Cancer Care Nova Scotia
Many Hearts • Many Minds • One Goal
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Cancer Information for Primary Caregivers
In Practice

Open Up and Say AHHH!

Management of Oral Complications from Cancer Therapy

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Overview

Cancer therapy can result in several different kinds of adverse events for patients. One such group of adverse events are the toxicities experienced in the oral cavity. Problems range from annoying through to debilitating, sometimes resulting in an inability to eat or drink. This issue of *In Practice* summarizes the management strategies for several oral complications, based on information included in the new *CCNS* Guideline, *'Best Practice Guidelines for the Management of Oral Complications from Cancer Therapy'*.

To begin, it is important to recognize that patients undergoing different kinds of cancer therapy are at different levels of risk for oral complications. Patients receiving chemotherapy after surgical removal of a solid tumour are at low risk (about 10%), whereas those receiving chemotherapy as the primary cancer treatment (e.g. some hematologic malignancies) and chemotherapy targeted to tumours of the head and neck or the GI tract are at intermediate risk (about 40%). Hematopoietic stem cell transplant patients (sometimes called bone marrow transplant) are at high risk (about 80%) and all patients who receive radiotherapy to the oral cavity will experience oral complications.

The types of complications experienced range in severity as well. The most common complications are oral mucositis (or stomatitis), salivary gland dysfunction (or xerostomia), oral pain, and oral infection *(Table 1)*. These may lead to other, more serious, complications, such as dehydration (unable to drink or eat), oral hemorrhage, or systemic infections. Management strategies (next page) are not always effective, so preventive measures must be considered in all patients, and especially those at intermediate or high risk.

The level of oral health before cancer treatment is an important risk factor for later development of oral complications. Patients who take meticulous care of their mouths are less likely to experience symptoms, and any symptoms they do experience will likely be less severe. There are at least two important prevention strategies to lessen oral complications:

- good oral self-care practices *(See Table 2)*, and
- preventative dentistry to eliminate adverse oral pathology prior to cancer treatment.

If possible, the guidelines recommend that each patient visit their dentist or oral surgeon for a complete examination BEFORE beginning chemotherapy or radiation therapy to the oral cavity. There are dental programs in the QEII Health Sciences Centre for high risk patient populations (i.e. stem cell transplant patients and head & neck cancer patients), but other patients need to see their community dentist. The dentist can perform necessary interventions or dental surgery to prevent future complications, and can reinforce the importance of good oral self-care practices. If there is dental pathology that requires surgery or other interventions, these must be completed in time for patient recovery before chemotherapy begins. Chemotherapy often causes neutropenia and thrombocytopenia- either of which would be risky to a patient still recovering from dental surgery. Therefore, patients should visit their dentist three or four weeks before chemotherapy is scheduled.

The organization of a pre-chemotherapy dental visit is a change in common practice, and will require collaboration between the physician referring patients for chemotherapy (often the surgeon), the oncologist receiving the referral, and action by an informed patient. For many types of cancer treatment, there is a delay between surgical removal of a tumour

and the start of chemotherapy. This provides an opportunity to deal with dental examination and necessary interventions. Urgent chemotherapy, however, should not be delayed to accommodate the dental visit. It is important that there be clear communication between the referring physician, the dentist/ dental team, and the oncology team. Some important communication points are listed in *Table 3*.

Prevention and management of oral mucositis

Prevention and management of oral mucositis has evolved from a long history of empiric practices, different from one practitioner to the next. In recent years, research evidence has emerged to support or deny many preventative and treatment interventions. Other practices remain untested. Agents which have been proven, unproven or inadequately researched are listed below. Of note, most of the research has been done in patients at high risk for oral mucositis, and it is not certain how to extrapolate this information to patients at lower risk (e.g. low risk chemotherapy patients):

Agents proven to be effective for mucositis prevention

- Benzydamine (radiation-induced mucositis in patients with head and neck cancer)
- Midline radiation blocks and three-dimensional radiation treatment to the oral cavity
- Oral cryotherapy (ice chips in the mouth for 30 minutes starting 5 minutes before chemotherapy administration) to prevent stomatitis in patients receiving 5-fluorouracil-based chemotherapy or high-dose melphalan as part of a conditioning regimen for stem cell transplant. (Exception: Oxaliplatin-based regimen.)
- Keratinocyte Growth Factor-1 (Palifermin- Kepivance®) in patients receiving high dose chemotherapy and total body irradiation for stem cell transplant

Agents which have not proven to be effective for prevention of mucositis in a specific population

- Chlorhexidine (radiotherapy patients head and neck cancer)
- Sucralfate (radiation-induced oral mucositis)
- Antimicrobial lozenges (radiation-induced oral mucositis)
- Acyclovir and its analogues
- Pentoxifylline (mucositis in patients undergoing hematopoietic stem cell transplant)

Agents for which there is insufficient evidence for prevention of mucositis

- Allopurinol Mouthwash
- Vitamin E
- Betacarotene
- Kamillosan Liquidum (chamomile)
- Prostaglandin E2 lozenges
- Filgrastim (G-CSF)

Management of oral mucositis has not been studied as well, and there are no evidence-based recommendations on how best to manage this problem if it occurs. There is evidence that chlorhexidine should not be used to treat established oral mucositis. (Although chlorhexidine may be used on the advice of the dentist for prevention of dental cavities, it should be held if there is mucositis). In the absence of definitive evidence, a stepwise approach to management *(Table 4)* is proposed in the guidelines, progressing from the least aggressive treatment for minor mucositis symptoms to more aggressive and more toxic treatment for more significant symptoms. Note that the use of local anesthetics is NOT the first step but is reserved for significant oral pain when coating agents alone and non-steroidal anti-inflammatories/analgesics are not effective *(see Oral Pain below)*. Also, the use of nystatin suspension is not recommended alone or in combination mouthwash formulations *(see Oral Infection below)*.

Oral pain

As noted in the previous section, oral pain is a common symptom of oral mucositis. The severity of pain may range greatly over time and depending on the type of cancer treatment given to the patient. Mild pain can often be managed by simple interventions, such as coating the mouth with an antacid or Kaopectate. If possible, an analgesic or a non-steroidal anti-inflammatory may be sufficient for moderate pain. If this is not effective, local anesthetics (alone or compounded in a pain relief mouthwash - *Table 5*) may be used, but with caution. Patients on these agents need to be properly educated about avoidance of aspiration from foods and liquids when the anesthetic numbs the gag reflex! Very severe oral pain is not uncommon in hematopoietic stem cell transplant patients, and often requires hospitalization and parenteral opioids.

Oral infection

Oral infections can be bacterial, fungal, viral, or due to other pathogens. A common type of oral infection is candidiasis (or thrush),

due to opportunistic overgrowth of endogenous candida (yeast) in the mouth, particularly associated with mouth ulcers. Clinicians often wish to use preventative antifungal agents, since it is believed easier to prevent candidiasis than to treat it. Despite established empiric practice, the evidence to date suggests that absorbable antifungal agents, such as fluconazole, are effective for both prevention and treatment, whereas non-absorbable agents, such as nystatin, are not effective. It is recommended that nystatin not be used for routine prevention or treatment, and this agent is not included in any mouthwash formulations. There is also no evidence that antibacterial or antiviral antibiotic agents are effective for prevention of these infections respectively. The guidelines only recommend that oral fluconazole be considered as prophylaxis for oral infection, and otherwise infections are only treated as they occur with appropriate antibiotics.

Conclusions

Oral complications may be a significant problem for patients receiving cancer treatment. There are some simple precautions that most patients can take, such as following a basic plan for mouth care and visiting the dentist before starting chemotherapy. Patients should be informed about the risks of oral complications and educated on self-care. It may be one of the few things patients can do for themselves before and during the difficult period of cancer treatment.

Medical prevention and management of oral mucositis, pain and infection is based largely on empiric practice, but should be adapted to include evidence-based practices (e.g. a change from nystatin to fluconazole for prevention and treatment of oral candidiasis). Some changes in common practice, such as the planning for a pre-chemotherapy dental visit, need to be considered within the full plan for patient management before, during, and after cancer treatment.

The full discussion of information and evidence is available to health care professionals in the *'Best Practice Guidelines for the Management of Oral Complications from Cancer Therapy'*. It is available on *Cancer Care Nova Scotia's* website at *www.cancercare.ns.ca*.

To request a print version, please email *info@ccns.nshealth.ca* or call 1-866-599-2267.

Table 1. **Oral Complications of Cancer Chemotherapy**

Complication	Direct Risk Factor	Indirect Risk Factors
Oral mucositis	Mucosal cytotoxicity	Decreased local/systemic immunity
	Physical/chemical trauma	Local infections
	Re-activation of HSV	
Oral infections		
Viral		Decreased systemic immunity
Fungal		Decreased systemic immunity
		Salivary gland dysfunction
		Altered oral flora (decrease bacterial flora)
Bacterial	Inadequate oral hygiene	Decreased systemic immunity
	Mucosal breakdown	Salivary gland dysfunction
	Acquired pathogens	
Taste dysfunction	Taste receptor toxicity	
Xerostomia	Salivary gland toxicity	Anticholinergic drugs
Neuropathies	Vinca alkaloid drug use	
Gastrointestinal mucositis		Nausea and vomiting
Hemorrhage	Oral mucositis	Thrombocytopenia

Table 2. **Basic Mouth Care Plan**

Flossing

- Flossing with dental floss allows a patient to clean surfaces between the teeth.
- Flossing is usually done before brushing, and before going to bed.
- The patient should continue their flossing practices, using the same type of dental floss as they have done in the past.
- If flossing causes bleeding of the gums which does not stop after 2 minutes, it should be discontinued.
- Patients who have not flossed routinely before cancer treatment should not begin flossing at this time.
- Patients with cancers in the mouth may not be able to floss.

Brushing

- Use a small, soft-headed, rounded-end, bristle toothbrush (electric toothbrushes are not preferred), and a fluoridated toothpaste or gel (preferably with a neutral taste).
- Brush teeth 4 times daily, within 30 minutes after eating and before bed. Brush after flossing.
- Rinse toothbrush in hot water water to soften it before using.
- Brush tongue gently from back to front.
- Rinse brush after using in hot water. Air dry.
- Change tooth brush when bristles are not standing up straight (about once per month).
- *Patients with Head & Neck Cancers:*
    - Brushing may not be appropriate because of tumour involvement. Patient may attempt to clean teeth with a moist gauze wrapped around the finger or a foam swab soaked in rinsing solution, if able. Otherwise patient should rinse mouth several times with rinsing solution.
- *Dentures:*
    - Remove dentures, plates and prostheses before beginning mouth care.
    - Rinse mouth thoroughly with rinse solution.
    - Brush and rinse dentures after meals and at bedtime. Rinse with rinsing solution before placing in mouth.
    - Remove from mouth for long periods (at least 8 hours/24). Soak in rinsing solution.

Rinsing

- Rinsing the oral cavity helps to maintain the moisture in the mouth, removes the remaining debris and toothpaste, and reduces the accumulation of plaque and infection.
- Rinse vigorously several times after brushing and flossing, using one of the rinsing solutions.

Lip Care

- Coat lips with an oil-based or water soluble lubricant to keep them moist. Water soluble lubricants may be used inside and outside the mouth, and can be used with oxygen, since there is no risk of aspiration.
- Apply the lubricant after each cleaning, at bedtime, and as needed. Water-based lubricants need to be applied more frequently.

Eating

- Avoid abrasive, rough, spicy, acidic and hot foods. All irritants should be avoided, especially alcohol and tobacco. Eat soft foods. Avoid foods containing a lot of sugar, and really cold foods. Encourage high-density and high-fibre foods to clean teeth and massage gums. Encourage a well-balanced diet, high in protein, vitamins B & C. Encourage a fluid intake of at least 2 litres per day to keep mucous membranes moist.

trim along this line

Table 3. Communication with Dentist/Dental Oncology Team

Pretreatment Dental Exam

The dentist should receive key information about the cancer patient prior to the assessment, including:

- Cancer diagnosis, such as type, stage, prognosis.
- Current CBC and other relevant bloodwork results; hematologic and immunologic status.
- Treatment planned for the patient, including planned date for first treatment.
- If radiation is planned, field and dose of radiation.
- If the patient is to receive a stem cell transplant, type of transplant, planned transplant date, conditioning regimen to be given.
- Other medical considerations, such as splenectomy, cardiopulmonary disease, indwelling venous access line.

Assess as early as possible - one month before cancer treatment if invasive oral procedure(s) needed.

Information to Send Back to Oncology Team

- Amount & severity of dental cavities.
- Number of teeth requiring restoration or extraction.
- Teeth requiring endodontic treatment, or other endodontic disease issues.
- Peridontal disease status.
- Teeth with pupal infection.
- Any other urgent dental care required.
- Time needed to stabilize any oral disease.

Table 4. A Stepwise Approach to Management of Oral Mucositis and Oral Pain

1. Mucosal Coating Agents

Alumina suspension (AmphojelTM) - constipating effects
Magnesia Suspension (Milk of MagnesiaTM) - laxative effects
Alumina and Magnesia Suspension (MaaloxTM) - balanced bowel effects
Attapulgite suspension (KaopectateTM) - mild constipating effects

- *May use 5-10mL 4-6 times daily to coat the mucosal surfaces.*

2. Water-Soluble Lubricating Agents

Artificial Saliva (e.g. Moi-Stir™, Salivart™) - 1-2 mL PRN
OraBase™

3. Topical Analgesics / Anti-inflammatory Agents

Benzydamine topical rinse (e.g. Tantum™) - No effect on gag reflex.

- *Rinse mouth with 10-15 mL q 4-6 hours; swish around mouth and spit out.*
- *May have a drying effect (from alcohol in formulation).*

May consider systemic analgesics (e.g. Acetaminophen) or NSAID (e.g. ibuprofen, naproxen) - unless patient at risk of febrile neutropenia.

4. Topical Anesthetics / Pain Relief Mouthwash Formulations

Lidocaine: Viscous, Ointment, Sprays (e.g. Xylocaine™) - Xylocaine Viscous is a thick paste, most patients dislike the sensation of this viscous product.

- *Swish and swallow slowly or spit out of mouth 5-10 mL q4h PRN; may inhibit gag reflex- do not eat or drink for at least 30 minutes after dose.*
- *Anesthetic effects occur in 5 minutes and last 20-30 minutes.*

Diphenhydramine liquid (e.g. Benadryl™) - may cause sensitization of the mucosal tissue; used in patients who cannot tolerate other anesthetics.

- *Swish and swallow 5-10 mL q4h PRN; Use non-alcoholic liquid formulation.*
- *Lidocaine and/or Diphenhydramine are components of the Pain Relief Mouthwash formulations.*

5. Systemic Analgesics

Opioid Drugs: Oral, IV Bolus Morphine or Hydromorphone
Continuous infusion, PCA dosing of Morphine or Hydromorphone for severe pain - Use according to institutional policy.

6. Cellulose Film-forming Agents

Film-forming Agents (e.g. Film-forming Hydroxypropylcellulose [GelclairTM], when available in Canada; or other available products)

Cancer Care Nova Scotia is a program of the Department of Health. Its mandate is to evaluate, coordinate and strengthen the cancer system in Nova Scotia.

Cancer Care Nova Scotia works with and supports professionals and stakeholders in the health care system to bring about patient-centred change. Its ultimate goal is to reduce the burden of cancer on individuals, families, communities and the health care system.

In Practice is a supplement to *Cancer Care Nova Scotia's* newsletter. It is written specifically for primary care practitioners with information that we hope will make a difference in your cancer practice.

Please contact Christine Smith, Communications Coordinator, *Cancer Care Nova Scotia,* by phone at 902-473-2932 or by email at christine.smith@ccns.nshealth.ca with comments or suggestions for future topics.

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Table 5. **Pain Relief Mouthwash Suspensions**

Pain Relief Mouthwash with Attapulgite (Kaopectate™) *(Mild constipating effect)*

• Diphenhydramine 6.25mg/5 mL (Benadryl™) liquid	50 mL
• Lidocaine (Xylocaine™) viscous 2%	25 mL
• Attapulgite (Kaopectate™) suspension	25 mL
TOTAL VOLUME	100 mL

Lidocaine may inhibit gag reflex. If this is a problem, order Pain Relief without Lidocaine.

Pain Relief Mouthwash with Antacid *(Balanced effect on the bowels)*

• Diphenhydramine 6.25mg/5 mL (Benadryl™) liquid	50 mL
• Lidocaine (Xylocaine™) viscous 2%	25 mL
• Magnesia-Alumina Concentrate Suspension (Maalox TC™)	75 mL
TOTAL VOLUME	150 mL

Lidocaine may inhibit gag reflex. If this is a problem, order Pain Relief without Lidocaine.

Pain Relief Mouthwash without Lidocaine (Mild constipating effect)

• Diphenhydramine 6.25mg/5 mL (Benadryl™) liquid	50 mL
• Attapulgite (Kaopectate™) suspension	50 mL
TOTAL VOLUME	100 mL

Used for patients who cannot tolerate lidocaine anesthetic. Diphenhydramine may cause sensitization of the oral tissues.

After brushing teeth and rinsing mouth, swish 10-15mL for up to 2 minutes, then spit out or swallow slowly. Repeat TID-QID PRN. Avoid putting anything in the mouth (including medications) for 30 minutes, especially if mouthwash swallowed. Systemic absorption of swallowed lidocaine may be contraindicated in patients with impaired cardiovascular function.

- Oral Fluconazole (or another absorbable systemic antifungal agent) is preferred for the prevention and/or treatment of oral candidiasis (Evidence-based statement).

For details on obtaining the full version of the *'Best Practice Guidelines for the Management of Oral Complications from Cancer Therapy'*, please refer to page 3 of this publication, under Conclusions.

If you have further questions or concerns on this topic, please email us at *info@ccns.nshealth.ca* or call 1-866-599-2267.