Mucositis: The Basics

What is mucositis?

Mucositis is a medical term that is used to refer to mouth sores, oral mucositis, or esophagitis. It can range in severity from a red, sore mouth and/or gums to open sores that can cause a patient to be unable to eat. The lining of the entire gastrointestinal tract (mouth, throat, stomach, and bowel) is made up of epithelial cells, which divide and replicate rapidly. Imagine this: if you bite your lip, the tissue is often able to heal by the next day because of this rapid growth. Chemotherapy and radiation therapy kill not only cancer cells, but other rapidly dividing cells as well, including the lining of the entire gastrointestinal tract. This article will discuss the effects on the lining of the mouth and throat (this lining is called the mucosa).

Oral mucositis leads to several problems, including pain, nutritional problems as a result of inability to eat, and increased risk of infection due to open sores in the mucosa. It has a significant effect on the patientÃ•s quality of life and can be dose- limiting (requiring a reduction in subsequent chemotherapy doses).

Signs and symptoms of mucositis include:

- Red, shiny, or swollen mouth and gums
- Blood in the mouth
- Sores in the mouth or on the gums or tongue
- Soreness or pain in the mouth or throat
- Difficulty swallowing or talking
- Feeling of dryness, mild burning, or pain when eating food
- Soft, whitish patches or pus in the mouth or on the tongue
- Increased mucus or thicker saliva in the mouth

Who gets mucositis?

Over forty percent of patients who receive chemotherapy will develop some degree of mucositis during the course of their treatment. Patients receiving radiation to the head, neck, or chest areas, and patients who undergo bone marrow or stem cell transplant, are even more likely to develop mucositis. Certain chemotherapy agents are more likely to cause this side effect (Table 1), as is total body irradiation, often used for bone marrow transplants.

Table 1: Chemotherapy agents known to cause mucositis

Alemtuzumab (Campath)	Bleomycin (Blenoxane)	Asparaginase (Elspar)
Cyclophosphamide (Cytoxan)	Cytarabine (Cytosar-U)	Busulfan (Myleran, Busulfex)
Docetaxel (Taxotere)	Doxorubicin (Adriamycin)	Capecitabine (Xeloda)
Fluorouracil (5-FU)	Gemcitabine (Gemzar)	Carboplatin (Paraplatin)
Gemtuzumab ozogamicin (Mylotarg)	Hydroxyurea (Hydrea)	Daunorubicin (Cerubidine)

Idarubicin (Idamycin)	Interleukin 2 (Proleukin)	Epirubicin (Ellence)
Lomustine (CeeNU)	Melphalan (Alkeran)	Etoposide (VePesid)
Mitomycin (Mutamycin)	Mitoxantrone (Novantrone)	Irinotecan (Camptosar)
Oxaliplatin (Eloxatin)	Paclitaxel (Taxol)	Methotrexate (Rheumatrex)
Pentostatin (Nipent)	Procarbazine (Matulane)	Mechlorethamine (Mustargen)
Topotecan (Hycamtin)	Trastuzumab (Herceptin)	Pemetrexed (Alimta)
Vinblastine (Velban)	Vincristine (Oncovin)	Thiotepa (Thioplex)
Tretinoin (Vesanoid)		

Factors that can increase the likelihood of developing mucositis, or that can make it worse if it does occur, include: poor oral or dental health, smoking, using chewing tobacco, drinking alcohol, dehydration, and diseases such as kidney disease, diabetes or HIV/AIDS.

Monitoring the development and resolution of mucositis can be difficult, given that the experience is different for every patient. The World Health Organization (WHO) oral toxicity scale is one of a number of grading systems developed to assist in evaluating the severity of mucositis:

Oral Mucositis			Severe Mucositis	
Grade 0	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
None	Soreness ± erythema	Erythema, ulcers Patients can swallow solid diet	Ulcers, extensive erythema Patients cannot swallow solid diet	Mucositis to the extent that alimentation is not possible

Adapted from WHO oral toxicity scale.

Examples of mucositis:

Severe mucositis

Mucositis with candida infection (thrush)

Prevention and treatment

There have been numerous studies trying many different medications and interventions to reduce the incidence and severity of oral mucositis. Unfortunately, only a few of these interventions have shown much success. It is known that a good oral care regimen (Table 2) can help in preventing or

decreasing the severity of mucositis and can help prevent the development of infection through open mouth sores. The mainstay of an oral care regimen is mouth rinses, and numerous studies have determined that just plain old salt water is the best and most cost effective mouth rinse available. A mouth rinse aides in removing debris and keeping the oral tissue moist and clean. Other important components include using mouth and lip moisturizers, using a soft-bristle toothbrush, maintaining adequate intake of fluids and protein, and avoiding irritating foods, alcohol and tobacco.

Table 2: Example of oral care protocol

- Rinse mouth (swish and spit) before and after meals and at bedtime with either:
  - Normal saline (1 tsp of table salt to 1 quart (32 oz.) of water)
  - Salt and soda (one-half tsp of salt and 2 tbsp of sodium bicarbonate in 1 quart of warm water)
- Use a soft-bristle toothbrush after meals and at bedtime. If the brush causes pain, toothettes may be used
- Use a non-abrasive toothpaste (or mix 1 tsp baking soda in 2 cups water). Avoid toothpastes with whiteners.
- Keep lips moist with moisturizers. Avoid using Vaseline (the oil base can promote infection).
- Avoid products that irritate the mouth and gums:
  - Avoid commercial mouthwashes and those with alcohol
  - Limit use of dental floss, DO NOT use with platelets below 40,000
  - Do not use lemon or glycerin swabs or toothbrushes without soft bristles
- Increase your fluid intake.
- Try to include foods high in protein in your diet.
- Avoid hot, spicy or acidic foods, alcohol, hard or coarse foods (crusty bread, chips, crackers).
- If you wear dentures:
  - Remove whenever possible to expose gums to air
  - Loose fitting dentures can irritate the mouth and gums and should not be worn
  - Do not wear dentures if mouth sores are severe

Do not smoke cigarettes, cigars or pipes. Do not use smokeless tobacco (chewing tobacco, snuff)

Cryotherapy, which involves sucking on ice chips during chemotherapy administration, has shown some effect in preventing mucositis caused by 5-FU (fluorouracil). Two agents, Gelclair® and Zilactin®, are mucosal protectants that work by coating the mucosa, forming a protective barrier for exposed nerve endings. These agents resulted in improved pain control, and ability to eat and speak in clinical trials. Amifostine (Ethyol®), a drug that protects against the damage to the mucosa caused by radiation, is approved by the FDA for patients receiving radiation therapy for cancers of the head and neck. Studies have demonstrated that amifostine can reduce dry mouth and may prevent mouth sores; however, more research is needed. Other agents that have been studied include: capsaicin (derived from chili peppers), glutamine, prostaglandin E2, Vitamin E, sucralfate, and allopurinol mouthwash.

Keratinocyte growth factor (KGF) is a substance produced naturally in the body that stimulates the growth, repair, and survival of cells that protect the lining of the mouth and GI tract. A manmade version of human KGF has been developed as the drug palifermin, and is currently indicated for use in patients with hematologic malignancies or blood cancers (leukemias, lymphomas and myelomas) who are undergoing bone marrow or stem cell transplant. Palifermin was found to decrease the length and severity of mucositis in these patients.

Pain control

Pain is a significant problem related to mucositis and warrants early intervention. In mild cases, ice pops, water ice, or ice chips may help numb the area, but most cases require more intervention for relief or pain.

Topical pain relievers include lidocaine, benzocaine, dyclonine hydrochloride (HCl), and Ulcerease® (0.6% Phenol). One of the issues of using topical agents is the inability to effectively coat all areas and that the pain relief is brief. In patients with mucositis that do not achieve pain relief with topical agents, narcotic analgesia is often necessary. This may require a hospital admission for intravenous (IV) pain medications until the mucosa begins to heal, particularly in patients unable to swallow. It is important to note that this side effect is temporary and the use of narcotics for the relief of pain caused by mucositis will be temporary as well. Patients should not "suffer through it" to avoid using narcotics, they will not become addicted to them when used for this very real pain.

One popular topical agent is "magic mouthwash" a mix of lidocaine, diphenhydramine and Maalox. This has not been proven effective and Maalox further dries the tissue, which can add to the complication. It is best to use lidocaine alone in a swish and spit method.

Patients receiving radiation therapy to the chest/head/neck area or chemotherapy should examine their mouths at least once a day for redness, sores, or signs of infection. The healthcare team should be notified if they notice worsening sores, white patches, pus, a "hairy" or thick feeling tongue, bleeding in the mouth, or development of a fever (temperature greater than 100.4).

Research continues into many new agents to prevent or treat mucositis, but at this point, it remains a challenging, costly, and distressing side effect.

References

Materials and photos adapted from Amgen Inc., 2006 teaching materials on Palifermin (Kepivance™)

Eilers J. Nursing interventions and supportive care for the prevention and treatment of oral mucositis associated with cancer treatment. Oncology Nursing Forum. Online. 31(4 Suppl):13-23, 2004 Jul.

Cawley MM. Benson LM. Current trends in managing oral mucositis. Clinical Journal of Oncology Nursing. 9(5):584-92, 2005 Oct.
National Cancer Institute website, www.cancer.gov

Sonis ST. Oral mucositis in cancer therapy. The Journal of Supportive Oncology. 2(6 Suppl 3):3-8, 2004 Nov-Dec.

Worthington HV. Clarkson JE. Eden OB. Interventions for treating oral mucositis for patients with cancer receiving treatment. Cochrane Database of Systematic Reviews. (2):CD001973, 2004.

More Information

Mucositis Tip Sheet: Here you will find helpful tips from our Oncology Nurse Educator about oral mucositis (mouth sores). You will find information that explains what oral mucositis is, why it happens, how it is treated, and what you can do to prevent yourself from developing it.

Mucositis Medications: Find out about medications which may be used to decrease the chance of developing oral mucositis (mouth sores) or to shorten the duration of oral mucositis in some cancer patients receiving chemotherapy and radiation therapy.

- Palifermin (Kepivance™)
- Amifostine (Ethyol®)