Summary of 2004 MASCC* Guidelines for the Treatment of Oral and GI Mucositis

**Oral Mucositis: Recommendations/Suggestions**
- Oral care protocol/education to reduce severity of mucositis (suggested)
- Midline radiation blocks and 3-dimensional radiation treatment (RT) to reduce mucosal injury (recommended)
- Oral cryotherapy (ice chips) for 30 minutes for patients receiving bolus 5-FU (recommended)
- Low-level laser therapy in patients receiving high-dose chemotherapy or chemoradiotherapy before stem cell therapy – provided technology and training are available (suggested)
- Use of a soft toothbrush that is replaced on a regular basis (recommended)

**Not Recommended**
- Chlorhexidine (Peridex) to prevent oral mucositis in patients with head and neck cancer undergoing RT or to treat established oral mucositis
- Routine use of acyclovir (Zovirax)/analogs to prevent mucositis except in seropositive patients for herpes simplex virus with high risk for reactivation
- Sucralfate (Carafate) or antibiotic lozenges should not be used to prevent radiation-induced oral mucositis

**Upper GI Mucositis: Recommendations/Suggestions**
- Ranitidine (Zantac) or omeprazole (Prilosec) for the prevention of epigastric pain after treatment with Cytoxan MTX and 5-FU or 5-FU + folinic acid (recommended)
- Amifostine (Ethyol) to reduce esophagitis induced by chemotherapy or RT in patients with Non Small Cell Lung Cancer

**Lower GI/Pelvic Mucositis: Suggestions**
- Sulfasalazine (Azulfidine) 500mg orally bid for patients receiving external beam radiation therapy to the pelvis plus rectal steroid enemas for advanced proctitis (suggested)
- Sucralfate (Carafate) enemas for the management of chronic RT-induced proctitis in patients with rectal bleeding (suggested)

The panel recommends that Kepivance (Palifermin) be used for the prevention of oral mucositis in patients receiving intense chemotherapy and RT for hematologic cancers or undergoing hematologic stem-cell transplantation but not for other treatments

* Multinational Association of Supportive Care in Cancer
1 Recommendations of the 2005 MASCC panel on oral mucositis.
CTCAE* V 4.0

Gastrointestinal Disorders

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade</th>
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<tbody>
<tr>
<td>Mucositis oral</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
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<tr>
<td>Asymptomatic or mild symptoms; intervention not indicated</td>
<td>Moderate pain; not interfering with oral intake; modified diet indicated</td>
<td>Severe pain; interfering with oral intake</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
<td>Death</td>
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Definition: A disorder characterized by inflammation of the oral mucosal.


**General Guidelines for Oral Care in the Treatment of Oral Mucositis**

1. Tailor an oral care program to the individual patient

2. Education: physicians, nursing staff, patients, and caregivers

3. If feasible, establish formal protocols and guidelines that are adaptable, appropriate and efficient for:
   - Adults
   - Children
   - Elderly
   - Patients with cognitive or sensory impairment

4. Before cancer therapy, optimize oral health:
   - Consider evaluation by dental professional
   - Eliminate/reduce oral infections, periodontal disease, gingivitis, deep caries/ pulp infections
   - Remove/modify potential sources of trauma/irritation Sharp teeth/fractured restorations
   - Poorly fitting or broken removable dentures
   - Orthodontic brackets or wires
   - Reduce risk for secondary infection
5. Encourage good, basic oral care:
   - Maintenance of dental and periodontal health throughout treatment and recovery
   - Dental plaque removal
   - Mechanical removal: tooth brushing, flossing, cleaning aids
   - Antibacterial rinses
   - Bland oral rinses

6. Viral and fungal prophylaxis (immunosuppressed patients) to reduce risk for infectious complications of mucositis.
   - Prevention of reactivation of herpes simplex virus
   - Prevent oral colonization by yeast/fungi

7. Prevention of trauma and irritation
   - Normal oral function
     - Soft-textured foods (such as puddings, mashed potatoes, cream of wheat), serve food at room temperature with avoidance of very hot foods
     - Oral habits-cheek/lip biting or chewing
     - Mouth breathing
   - Avoid certain products/medications
     - Oral rinses or medications containing alcohol
     - Highly flavored products (mint, cinnamon)
     - Minimal viscosity

8. Denture care
   - Adjust to prevent trauma/irritation
   - Instruct patients
     - Minimal use of dentures from start of therapy
     - Clean dentures daily
Tiered Strategy for the Management of Oral Mucositis Pain

**Foundation Level Care**
Basic oral hygiene + bland rinses + trauma prevention

Persistent or Increased Oral Mucositis Pain

**Level 1 Care: Mild Pain**
Foundation level care + Topical anesthetics + Mucosal surface protectants (such as “magic mouthwash” – a solution with viscous lidocaine, Maalox, benadryl with or without carafate) + Adjuvant drugs + Nonpharmacologic pain management

Persistent or Increased Oral Mucositis Pain

**Level 2 Care: Mild to Moderate Pain**
Foundation level care + Level 1 care + Non-opioid analgesics

Persistent or Increased Oral Mucositis Pain

**Level 3 Care: Moderate Pain**
Foundation level care + Level 1 and 2 care + Opioids for moderate pain + Management of opioid side effects
Risk Factors for the Development of Oral Mucositis (Stomatitis)

1. Seropositive for herpes simplex virus or history of flare
   - The use of prophylactic acyclovir (Zovirax) or valacyclovir (Valtrex) should be mandatory for patients at high risk for reactivation [patients undergoing bone marrow transplant (BMT) or profound myelosuppression]

2. Radiation therapy as follows:
   - Concurrent or sequential chemotherapy/radiation
   - Radiation therapy to head and neck region above 40-50 Gy
   - Total body irradiation
   - Radiation to major salivary glands produces decreased salivation and xerostomia
   - The severity of mucositis caused by radiation is dependent on total dosage and length of treatment

3. Patients undergoing transplantation or receiving chemotherapy for lymphoma

4. Chemotherapy-commonly used agents: severity dependent on total dosage and schedule of administration
   - Alkylating agents: cyclophosphamide (cytoxan)
   - Anthracyclines: doxorubicin (adriamycin), epirubicin (ellence), liposomal doxorubicin (doxil)
   - Antimetabolites: cytosine arabinoside (ara-C), 5-FU, MTX, capecitabine (xeloda)
   - Antitumor antibiotics: bleomycin (blenoxane), etoposide (VP-16), mitoxantrone (novanthrone)
   - Taxanes: docetaxel (taxotere), paclitaxel (taxol)
   - Vinca alkaloids: vinblastine (velban), vinorelbine (navelbine)

5. Patient factors:
   - Patients who smoke
• Patients with history of poor oral hygiene
• Acute or chronic periodontal disease
• Pediatric age/older age
• Female gender
• Poor nutritional status
• Immunosuppression
• Alcohol consumption

Key Points: Management of Oral Mucositis (Stomatitis, OM) and GI Mucositis

1. Oral mucositis is a common, painful side effect of chemotherapy and radiation therapy noted by varying degrees of mucosal erythema, atrophy, and ulceration. It has a profound negative impact on patient Quality of Life (QOL) cost of care, and the success of cancer therapy.

2. Mucositis is not limited to the mouth but extends throughout the entire gastrointestinal tract and it probably affects all other mucosal surfaces, such as those of the nasal passages, eyes, and genitourinary and respiratory tracts.

3. Mouth pain and ulceration characterize oral mucositis, symptoms of esophageal mucositis include retrosternal chest pain and odynophagia, and in the small intestine there is abdominal pain, bloating and diarrhea. Mucositis in the distal bowel leads to pain on defecation and bloody mucous stool. Mucositis can also cause nausea, fatigue, malnutrition, systemic infection and death.

4. In several studies of hematologic stem cell transplantation patients (HSCT) 42-50% of patients rated OM as the most severe and debilitating complication.

5. OM when present in HSCT treatment or treatment for head or neck cancer is associated with more days of fever, increased risk of significant infection, higher utilization of TPN, more days of narcotic usage and longer hospital stays. Patients undergoing HSCT who developed grade 3-4 OM had a mortality rate of 40% whereas those with little or no OM had a mortality of only 1%.

6. Kepivance (Palifermin), a recombinant human keratinocyte growth factor, has only been approved for the prevention of OM in patients receiving intensive chemotherapy and radiotherapy for hematologic cancers and HSCT but not for other treatments. There is no generally proven effective agent for prophylaxis of oral mucositis and no “gold standard” exists for therapy.

7. Grade 3-4 OM or GI mucositis is associated with:
• 3-fold increase in risk for chemotherapy dose reduction
• 3-fold increase in risk for infection-related death during myelosuppression
• 10-fold increase in use of TPN and fluids
• 10-fold increase in use of opioid analgesics
• 2-fold increase in ER visits
• Additional 7 days of hospitalizations per episode
• Incremental cost of >$3,500 per episode

References:


10. NCCN Practice Guidelines in Oncology v.2.2009 – Prevention and Treatment of Cancer-Related Infection