



Oral Mucositis

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Oral/Dental Complications

- Oral and dental care:
 - prevention and intervention
 - before, during and following cancer therapy:
- Acute complications:
 - mucositis, stomatitis, saliva (quantity, quality), taste, pain, infection
- Chronic complications:
 - Mucositis/stomatitis, pain, saliva (quantity, quality), infection, taste, tissue necrosis, caries, periodontal disease, oral function, rehabilitation
- Impact: cost of care, hospitalization, diet/nutrition, speech, esthetics, infection risk, pain, systemic health, activity of daily living, quality of life

Why does mucositis matter in the treatment of potentially fatal disease:

- Common & debilitating
- Pain, functional impact:
 - Oral intake, dysphagia, dehydration, weight loss, (need for nutritional support), speech, infection risk
- Impact on cancer therapy:
 - Dose delay, dose reduction, change in CT, treatment breaks, hospitalization, discontinuing treatment

- Increased costs

- Barasch A, Epstein JB. *Dermatol Ther* 2011;24:424-31
 - Murphy BA, Beaumont JL, Isitt J, et al.. *J Pain Symp Manage* 2009; 38:522-32.
- Scully C, Epstein JB, Sonis S. *Head Neck* 2003;25:1057-70.; *Head Neck* 2004;26:77-84
 - Gabriel DA, Shea T, Olajida O, Serody JS, Comeau T. *Semin Oncol* 2003;30:76-83
 - Rose-Ped AM, Bellm LA, Epstein JB, et al. *Cancer Nursing* 2002;25:461-467
 - Bellm LA, Epstein JB, Rose-Ped A, et al. *Supp Care Cancer*. 2000; 8:33-39

Impact of Mucositis

- Impact QOL & completion of Cancer TX
- Symptom clusters: shared pathobiology^{1,2}
- True incidence under-estimated
 - Most clinical trials toxicity not primary endpoint
 - Most clinical trails report based on PRO, NCI CTCAE³
 - Health professionals assessment of incidence & severity less than patient report⁴
 - Pain, swallowing, speech, eating, feeling ill, wght loss, overall QoL (all $p < 0.01$)⁵
- ↑ toxicity in elderly ($p = 0.04$)⁵

¹ Aprile G, Ramoni M, Keefe D. Curr Opin Supp Palliat Care 2009;3:50-4

² Nishimura N, Nakano K, Ueda K. Support Care Cancer 2011

³ Saed ED. Ind J Med Res 2011;134:413-8

⁴ Bateman E, Keefe D. Semin Oncol 2011;38:358-61

⁵ Liu Y, Guan X, Zhu G. Oral Oncol 2012

Outcomes of Oral Mucositis in HNC

- 103 consecutive HNC, chart review
- 81% males; 80% Caucasian; average 66 Gy
- Mucosal ulcers associated with:
 - ↑ topical & opioid analgesics ($p < 0.001$)
 - ↑ weight loss ($p = 0.02$)
 - ↑ feeding tubes ($p = 0.07$)
 - RT delay 6% vs 0% without ulcers

Elting L, Cookelsy C, Garden A. Supp care Cancer 2005;13:443

Outcomes of Oral Mucositis in HNC

- Retrospective review 204 consecutive pts treated 2002, single center
- Mucositis 91%
 - 66% severe (gr 3-4); severity & duration ↑ with RT+CT
- OM more common:
 - combined CT/RT (OR 7.8) $p=0.02$,
 - altered fractionation RT (OR 6.3, $p=0.03$)
- Severe mucositis:
 - associated with severe pain (54% v 6%, $p<0.001$)
 - weight loss >5% (60% v 17%, $P<0.001$)
- OM associated with ↑cost: \$1,700 (mild mucositis) to \$6,000 (severe mucositis)
 - Elting LS, Cooksley CD, Chambers MS, Garden AS. Int J Radiat Oncol Biol Phys 2007;68:1110-20

Mucositis in HNC: morbidity & resource utilization

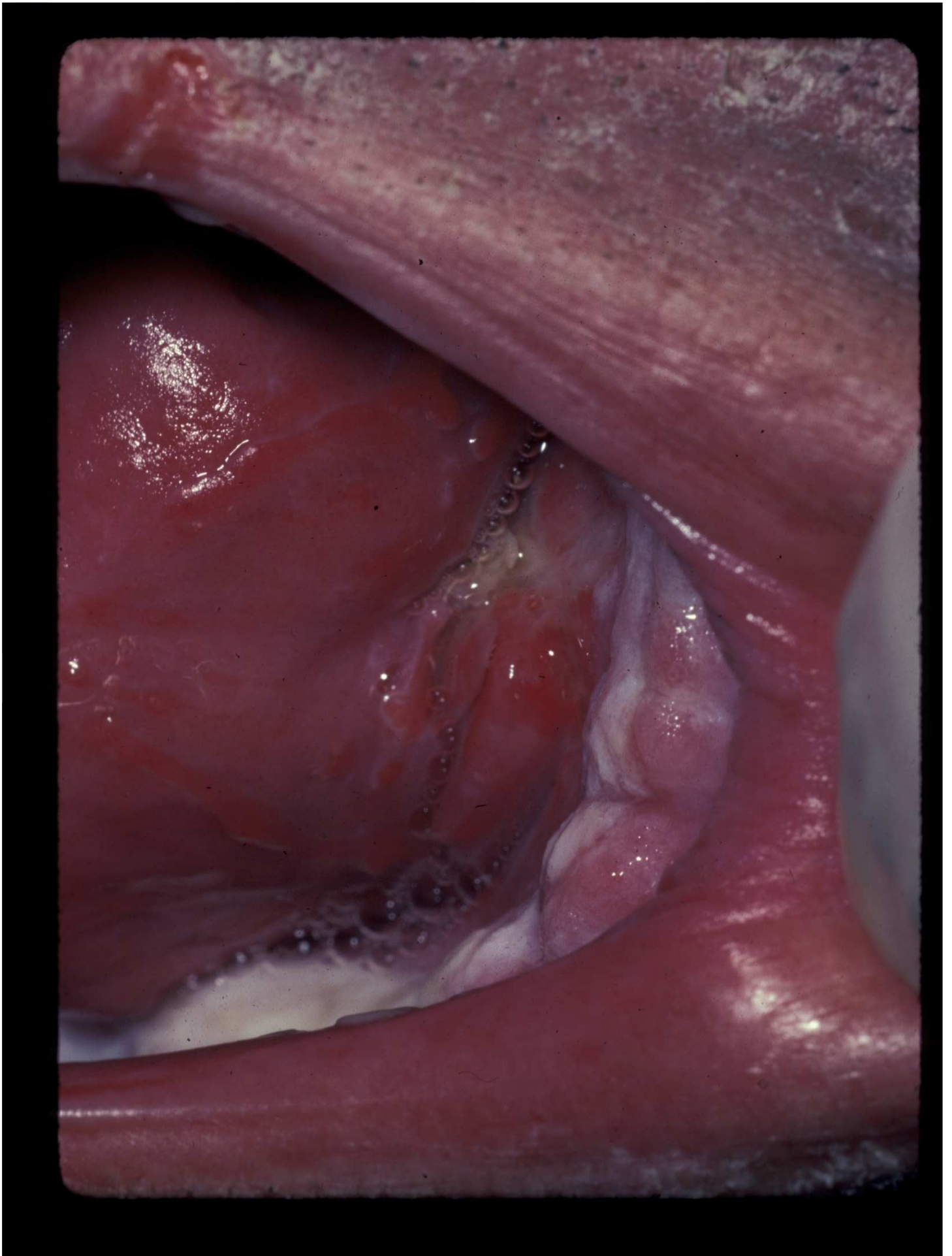
- 75 pts, 6 centers; RT+CT 67%, 33% RT alone
- 76% mouth/throat soreness, opioids in 85%
- Mucositis pain affects function despite opioids
- Resource utilization:
 - tube feeding 51%
 - hospitalization 31% (30% recorded due to mucositis), average LOS 4.9 days
- Murphy BA, Beaumont JL, Isitt J, Garden AS, Gwede CK, et al. J Pain Symp Manage 2009; 38(4):522-32.

Oral Mucositis: Resource utilization in HNC

- Prospective study: 69 pts; 75% OSCC or OPC; 49% IMRT with chemo; 72% male
- 90% mouth & throat soreness (MTS) ≥ 2 ; only 6% no MTS
- Patients with MTS:
 - non-prophylactic G-tubes 25%
 - unplanned office visits 37%
 - hospitalization 18%

• Keefe D et al. Supp Care Cancer 2007:395







Survey of Professional Burden of Mucositis in HNSCC

- 50 Rad Onc & 51 Oncol Nurses, tx average of 6-12 HNC pts/mo
 - Mean target RT 72 Gy; 92% developing mucositis, 71% Gr 2 or 3 (WHO), 16% Gr 4
 - Rad Onc spend 7.2hrs, nurses 12.1 hrs managing mucositis, increasing time as mucositis increased
- Xiao X, Barron RL, Mautner B et al. J Support Care Cancer 2010

Targeted Agents, immunotherapy & oral complications

- EGFRi (cetuximab): erythema, pain; ↑mucositis with cytotoxic TX, anterior mucositis, in field/ out of field mucositis/dermatitis; taste change
- Anti-VEGF (bevacizumab): bleeding, delayed healing, osteonecrosis; taste
- Tki (sunitinib/sorafenib): osteonecrosis, lichenoid mucositis; taste
- mTORi (tacro-, siro-, evero-, ridaforo-limus): stomatitis (aphthous-like), pain; lichenoid; taste
- Immunotherapy
- Different pathobiology, different management

MASCC/ISOO Evidence-Based Clinical Practice Guidelines for Oral Mucositis (2014)

- Recommend for prevention:
 - Cryotherapy 30 mins bolus 5-FU CT (level evidence II)
 - KGF-1-palifermin for high-dose CT + TBI in auto-HSCT (level evidence II)
 - LLLT ($2\text{J}/\text{cm}^2$; 2 secs/point) for HSCT with high dose CT, with or without TBI (level evidence II)
 - Benzydamine HNC for standard dose RT (level evidence I)
- Recommend for Treatment:
 - PCA for oral pain in HSCT (level evidence II)

MASCC/ISOO Evidence-Based Clinical Practice Guidelines for Oral Mucositis (2014)

- Suggestions in favor: Prevention:
 - Oral care protocols (level of evidence III)
 - Oral cryotherapy high dose melphalan HSCT with/without TBI (level of evidence III)
 - LLLT (wavelength ~633nm) HNSCC Tx RT with/without CT (level of evidence III)
- Suggestions for Pain
 - Transdermal fentanyl conventional & high dose CT in HSCT with/without TBI (level of evidence III)
 - 2% morphine mouthrinse HNSCC RT (level of evidence III)
 - 0.5% doxepin mouthrinse for mucositis pain (level of evidence IV)

MASCC/ISOO Evidence-Based Clinical Practice Guidelines for Oral Mucositis (2014)

- Recommendations against (prevention):
 - Antimicrobials: BCoG, PTA, chlorhexidine [HNSCC], chlorhexidine, Isegran [RT, HSCT] (Level of evidence II)
 - Sucralfate CT/RT (Level of evidence I); HNSCC RT+CT (Level of evidence II)
- Recommendation against use (treatment):
 - Sucralfate CT (Level of evidence I); RT (Level of evidence II)
 - IV glutamine CT with/without TBI HSCT (Level of evidence II)

MASCC/ISOO Evidence-Based Clinical Practice Guidelines for Oral Mucositis (2014)

- Suggestions against (Prevention):
 - Chlorhexidine in RT (Level of evidence III)
 - GM-CSF mouthrinse in Auto- allo-HSCT (Level of evidence II)
 - Misoprostol mouthrinse in RT (Level of evidence III)
 - Systemic pentoxifylline in HSCT (Level of evidence III)
 - Pilocarpine in HNSCC RT (Level of evidence III), HSCT with/with TBI (Level of evidence II)



Trends in Oncology Therapy impacting Oral Mucositis

- Increasing toxicity in HNC
- Increasing use of targeted therapies
- Decreasing toxicity in Hematopoietic Stem Cell Transplant:
 - Mini-transplant
 - Reduced intensity conditioning
 - Changing medications in conditioning
 - Kepivance first FDA approved intervention
- Oral care in cancer therapy, developing interventions

Mucositis and QOL

- Impact QOL & completion of Cancer TX
- Symptom clusters: shared pathobiology^{1,2}
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Advances in Cancer Therapy:

Targeted Therapy/Immunotherapy

Personalized Medicine

- New drug or TX presents new toxicity(s)
- Understanding mechanism of action is key to management
- Multimodality TX
- Symptoms clusters
- Toxicity assessment: validated PROs, scales
- Antitumor effect must not be compromised by TX of toxicity
- Risk prediction (personalized medicine)

Mucositis

A fish hook lodges in my throat.

Splittle, kindergarten paste, thickens everything-even vision.

Mouth packed with sores and blisters, swollen ulcerated tongue.

Topside sandpapered with number 7 coarsest grade.

Taste buds, saliva glands seared.

Cool water, corrosive acid now.

The tongue rests; the teeth become enemies now.

Coiled steel razored wire stop dentate prison walls.

Only moans escape my lips. I cannot eat or speak.

Inside a howl festers.

Pain lengthens time.

-Anita Hart Balter