

Graft-versus-Host Disease: Mouth

Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023



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Learning Objectives

Participants will learn about:

1. General oral care after transplant
2. Oral complications after transplant
3. How to recognize cGVHD in the mouth
4. Types of Oral cGVHD
5. Treatment for different types of oral cGVHD

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Overview

- Take care of your mouth!
- Establish community dental care: Who, What, When
- Oral cancer screenings
- Non-GVHD post-transplant complications
- GVHD and your mouth
 - Symptoms
 - Appearance
 - Therapies

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The Oral Cavity is the Gateway to the Body



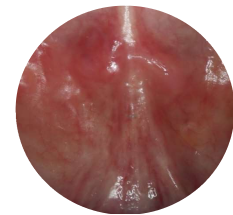
Gingiva



Buccal Mucosa



Tonsils



Sublingual Immune Response

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Take Care of Your Mouth - Brush

- Use toothpaste with fluoride
- Sensitive mouth?
 - Fruit-flavored or children's toothpaste
- Sensitive teeth?
 - Fluoride rinse/gel or desensitizing toothpaste (Sensodyne, ProNamel, Colgate Sensitive, etc.)
 - Professional desensitizing treatment (several options in the dental office)
- Limited joint mobility?
 - Electric toothbrush (any kind from the drugstore)



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Take Care of Your Mouth - Floss

- Floss picks
- Waterpic or other electric flosser
- See your Dentist 😊



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Finding Community Dental Care (a dentist!)

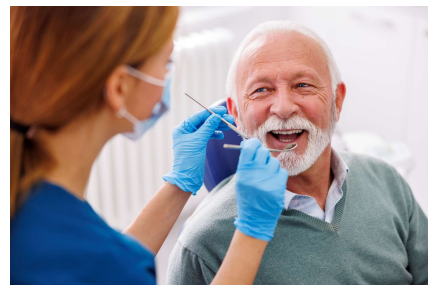
- **Tell** your dentist that you are a transplant survivor
- **Show** your dentist anything unusual or new that you see or feel in your mouth
 - Mouth ulcers, lumps and bumps should heal within 3 weeks***
 - Teeth, gums, lips, tongue and cheeks
- **Do** ask for an oral cancer screening

***This time projection does not include GVHD, unfortunately

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Finding Community Dental Care (a dentist!)

- Not every dentist appreciates your complex medical history and needs.
- If your dentist is not a good fit, interview other dental offices
- Ask, “Do you have experience treating medically complex patients?”
- University (dental school faculty or resident practice) or Medical Center Clinics are a good option



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Get an Annual Oral Cancer Screening

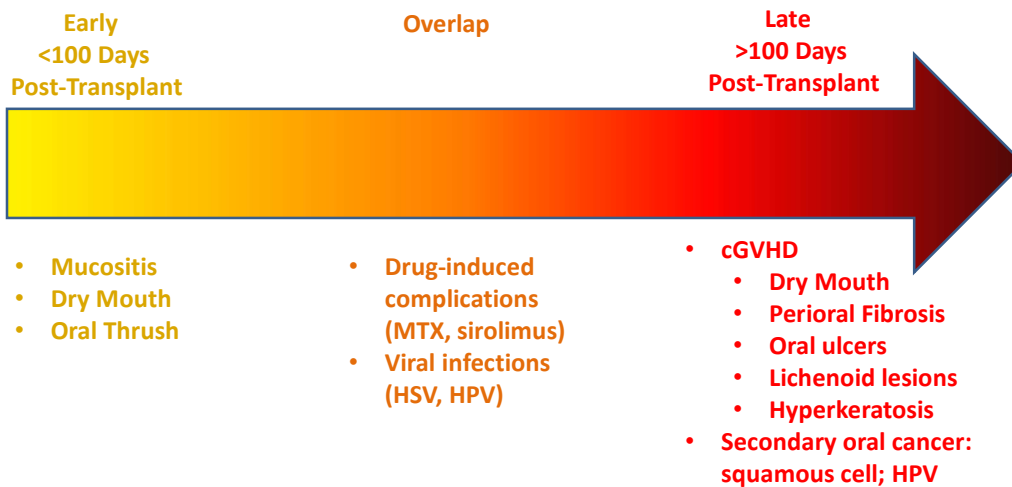
- Highest risk in patients with oral cGVHD history
- 5-10+ years post-transplant
- Tongue is the most common site



5 years post-transplant
Patient noticed the lesion 2-3 weeks prior to photo

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Timing of Oral Post-Transplant Complications



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Non-GVHD Post-Transplant Complications

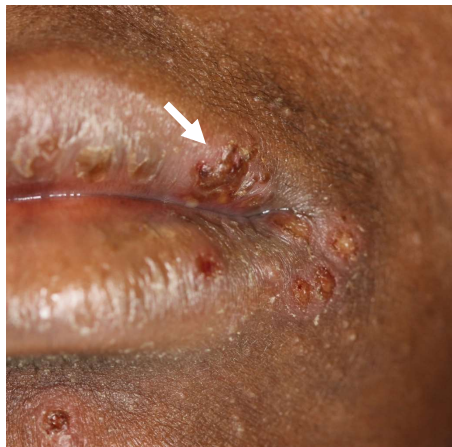
- Loss or change in taste
- Radiation-induced dry mouth
- Medication-related oral ulcers or lesions
- Infections (thrush, bacterial or viral)
- Cold sores (herpes simplex virus recrudescence)



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Herpes Simplex Virus (HSV) Recrudescence

- **HSV reactivation is common:** acute onset, exquisitely painful oral ulcers
 - **Diagnosis:** swab ulcer for PCR lab test for HSV DNA
- Management:** lidobenalox, systemic antivirals



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Common Post-Transplant Complications: Oral Thrush (Candidiasis overgrowth)

- Pseudomembranous or erythematous
- **Management:** topical antifungals (clotrimazole troches, etc) in addition to systemic antifungal prophylaxis



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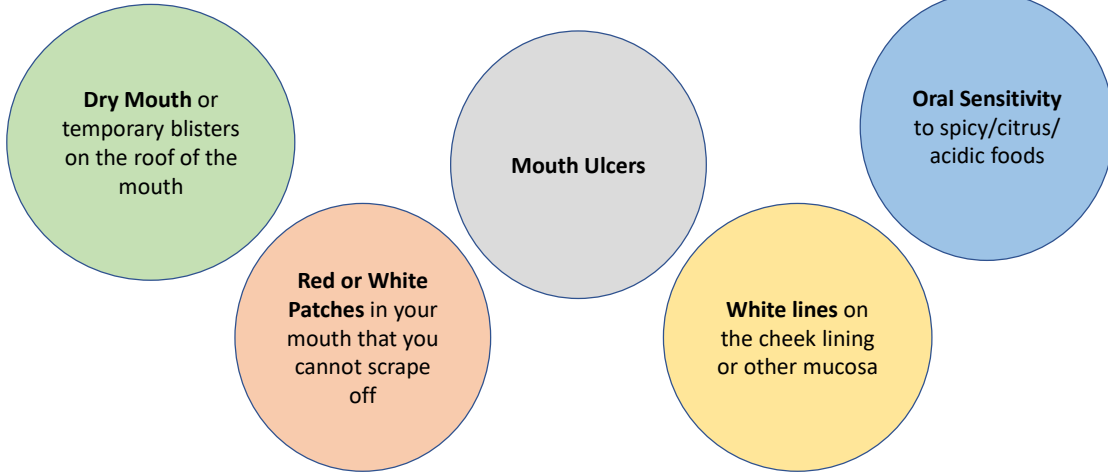
mTOR inhibitor/ Sirolimus-Induced Oral Stomatitis

- Excess circulating levels of mTOR (Mammalian target of rapamycin) inhibitors such as sirolimus may induce **painful** aphthous-like **ulcers** with well-demarcated borders and focal erythema
- **Management:** topical steroids, magic mouthwash, adjustment of sirolimus dose



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Symptoms of Oral cGVHD



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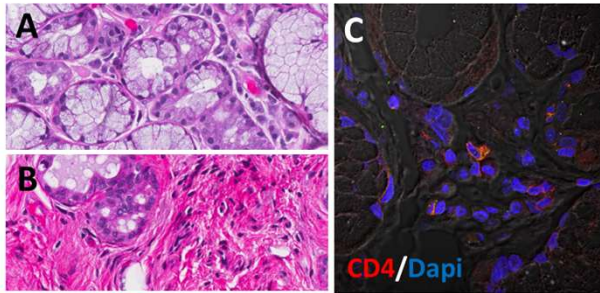
Oral Manifestations of cGVHD



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Salivary Glands are a target of cGVHD

Immune cells infiltrate salivary glands:



Salivary glands can be targeted by cGVHD without oral mucosal involvement:



Dry mouth can lead to smooth surface cavities

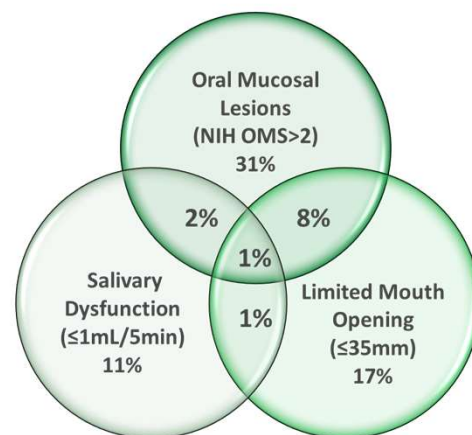
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Oral cGVHD is Three Distinct Diseases

- Oral mucosal disease
- Salivary Dysfunction
- Limited mouth opening
- Different types of oral cGVHD may need different treatment
- The underlying pathology is different
- The prognosis is different



2015 Bassim et. al. Oral disease profiles in chronic graft versus host disease. J Dent Res. 2015 Apr;94(4):547-54.a

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Oral cGVHD Diagnostic Criteria

1) **Sufficient for diagnosis:** Lichen planus-like changes



2) - or -

The presence of at least 1 distinctive manifestation (xerostomia, mucoceles, mucosal atrophy, pseudomembranes, ulcerations) **confirmed by pertinent biopsy or other relevant tests**

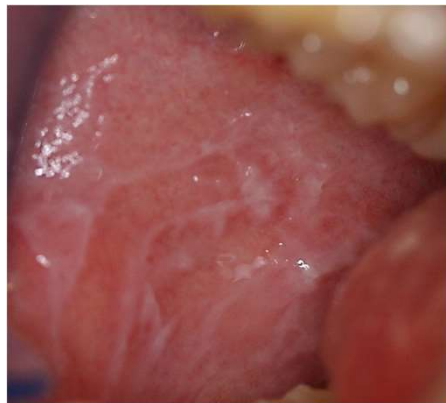
3) **The exclusion of other possible diagnoses**

- Oral infections
- Drug reaction
- New cancers

National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: I. Diagnosis and staging working group report. *Jagasia MH, Biol Blood Marrow Transplant.* 2015 Mar;21(3):389-401

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Diagnostic Features of Oral cGVHD: Lichenoid Lesion



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Distinctive Features of Oral cGVHD: Palate



Palatal hyperkeratosis



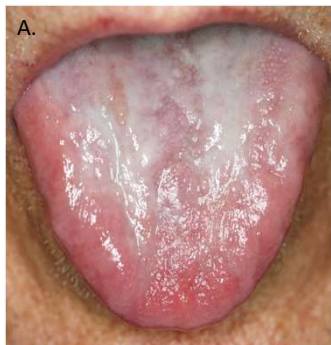
Mucocelles



Erythema

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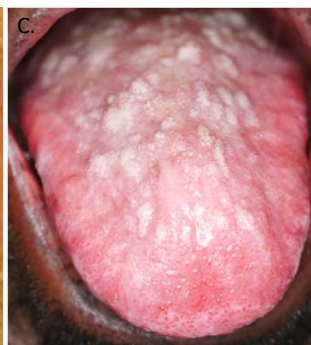
Distinctive Features of Oral cGVHD: Tongue



A. Atrophic glossitis



B. Hyperkeratosis with patchy atrophy and associated erythema



C. Patchy tufted hyperkeratosis

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Distinctive Features of Oral cGVHD: Pseudomembranous Ulcerations



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Salivary Gland cGVHD Diagnosis

- Is your mouth suddenly drier?
- Is your mouth progressively drier?
- Can you chew and swallow food without drinking water?
- Are you taking medications that can cause dry mouth?
- Did you have irradiation (total body irradiation or targeted to the head and neck) as part of your cancer therapy or transplant preparation?
- * A biopsy of the minor salivary glands is needed for formal diagnosis.

National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: I. Diagnosis and staging working group report. *Jagasia MH, Biol Blood Marrow Transplant.* 2015 Mar;21(3):389-401

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Preventive Measures

- Stringent oral / dental hygiene
- Routine dental cleaning with possible endocarditis prophylaxis
- Surveillance for infection and malignancy

TOPICAL THERAPY FOR MUCOSITIS (EARLY POST-TRANSPLANT)

- Cryotherapy
- Supersaturated calcium phosphate rinses
- Pain control (opioid analgesics)

TOPICAL THERAPY FOR ORAL cGVHD

- First Line: Dexamethasone oral suspension (0.1mg/ml) - Expected ~29-58% patient response rate¹⁻²
- Second Line: Not well established

¹A.R. Park, H.O. La, B.S. Cho, et al. Comparison of budesonide and dexamethasone for local treatment of oral chronic graft-versus-host disease. *Am J Health Syst Pharm*, 70 (2013), pp. 1383–1391. PMID: 23903476

²Treister N, Li S, Kim H, Lerman M, Sultan A, Alyea EP, Armand P, Cutler C, Ho V, Koreth J, Antin JH, Soiffer R. An Open-Label Phase II Randomized Trial of Topical Dexamethasone and Tacrolimus Solutions for the Treatment of Oral Chronic Graft-versus-Host Disease. *Biol Blood Marrow Transplant*. 2016 Nov;22(11):2084-2091. PMID: 27590106

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TOPICAL THERAPY FOR ORAL cGVHD: MOUTH SORES

- Lichen planus-like changes:
 - Steroid rinses
 - Calcineurin-inhibitor rinses
- Oral ulcers (isolated)
 - Topical steroid gel
 - Tacrolimus gel
 - Intra-lesional triamcinolone injection

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Aids for Dry Mouth

- Sugar-free gum or candies
 - Xylitol is an alcohol-based sugar that can also reduce tooth decay – look for it in your sugar-free gum or candy
 - Lemon flavors can stimulate saliva
- Frequent sips of water
- Lubricating rinses such as biotene

Xylitol



Aids for Dry Mouth: Prescriptions

- Prescription medications can stimulate saliva production from intact salivary glands
 - **Pilocarpine (Salagen)**
 - **Cevimeline (Evoxac)**
 - → May take a few weeks to show an effect
 - → Only work if you have saliva-producing cells left in your glands
 - → Not appropriate for everyone



Fluoride is Important

- Check your toothpaste: does it contain fluoride?
- Fluoride re-builds dental enamel that has mild damage
- Active Hydroxyapatite (nHA or Zn-HA) can also help rebuild tooth enamel
- Saliva washes food away from the teeth, buffers acids and bases in the mouth and returns calcium to damaged tooth enamel.
- Dry mouth = less saliva = less protection from decay! ☹️

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Aids for Reduced Opening

- Progressive gentle stretching can maintain or improve mouth opening
- Aids to help:
 - Stacked tongue depressors
 - **Physical therapy**
- In severe cases:
 - Perioral steroid injections
 - Surgical intervention



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Key Points

- See your dentist regularly after your transplant has stabilized.
- Call your dentist if you notice any problem or change in your mouth.
- Take care of your mouth by brushing and flossing every day. A healthy mouth is less likely to develop problems (but cannot prevent every challenge!).

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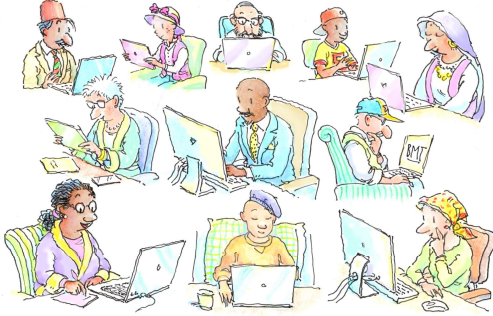
QUESTIONS?



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LET US KNOW HOW WE CAN HELP YOU



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