Oral Mucositis: Addressing the Causes, Challenges, and Clinical Management

CARRIE F. DALY, MS, RN, AOCN®, and ANNETTE M. QUINN, MSN, RN

From Rush University Medical Center, Chicago, Illinois, and University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

Author's disclosures of potential conflicts of interest are found on page 2 and at the end of this article.

Correspondence to: Carrie F. Daly, MS, RN, AOCN®, Rush University Medical Center, Department of Radiation Oncology, Chicago, IL 60612. E-mail: carrie_f_daly@rush.edu; Annette M. Quinn, MSN, RN, University of Pittsburgh Medical Center, Radiation Oncology, 5230 Centre Ave, Pittsburgh, PA 15232. E-mail: quinnae@upmc.edu

Abstract

Oral mucositis remains one of the most painful and debilitating side effects of cancer therapy. A working knowledge of the risk factors for oral mucositis and oral cavity assessment protocols is essential to early identification of signs and symptoms in high-risk patients. The use of evidence-based guidelines and patient education will facilitate symptom management and supportive care strategies designed to avoid reductions, delays, or discontinuation of cancer treatment.

J Adv Pract Oncol 2011;2(Suppl 1):4–13

Despite significant advances in the treatment of cancer during the past decade, oral mucositis (OM) remains one of the most painful, debilitating, and menacing side effects of cancer therapy. An estimated 400,000 patients develop oral complications related to cancer therapy each year. Oral mucositis poses a significant threat to patients by causing treatment delays and dose reductions, increasing their risk for local and systemic infections, and impairing their quality of life (American Cancer Society, 1999). In addition, OM increases health-care delivery costs by at least $1,700 per patient, depending on its severity (Elting et al., 2003). Advanced practitioners play an important role in assessing oral cavity changes and using valid and reliable tools to predict the risk for OM and evaluate the effectiveness of protocols for its prevention and treatment.

Pathogenesis

Oral mucositis is characterized by inflammatory lesions of the oral cavity caused by high-dose cancer therapy. These lesions result from a complex interaction between local tissue damage, the oral environment, the level of myelosuppression present, and the patient's genetic predisposition. Until fairly recently, OM was thought to arise solely from epithelial injury. The nonspecific effects of chemotherapy and radiation on the rapidly proliferating cells of the basal epithelium were believed to have a direct inhibitory effect on DNA replication and mucosal cell proliferation. This was hypothesized to lead to a reduced renewal capability of the basal epithelium, resulting in atrophy, collagen breakdown, and eventual ulceration. The ulcerations in turn served as portals for microorganisms that promoted further tissue injury (Sonis, 2004a). However, recent research performed at the cellular level

has shown that a multitude of molecular events are responsible for OM beyond direct damage to the epithelium alone. In addition, the submucosa has been shown to play a vital role in the damage to and healing of the oral epithelial lining (Sonis, 2004a).

In 2004, Sonis proposed a five-phase model for the pathobiology of OM (Sonis, 2004a). The initiation phase begins within seconds of chemotherapy or radiation therapy and is characterized by the release of reactive oxygen species (ROS) by the basal epithelium. These free radicals, which are a natural by-product of oxygen metabolism and play an important role in cell signaling, promote a cascade of injurious molecular events. The ROS surge leads to trauma of the cells and blood vessels in the submucosa. Although the mucosa still appears normal on examination, the events that ultimately lead to ulceration are already triggered.

The signaling phase is characterized by ROS-induced apoptosis, or programmed cell death, which further contributes to the cascade of injurious events. Breaks in DNA strands result in the activation of several transduction pathways that activate factors such as p53 and nuclear factor-κB (NF-κB). NF-κB is involved in the upregulation of up to 200 genes, many of which affect mucosal toxicity (Sonis, 2004a, 2004b). The upregulation of these genes results in the production of large quantities of cytokines, including tumor necrosis factor–α (TNF-α), interleukin (IL)-1β, and IL-6. These proinflammatory cytokines mediate inflammation and dilate vessels, possibly increasing the concentration of chemotherapeutic agents at the site of injury. They are major contributors of injury, and increased levels correlate with nonhematologic toxicities induced by chemotherapy and radiation. Effective pharmacologic blockade of their production is associated with less frequent and severe mucositis in experimental models (Sonis et al., 2007). In addition, the signaling phase involves the activation of metalloproteinases that target fibroblasts, thus leading to the destruction of the collagenous subepithelial matrix and the breakdown of the epithelial basement membrane (Skulason, Holbrook, & Kristmundsdottir, 2009).

In the amplification phase, many of the proinflammatory cytokines produced during the signaling phase stimulate further injury through positive feedback loops. For example, TNF-α releases additional cytokines creating a feedback loop that magnifies the biological effects. These feedback loops increase tissue injury and prolong damage by continuing to provide signals for days after the original chemotherapeutic or irradiation insult. There may be some mucosal erythema at this stage, but generally the tissue integrity remains intact and patients have few symptoms (Sonis, 2004a).

In the ulceration phase, the epithelial integrity breaks down and lesions develop. These lesions are typically deep and painful, allowing for both gram-positive and gram-negative bacterial colonization. The colonizing bacteria further increase injury by shedding cell wall products that penetrate into the submucosa, causing the release of additional cytokines.

The healing phase begins when signals from the extracellular matrix lead to the proliferation and differentiation of bordering epithelium cells that fill in ulcerations (Sonis, 2004a). Most cases of OM heal spontaneously. Of all the stages of mucositis, the healing phase is the least understood. Even after the full replenishment of the epithelium, the structure of the reconstituted submucosa is not identical to its state prior to mucotoxic damage (Sonis, 2004a; Fischer et al., 2003).

Risk Factors

The incidence of OM varies greatly among cancer patients and is generally associated with treatment modality rather than tumor type. Patients receiving high-dose chemotherapy, radiation therapy, or chemoradiation therapy delivered to the head and neck region are at the highest risk for OM (Silverman, 2007). The risk for developing mucosal injury increases with the number of chemotherapy cycles and previous episodes of chemotherapy-induced mucositis. Chemotherapeutic agents associated with the highest risk for OM include fluorouracil (5-FU), cyclophosphamide, methotrexate, and cisplatin. Drug dose, schedule, and route of administration are key contributing factors to OM occurrence, with weekly regimens associated with increased risk (Kostler, Hejna, Wenzel, & Zielinski, 2001). In general, the incidence of OM in cancer patients undergoing chemotherapy at standard doses is 40% to 60% (Rubenstein et al., 2004). Oral mucositis occurs in nearly all patients who receive high-dose myeloablative therapies (Epstein & Schubert, 2003) and in those receiving chemoradiation therapy for head and neck cancer (Trotti et al., 2003).

Patient-related risk factors for OM are listed in

Table 1. The severity and duration of OM are related to the number of risk factors present. In general, younger patients are at increased risk due to a rapid epithelial mitotic rate, or the increased presence of epidermal growth factor receptors. The elderly are more prone to mucositis, in part, due to their physiologic decline in renal function. Women are at a significantly higher risk than men (86% vs. 60%), and their OM is generally more severe and longer in duration (Sonis et al., 1999). Poor oral hygiene and ill-fitting dental prostheses may worsen OM, but can be managed with the elimination of periodontal disease, the extraction of offending teeth, and the use of oral care protocols. In addition, patients who are nutritionally compromised are at risk for poor mucosal regeneration, which may contribute to the development of severe mucositis.

Table 1. Risk Factors for Oral Mucositis

Patient-related risk factors
Neutropenia
Poor oral hygiene
Impaired salivary function
Use of alcohol and tobacco
Poor nutrition
Age (children and elderly)
Genetic factors
Gender
Treatment-related risk factors
Specific chemotherapy
Chemotherapy dose
Regimen
Radiation therapy plus chemotherapy
Concomitant medications

Note. Information from Sonis et al. (1999), Barasch et al. (2003), and Brown (2010).

Consequences

Patients with OM are at increased risk for impaired quality of life. Severe pain, which may require the use of opioids, coupled with the inability to chew or swallow, often leads to dehydration, malnutrition, anorexia, cachexia, and the need for a feeding tube or total parenteral nutrition. This, in turn, prolongs hospitalization, reduces quality of life, and increases medical costs. Patients with OM and its sequelae often become depressed, agitated, and fatigued. In addition, the ulcerations associated with OM may lead to systemic infection with downstream effects including anti-infective use, a delay in treatment, hospitalization, increased medical costs, and ultimately, the potential for suboptimal long-term survival (Elting et al., 2003; Scully, Sonis, & Diz, 2006). Oral mucositis is recognized as a key dose-limiting toxicity of cancer treatments that include mucositis-inducing agents (McGuire, Correa, Johnson, & Wienandts, 2006).

The financial burden associated with OM can be significant. Severe ulcerative mucositis has been shown to increase treatment costs by as much as $43,000 compared with less severe mucositis (Sonis et al., 2001). Results from an analysis of a phase III trial comparing the keratinocyte growth factor palifermin (Kepivance) with placebo showed that the daily hospital rate for patients treated with stem cell transplant including total-body irradiation and placebo was $2,834. The downstream consequences of OM such as bacteremia, febrile neutropenia, intubation, and total parenteral nutrition raised the cost to $4,663 per day (Elting et al., 2004, 2007).

Mucositis Symptoms

Patients typically present with erythema of the oral mucosa followed by dryness of the mouth and a burning sensation in the lips. Ulcerations are mostly seen on the movable mucosa of the buccal mucosa and the lateral and ventral surfaces of the tongue while the hard palate and the gingiva appear to be resistant. Chemotherapy-induced OM lasts approximately 1 week and heals spontaneously in approximately 21 days (Sonis, 2000).

Pain is a hallmark symptom of OM and most often the first indicator of its development. It is the most distressing symptom noted by patients and often requires administration of opioid analgesics as well as local and topical agents (Wojtaszek, 2000). Pain triggers a symptom cluster, including fatigue and depression, which can have a detrimental effect on quality of life. In addition, excessive pain may result in a delay, reduction, or cessation of chemotherapy. It is critical that advanced practitioners monitor pain response in patients with OM using validated scales and provide patient education regarding the undesired side effects of opioids, including constipation, nausea, and sedation, to achieve a balance between pain relief and quality of life.

Oral Cavity Assessment

The first step in evaluating OM is to complete a baseline assessment of the patient's oral cavity. This should include identifying any changes in the oral mucosa, assessing for poor dentition, and recognizing any areas with signs of infection. Once the

patient has commenced treatment, weekly examination of the oral cavity, including the lips, tongue, oral mucosa, and gingival region, is critical. This objective assessment should document the presence of erythema, lesions, or any edema, and should be supported by a subjective assessment evaluating pain, sensitivity, and dryness. It is also important to perform a functional assessment evaluating the patient's voice, chewing, and swallowing (Bruce & Quinn, 2007; Cawley & Benson, 2005).

Tongue blades and a good light are invaluable tools for oral cavity assessment. Tongue blades can be used to gently move the soft tissue (ie, tongue) and allow complete inspection of the areas of interest. Ill-fitting dentures can cause more pain and exacerbate OM; they should be removed for a thorough oral examination. A head mirror with headlights and a penlight are the most useful tools in visualizing the oral cavity (Cawley & Benson, 2005).

The lips, buccal mucosa, and the gingivobuccal sulcus should be inspected first, followed by the teeth and alveolar areas. The dorsal and ventral surfaces of the tongue, floor of the mouth, and the gingivobuccal sulcus should be then be examined. It is effective to have the patient say "ahh" and open the mouth wide to assist in observing the back of the throat. After the hard palate is visualized, the tongue should be inspected for immobility and deviation. Typically ulcerative lesions on the mucosal surface bleed when touched. The signs of OM should be assessed or a differential diagnosis established before every chemotherapy administration and during follow-up; see Figure 1 (Cawley & Benson, 2005; Brown, 2010).

Toxicity Assessment Scales

Performing regularly scheduled oral assessments with a valid and reliable rating scale specifically designed for OM promotes more effective monitoring of OM progression and the use of appropriate measures to ease patient discomfort and distress (see Table 2). Unfortunately, a lack of a standardized scoring system for OM has hampered high-quality research in this field. The

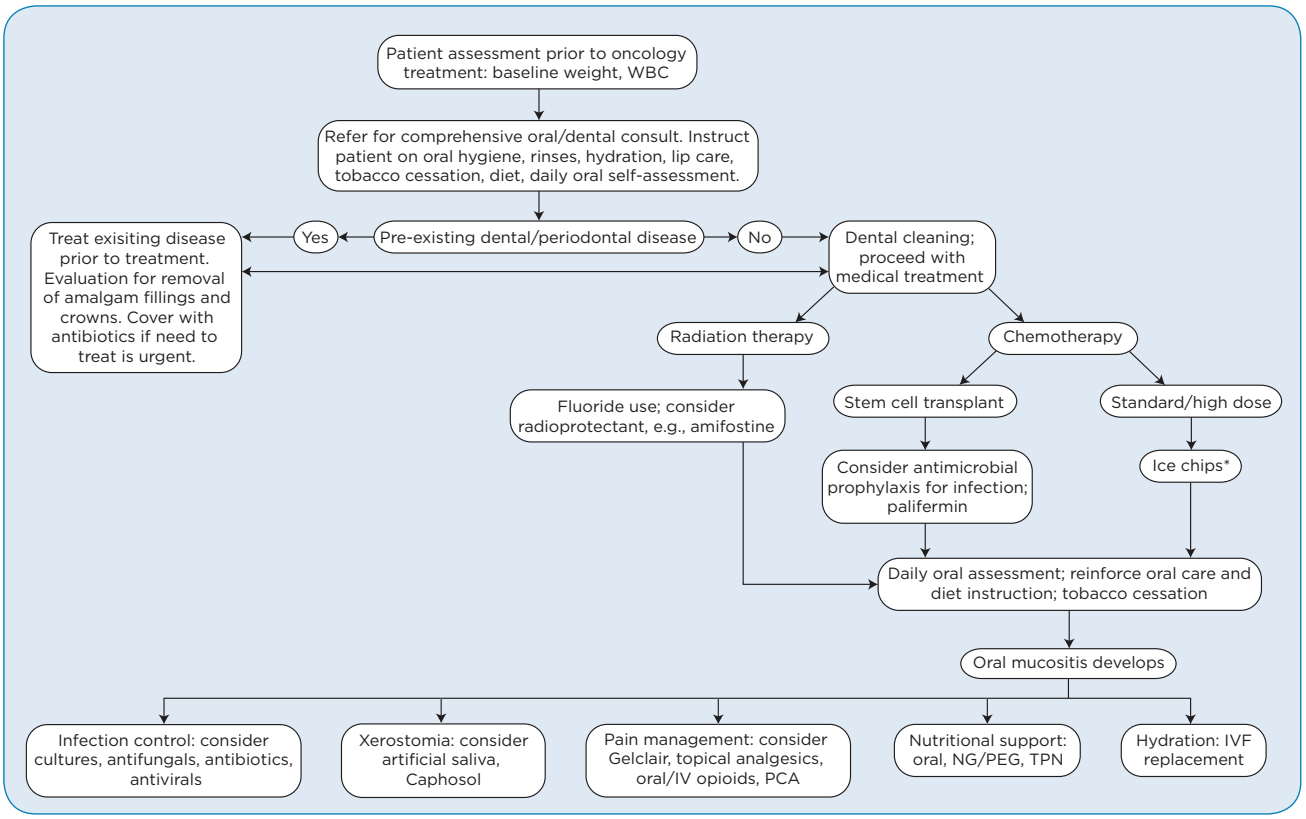

Figure 1. Oral assessment and management (Bruce & Quinn, 2007). IVF = intravenous fluids; NG/PEG = nasogastric/percutaneous endoscopic gastrostomy; PCA = patient-controlled analgesia: TPN = total parenteral nutrition. Figure reprinted with the permission of author.
*Ice chips x 30 minutes with bolus short-acting chemotherapy.

World Health Organization (WHO) scale, which is the most widely used instrument, assesses all three components of mucositis: the anatomical location of the lesions, objective mucosal changes (redness and ulceration), and functional outcomes (ability to eat); see Table 3.

National Cancer Institute Common Toxicity Criteria (NCI-CTC) for mucositis have been developed for patients receiving radiation therapy, chemotherapy, and conditioning regimens for bone marrow transplant (see Table 4). The NCI-CTC scale for radiation-induced mucositis is based solely on objective findings, whereas the scale for chemotherapy and bone marrow transplant–associated mucositis includes elements such as difficulty with swallowing, IV fluid support, and intubation.

The Oral Mucositis Assessment Scale was developed and tested by a panel of experts for the purpose of investigative applications (see Table 5). The panel included nurses, dental hygienists, physicians, dentists, statisticians, and representatives from the pharmaceutical and biotechnology industries. This scale scores objective and subjective findings separately. Primary indicators of mucositis include the degrees of ulceration and redness measured in specific sites in the mouth. Secondary indicators included oral pain, difficulty swallowing, and the ability to eat as assessed by the patient.

Table 2. Commonly Used Mucositis Assessment Scales

Assessment	Measures
World Health Organization Oral Toxicity Scale	OM appearance and difficulty swallowing
National Cancer Institute Common Toxicity Criteria	OM appearance only; standardizes adverse events in clinical trials
Oral Mucositis Assessment Scale	Records anatomical distribution of oral lesions; no functional assessment
Oral Assessment Guide	Anatomical and functional assessment

Note. OM = oral mucositis.

Evidence-Based Management

Ongoing assessment, monitoring, evidence-based interventions, and patient education on oral hygiene are essential to optimizing OM management (Eilers & Epstein, 2004; Cawley & Benson, 2005; Kwong, 2004). While these measures will not prevent OM, they can reduce the duration and severity of the toxicity. A study involving pediatric patients compared the use of specific oral care protocols with general oral care. Results showed that preventative oral care consisting of patient education and oral rinses effectively alleviated OM in children with cancer (Cheng, Chang, & Yuen, 2004).

Many agents have been investigated for the treatment and/or prevention of OM, including antimicrobials, anti-inflammatory agents, and granulocyte-macrophage colony-stimulating factors. However, the quality of evidence has been variable and no single intervention has been shown unequivocally to be effective. Evidence-based guidelines from the Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology (MASCC/ISOO) are an important tool in OM management. Although the guidelines offer limited choices for prevention and management, they reflect several therapeutic advances since their original publication in 2004 (see Table 6).

Table 3. World Health Organization Oral Toxicity Scale

Grade	Manifestation
0	None
1	Erythema and soreness No ulcers May include buccal mucosal scalloping with/without erythema
2	Ulcers Able to eat a solid diet Ulcers with/without erythema
3	Ulcers Requires a liquid diet Subject not able to eat solids Ulcers with/without erythema
4	Ulcers Not able to tolerate solid/liquid diet Requires IV or feeding tube Mucositis to the extent that alimentation is not possible Liquids tolerated for medication use only A subject's ability to eat must be determined based on the extent of the subject's mucositis

Note. Based on information from the World Health Organization (1979).

Table 4. National Cancer Institute Common Toxicity Criteria

Grade	Clinical examination	Functional/symptomatic assessment
1	Erythema of mucosa	Asymptomatic or mild symptoms; intervention not indicated
2	Patchy ulcerations or pseudomembranes	Moderate pain; not interfering with oral intake; modified diet indicated
3	Confluent ulcerations or pseudomembranes; bleeding with minor trauma	Severe pain; interfering with oral intake
4	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences	Life-threatening consequences; urgent intervention indicated
5	Death	Death

Note. Based on information from the National Cancer Institute (2010).

MASCC/ISOO guidelines recommend the use of palifermin in patients with hematologic malignancies who are receiving high-dose chemotherapy and total-body irradiation with autologous stem cell transplant, at a dose of 60 mg/kg per day for 3 days prior to conditioning treatment and for 3 days posttransplant for the prevention of OM (Keefe et al., 2007). The agent helps to stimulate the replication and maturation of epithelial cells, and has been shown to reduce the severity and duration of mucositis in patients with hematologic malignancies receiving high-dose chemotherapy and total-body irradiation with autologous stem cell transplant. Phase III trials conducted by Spielberger and colleagues showed that palifermin administered 3 days before transplant and 3 days after transplant reduced the incidence of grades 3 and 4 mucositis (63% with palifermin vs. 98% with placebo; Spielberger et al., 2004). In addition, the duration of grades 3 and 4 OM was reduced from 9 to 6 days with the use of palifermin (Spielberger et al., 2004).

Table 5. Oral Mucositis Assessment Scale Scoring

Location	Ulceration	Erythema
Lip		
Upper	0, 1, 2, 3	0, 1, 2
Lower	0, 1, 2, 3	0, 1, 2
Buccal muosa		
Right	0, 1, 2, 3	0, 1, 2
Left	0, 1, 2, 3	0, 1, 2
Ventrolateral tongue		
Right	0, 1, 2, 3	0, 1, 2
Left	0, 1, 2, 3	0, 1, 2
Floor of mouth	0, 1, 2, 3	0, 1, 2
Palate		
Hard	0, 1, 2, 3	0, 1, 2
Soft	0, 1, 2, 3	0, 1, 2

Note. Objective and subjective findings are scored separately (Sonis et al., 1999).

MASCC/ISOO guidelines also recommend cryotherapy to prevent OM in patients who are receiving high-dose melphalan as a conditioning agent for hematopoietic stem cell transplant (Keefe et al., 2007). This recommendation is based on the theory that vasoconstriction will decrease exposure of the oral cavity mucous membranes to toxic agents. The guidelines recommend 20 to 30 minutes of oral cryotherapy to decrease mucositis in patients receiving bolus doses of 5-FU and or high-dose melphalan (Keefe et al., 2007).

A number of palliative rinses and gels are available, but the evidence supporting their benefit is conflicting. Findings from an Oncology Nursing Society survey indicated that oncology nurses prefer magic mouthwash—a multiagent rinse consisting of lidocaine, diphenhydramine, and aluminum hydroxide–magnesium hydroxide—as front-line therapy for mucositis pain. However, a recent study showed that the combination provided little benefit compared with standard oral hygiene and symptomatic treatment of OM (Kostler, Hejna, Wenzel, & Zielinski, 2001). An additional caveat to the use of magic mouthwash is the associated numbing effect that creates a potential for injury.

The use of low-level laser therapy (LLLT) has demonstrated promising results in mucositis trials (Nes & Posso, 2005). In 2004, Rubenstein and colleagues showed that LLLT reduced the incidence of

Table 6. MASCC/ISOO Clinical Practice Guidelines for the Management of Mucositis: 2007 Update

Foundations of Care	
Previous guideline	**Updated or new guideline**
The panel suggests that oral care protocols that include patient education be used to attempt to reduce the severity of mucositis from chemotherapy or radiation therapy.	The panel suggests multidisciplinary development and evaluation of oral care protocols, and patient and staff education in the use of such protocols to reduce the severity of oral mucositis from chemotherapy and/or radiation therapy. As part of the protocols, the panel suggests the use of a soft toothbrush that is replaced on a regular basis. Elements of good clinical practice should include the use of validated tools to regularly assess oral pain and oral cavity health. The inclusion of dental professionals is vital throughout the treatment and follow-up phases.
The panel recommends patient-controlled analgesia with morphine as the treatment of choice for oral mucositis pain in patients undergoing HSCT.	The panel recommends patient-controlled analgesia with morphine as the treatment of choice for oral mucositis pain in patients undergoing HSCT. Regular oral pain assessment using validated instruments for self-reporting is essential.
Radiation Therapy—Prevention	
Previous guideline	**Updated or new guideline**
None	The panel recommends that sucralfate not be used for the prevention of radiation-induced oral mucositis
None	The panel recommends that antimicrobial lozenges not be used for the prevention of radiation-induced oral mucositis
The panel recommends the use of midline radiation blocks and three-dimensional radiation treatment to reduce mucosal injury.	No change
The panel recommends benzydamine for prevention of radiation-induced mucositis in patients with head and neck cancer receiving moderate-dose radiation therapy	No change
The panel recommends that chlorhexidine not be used to prevent oral mucositis in patients with solid tumors of the head and neck who are undergoing radiotherapy.	No change
Standard-Dose Chemotherapy—Prevention	
Previous guideline	**Updated or new guideline**
The panel recommends that patients receiving bolus 5-fluorouracil chemotherapy undergo 30 minutes of oral cryotherapy to prevent oral mucositis. The panel suggests that 20 to 30 minutes of oral cryotherapy be used to attempt to decrease mucositis in patients treated with bolus doses of edatrexate.	No change
The panel recommends that acyclovir and its analogues not be used routinely to prevent mucositis	No change

Note. HSCT = hematopoietic stem cell transplantation; LLLL = low-level laser light therapy. Adapted from Keefe et al. (2007).

Continued

Table 6. MASCC/ISOO Clinical Practice Guidelines for the Management of Mucositis: 2007 Update (cont.)

Standard-Dose Chemotherapy—Treatment	
Previous guideline	**Updated or new guideline**
The panel recommends that chlorhexidine not be used to treat established oral mucositis	No change
High-Dose Chemotherapy With or Without Total Body Irradiation Plus HSCT—Prevention	
Previous guideline	**Updated or new guideline**
None	In patients with hematological malignancies receiving high-dose chemotherapy and total body irradiation with autologous stem cell transplant, the panel recommends the use of keratinocyte growth factor-1 (palifermin) in a dose of 60 µg/kg/day for 3 days prior to conditioning treatment and for 3 days posttransplant for the prevention of oral mucositis.
None	The panel suggests the use of cryotherapy to prevent oral mucositis in patients receiving high-dose melphalan.
The panel does not recommend the use of pentoxifylline to prevent mucositis in patients undergoing HSCT	No change
None	The panel suggests that granulocyte-macrophage colony-stimulating factor mouthwashes not be used for the prevention of oral mucositis in patients undergoing hematopoietic stem cell transplantation
LLLT requires expensive equipment and specialized training. Because of interoperator variability, clinical trials are difficult to conduct, and their results are difficult to compare; nevertheless, the panel is encouraged by the accumulating evidence in support of LLLT. The panel suggests that, for centers able to support the necessary technology and training, LLLT be used to attempt to reduce the incidence of oral mucositis and its associated pain in patients receiving high-dose chemotherapy or chemoradiotherapy before HSCT.	No change

Note. HSCT = hematopoietic stem cell transplantation; LLLL = low-level laser light therapy. Adapted from Keefe et al. (2007).

OM and associated pain in patients receiving chemotherapy or chemoradiation before hematopoietic stem cell transplant. The use of LLLT is recommended by MASCC/ISOO guidelines (Keefe et al., 2007).

Interdisciplinary Management

Optimal management of OM requires an interdisciplinary effort with representation from dentistry, psychosocial oncology, audiology, nutrition, speech/swallow therapy, smoking cessation, integrative medicine, palliative care (to assist in pain control), and social work. Oral care protocols should begin before cancer therapy is initiated to achieve optimal outcomes and patient adherence (see Figure 1). Effective pretreatment oral protocols include dental cleanings, dental work to eliminate caries and existing gum disease, adjustment or fitting for dentures or partial plates, and patient education regarding the importance of daily oral hygiene, proper brushing techniques, and oral care. Effective oral care protocols during cancer treatment are similar. Patients should be instructed to clean their teeth and gums after every meal and before bed and use non–alcohol-based rinses (e.g., Biotene) regularly. Dentures should be removed and cleansed daily. Painful stimuli such as hot foods, spicy foods, alcohol, and smoking should be avoided. In addition, patients should be instructed to assess their mouth daily

and report any pain, redness, or sores, keep their lips lubricated, and drink plenty of fluids (Treister & Sonis, 2007; Peterson, 2006; Lalla et al., 2008). Education on the importance of good nutrition and a diet high in calories and protein is essential (Peterson, 2006; Lalla et al., 2008).

Case Study: An Older Adult Receiving Chemotherapy for PTCL

Mrs. Y is a 76-year-old Asian woman who was originally diagnosed with stage II high-grade peripheral T-cell lymphoma (PTCL) in March 2009. She was treated with conventional chemotherapy, which did not control her disease. She presented with an enlarged lymph node under the right axilla and a grape-sized swollen lymph node in the right neck area. Mrs. Y claimed the enlarged nodes were not painful but indicated that her skin was discolored. She believed both nodes had grown during the past few weeks. Tissue diagnosis confirmed the recurrence of PTCL.

Mrs. Y was started on pralatrexate (Folotyn), a folate analog metabolic inhibitor approved for the treatment of relapsed/refractory PTCL. Pralatrexate was administered once a week for 6 consecutive weeks, with the seventh week off. She began her first 7-week cycle of 30 mg/m^2 pralatrexate IV push over 3 to 5 minutes. She was to continue this therapy until the lymphoma progressed or an unacceptable toxicity occurred (Allos Therapeutics, 2011). In addition, Mrs. Y received oral folic acid and vitamin B12 injections every 8 to 12 weeks.

The most common adverse effects of pralatrexate include oral mucositis, low platelet count, and elevated liver functions (Allos Therapeutics, 2011). While Mrs. Y had requested aggressive treatment for her PTCL recurrence, her past medical history showed that she was nonadherent with dental examinations and oral care regimens. Therefore, she was considered at high risk for OM and underwent regular oral cavity assessments.

At week 4, Mrs. Y was seen prior to chemotherapy administration, during which time she complained of acute pain and burning in her mouth, in the back of her throat, and on her tongue. Upon examination of her mouth with a tongue blade, the mucosal area began to bleed. White patches were also seen in the back of her throat and her tongue was red and bumpy. Red ulcers and swelling were also noted. Using the WHO toxicity scale, Mrs. Y was diagnosed with grade 3 OM. She was not able to eat solid foods and required a liquid diet. Using a pain scale of 1 through 10 with 10 being the worst pain, the patient stated that she was in severe pain with a score of 8. She described the pain as a burning sensation. Although the duration of pain was constant and became worse when she consumed any liquids or solids, she had not taken anything for pain management. She had lost 5 pounds in 1 week and appeared to be dehydrated.

Due to her weight loss, a dietician and an advanced practitioner were scheduled to see Mrs. Y to discuss diet, hydration, and food supplements. Treatment with 1 liter of intravenous fluid was recommended and chemotherapy was delayed for 1 week. Mrs. Y was asked to return the next day for IV fluid and reassessment (Lalla, Sonis, & Peterson, 2008; Peterson, 2006; Keefe et al., 2007).

Summary

Advanced practitioners play a critical role in helping patients with cancer achieve the maximum benefit of therapy. They must be knowledgeable about the risk factors and pathogenesis of OM in order to identify high-risk patients and implement the appropriate interventions. The clinical appearance of OM should be documented and graded using a validated tool such as the WHO or NCI-CTC scale. Pain should be assessed, documented, and controlled using comfort measures and nonopioid and opioid analgesia as necessary. The use of evidence-based practice guidelines and education on the importance oral care regimens and a healthy diet will help minimize the effects of this debilitating toxicity of cancer treatment.

DISCLOSURES

Carrie F. Daly, MS, RN, AOCN®, reported a financial interest/relationship or affiliation in the form of: Speakers' Bureau, Roche Laboratories, Inc. Annette M. Quinn, MSN, RN, has no real or apparent conflicts of interest to report.

REFERENCES

Allos Therapeutics, Inc. (2011). Folotyn prescribing information. Retrieved from http://www.folotyn.com/sites/default/files/pdf/Folotyn_PI.pdf

American Cancer Society. (1999). Mouth sores painful for patients: New scoring system to aid in treating mouth sores. Retrieved from http://www.cancer.org/doc-root/NWS/content/NWS_1_1x_Mouth_Sores_Painful_for_Patients.asp

Barasch, A., & Peterson, D. (2003). Risk factors for ulcerative oral mucositis in cancer patients: Unanswered questions. *Oral Oncology, 39*(2), 91–100.

Brown, C. (2010). Oral mucositis. In C. Brown (Ed.), *A guide to*

oncology symptom management (pp. 333–346). Pittsburgh, PA: Oncology Nursing Society.

Bruce, S. D., & Quinn, A. (2007). The pain of oral mucositis. *U.S. Oncological Disease, 1,* 86–90.

Cawley, M. M., & Benson, L. M. (2005). Current trends in managing oral mucositis. *Clinical Journal of Oncology Nursing, 9*(5), 584–592.

Cheng, K. K., Chang, A. M., & Yuen, M. P. (2004). Prevention of oral mucositis in paediatric patients treated with chemotherapy: A randomised crossover trial comparing two protocols of oral care. *European Journal of Cancer, 40*(8), 1208–1216. doi:10.1016/j.ejca.2003.10.023

Eilers, J., & Epstein, J. B. (2004). Assessment and measurement of oral mucositis. *Seminars in Oncology Nursing, 20,* 22–29. doi:10.1053/j.soncn.2003.10.005

Elting, L. S., Cooksley, C., Chambers, M., Cantor S. B., Manzullo, E., & Rubenstein, E. B. (2003). The burdens of cancer therapy. Clinical and economic outcomes of chemotherapy-induced mucositis. *Cancer, 98*(7), 1531–1539. doi:10.1002/cncr.11671

Elting, L. S., Shih, Y.-C. T., Stiff, P. J., Bensinger, W., Cantor, S. B., Cooksley, C., & Spielberger R. (2005). Palifermin reduces estimated downstream costs of autologous stem cell transplant: Analysis of phase 3 trial results. *The Journal of Supportive Oncology, 3*(2 suppl), 76–77.

Elting L. S., Shih Y. C., Stiff P. J., Bensinger, W. Cantor, S. B., Cooksley, C.,...Emmanoulides, C. (2007). Economic impact of palifermin on the costs of hospitalization for autologous hematopoietic stem-cell transplant: Analysis of phase 3 trial results. *Biology of Blood and Marrow Transplantation, 13*(7), 806-813. doi:10.1016/j.bbmt.2007.03.004

Epstein, J. B., & Schubert, M. M. (2003). Oropharyngeal mucositis in cancer therapy. *Oncology, 17*(12), 1767–1776.

Fischer, D. S., Knobf, M. T., Durivage, H., & Beaulieu, N. (2003). *The cancer chemotherapy handbook* (6th ed.). Philadelphia, PA: Mosby.

Keefe, D. M., Schubert, M. M., Elting, L. S., Sonis, S. T., Epstein, J. B, Raber-Durlacher, J. E.,...Peterson, D. E. (2007). Updated clinical practice guidelines for the prevention and treatment of mucositis. *Cancer, 109*(5), 820–831. doi:10.1002/cncr.22484

Köstler, W., Hejna, M., Wenzel, C., & Zielinski, C. C. (2001). Oral mucositis complicating chemotherapy and/or radiotherapy options for prevention and treatment. *CA: A Cancer Journal for Clinicians, 51*(5), 290–315. doi:10.3322/canjclin.51.5.290

Kwong, K. K. (2004). Prevention and treatment of orophyaryngeal mucositis following cancer therapy: Are there new approaches? *Cancer Nursing, 27*(3), 183–205.

Lalla, R. V., Sonis, S. T., & Peterson, D. E. (2008). Management of oral mucositis in patients with cancer. *Dental Clinics of North America, 52*(1), 61–77, viii. doi:10.1016/j.cden.2007.10.002

McGuire, D. B., Correa, M. E., Johnson, J., & Wienandts, P. (2006). The role of basic oral care and good clinical practice principles in the management of oral mucositis. *Supportive Care in Cancer, 14*(6), 541–547. doi:10.1007/s00520-006-0051-8

National Cancer Institute. (2010). Common Terminology Criteria for Adverse Events (v.4.0). Retrieved from http://evs.nci.nih.gov/ftp1/CTCAE/About.html

Nes, A. G., & Posso, M. B. (2005). Patients with moderate chemotherapy-induced mucositis: Pain therapy using low intensity lasers. *International Nursing Review, 52*(1), 68–72. doi:10.1111/j.1466-7657.2004.00401.x

Peterson, D. (2006). New strategies for management of oral mucositis in cancer patients. *The Journal of Supportive Oncology, 4*(2 suppl), 9–13.

Rubenstein, E. B., Peterson, D. E., Schubert, M., Keefe, D., McGuire, D., Epstein, J.,...Sonis, S. T. (2004). Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer, 100*(9 suppl), 2026–2046. doi:10.1002/cncr.20163

Scully, C., Sonis, S., & Diz, P. D. (2006). Oral mucositis. *Oral Diseases, 12*(3), 229–241. doi:10.1111/j.1601-0825.2006.01258.x

Silverman, S. (2007). Diagnosis and management of oral mucositis. *The Journal of Supportive Oncology, 5*(suppl 1), 13–21.

Skulason, S., Holbrook, W. P., & Kristmundsdottir, T. (2009). Clinical assessment of the effect of a matrix metalloproteinase inhibitor on apthous ulcers. *Acta Odontologica Scandinavica, 67*(1), 25–29.

Sonis, S. T. (2000). Oral complications. In R. C. Bast, D. W. Kufe, & R. E. Pollock (Eds.), *Cancer medicine* (5th ed., chap. 153). Hamilton, Ontario: Decker Publishing, Inc.

Sonis, S. T. (2004a). Pathobiology of mucositis. *Seminars in Oncology Nursing, 20*(1), 11–15. doi:10.1053/j.soncn.2003.10.003

Sonis, S. T. (2004b). A biological approach to mucositis. *The Journal of Supportive Oncology, 2*(1), 21–32.

Sonis, S. T. (2007). Pathobiology of oral mucositis: Novel insights and opportunities. *The Journal of Supportive Oncology, 5*(9 suppl 4), 3–11.

Sonis, S. T. (2009). Mucositis: The impact, biology and therapeutic opportunities of oral mucositis. *Oral Oncology, 45*(12), 1015-1020. doi:10.1016/j.oraloncology.2009.08.006

Sonis, S. T., Ellers, J. P., Epstein, J. B., LeVeque, F. G., Liggett, W. H. Jr., Mulagha, M. T.,...Wittes, J. P. (1999). Validation of a new scoring system for the assessment of clinical trial research of oral mucositis induced by radiation or chemotherapy. Mucositis Study Group. *Cancer, 85*(10), 2103–2113. doi:10.1002/(SICI)1097-0142(19990515)85:10<2103::AID-CNCR2>3.0.CO;2-0

Sonis, S. T., Haddad, R., Posner, M., Watkins, B., Fey, E., Morgan, T. V.,...Ramoni, M. (2007). Gene expression changes in peripheral blood cells provide insight into the biological mechanisms associated with regimen-related toxicities in patients being treated for head and neck cancers. *Oral Oncology, 43*(3), 289–300. doi:10.1016/j.oraloncology.2006.03.014

Sonis, S. T., Oster, G., Fuchs, H., Bellm, L., Bradford, W. Z., Edelsberg, J.,...Horowitz, M. (2001). Oral mucositis and the clinical and economic outcomes of hematopoietic stem cell transplantation. *Journal of Clinical Oncology, 19*(8), 2201–2205.

Spielberger, R., Stiff, P., Bensinger, W., Gentile, T., Weisdorf, D., Kewalramani, T.,...Emmanouiliades, C. (2004). Palifermin for oral mucositis after intensive therapy for hematologic cancers. *The New England Journal of Medicine, 351*(25), 2590–2598.

Treister, N., & Sonis, S. (2007). Mucositis: Biology and management. *Current Opinion in Otolaryngology & Head and Neck Surgery, 15,* 123–129. doi:10.1097/MOO.0b013e3280523ad6

Trotti, A., Bellm, L. A., Epstein, J. B., Frame, D., Fuchs, H. J., Gwede, C. K.,...Zilberberg, M. D. (2003). Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: A systematic literature review. *Radiotherapy Oncology, 66,* 253–262. doi:10.1016/S0167-8140(02)00404-8

Wojtaszek, C. (2000). Management of chemotherapy-induced stomatitis. *Clinical Journal of Oncology Nursing, 4*(6), 263–270.

World Health Organization. (1979). WHO handbook for reporting results of cancer treatment. Geneva, Switzerland: World Health Organization.

Claim Certificate Online Only

To receive acknowledgement of participation for this CE-certified activity, you must complete the evaluation and posttest online. Please visit **http://www.IMERonline.com/570_jadpro** and follow the directions provided. You must have an account with IMER or you will be directed to create one. Creating an IMER account and claiming a certificate are free of charge.

Method of Participation

Participants must complete the posttest by recording the best answer to each question. Once you have finished your test and completed the subsequent evaluation form, click Submit Test to send your responses to us. Your test will be immediately reviewed and if you receive a passing grade of 70% or better, you will then be directed to print your certificate online.

Free Oral Mucositis Toolkit

Up to 500 free oral mucositis toolkits will be available and mailed to requestors on a first-come, first-serve basis. To request your toolkit, please visit **http://www.IMERonline.com/570_jadpro**. You must have an account with IMER or you will be directed to create one. The toolkit includes:

- A high-intensity battery-operated pen light
- Tongue blades
- Pocket-sized laminated assessment tools that can be utilized in daily clinical practice