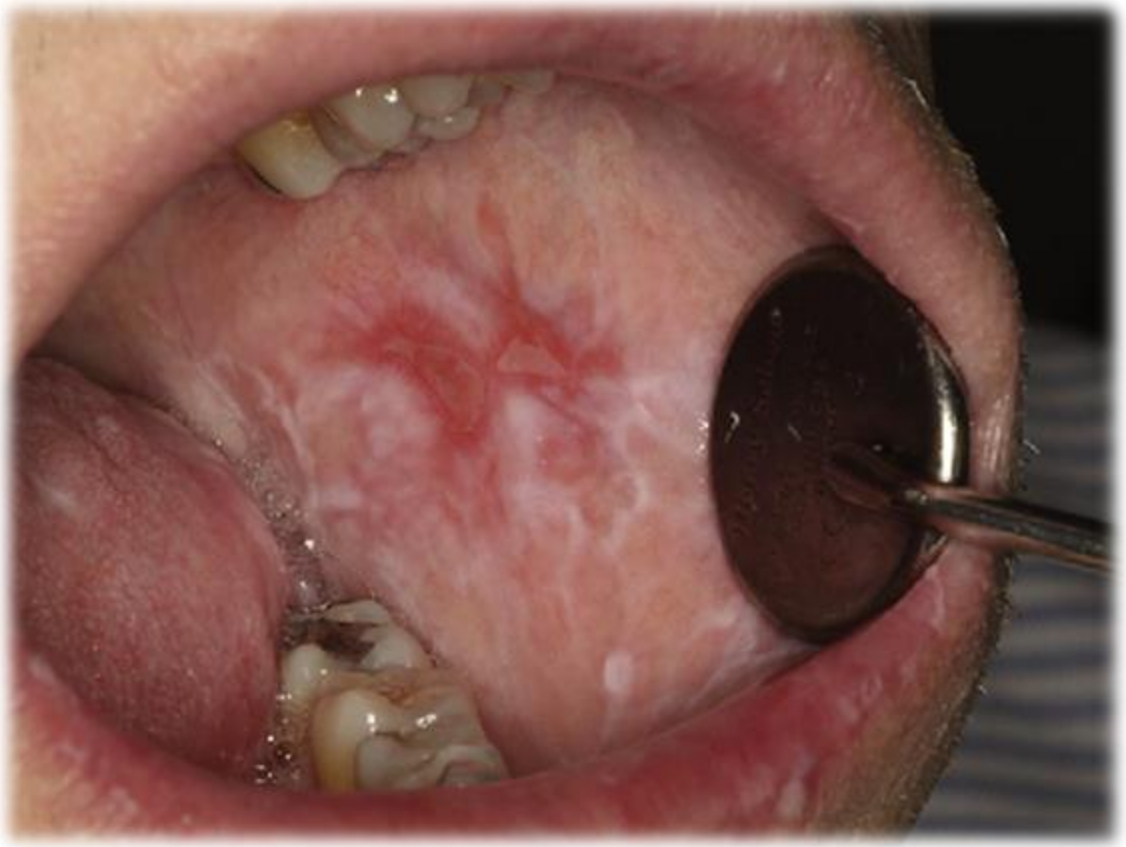
ULCERATIVE GVHD



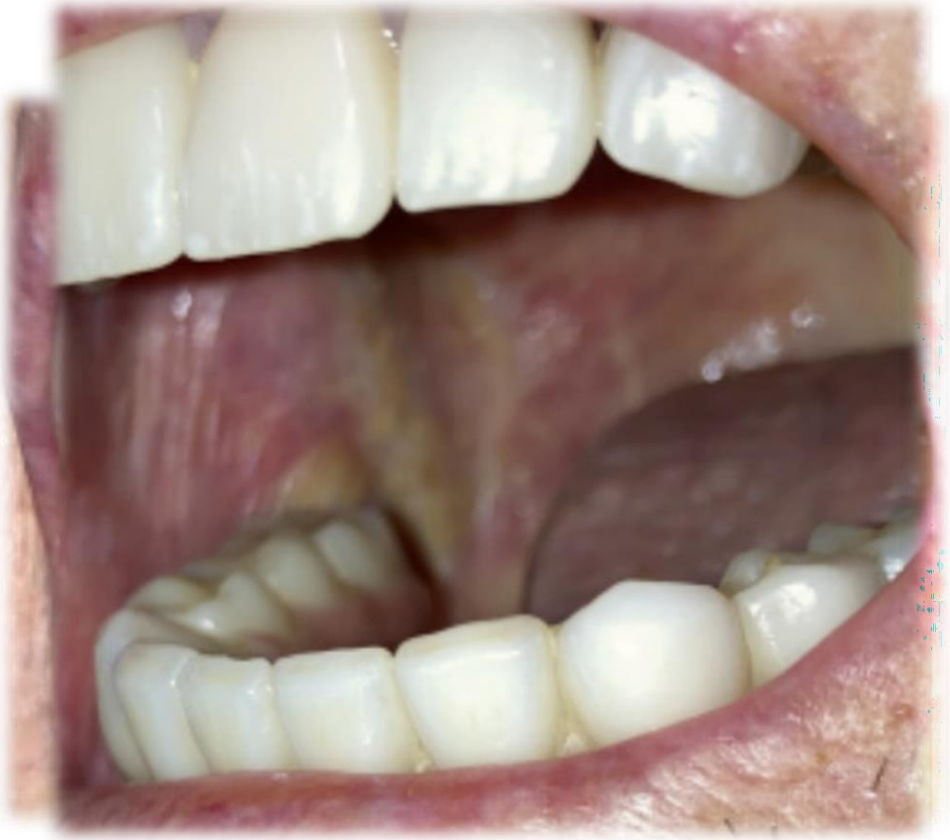
- appears smooth, red, and yellow and is often very painful
- may look like canker sores and can be quite large

RETICULAR & ULCERATIVE GVHD

- Ulcerations surrounded by wispy white lines
- Areas of healing and active disease



SCLERODERMATOUS GVHD



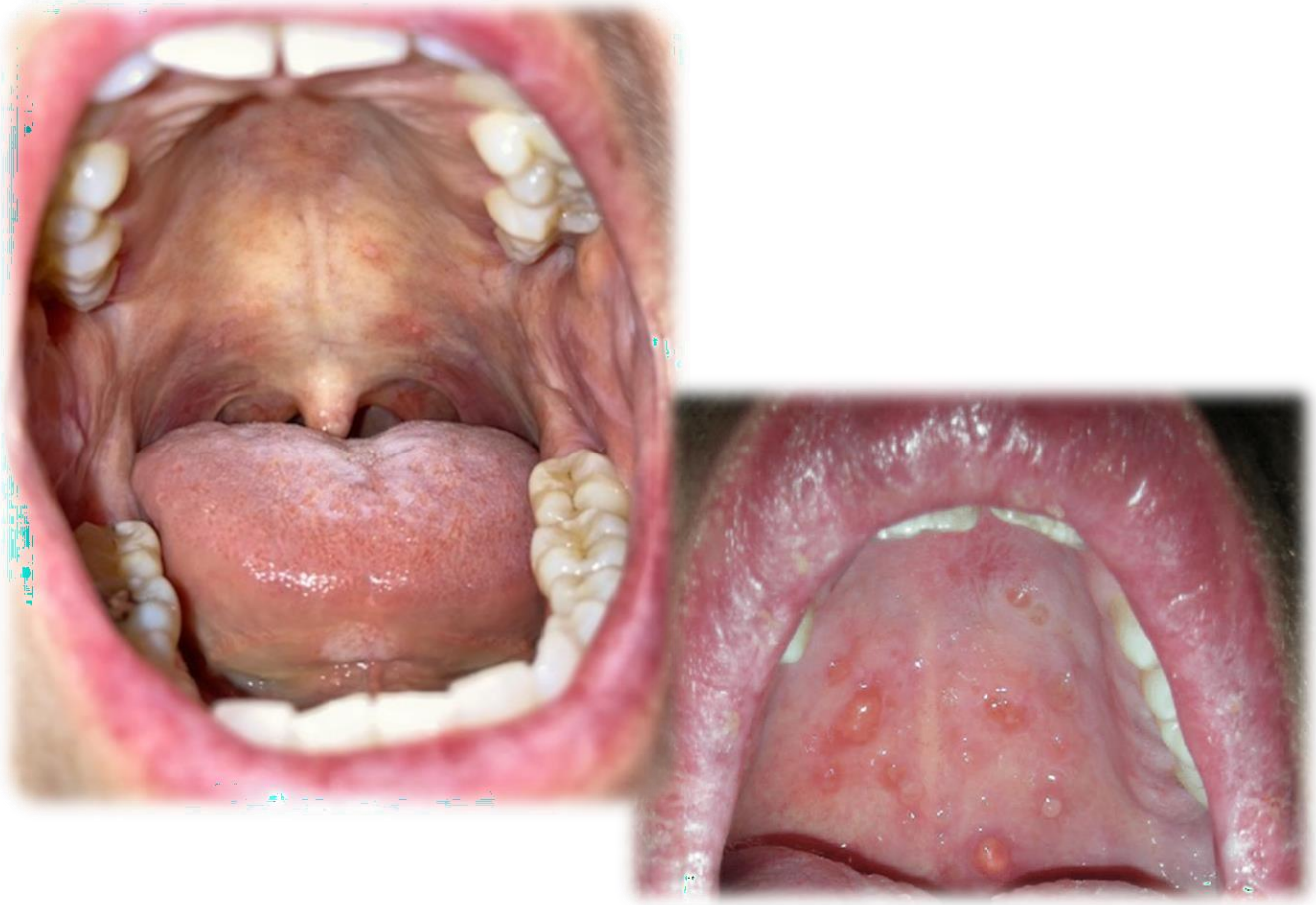
- results in thickening and hardening of the skin on the face and neck
- in some cases, soft tissues inside of the mouth may feel “tight”
- may be difficult and even painful to open the mouth for normal daily functions

TRISMUS (Limited Opening)

- Limited mouth opening and limited mouth mobility can occur due to scarring
- Makes eating, chewing and swallowing difficult
- Normal opening is 50-60 mm between front teeth

GVHD of SALIVARY GLANDS (SPIT GLANDS)

- dry mouth
- superficial mucoceles:
  - small blisters on the inside of the lips and the palate
  - come and go with meals
  - more of a nuisance than painful



What Should I Expect after I've Been Diagnosed with Oral GVHD?

Duration and Intensity of GVHD Symptoms

- will come and go
- can worsen if your body is stressed, both physically (such as having a cold) and emotionally
- can worsen with certain foods
- can persist for many years, although GVHD sometimes burns out after the first couple of years

How are Oral GVHD Mucosal Lesions Treated?

Treatment

- Systemic Immunosuppressive Medications: prednisone, tacrolimus (Prograf®), sirolimus (Rapamune®), mycophenolate (Cellcept®), Jakafi®, Rezurok®

- Topical agents: steroid gels, steroid risnes(fluocinonide, clobetasol, budesonide, dexamethasone), tacrolimus ointment

- Intralesional treatment: For large or slow-growing ulcers, the area can be treated “intralesionally” (with a steroid injection directly into the involved area) to speed the healing process.

- Yeast prevention

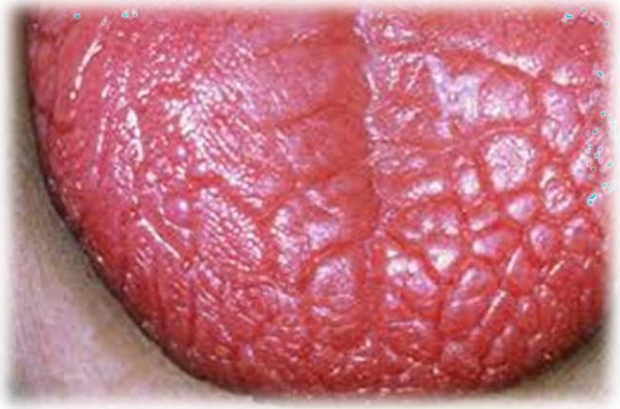
Long Term Management

- After symptoms are controlled, treatment should be reduced to the lowest amount needed to maintain comfort, increasing the frequency during flare-ups as needed
- If there is no discomfort, it is a good idea to stop treatment completely to let your mouth rest rather than use the topical therapy continuously

Substances to Avoid: May Exacerbate or Cause a Flare

- Mint flavoring including mint-flavored toothpastes and mouthwashes
- "Tartar Control" or "Whitening" toothpastes or products
- Oral hygiene products that have sodium lauryl sulfate (SLS)
- Cinnamon
- Certain flavored coffee/tea
- Tomato sauce or acidic foods
- Spicy foods
- Citrus fruits
- Vinegar
- Ginger
- Garlic
- Red wine
- Tobacco
- Pineapple
- Strawberries

How is Xerostomia (Dry Mouth) Treated?



Major Functions of Saliva

Protective Functions

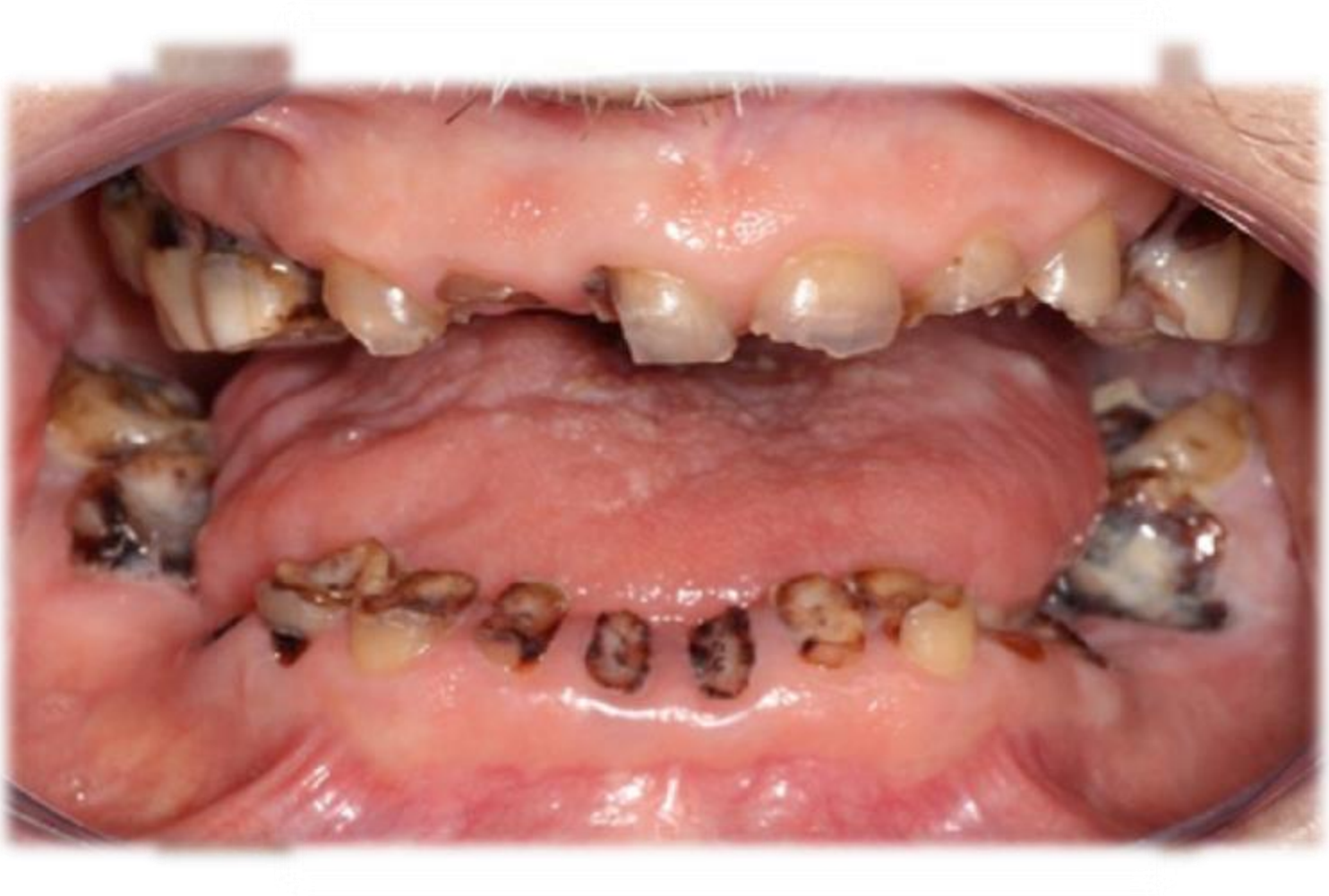
- lubrication
- antimicrobial
- mucosal integrity
- lavage/cleansing
- buffering
- remineralization

Food & Speech Related Functions

- food preparation
- digestion
- taste
- speech

Complications of Dry Mouth

- Mucosal abnormalities
- Candidiasis
- Coated tongue
- Halitosis
- Difficulty swallowing
- Periodontal disease
- Caries



Behavior Modifications

- Limit alcoholic/caffeinated beverages
- Do not use mouthrinses with alcohol
- Frequently sip water; stay hydrated
- Ice chips
- Humidfier at night
- Use sugarless salivary stimulants
  - Sugarless chewing gum
  - Sugarless hard candies, lozenges

Salivary Stimulants

SUGAR-FREE SALIVARY STIMULANTS. The regular use of **SUGAR-FREE** gums, mints, and candies can help stimulate salivary flow (see below examples) Products containing xylitol can help protect the teeth. **Xylitol is a natural sweetener product that differs chemically from others sweeteners such as sorbitol, fructose, and glucose. Xylitol can interfere with the growth of bacteria that cause cavities.**

Chewing Gums *(manufacturer)*	**Mints / lozenges *(manufacturer)***	**Adherent Lubricating Products**
MightTeaFlow *(Camellix)* Ice Cubes *(Ice Breakers)* Trident Gum with Xylitol *(Cadbury)* Orbit Sugarfree Gum (*Wrigley*)	MightTeaFlow *(Camellix)* Spry Mints *(Xlear)* TheraMints *(3M)* ACT Dry Mouth Lozenges Sugar Free Sour Candy	Xylimelt Mucoadhesive Tablet (*Quest*) Xerostrip (*Xerostrip*)

Oral Moisturizers

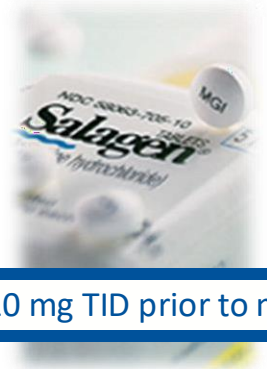
ORAL MOISTURIZERS, LUBRICANTS & GELS: There are many over-the-counter products that may help in moisturizing and lubricating the oral tissues (see below examples). These agents are typically available as gels or liquids. Their effects are temporary but can provide comfort while speaking and eating. Using a saliva substitute instead of drinking water prior to sleep and when awakened, may reduce the need go to the bathroom during sleep.

Oral Moisturizers & Lubricants *(manufacturer)*

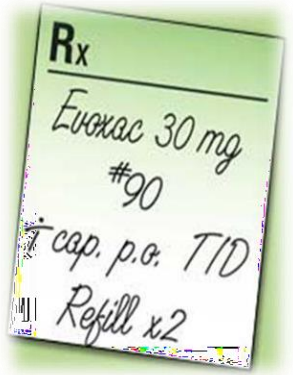
Biotene Oral Balance Moisturizing Gel (*GSK*)
MouthKote Moisturizing Spray (*Parnell*)
Oasis Mouth Spray *(GSK)*
Lubricity *(You First)*
Store Brand "Dry Mouth Spray"
Aquoral *(K Pharmaceuticals)*

Sialogogue Therapy

- Medications to increase salivary flow
- Two prescription drugs available:
  - pilocarpine (Salagen, *MGI Pharma*)
  - cevimeline (Evoxac, *Daiichi Sanko, Inc*)



5 – 10 mg TID prior to meals



- GI, sweat, and cardiac side effects:
  - Should be avoided in patients with significant heart disease, asthma, and narrow-angle glaucoma
- **<u>Require functioning glands</u>**

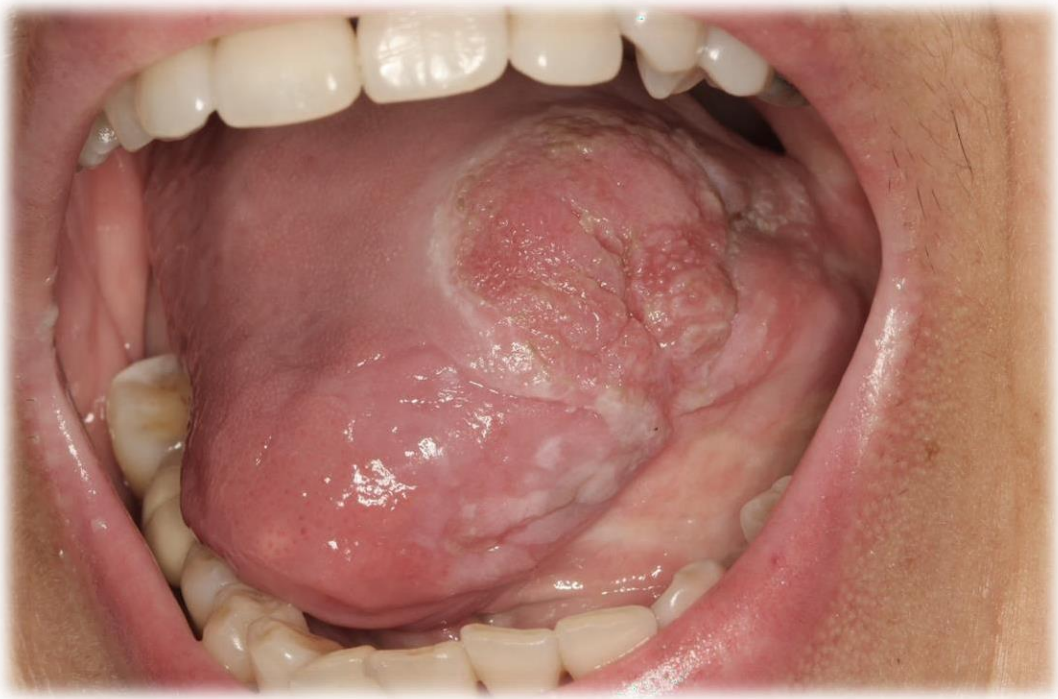
Other Important Information

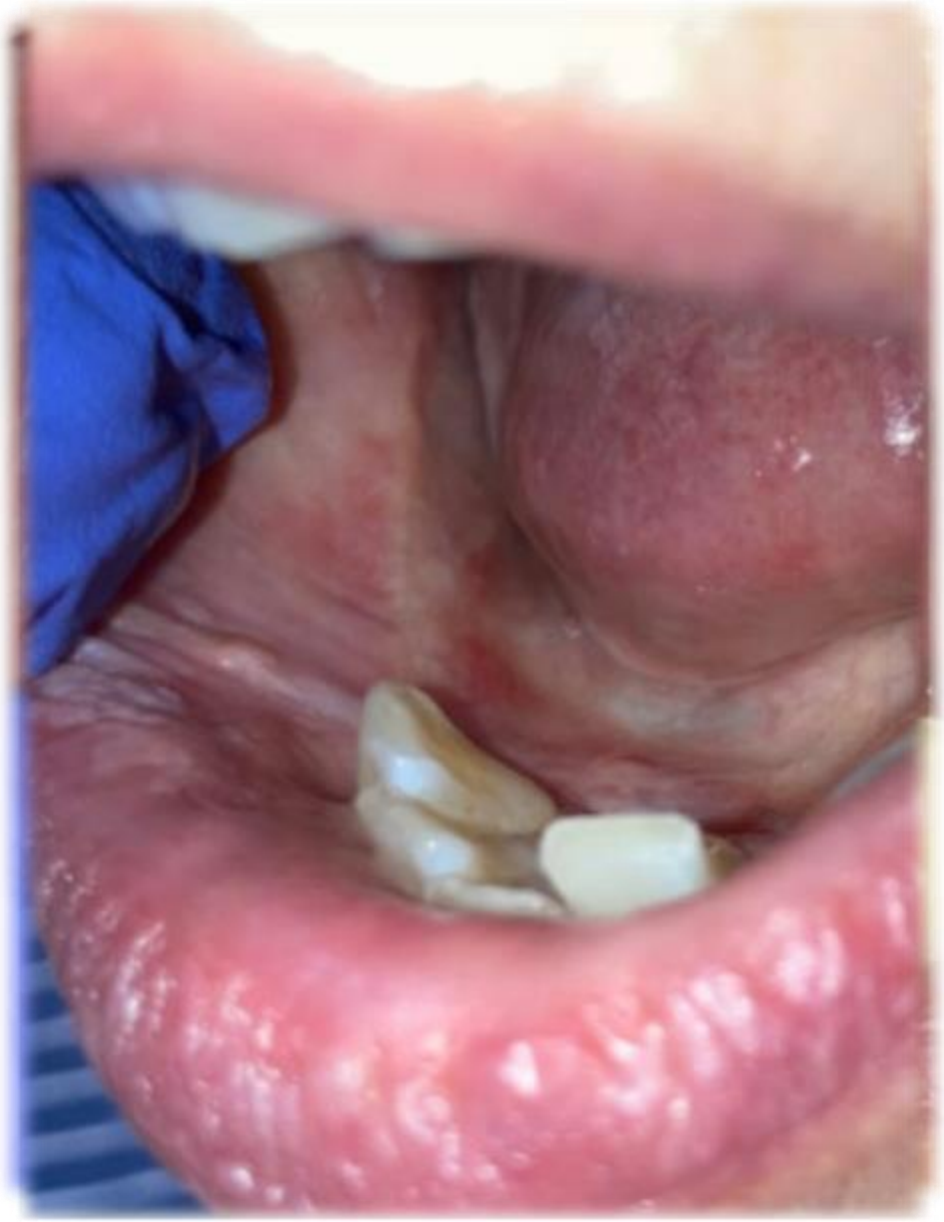
- **See dentist regularly**:
  - may recommend you undergo more frequent check-ups, professional cleanings and in-office fluoride applications
- **Perform oral hygiene as instructed**:
  - may recommend a **prescription strength fluoride** to be used in addition to your regular toothpaste
  - consistently accomplishing daily oral hygiene measures is one of the most important steps in successfully managing the dental complications of oral dryness.
- **Avoid sugary food and drinks**:
  - Decrease intake of sweet or sticky foods
  - avoid the frequent intake of acidic beverages (such as most carbonated and sports replenishment drinks) and lemon products.

Is Oral Chronic GVHD a Risk Factor for Oral Cancer?

Oral GVHD and Oral Cancer

- Patients with cGVHD have a significantly increased risk of developing oral cancer and should undergo an oral cancer screening at least once a year.
- Since oral cGVHD can look similar to early oral cancer, it is best to be seen by a specialist who is familiar with these conditions.
- Periodic biopsies of suspicious lesions may be necessary.



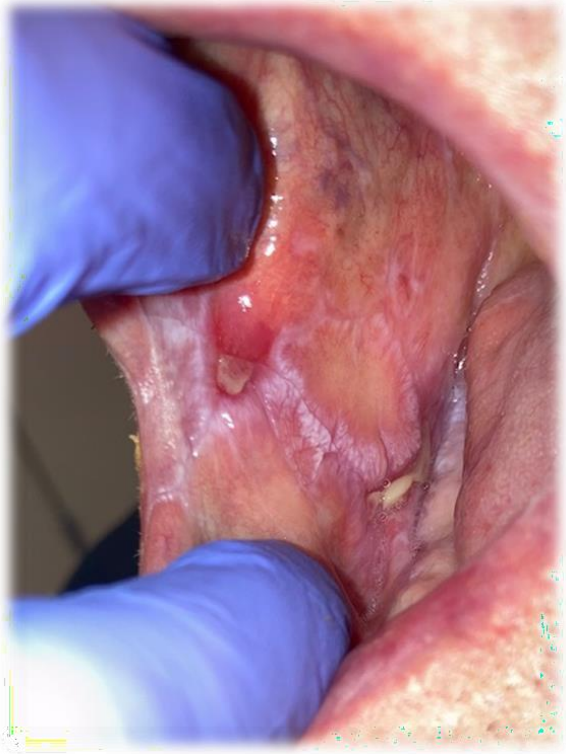


Oral Squamous Cell Carcinoma

- Can affect cGVHD patients more frequently than non-cGVHD patients
  - probably because of the combination of extended tissue inflammation and immunosuppression

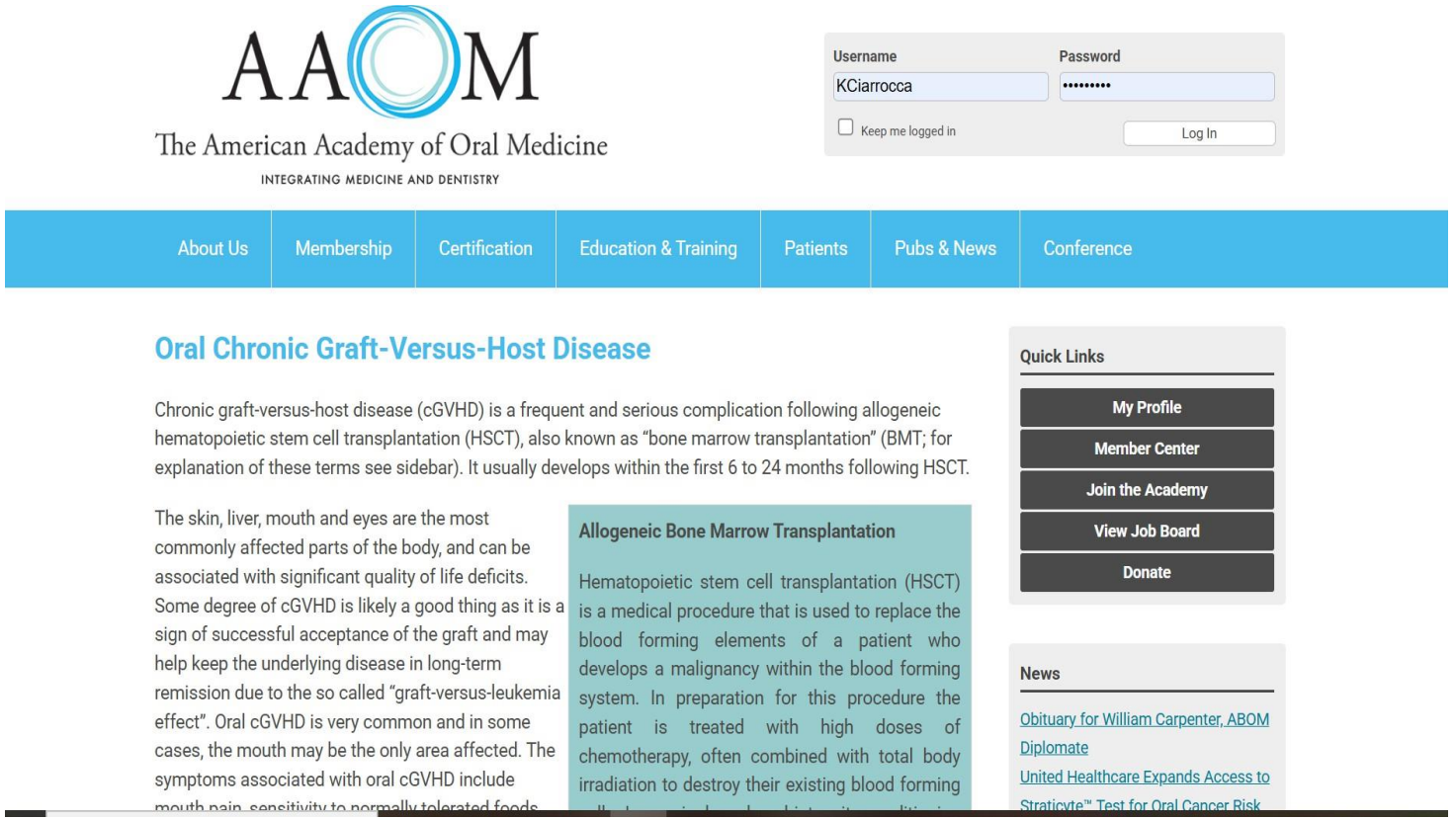
Final Thoughts

- Oral GVHD can cause painful and annoying effects on your mouth that affect your ability to eat, speak, and your quality of life … BUT ….
- You do **not** have to live with the pain or the nuisance
- Decrease inflammation
- Keep mouth moist
- Self-exams
- Careful attention to what you eat
- Regular follow-up with someone who treats oral GVHD



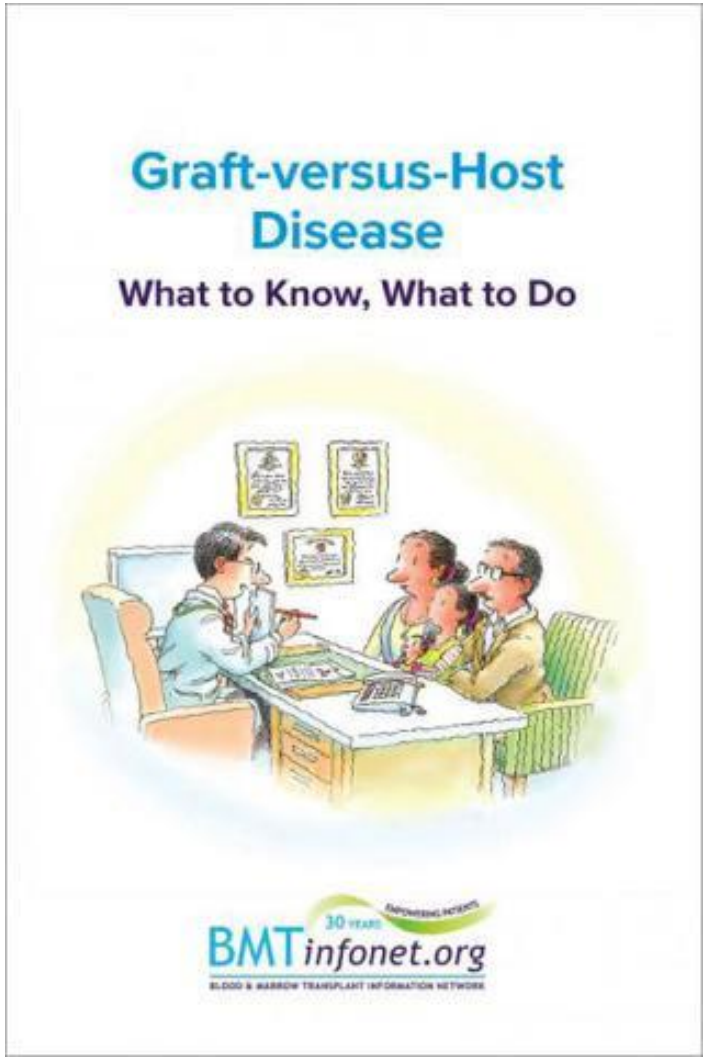
Helpful Resources

SCAN ME



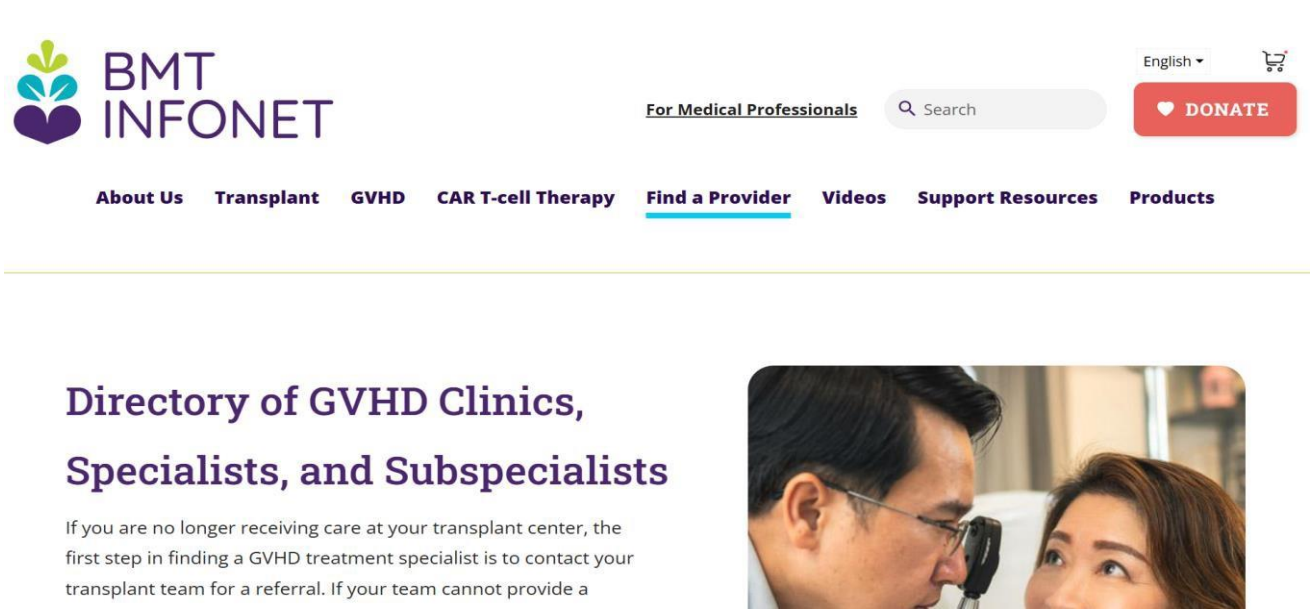
Helpful Resources

SCAN ME



Directory of GVHD Clinics and Providers

bmtinfonet.org/gvhd-directory



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Questions?

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Let Us Know How We Can Help You

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

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