Current Trends in Managing Oral Mucositis

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Oral mucositis is an inflammatory and ulcerative process of the oral cavity that results from an assault on the epithelial mucous membrane tissue and most commonly is associated with the administration of radiotherapy and chemotherapy. The incidence of oral mucositis ranges from 15%–40% in patients receiving stomatotoxic chemotherapy or radiotherapy and 70%–90% in bone marrow recipients. Knowledge regarding the pathophysiology of oral mucositis has evolved and now guides practice. Assessment tools to measure the level of mucositis provide valuable data concerning the status of the oral cavity. No single oral assessment tool has been found to be appropriate in all clinical settings. Mucositis has a significant impact on patients' quality of life and treatment plan. Management of oral mucositis is aimed at minimizing this side effect and its subsequent sequelae. The strategies of care are geared toward early intervention and supportive care for patients at risk for developing mucositis and include specific targeted therapies for the management of debilitating side effects. This article provides an overview of the risk factors, pathophysiology, incidence, impact, clinical presentation, oral assessment tools, management strategies, and nursing implications related to oral mucositis.

Oral mucositis is an inherent complication of cancer therapy for many patients. A basic definition of mucositis is erythema and ulceration of the mucosa. Oral mucositis plays a significant role in the physical and psychosocial aspects of patients undergoing cancer therapy. From a public health perspective, oral mucositis is a larger problem than is currently recognized. Because of the significant number of patients affected by this side effect, nursing knowledge and research regarding oral mucositis must increase. Managing oral mucositis is as important as managing decubiti, fatigue, nausea and vomiting, and many other side effects that can occur in patients with cancer.

Oral mucositis has emerged as one of the most frequent causes of treatment delay and dosage reductions in cancer therapy, and it affects patients across all treatment modalities. Patients' quality of life can be affected by pain, infection, altered nutrition, and impairment of oral function, resulting in potential treatment delays and economic burden. Through education and research, nurses can be actively involved in reducing and managing these debilitating effects.

Incidence and Impact

The incidence of oral mucositis varies widely based on the specific type of cancer and the modality used for treatment, but about 400,000 people develop oral complications from cancer therapy each year (Brown & Wingard, 2004). Mucositis often is associated with radiotherapy to the head and neck and with high-dose chemotherapy regimens, especially those used in stem cell transplantation. According to Elting et al. (2003), mucositis also occurs with the use of myelosuppressive chemotherapy for solid tumors (see Table 1).

In their review of the literature, Epstein and Schubert (2003) found that 30%–75% of chemotherapy patients experienced oral mucositis. In head and neck radiotherapy (i.e., doses greater than 5,000 cGy) and in stem cell transplants, the incidence was 100% and almost 90%, respectively.

In a retrospective study of clinical outcomes, Elting et al. (2003) reviewed the records for a random sample of 599 patients who had myelosuppression related to chemotherapy. Oral mucositis occurred in 37% of the 1,236 cycles of chemotherapy. The researchers found that therapy dosage reductions occurred at a rate of 21% after cycles with mucositis episodes (grades 3 and 4) versus 11% for cycles without mucositis episodes. In addition, the review identified bleeding, infections, and the need for nutritional support in more cycles when grade 4 oral mucositis was present. Oral mucositis was discovered more frequently during cycles with fluorouracil (5-FU) (51%) than during cycles without 5-FU (27%, $p < 0.001$).

Oral mucositis obviously has a potential impact on clinical outcomes. Delayed treatment and reduced dosages may be necessary to provide time to heal damaged tissues. Therefore, managing

Submitted December 2004. Accepted for publication April 6, 2005. Editorial assistance was provided by the Curry Rockefeller Group. OSI Pharmaceuticals, Inc., a marketer of Gelclair® Bioadherent Oral Gel, which is mentioned in this article, provided financial support and employs the second author. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing *or the Oncology Nursing Society.)*

Digital Object Identifier: 10.1188/05.CJON.584-592

Table 1. Chemotherapy and Levels of Mucositis

Chemotherapy Agent	More Common	Less Common	Rare
Bleomycin	X		
Cisplatin		X	
Cyclophosphamide	X		
Cytarabine	X		
Dactinomycin	X		
Daunorubicin			X
Docetaxel		X	
Doxorubicin		X	
Etoposide	X		
Fluorouracil	Continuous infusion	Single dose	
Methotrexate	X		
Mitomycin		X	
Paclitaxel	X		
Vinblastine			X
Vincristine			X
Vinorelbine		X	

Note. Based on information from Wilkes & Ades, 2004.

debilitating symptoms that may have a severe impact on patients' quality of life is a pivotal role of oncology nurses (Elting et al., 2003).

Risk Factors

The etiology of oral mucositis is directly related to the impact of radiotherapy and chemotherapy on the oral mucosa. When discussing any side effect of therapy, reviewing the risk factors is essential so that healthcare providers can identify which patients are at risk, why they are at risk, and how best to reduce their risk.

Patient-Related Risk Factors

Age is a universally acknowledged risk factor, but numerous studies have offered differing views on which age population is at greatest risk. Barasch and Peterson (2003) reviewed research dealing with age and gender as risk factors for mucositis and found that older populations appear to be at increased risk. However, according to Sonis and Fey (2002), younger populations appear to be at greater risk, which may be related to their more rapid rate of epithelial proliferation. Overall, the data suggest that women are at greater risk than men, particularly if they are receiving 5-FU–based chemotherapy. Smoking and excessive alcohol use also are risk factors because they alter the epithelial mucosal environment (Raber-Durlacher, 1999).

Treatment-Related Risk Factors

Treatment-related risk factors are directly linked to radiotherapy and chemotherapy regimens. A recent compilation of the literature (Avritscher, Cooksley, & Elting, 2004) identified the treatment modalities with the greatest risk for the development of oral mucositis.

Radiotherapy directly assaults the oral mucosa. Repetitive, daily radiation treatment has an additive effect, causing inflammation and ulceration of the oral mucosa. Radiation delivered directly to the head and neck and total body irradiation for bone marrow transplantation result in the most common occurrences of mucositis.

The chemotherapeutic agents most frequently associated with mucositis are antimetabolites, which include etoposide, 5-FU, and methotrexate. Other agents associated with oral mucositis include bleomycin, cisplatin, cyclophosphamide, cytarabine, dactinomycin, daunorubicin, docetaxel, doxorubicin, mitomycin, paclitaxel, vinblastine, vincristine, and vinorelbine (Wilkes & Ades, 2004). Even at standard doses these agents are known to cause mucositis. In addition, research has demonstrated that high-dose chemotherapy regimens are linked more frequently with the occurrence of mucositis (Avritscher et al., 2004). A combined regimen of chemotherapy and radiotherapy also significantly increases the risk and severity of oral mucositis (Trotti et al., 2003).

All bone marrow recipients are at risk. In addition, allogeneic transplant recipients have higher rates of oral mucositis than autologous transplant recipients (Woo, Sonis, Monopoli, & Sonis, 1993; Zerbe, Parkerson, Ortleib, & Spitzer, 1992).

Pathophysiology

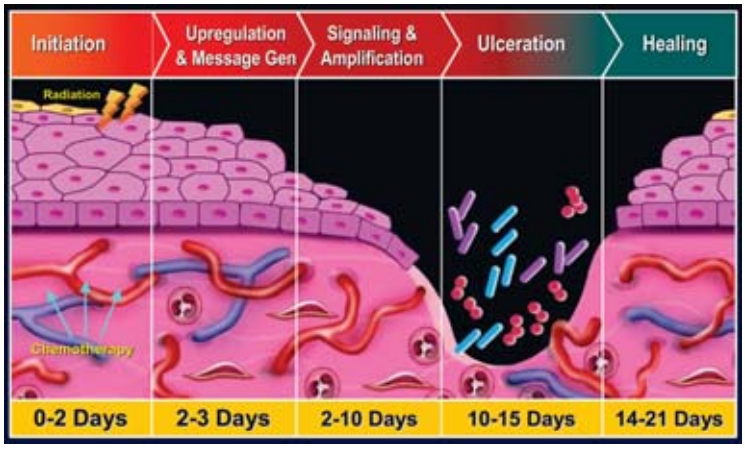
Understanding the physiology of oral mucosa is pivotal when discussing oral mucositis. The mucosa is composed of stratified epithelial cells that cover the connective tissue and submucosa. As epithelial cells are sloughed, new epithelial cells arise from the stem cells in the submucosa to the surface, which takes about two weeks; therefore, the integrity of the mucosa is linked to the ability of the stem cells to continuously reproduce (Sonis, 2004c).

Historically, mucositis was believed to be the result of damage to the epithelium: Radiotherapy and chemotherapy affected the replication of epithelial cells and thus caused mucositis. However, the pathobiology of oral mucositis is more complex, involving more than simply a process of damage to the epithelial cells. The development of animal models led to a comprehensive study of the pathobiology of oral mucositis. An animal model using the oral mucosa of hamsters was developed because the oral mucosa and bone marrow in hamsters respond in much the same way as those of humans when exposed to chemotherapy and radiotherapy (Sonis, 2004c). Through the availability of animal models and clinical observations, a more in-depth approach has been derived for the biology of mucositis development. Research performed at the cellular level has demonstrated that a multitude of molecular events are triggered and that the target is the submucosa rather than the epithelial lining (Sonis, 2004a, 2004c).

Sonis (2004c) coined the term "pathobiology" in his work to explain the mechanism by which oral mucositis occurs. His model of pathophysiology for oral mucositis (Sonis, 2004a, 2004c; Sonis et al., 2004) consists of five phases (see Figure 1). The first phase is initiation (0–2 days), which occurs when radiotherapy or chemotherapy is delivered. Direct damage to the epithelial cells injures the DNA and results in the death of a small portion of cells.

Phase two of the oral mucositis model is upregulation and message generation (2–3 days). In this phase, inflammatory cytokines are released that cause further tissue injury and cell death. The mucosa starts to thin, and erythema may be present. Tumor necrosis factor-alpha (TNF-α), a proinflammatory cytokine, is a protein produced by monocytes and macrophages that is increased because of inflammation. TNF-α has the ability to cause necrosis by interfering with blood flow, cytotoxic inflammation, and regulation of immune responses (Rieger, 2001).

The third phase is signaling and amplification (2–10 days), which consists of direct damage to cells and escalation of the process initiated by proinflammatory cytokines. In this phase, TNF-α activates



Initiation (phase 1)
- Damage to DNA causes cell death.
- Generation of reactive oxygen species
- Stimulation of transcription factors

Upregulation and message generation (phase 2)
- Activation of transcription factors nuclear factor-kappa beta (NF-κB) > proinflammatory cytokines
- Angiogenesis
- Fibroblast breakdown: macrophages > metalloproteinases > tissue injury or production of tumor necrosis factor-alpha (TNF-α)

Signaling and amplification (phase 3)
- Direct damage continues.
- TNF-α activates NF-κB.
- Feedback loop amplifies effects.

Ulceration (phase 4)
- Ulceration from epithelium to submucosa
- Pseudomembrane over ulcer
- Bacterial colonization
  - Bacterial wall products activate macrophages.
  - Macrophages stimulate proinflammatory cytokines.

Healing (phase 5)
- Signal from extracellular matrix
- Migration and proliferation
- Layering of cells
- Normal oral flora is established.

Figure 1. Phases of Mucositis

Note. Based on information from Sonis, 2004b.

additional cytokines, creating a feedback loop that amplifies the biologic effects. Most of the damage occurs below the level of the mucosa.

Phase four, ulceration (10–15 days), is the most clinically obvious, extending from the epithelium into the submucosa. The ulcers tend to be deep and have no regular shape. A pseudomembrane frequently coats the lesions. As this fibrinous exudate is filled with bacteria, colonization can occur. Bacterial wall products activate macrophages and can lead to further stimulation of the proinflammatory cytokines. Nerve endings are exposed, causing pain that can be debilitating.

In phase five, healing (14–21 days), the epithelial cells that border the ulcer begin to migrate to the ulcer where they proliferate into the wound bed. The tissue will start to form layers, and normal oral microbial flora will be established. However, cells below the surface never fully return to their previous state, which puts the oral mucosa at risk for future injury or occurrences of mucositis.

This new model is important because it enhances nursing knowledge, thus assisting nurses in anticipating when oral mucositis will occur. Proactive management (i.e., optimal oral care) and patient education are imperative because damage occurs before mucosal changes can be seen.

Assessment Tools

No standard of practice exists for the assessment of oral mucositis. Oral assessment scales are evolving, and the number of scales used in clinical practice and research continues to grow. The clinical goal of oral cavity assessment is to improve or maintain patients' functional status.

In an ideal environment, a mucositis assessment scale should be objective, reliable, and valid for all clinical and research situations (Sonis et al., 2004). To date, none of the available scales meets all of the criteria. Lack of patient input and difficulty of use are disadvantages for all currently available assessment scales (Cella et al., 2003).

Most scales can be divided into one of two groups. The first group of scales is very general in nature and usually consists of a four- or five-point rating scale that allows for a basic assessment of the oral cavity (see Table 2). The second group of scales uses multiple variables that allow for the assessment of a number of factors in relation to oral condition and function (see Table 3). In the scales, scores are totaled for a mucositis severity score (Schubert, 1993). Beck's (1979) Oral Exam Guide and Sonis et al.'s (1999) Oral Mucositis Assessment Scale require use by an experienced nurse and may not be as appropriate as other more clinical scales for bedside nurses. The most relevant scale for clinical assessment in the United States appears to be based on the National Cancer Institute's design (see Figure 2). In addition, the Radiation Therapy Oncology Group scale is used frequently for radiotherapy trials (Sonis et al., 2004).

All oral assessment needs to begin with visualization of the oral cavity. The assessment should be initiated before the start of therapy, which allows healthcare providers to have a baseline for future assessment. A single, agreed-upon assessment scale should be used by all members of the patient care team, who must be educated regarding the specific areas to be assessed as well as how to use the scale. Oral cavity examinations should be ongoing, and all findings must be documented in patients' records. A key element of success with any oral cavity examination is patients' cooperation and participation. Patients need to have a clear understanding of the symptoms as well as the assessment, progression, and management of oral mucositis.

Clinical Presentation

Visual signs of mucositis usually occur 7–14 days after radiotherapy or chemotherapy has started (Epstein & Schubert, 2003).

Table 2. General Mucositis Assessment Scales

Scale	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
NCI-CTC dysphagia	None	Symptomatic, able to eat regular diet	Symptomatic and altered eating or swallowing; IV fluids indicated < 24 hours	Symptomatic and severely altered eating or swallowing; IV fluids, tube feedings, or total parenteral nutrition indicated ≥ 24 hours	Life-threatening consequences (obstruction, perforation)	Death related to toxicity
NCI-CTC mucositis and stomatitis	None	Erythema of the mucosa	Patchy ulcerations or pseudomembranes	Confluent ulcerations or pseudomembranes, bleeding with minor trauma	Tissue necrosis, significant spontaneous bleeding, life-threatening consequences	Death related to toxicity
World Health Organization	None	Oral soreness, erythema	Oral erythema, ulcers, solid diet tolerated	Oral ulcers, liquid diet only	Oral alimentation impossible	–

NCI-CTC—National Cancer Institute Common Toxicity Criteria

Note. Based on information from National Cancer Institute, 2003; World Health Organization, 1979.

Although the mucosa may not be altered, damage already may be occurring during treatment. The nadir of the neutrophil count often signals the onset of visual mucositis, and the healing process occurs with the elevation of the neutrophil count (Khan & Wingard, 2001).

Assessing the appearance and functional ability of the oral cavity is essential for minimizing the effects of oral mucositis. Because no oral assessment tool is accepted universally, nurses must ensure the use of a standard approach to oral assessment in their specific clinical setting. All healthcare providers and patients need to understand and actively participate in oral assessment.

A mucositis diagnosis is based on clinical examination of the oral cavity. Early signs include erythema and inflammation of the oral mucosa. In patients receiving chemotherapy, mucositis usually begins in the nonkeratinized mucosa of the ventral tongue, floor of the mouth, soft palate, and buccal mucosa (see Figure 2a). In general terms, this would be described as mild mucositis (Epstein & Schubert, 2003).

As mucositis progresses, ulcers that may be painful appear. Erythema and inflammation continue (see Figure 2b), and patients will complain of soreness and an altered ability to eat and drink. These symptoms are described as moderate mucositis (Epstein & Schubert, 2003).

As ulceration spreads, pseudomembranes often coat the ulcers and the exposure of nerve endings results in pain (see Figures 2c and 2d). Ulcers are deep and have no regular shape. Patients may not be able to eat or drink normally because of pain and a reduced ability to swallow. The presence of pseudomembranes dramatically increases the risk for complications (Epstein & Schubert, 2003).

During healing, which is a slow process, the risk for injury remains. On average, healing after the end of chemotherapy occurs in two to three weeks, but healing after the completion of radiation therapy takes three to six weeks (Epstein & Schubert, 2003).

The process of oral mucositis, from its onset to complete healing, may last three to four weeks. Current scheduling regimens (i.e., daily, weekly, or biweekly) may not permit sufficient time for complete healing of the oral mucosa. This ongoing assault places patients at even greater risk for multiple complications.

Table 3. Multiple-Variable Mucositis Assessment Scales

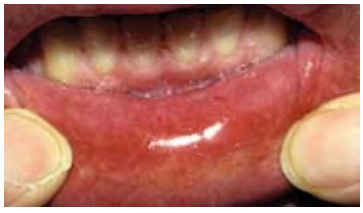
Scale	Study	Measurement	Comments
Oral Exam Guide	Beck, 1979	Visual inspection of 15 items rated on a scale of 1–4; oral perception guide has 9 patient-described items.	Research tool that gains subjective data from patients
Oral Assessment Guide	Eilers et al., 1988	Erythema, pain, salivation, swallowing, and voice measured on a 3-point rating scale.	Visualization, palpation, and tongue blade examination; does not measure lesions; easy to use in clinical setting
Oral Mucositis Index 34 for BMT	Schubert et al., 1992	11 items about atrophy, 11 about ulceration, 10 about erythema, and 2 about edema; items scored from 0–3.	Research tool developed for use by dental professionals
Oral Mucositis Assessment Scale	Sonis et al., 1999	Clinical assessment in 8 oral cavity sites; measures extent and severity of erythema and ulceration; pain and difficulty swallowing measured by patient.	Research tool for radiotherapy and chemotherapy that measures functional, subjective, and objective items and accurately measures lesion size; requires detailed training
Oral Mucositis Index 20 for PBSCT	McGuire et al., 2002	1 item about atrophy, 9 about ulceration, 9 about erythema, and 1 about edema; scored from 0–3	Research tool adapted from the Oral Mucositis Index 34; used by trained nondental professionals

BMT—bone marrow transplant; PBSCT—peripheral blood stem cell transplant

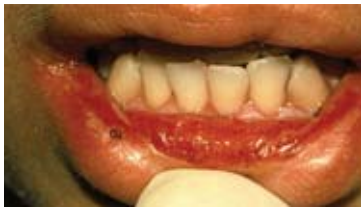
Complications

Any discussion of oral mucositis must address the issue of complications, which have the most impact on patients' treatment plans and quality of life. The three most common complications are pain, infection, and altered nutrition.

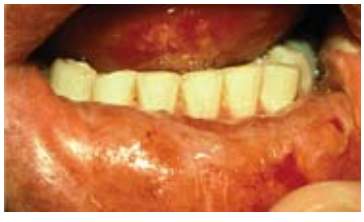
The primary complaint of patients with oral mucositis is pain. In 1999, a panel of healthcare providers met to discuss oral mucositis and review its most important outcomes



a. Grade 1: erythema of the mucosa



b. Grade 2: patchy ulcerations or pseudomembranes



c. Grade 3: confluent ulcerations or pseudomembranes; bleeding with minor trauma

d. Grade 4: tissue necrosis, significant spontaneous bleeding, life-threatening consequences

Figure 2. Examples of Grades of Mucositis Based on National Cancer Institute Criteria

Note. Photos courtesy of Mark Schubert, MSD. Reprinted with permission.

from patients' and healthcare providers' perspectives (Bellm et al., 2002). Healthcare providers ranked oral pain third after airway obstruction and fever, but patients ranked oral pain as the most significant complication.

Because patients identify pain as the most problematic effect of mucositis, agents that reduce pain are of clinical importance. In a study of pain associated with oral mucositis after high-dose chemotherapy, Cella et al. (2003) found that the scores for mouth pain increased as mucositis scores increased and decreased as mucositis scores decreased. The goal of treatment is to eliminate pain, so analgesics must be incorporated into patients' care plan. Additionally, other agents, including rinses and coating agents, may be used to reduce oral pain locally.

Oral pain causes a number of complications in patients with cancer. It can affect oral hygiene because patients may not be able to perform adequate mouth care. Impaired swallowing impacts patients' nutritional status as well as their ability to take oral medications. Some patients have described swallowing their saliva as "swallowing glass." At times, patients may require hospitalization for pain management.

The inability to take oral medications may further complicate patients' pain or negatively affect the treatment plan for cancer and other medical disorders. Other routes for administration of pain medication must be assessed in patients who cannot take oral pain medication. Because pain is a subjective experience, it must be managed from patients' perspectives.

The second major complication of mucositis is infection. Three types of infections can occur in patients with oral mucositis: bacterial, fungal, and viral. The use of broad-spectrum antibiotics in neutropenic patients has reduced the incidence of bacterial infections, but they still represent a threat to patients with oral mucositis. The most common gram-negative pathogens are *Pseudomonas, Klebsiella, Serratia,* and *Escherichia coli* (Schubert, 1993). Gram-positive pathogens include staphylococci and streptococci. Currently, the most severe bacterial infections arise from the gram-positive pathogen *Streptococcus viridans*. This pathogen is responsible for as many as 39% of infections in neutropenic patients (Khan & Wingard, 2001). Antibiotics sensitive to the offending pathogen will be administered via IV or orally.

Fungal infections also occur frequently. In patients receiving chemotherapy, the most common fungal pathogens are *Candida* and *Aspergillus* species (Khan & Wingard, 2001). In patients receiving radiotherapy to the head and neck, the most common pathogen is *Candida,* which occurs as an opportunistic infection because it naturally develops in the oral cavity. Antifungals can be administered to manage the infection, which can progress from a local to a life-threatening systemic infection. Therefore, identifying and treating these pathogens early are imperative (National Cancer Institute, 2005).

Viral pathogens cause infections in patients with oral mucositis and consist primarily of herpes simplex and cytomegalovirus; however, herpes simplex occurs most commonly (Khan & Wingard, 2001). Both of these pathogens cause pain and can escalate patients' experience of pain. Antivirals often are used to eradicate the condition and assist in healing.

The third complication of oral mucositis is altered nutrition. Adequate nutrition is not only essential to wound healing but is a major factor in the ability to perform activities of daily living. Ulcerations can impair patients' ability to chew and swallow solid food or liquids. If left untreated, dehydration and impaired nutrition can become serious complications that may require hospitalization and parenteral nutrition. The importance of optimal pain management cannot be overemphasized because it enhances patients' ability to eat and maintain adequate hydration.

Oral Care Protocol

The cornerstone of preventing or minimizing the effects of oral mucositis is an oral care protocol (see Figure 3). A review of the literature indicates that no single evidence-based protocol is used universally in caring for patients with cancer. In 1979, Beck evaluated the effects of oral care protocols and found no individual protocol to be more effective than the others but observed that the implementation of an oral care routine did have a positive impact. The result of this research was the Oral Exam Guide.

The foundation of any oral care protocol is good oral hygiene. Before radiotherapy or chemotherapy is initiated, a baseline oral examination should be completed and a dentist should be consulted. The dentist should conduct a baseline examination, repair dental caries, thoroughly clean the teeth, and repair any broken teeth or dentures.

The most important element of an oral care protocol is keeping the mouth clean, which begins with regular brushing and flossing. Patients need to be educated to use a soft toothbrush and floss after every meal. Flossing can be discontinued if it causes pain and if the platelet count is less than 40,000/mm^3 (Brown & Wingard, 2004). Rinsing the mouth with a saline or sodium bicarbonate solution after meals and several times every day also will aid in keeping the mouth clean and moist and will reduce the amount of bacteria (Shih, Miaskowski, Dodd, Stotts, & MacPhail, 2002).

Daily routines that can directly or indirectly negatively impact the oral mucosa should be avoided. If a mouthwash is used, it must not contain alcohol because alcohol acts as a drying agent and irritant. In the hospital setting, lemon glycerin swabs

DOs

- Practice preventive dental care.
  - Clean teeth.
  - Treat dental caries.
  - Repair broken teeth or dentures.
- Brush teeth (using a soft toothbrush or toothette) or dentures after each meal.
- Remove dentures or bridges until mouth sores heal.
- Floss teeth.
  - Can discontinue if pain arises or the platelet count is less than 40,000/mm^3.
- Keep mouth and lips moist.
  - Frequently sip water.
  - Use a saliva substitute.
  - Keep lips moisturized.
  - Suck on hard candy to stimulate saliva.
- Maintain good fluid intake.
- Maintain intake of protein and vitamins.
- Eat bland, soft foods.

DON'Ts

- Avoid mouthwashes containing alcohol.
- Do not use lemon glycerin swabs.
- Avoid spicy, acidic, and coarse foods.
- Do not consume extremely hot or cold foods.
- Do not consume alcohol.
- Do not use tobacco.

Figure 3. Example of an Oral Care Protocol

should not be used because they also dry out the mucosa. Other behaviors that cause a dry oral environment include smoking (i.e., cigars or cigarettes) and drinking alcoholic beverages (Raber-Durlacher, 1999).

Healthcare providers generally should recommend that patients avoid foods that can cause irritation or pain. Foods that are acidic, spicy, or coarse should be eliminated from the diet. Heat and extreme cold also cause irritation and are not recommended (Epstein & Schubert, 2003). Foods that provide high caloric intake and protein (e.g., pudding, eggs, milk shakes, pasta, nutritional supplements) should be consumed. Some patients may need dietary consultation.

Patient compliance is an integral part of the oral care process. Active participation in oral care and assessment should be reinforced at every opportunity. Because mucositis most often occurs after patients receive chemotherapy or radiotherapy in an ambulatory setting, they must receive educational materials to take home. These instructional materials should include signs and symptoms to watch for, how to prepare food appropriately, how to reduce the effects of mucositis, and when to contact healthcare providers.

Educational information should use understandable language and simple illustrations so that patients can refer to it outside the clinic. In addition, to increase their utility, education sheets can be translated into different languages.

Each patient will be prescribed a treatment plan that depends on his or her diagnosis, with many requiring treatments extending over several months. The physical and psychological ramifications associated with the sequelae of mucositis can be enormously debilitating, and they require that oncology nurses provide ongoing support, encouragement, and availability to their patients.

Targeted Therapies

The goal of clinical management is to prevent oral mucositis; however, in reality, prevention is rare. Therefore, clinical management using current therapies is aimed at reducing the severity of mucositis. The following review of targeted therapies is not intended to be all inclusive but rather highlights the agents and strategies that are currently in the forefront of clinical practice (see Table 4).

The most commonly known and used rinsing agent is "magic mouthwash," which is a mixture of lidocaine, diphenhydramine, and magnesium or aluminum hydroxide. In some clinical settings, nystatin may be included or substituted in the mixture. In a study comparing magic mouthwash with chlorhexidine gluconate mouthwash and saline or sodium bicarbonate mouthwash, no clinical differences were found in the timeline of mucositis (Dodd et al., 2000). Pain reduction with the rinses is minimal and of short duration.

The agent Gelclair® Bioadherent Oral Gel (Helsinn Healthcare SA, Lugano, Switzerland) is a concentrated bioadherent gel composed of polyvinylpyrrolidone, sodium hyaluronate, and glycyrrhetinic acid that is diluted then rinsed around the mouth for at least one minute. The agent can be used as needed, depending on patients' level of pain. Gelclair is recommended for use one hour before meals (Buchsel, 2003). The mucoadherent and lubricating agents in this gel coat the oral mucosa and rapidly decrease pain (OSI Oncology, 2003). Gelclair was evaluated for its effectiveness in reducing pain in a study of 30 hospice patients with varying pathologies of the oral cavity. The findings indicated that pain was reduced by 92% in a five- to seven-hour period following use. Eighty-seven percent of patients indicated improvement in pain related to swallowing food and liquids after 7–10 days of repeated use of Gelclair (Innocenti, Moscatelli, & Lopez, 2002).

Recombinant human kertainocyte growth factor 1, also known as palifermin, stimulates the replication and maturation of epithelial cells (Peterson, Beck, & Keefe, 2004). Palifermin was studied in a phase III trial in patients with hematologic malignancies who were receiving total body irradiation and high-dose chemotherapy in preparation for peripheral blood stem cell transplant (Spielberger et al., 2004). Palifermin or placebo was administered for three days before transplant and again three days after transplant. The results showed that the incidence of grades 3 and 4 oral mucositis, according to the World Health Organization scale, were 63% with palifermin versus 98% with placebo. Spielberger et al. also found that the duration of grades 3 and 4 mucositis was reduced from nine days with placebo to six days with palifermin. Palifermin has been approved in the United States to decrease the incidence and duration of severe oral mucositis in patients with hematologic

Table 4. Targeted Therapies

Agent	Comments
Magic mouthwash	Lidocaine, Benadryl® (Pfizer, Inc., New York, NY), or Maalox® (Novartis, East Hanover, NJ), with or without nystatin
Gelclair® Bioadherent Oral Gel	Gel that forms a barrier over oral mucosa and provides rapid and durable pain relief in five to seven hours
Amifostine	Radioprotective antioxidant administered by IV or subcutaneously; does not reduce incidence of mucositis, but improves ability to produce saliva
Iseganan hydrochloride	Antimicrobial peptide that is associated with a decreased incidence with stomatotoxic chemotherapy
Glutamine (AES-14)	Amino acid; oral delivery system
Keratinocyte growth factors	Stimulates replication and maturation of epithelial cells; prevents and reduces mucositis
• Palifermin	Studied in peripheral blood stem cell transplant recipients; significantly decreases oral mucositis incidence and duration
Low-level laser therapy	Promotes healing and reduces pain and inflammation

Case Study

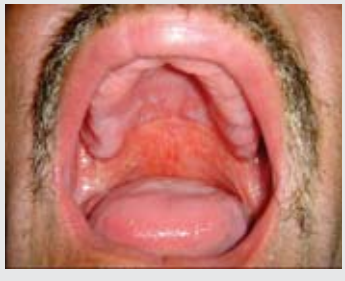
R.H. is a 49-year-old man who is married with two children and works as a supervisor in the removal of asbestos material. The patient presented with a change in his voice, weight loss, and pain in his throat for two months. Following a biopsy, R.H. was diagnosed with infiltrating, moderately differentiated carcinoma of the right tonsil (T2N1M0). R.H. wears upper and lower dentures and has a history of smoking one pack of cigarettes per day for 38 years right up to the day he started treatment, which consisted of combination chemotherapy and radiation (40 sessions). A percutaneous endoscopic gastrostomy tube was placed to facilitate feedings because of the anticipated inability to eat secondary to severe stomatitis and esophagitis.

On the tenth session of radiation therapy, the oncology clinical nurse specialist assessed R.H. for symptom control related to severe stomatitis and difficulty in swallowing. Assessment revealed a pseudomembranous plaque covering two-thirds of the tongue (see Figure A) and erythema extending throughout the gingiva. White patches were present on the back of the throat and soft palate. R.H. identified his pain as a 10+ on the visual analog scale, and he had extremely thick saliva and xerostomia.

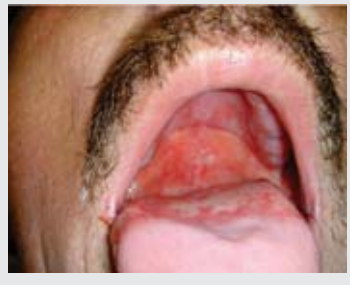
R.H. was given a less demanding position at work, but he still worked outdoors where the weather was hot and very humid. A care plan was initiated and consisted of (a) rinsing his mouth with baking soda in tepid water several times a day, (b) using a bioadherent oral gel mixed with water every eight hours, and (c) applying a fentanyl (Duragesic®, Janssen Pharmaceutica Products, L.P., Titusville, NJ) patch every 72 hours. The patient already had been prescribed nystatin to rinse with and expectorate.

As the treatment sessions continued, R.H. needed to use the bioadherent oral gel every four hours and stated that "it was a burst of relief" that enabled him to drink small amounts of water and continue to work. Within two days of using the gel every four hours or as needed, the patient reported his pain was a 4–5 on the visual analog scale, and he referred to the gel as his lifesaver. R.H. believed that without the bioadherent oral gel and Duragesic patch, he would have stopped treatment and, as a result, would not have been able to go to work. Throughout his treatment, R.H.'s Karnofsky performance status remained at 90 and his stomatitis scale wavered from 2.0–3.0 (on a scale from 0 = no stomatitis to 4 = tissue necrosis, significant bleeding, and life-threatening consequences).

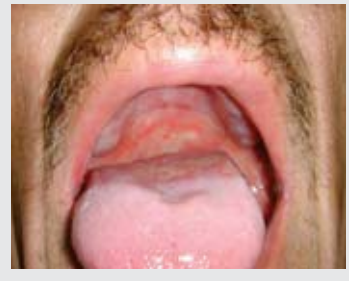
Through the use of multiple interventions during his therapy, R.H. was able to reduce his pain, maintain a good performance status, and maintain his lifestyle without severe changes.



Day 11: Patient rates pain as a 12 on a scale of 1–10.



Day 15: After pain measures are in place, patient rates pain as a 4.



Day 21: Pain measures are continued (pain = 4); course of antifungals completed.

Figure A. Patient With Oral Mucositis at Three Points During Treatment

Note. Photos courtesy of New York Hospital Queens. Reprinted with permission.

malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support (Amgen Inc., 2004).

Other targeted treatments are aimed at preventing or minimizing oral mucositis. The following agents are currently in clinical trials.

Amifostine, a radioprotective compound, is an antioxidant that can be administered via IV or subcutaneously. Its current indication is for the prevention of radiotherapy-induced xerostomia, and it acts as a free radical scavenger to protect healthy cells against the effects of radiotherapy or chemotherapy. Amifostine was studied as a radioprotector in patients with head and neck cancer. Investigators found that it did not reduce the incidence of mucositis but did improve patients' ability to produce saliva, which is important for speaking, chewing, and swallowing (Brizel et al., 2000). A potential limiting effect of amifostine is nausea, which occurs in about 53% of patients. Less than 1% of patients experience hypotension. The recommended dose of amifostine in the radiotherapy population is 200 mg/m^2 (Brizel et al.; MedImmune Oncology, Inc., 2003).

Saforis™ (MGI Pharma, Inc., Bloomington, MN) is an oral suspension with L-glutamine, an amino acid needed during periods of rapid cell turnover and for protein synthesis. It is administered orally for the purpose of increasing the uptake of L-glutamine to the cells lining the oral mucosa. In Peterson and Petit's (2003, 2004) study evaluating the effectiveness of Saforis in chemotherapy patients, a 20% reduction in moderate to severe mucositis was identified (National Cancer Institute scale > grade 2).

Finally, the use of low-level laser therapy has been receiving attention. Lasers (i.e., light amplification by stimulated emission of radiation) produce pure light in a single wavelength. This noninvasive treatment mo-

dality uses the pure light of a low-intensity laser to produce photochemical reactions in the cells (Sandoval, Koga, Buloto, Suzuki, & Dib, 2003; Zeischegg, n.d.). The effects noted in chemotherapy-based studies indicate that low-level laser therapy decreases the duration of mucositis and the pain experienced by patients (Pourreau-Schneider et al., 1992; Sandoval et al.).

Other management strategies are being developed and studied for their impact on reducing the incidence and duration of oral mucositis. The basic strategy for management will continue to be based on early intervention and supportive care. Early intervention needs to include routine oral care and pain management, and supportive care should be focused on maintaining hydration, managing infection, and providing nutritional intervention.

Future Directions

Oral mucositis treatment strategies traditionally have been based on palliation of symptoms and prevention of infection. Targeted therapies can positively impact the risk and incidence of oral mucositis, and multiple targeted therapies may be the standard of practice in the future. Because nurses are in a unique position to participate in the evaluation of specific therapies, they should be proactive in initiating oral care protocols and educating patients about the benefits of basic oral care. Education, nursing research, and evidence-based practice are the foundations for success in creating a positive outcome in patients with oral mucositis. The key player in creating successful outcomes is and will continue to be the nurse.

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Rapid Recap

Current Trends in Managing Oral Mucositis

- Oral mucositis is a common complication of cancer therapy.
- New information is available that defines the pathobiology of mucositis and helps nurses to understand how mucositis occurs at the cellular level and how to anticipate when it will occur.
- Agents are available to assist nurses in managing mucositis.
- The appearance and functional ability of the oral cavity must be assessed on a regular basis to minimize the effects of oral mucositis.
- Nurses must be proactive in initiating oral care protocols and educating patients about the benefits of basic oral care.