

Oral mucositis

Oral mucositis, sometimes called stomatitis, describes inflammation of oral mucosa, which occurs as a result of exposure to chemotherapeutic agents and ionizing radiation.¹

In a survey of 558 nurses, 89% identified oral mucositis as a significant problem and a huge

majority (92%) ranked oral mucositis 'very high' relative to other supportive care issues faced by cancer patients. 93% reported the pain of oral mucositis as 'most important' to their patients, followed by difficulty swallowing (87%) and speaking (73%).²

Prevalence

The overall risk of developing oral mucositis varies and is influenced by the patient's diagnosis, age, level of oral health, and type, dose, and frequency of drug administration.³ However, all patients receiving radiotherapy for head and neck cancer will experience oral mucositis, as will 80% of patients receiving Hematopoietic Stem Cell Transplants (HSCT) and 40% of patients treated with standard dose chemotherapy.²

There are many types of chemotherapy that are mucotoxic. Some of these include:³

- 5-fluorouracil
- methotrexate
- doxorubicin
- etoposide
- melphalan
- cytosine arabinoside
- cyclophosphamide

Pathophysiology

Oral mucositis is characterised by physiological changes to epithelial cells ranging from erythema to ulceration. However, endothelial, microvascular

and connective tissue damage precedes epithelial injury, meaning oral mucositis begins at a very early stage of radiation therapy.⁴

The phases of oral mucositis⁴

Initiation	Cell exposure to chemo- and radiotherapy causes DNA damage and generates reactive oxygen species (ROS), which are able to injure cells, tissues and blood vessels
Signalling	ROS cause further DNA damage and stimulate expression of transcription factors that lead to tissue injury and apoptosis
Amplification	Release of pro-inflammatory cytokines result in further tissue damage, which amplifies the signalling cascade
Ulceration	Painful ulcers form that provide an entry point for bacteria, viruses and fungi. Bacterial cell wall components can further induce inflammation
Healing	A signal from submucosal tissue allows renewed cellular proliferation and differentiation restoring the lining of the oral cavity

The World Health Organisation (WHO) classify oral mucositis in 5 clinical categories⁵

WHO oral toxicity scale⁵

Oral mucositis			Severe oral mucositis	
Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
No change	Soreness/erythema	Erythema and ulcers	Ulcers (liquid only diet)	Alimentation not possible

Adapted from the WHO oral toxicity scale.⁵

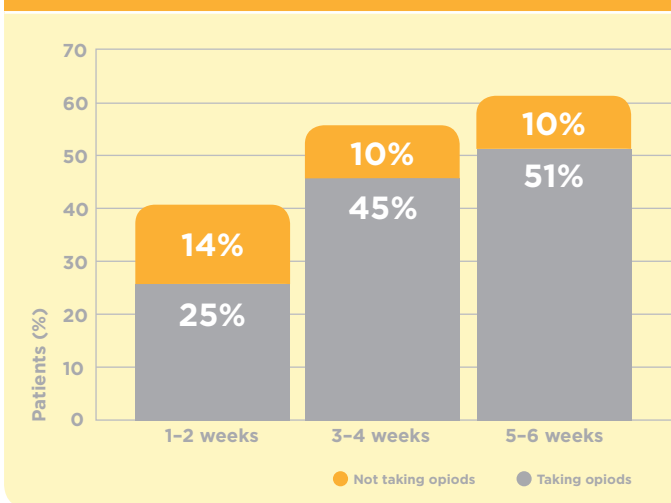
Impact

Severe oral mucositis can cause other debilitating comorbidities

- Pain that is severe enough to require opioid analgesics^{6,7}
 - Opioid analgesics are associated with incapacitating side effects, such as constipation², hallucinations⁶ and loss of mental acuteness⁶

- Hospitalisation and parenteral nutrition can be required when mouth soreness becomes too painful for patients to eat at all^{3,7}
- The ulcers associated with oral mucositis act as a site for infection⁴ and subsequent septicaemia.³ Mortality rates as a result of oral mucositis related infections are between 6 and 30%⁸
- The pain and its associated effects can damage patients' psychological well being⁹
- Severe oral mucositis may interfere with the intended course of treatment, potentially affecting patient survival³

Severity of mouth and throat soreness in relation to opioid use over time⁷



Adapted from Murphy BA *et al.*⁷ A 6-week multicentre study to investigate healthcare utilisation in head and neck cancer patients (n=75). Changes in mouth and throat soreness at each time point versus baseline and overall test for the effect of time were statistically significant (P<0.001).

The economic burden of mucositis is high⁷

Mucositis-related pain and its functional impairment is associated with increased use of costly healthcare resources.⁷

References:

1. National Cancer Institute. Oral complications of chemotherapy and head/neck radiation. Last modified 10th June 2009. Available at: www.cancer.gov/cancertopics/pdq/supportivecare/oralcomplications/HealthProfessional. Last accessed January 2010. 2. Bruce SD, Quinn A. *US Oncological Disease* 2007;**1**:86-90. 3. Pico J-L *et al.* *The Oncologist* 1998;**3**(6):446-451. 4. Sonis ST *et al.* *CANCER Supplement* 2004;**100**(9):1995-2025. 5. World Health Organisation. Handbook for reporting results of cancer treatment. Geneva, Switzerland: World Health Organisation, 1979. 6. Bellm LA *et al.* *Support Care Cancer* 2000;**8**(1):33-39. 7. Murphy BA *et al.* *J Pain Symptom Manage* 2009;**38**(4):522-532. 8. Treister N, Sook-Bin W. Chemotherapy-Induced Oral Mucositis, 2008. Available at <http://emedicine.medscape.com/article/1079570-overview>. Last accessed January 2010. 9. Borbasi S *et al.* *Oncol Nurs Forum* 2002;**29**(7):1051-1057.