Guidelines for Prevention and Management of Oral Mucositis

These guidelines apply to all chemotherapy patients, as well as patients receiving radiotherapy to head, neck or oesophagus

Mucositis is defined as the damage that occurs to the oral mucosa and gastrointestinal tract following chemotherapy or radiotherapy (especially radiotherapy to the head, neck or oesophagus), leaving the tissue exposed to infection.

Stomatitis refers to the diffuse inflammatory, ulcerative condition affecting the mucous membranes lining the mouth.

All chemotherapy drugs have the potential to cause oral mucositis. Treatments most commonly associated with oral mucositis include

- Anti-metabolites e.g. 5-FU, capecitabine, methotrexate
- Anthracyclines e.g. epirubicin, doxorubicin
- All lymphoma or leukaemia patients who have recently had treatment
- Tyrosine kinase inhibitors (such as sunitinib, pazopanib, afatinib) and everolimus
- Radiotherapy to the head and neck region

Oral mucositis typically occurs 7 to 14 days after chemotherapy or radiotherapy and may last for 2-3 weeks after the completion of treatment. It may result in pain, discomfort and difficulty eating.

It is important to take preventative measures against mucositis (see page 3) and to recognise and treat it promptly and effectively if it occurs.

Management involves mouth care, management of oral pain and consideration of nutritional support in severe cases.

Assessment of patient

Patients presenting with acute oncological problems, during and immediately after their treatment, should be assessed for the presence of oral mucositis.

- Clinical examination of oral mucosa – see page 3 for more details
- Functional status - ability to eat
- Bloods – FBC (check if neutropenic), U&Es, CRP

Grading of Oral Mucositis (CTC criteria)

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

Reason for Update: reviewed to align with AOS requirements	Approved by Chair of Alliance Chemotherapy Group: Dr J De Vos
Version: 4	Date: 1.6.16
Supersedes: Version 3	Review Date: July 2018
Prepared by: S Taylor	Checked by: C Tucker

Management of Oral Pain

Patients **currently** receiving radiotherapy or chemotherapy (or within last 2-4 weeks) and with oral, pharyngeal or oesophageal mucositis

Encourage good oral hygiene and frequent mouth washing (see page 3)
Check to see if patient has any evidence of oral infection **

Grade 1 or 2 *

1st line
Difflam (benzydamine) mouthwash: 15ml up to every 1½ hours, to provide local pain relief for stomatitis.
It may be diluted with a little water if stinging occurs.

2nd line options
The options below may be considered according to the affected area, clinical situation and patient preference:

Systemic options:

Co-codamol 30/500 dispersible tablets - 2 tablets up to QDS (remember to co-prescribe laxative as required)
Soluble Paracetamol 1g QDS

Topical options:

Mucaine equivalent* (antacid and oxetacaine)
10ml QDS, taken before meals to aid eating, in patients with oral or oesophageal ulceration.
May be used alongside other pain relief options.

Hydrocortisone 2.5mg buccal tablets

- one tablet to be allowed to dissolve slowly in the mouth in contact with the ulcer 4 times daily
- are considered useful, particularly in localised radiotherapy reactions, for patients with a single ulcerated area.

Lidocaine 1 - 2% gel* (e.g. Optilube) applied qds

Bonjela (Choline salicylate dental gel) applied to mouth ulcers up to every 3 hours

Orabase (carmellose sodium paste)
Apply to affected areas after meals and before bedtime, or more frequently

Soluble aspirin 300mg

- An option for radiotherapy-induced mucositis, for patients who cannot tolerate Difflam but who wish to continue to try a topical option as well as systemic analgesia
- 1-2 tablets dissolved in a little water and used as a mouthwash up to QDS, and gargled if any oro-pharynx pain (may be swallowed unless any contra-indications e.g. risk of thrombocytopenia, history of peptic ulcers)

*Due to its local anaesthetic effect, advise patients to take care to ensure that food/drinks are not too hot.

Grade 3 *

Grade 4 *

ADMIT, RESUSCITATE
Discuss with consultant ASAP
Manage as for Grade 3

As for Grade 1 and 2, PLUS:

Immediate release opioids
e.g. oral morphine sulphate solution (Oramorph®) 10mg every 4 hours, if the patient can tolerate the oral route.
Otherwise, consider fentanyl patches (C/I if patient on aprepitant) or s/c syringe driver.
Consult palliative care/pain team.

- remember to co-prescribe laxative and antiemetics as required

Gelclair oral gel (15ml sachets)

This is classified as a device, not a medicine, and is not included in local formularies. Its use is restricted to patients with Grade 3 / 4 mucositis.
It does not contain any active drug, and does not promote healing. However, it may provide symptomatic relief in some patients.
The contents of one sachet are rinsed around the mouth to form a protective layer over the sore areas, which may make it more comfortable to eat and drink. The manufacturers state that it may provide relief for up to 7 hours.
Discontinue if the patient does not report any benefit.

If bleeding from mouth, consider **tranexamic acid 5% mouthwash**, 10ml rinsed around the mouth qds, then spit out

Consider **enteral feeding** – refer for dietician review

Reason for Update: reviewed to align with AOS requirements	Approved by Chair of Alliance Chemotherapy Group: Dr J De Vos
Version: 4	Date: 1.6.16
Supersedes: Version 3	Review Date: July 2018
Prepared by: S Taylor	Checked by: C Tucker

*** For patients on capecitabine or continuous 5FU, ensure they have their treatment interrupted for Grade 2 or above mucositis.**

- Severe mucositis (and diarrhoea) early in the first treatment cycle can be the first presenting toxicity due to DPD deficiency#, in which case potentially fatal neutropenia can quickly follow.
- (#A genetic disorder in which there is significantly decreased activity of dihydropyrimidine dehydrogenase, an enzyme involved in the metabolism of active 5FU to inactive metabolites)
- For further information specific to the regimen, including subsequent dose reductions, refer to the relevant chemotherapy or radiotherapy protocol.

**** Anti-Infectives**

- Susceptibility to mouth ulcers associated with Herpes simplex or Candida is increased with prolonged neutropenia and monocytopenia. Antiviral or antifungal prophylaxis may be required for highly myelosuppressive chemotherapy regimens (refer to specific protocols).
- If any signs of infection, take oral swabs
- Candida – fluconazole 50mg daily for 7 - 14 days (100mg od if immunocompromised)
- Viral – consider topical aciclovir 5% for local infection in low risk patients. If highly immunocompromised, consider oral or IV aciclovir. If in doubt, discuss with Consultant.
- Patients who are neutropenic and have signs of infection should be treated according to local neutropenic sepsis guidelines.

Oral Assessment

An oral assessment should be carried out and recorded **once daily** for all haematology and oncology in-patients, according to a locally agreed assessment tool. This requires visual inspection of the oral cavity using a torch, and tongue depressor if necessary, to examine the oral mucosa.
Nutrition, hydration and pain should all be managed according to a locally agreed care plan, and with reference to the oral pain management options listed above.

For out-patients, an oral assessment should be carried out at each out-patient chemotherapy appointment.

Prevention of Oral Mucositis - Maintaining Good Oral Hygiene

A Good Mouth Care leaflet, containing the following information, should be given to all patients before starting the relevant treatment:

1. **All patients** should be encouraged to clean teeth with toothpaste and a soft toothbrush or electric toothbrush after each meal, as well as at bedtime.
   Advise patients to replace their toothbrush regularly to minimise infection risk.
2. All patients should also be encouraged to rinse the mouth thoroughly four times a day (see below for mouthwash options), after each meal and at bed-time, after brushing teeth.
3. Careful dental flossing once daily to reduce plaque should be encouraged. However, if the patient is at risk of thrombocytopenia, flossing should be avoided as this may irritate the gums, thereby causing excessive bleeding.
4. Dentures should be cleaned after each meal and soaked overnight in patient's usual solution.
5. Lips may also be moistened with Vaseline or soft paraffin, or the patient's own lip salve.

6. Adequate oral fluid intake and diet should be encouraged, although alcohol and tobacco should ideally be avoided. Advise patient that spicy foods may irritate the mouth, and care should be taken with rough or crunchy foods as they may damage the mucosal lining or gums.

7. For patients receiving chemotherapy, assuming time permits, ask them to have a dental check-up before chemotherapy starts. Routine annual dental appointments should also continue throughout treatment and follow-up.
   For patients receiving head and neck radiotherapy, a **pre-treatment** dental examination **must** be undertaken.

   If any urgent dental work is required once chemotherapy has started, it is important that a blood test is performed within 48 hours of any dental treatment and their doctor consulted, so as to determine the need for a platelet transfusion pre-treatment or for any prophylactic antibiotic cover.

8. It is recommended that patients do **not** visit a dental hygienist whilst undergoing chemotherapy, so as to avoid unnecessary trauma to the gums.

9. Chemotherapy patients may be directed to the Macmillan leaflet "Mouthcare during Chemotherapy" http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Symptomssideeffects/Mouthcare/Mouthcare.aspx
   There is also a Macmillan leaflet "Dry Mouth" specifically for patients receiving radiotherapy to the head, neck or mouth.
   http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Symptomssideeffects/Mouthcare/Radiotherapy.aspx

Choice of Mouthwash

1. Despite numerous trials, there is no mouthwash that has been proven to be superior to any other in chemotherapy patients. Frequency of mouthwashing is considered the most important factor, although the optimum frequency has not been defined.

2. For the above reason, local expert opinion is that water should be the standard solution used to rinse the mouth. It is important to encourage vigorous rinsing using a ballooning and sucking motion of the cheeks for at least 30 seconds, as it is this action that removes loose debris from the teeth.

3. If preferred, normal saline mouthwashes may be used instead. Ready-made saline is available from Pharmacy as 1 litre plastic bottles of Sodium Chloride 0.9% for Irrigation. This is well tolerated, economical and may also help with healing if stomatitis does occur.

   Alternatively, patients can be advised to make their own salt solution by adding a little salt (¼ to ½ a teaspoon) to a cup of warm water.

4. There is no clinical benefit in using a commercial mouthwash instead of water. However, if the patient prefers to use one, recommend that they choose an alcohol-free product. (Examples include Dentyl, Colgate Plax, Oral B Alcohol Free)

5. **For patients receiving radiotherapy to head and neck:**
   Benzydamine (Difflam) mouthwash has been shown to be useful for both prevention and treatment of mucositis in this patient group, and so is recommended as the mouthwash of choice[1, 2]
   Chlorhexidine mouthwash is not recommended for this group of patients.[1, 2]

References: [1]Rubenstein, EB et al; Cancer 2004; 100 (9 suppl): 2026 – 2046
[2]Keefe, DM et al; Cancer 2007; 109: 820 – 831
Lalla, R et al; Cancer 2014; 1453 – 1461

Reason for Update: reviewed to align with AOS requirements	Approved by Chair of Alliance Chemotherapy Group: Dr J De Vos
Version: 4	Date: 1.6.16
Supersedes: Version 3	Review Date: July 2018
Prepared by: S Taylor	Checked by: C Tucker