



# **HOSPICE PALLIATIVE CARE ASSOCIATION of SOUTH AFRICA**

## **CLINICAL GUIDELINES**

**2012**



## **FORWARD**

It is with great pleasure that I introduce the updated HPCA Clinical Guidelines and thank the team that has contributed to the development of the guidelines. It has taken some time to complete this update on the 2006 guidelines and to ensure the inclusion of guidelines for paediatric palliative care so that care is available to adults and children and their families.

Palliative care is an important approach to assisting patients with life-threatening illness and life-limiting conditions. The World Health Organisation (WHO) definition of palliative care describes that palliative care is applicable early in the illness – in fact from the time of diagnosis of the illness - in conjunction with treatment intended to prolong life. Palliative care can be provided in any setting such as hospitals, community health centres, care homes, the patient's own home, as well as in hospices.

We hope that health care professionals will find these guidelines useful in ensuring that patients not only receive treatment directed at the disease, but also holistic care that addresses distressing symptoms and psychosocial and spiritual problems. The guidelines focus on clinical issues but there is an important section that addresses psychosocial problems such as bereavement care and also spiritual care.

In order to provide holistic care, the WHO requires us to conduct an “impeccable assessment” to discover the patient's physical, psychosocial and spiritual problems. It is useful when faced with a patient with advanced illness to identify the list of problems they experience and to ensure that a care plan addressing each of these problems is developed and reviewed regularly.

The clinical guidelines provide advice on assessment, on pharmacological and non-pharmacological management of symptoms, on how to explain to patient and family members the goals of treatment and provide a reminder to involve the interdisciplinary team or refer to a more experienced clinician when necessary.

There is also a reminder at the beginning of this document to provide care in accordance with bioethical principles. In addition to the recognised principles of beneficence, non-maleficence, autonomy and justice, palliative care also recognises a principle of non-abandonment. As described by Dr Balfour Mount above, people requiring palliative care are “the sickest of the sick and deserve the best the health system can offer them.” Patients who are discharged from hospital should have a care plan, the required medication and referral to a home care service that will provide continuity of care to patient and family.

Palliative care complements acute and chronic care provided to patients. We hope these guidelines will assist clinicians to manage patient symptoms to improve the quality of life of their patients

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**Acknowledgements:**

The Hospice Palliative Care Association of South Africa acknowledge the following in the development of the 2012 Clinical Guidelines in Palliative Care:

Dr Janet Stanford  
Dr Charmaine Blanchard  
Dr Roger Cummins  
Dr Sarah Fakroodeen  
Dr Liz Gwyther  
Dr Margie Hardman  
Dr Sonia Hitchcock  
Dr Rene Krause  
Dr Lize Louw  
Dr Debbie Norval  
Mrs Susan McGarvie  
Mrs Fran Tong  
Dr Sonia van der Spuy  
Mrs Russel van Rensburg

Thanks also to the contributors to the 2006 Clinical Guidelines which formed the foundation of this booklet

Brenda Dass  
Sandie de Villiers  
Deidre Dimbleby  
Kennedy Lata  
Lindsay Lombard  
Trish Lück  
Patrick Mashele  
Lynelle Ruthvin

**Disclaimer:**

In composing these guidelines, the authors have been diligent in their efforts to verify its content through the date of its publication (August 2012). However, it is important to note that drug dosing, uses, side-effects, and contra-indications change over time. All clinicians prescribing from these guidelines should take the time to ensure that drug information is consistent with the manufacturer's current recommendations. Prescribers must also use their own discretion in advising routes of administration that may be common practice in palliative care, but unlicensed by the manufacturer.

## **Contents**

How to use these guidelines	8
Ethical considerations	9
WHO definition of Palliative Care	10
Guidelines for Management of Pain	
1. Pain assessment and management	11
2. Bone pain	17
3. Neuropathic pain	18
4. Incident pain	22
5. Muscle spasm, myoclonus & dystonia	23
Management of Respiratory Symptoms	
1. Breathlessness	32
2. Cough	35
3. Hiccup	38
4. Oxygen therapy	39
Management of Gastro-intestinal Symptoms	
1. Dysphagia	42
2. Nausea and vomiting	44
3. Intestinal obstruction	47
4. Ascites	49
5. Diarrhoea	50
6. Constipation	53
Constitutional Symptoms	
1. Anorexia, Asthenia and Cachexia	65
2. Fever and Sweating	61
Infective symptoms	
1. Immune reconstitution inflammatory syndrome	65
2. Neutropaenic sepsis	67
Management of Neuro-psychiatric symptoms	
1. Delirium	69
2. Anxiety	75
3. Depression	78
4. Insomnia	82
5. Convulsions	83
Management of Urinary Symptoms	
1. Incontinence	88
2. Urinary Tract Infection	90
3. Urinary haemorrhage	93
4. Bladder and ureteric spasm	94

Guidelines for Pressure Care and Wound Care	
1. Pressure Care	96
2. Wound Care	97
The Terminal Phase	104
Vascular and haematological disorders	
1. Anaemia and blood transfusions	108
2. Lymphoedema	110
3. Thromboembolism	114
Palliative Care Emergencies	
1. Haemorrhage	119
2. Hypercalcaemia	121
3. Spinal cord compression	125
4. Superior Vena Cava obstruction	129
General Aspects of Mouth Care	132
Specific Aspects of Oral Care	139

These Guidelines have been developed as an approach to Symptom Management as a Best practice developed from Evidence-Based Medicine as recommended by the Hospice Palliative Care Association of South Africa.

### How to use these guidelines:

- HPCA guidelines have been developed as a tool to guide decision making in the management of patients with life-threatening illness
- We recognize and recommend that management is individualized according to each patient's condition and need. Guidelines will provide a framework for management.
- Comprehensive assessment (The WHO challenge to clinicians is for “**impeccable assessment**” see Appendix 1) is essential for effective management
- It is recommended that the guidelines are used in conjunction with other palliative care reference materials, including SAMF
- The guidelines promote standardized clinical palliative care management and standardized palliative care training.
- The Guidelines have been developed using the following format:
  1. Appropriate assessment to identify cause and severity of symptoms
  2. Explanation to patient and family at all stages
  3. Correct reversible factors
  4. Consider disease-specific palliative therapy
  5. Institute non-pharmacological interventions
  6. Prescribe appropriate first-line treatment
  7. Consider adjuvant/second-line treatment
  8. Review assessment and managementAt all stages of management consider:
  9. Involvement of interdisciplinary team
  10. Referral to appropriate service/more experienced clinician



### Ethical considerations:

We recognize that patients diagnosed with life-threatening or terminal illness are vulnerable in their emotional state and dependence on their health care professionals (and non-professionals) for compassionate empathetic care, sensitive sharing of information to promote participation in decision-making and effective symptom management. It is essential that HCPs caring for patients with life-threatening illness base their care on sound ethical principles and practice. The following is an outline of ethical principles as applicable to end-of-life care.

### Beneficence and Non-maleficence:

- Treatment can only be justified if there is benefit to the patient
- In clinical care, balance benefit of treatment vs risk of treatment
- If there is no longer any benefit to the patient withholding or withdrawing treatment is a sound medical decision which may be reached in discussion with patient, family & carers
- Continuity of care
- Non-abandonment, there is always an appropriate treatment plan
- Referral to hospice or palliative care service if symptom control is not achieved within time frame specified in individual care plan.
- Rigorous and effective professional education of HCPs to develop competence in palliative care will promote beneficence, as will effective medical & palliative care research

### Respect for autonomy (self-rule)

- Informed consent
- Participation in decision-making
- Confidentiality and privacy
- Refusal of treatment
- Based on good communication, assessment of patient's understanding
- Empowerment combines autonomy & beneficence

### Justice

- Distributive justice - distribution of scarce resources
- Rights based justice
  - equal access to health care
  - right to palliative care
  - right to pain and symptom control
  - right to competent, trained clinician
- Legal justice
  - in accordance with the laws of the state

## **World Health Organisation Definition of Palliative Care**

Palliative Care is an approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, through the prevention and relief of suffering, the early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Palliative Care:

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process;
- Intends neither to hasten or postpone death;
- Integrates the psychological and spiritual aspects of patient care;
- Offers a support system to help patients live as actively as possible until death;
- Offers a support system to help the family cope during the patient's illness and in their bereavement;
- Uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated;
- Will enhance the quality of life, and will also positively influence the course of illness;
- Is applicable early in the course of illness, in conjunction with other therapies that are implemented to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

<http://www.who.int/cancer/palliative/definition/en/>

## **Guidelines for Management of Pain**

- 1. Pain assessment and management**
- 2. Bone pain**
- 3. Neuropathic pain**
- 4. Incident pain**
- 5. Muscle spasm, myoclonus & dystonia**

### **1. Pain assessment and management**

Patients have the right to appropriate and effective relief of pain. A clinician who follows the basic principles of pain management will be able to control pain in 75 to 80 percent of patients. This section is based the World Health Organisation (WHO) guidelines for cancer pain control.

#### **Definition of pain:**

According to the International Society for the Study of Pain, pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Pain may involve physical, emotional, social and spiritual dimensions that may need to be addressed to achieve effective pain relief.

#### **Clinical assessment of cause and severity of pain**

- a) History
  - Accept patients' description of the pain as being real for them.
  - Careful pain history using:
    - P - precipitating and relieving factors
    - Q - quality
    - R - radiation
    - S - site and severity
    - T - timing and treatment
  - Use a formal pain assessment tool, e.g. Numerical Rating Scale, Verbal Descriptor Scale or Visual Analogue Scale.
  - Assess every pain.
  - Elicit the meaning of the pain to the patient.
  - Consider all dimensions of pain.
- b) Examination

A careful and appropriate clinical examination is essential.
- c) Special investigations may be appropriate in some patients.

Eg. An X-ray or scan may help to detect bone metastases. On the other hand blood tests to determine the levels of tumour markers are seldom needed to treat pain. Consider if the result will actually change the management plan.

#### **Explanation to patient and family:**

Discuss treatment options, fears, anxieties regarding pain management with opioids, adjustment of activities to reduce painful episodes. Reach consensus regarding the proposed management plan.

Correct reversible factors such as dehydration and constipation.

Consider disease specific palliative treatment

Single dose of radiotherapy for bone metastases

Fluconazole for cryptococcal meningitis,

Antiretroviral treatment for HIV neuropathy.

Consider non-pharmacological approaches. (not all are evidence based)

- Application of heat/cold
- Massage
- Meditation
- Relaxation
- Distraction
- Music therapy.
- Reflexology
- Positioning
- Passive movements
- Splinting fractured limb
- Mobility aids

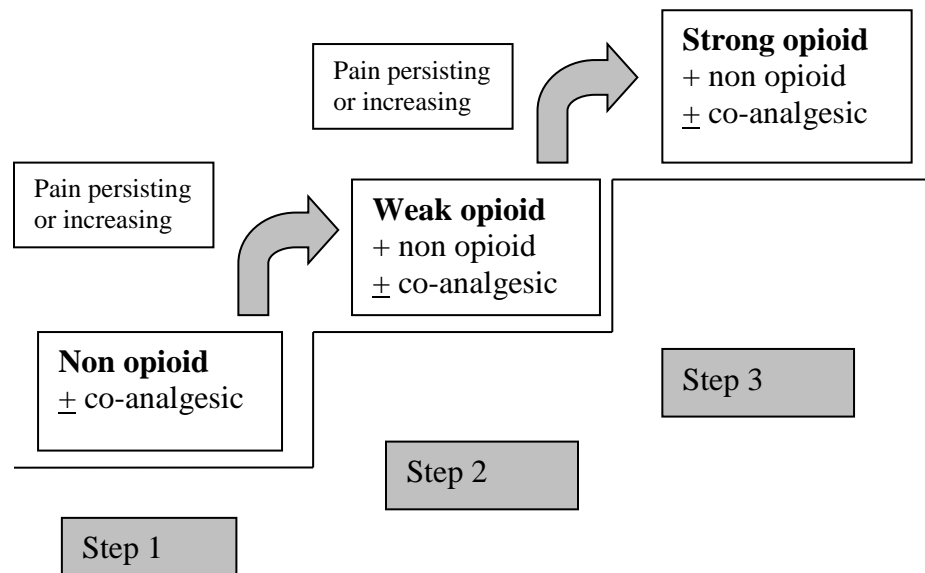
Prescribe appropriate first-line treatment

First line analgesia following the recommendations of the World Health Organisation (WHO) Analgesic Guidelines.

General principles of pain management:

- By mouth: use oral medications unless the patient is vomiting or comatose.
- By the clock: for persistent pain, analgesics should be given regularly at a fixed dose on a fixed schedule.
- By the ladder (see below)
- For the individual: the choice of analgesic is determined by the severity, site and type of pain. Individual requirements for analgesics vary enormously and the dosage of analgesic must be titrated against the particular patient's pain.
- Use of adjuvants: to enhance analgesic effect, e.g. corticosteroids, anti-convulsants.
- Attention to detail:
  - Take nothing for granted.
  - Be precise in history taking.
  - Give precise instructions, verbally and in writing.

## The WHO Three-Step Analgesic Ladder



Non-opioids: paracetamol, NSAIDs

Weak opioid: tramadol 50-100mg 6 hourly. Tramadol crosses to step three but does have a ceiling dose

Strong opioids: morphine, fentanyl, methadone, oxycodone, hydromorphone

If a weak opioid ceases to be effective, it is important not to switch to another weak opioid on step 2, but to switch to step 3.

The guidelines describing starting a patient on morphine as a strong opioid as morphine is available on the Essential Drug Lists at all levels.

### GUIDELINES ON COMMENCING MORPHINE

When a patient needs to start on a strong opioid, it is usual to commence oral morphine. Morphine syrup has the advantage of allowing review of the dose every four hours, and is thus better than slow release morphine to achieve rapid control of pain (and to reduce the dose if side-effects occur). Consider starting with slow release morphine in situations where there are too few nurses to administer morphine every 4 hours.

Starting dose:

- Morphine syrup 2.5 – 10mg 4-hourly.
  - 10mg 4-hourly
  - 2.5 – 5mg 4-hourly elderly, cachectic, Patients who are HIV positive also respond well to low dose morphine syrup

Anticipate side effects routinely:

- Constipation: Lactulose 15 – 30ml daily

- Nausea: Milk of Magnesia/Liquid Paraffin (3:1) 15 – 30ml daily  
Haloperidol 1.5mg – 5mg nocté for five to seven days  
Metoclopramide 10mg tds for five to seven days.
- Confusion/Drowsiness: is a temporary side effect and usually wears off after a few days.

#### Increasing dose

- Increase in increments of 30-50 percent of dose., eg  
5 mg → 10 mg → 15 mg → 20 mg → 30 mg → 45 mg → 60 mg →  
90/100 mg → 120/160 mg
- There is no ceiling (maximum) dose of morphine. The dose of morphine is titrated to the patient's pain control requirement.

#### Review patient regularly

- Severe pain: dose can be increased twice a day. If less severe, increase every one or two days to minimise side-effects.
- Once tolerant, a double dose can be given at bedtime to avoid waking for 2am dose.
- Consider converting to slow release opioid once pain controlled for ease of administration.

#### Breakthrough doses

- Breakthrough doses may be used when pain is not controlled on the regular dosing schedule (e.g. a patient on morphine syrup 20mg 4-hourly will receive 10-20mg morphine syrup stat).
- Use 50 – 100 percent 4-hourly dose (e.g. a patient on morphine syrup 20mg 4-hourly will receive 10-20mg morphine syrup stat).
- Consider increasing morphine dose if more than two breakthrough doses in previous 24-hours.
- To increase the morphine dose add previous 24-hour use of morphine of regular and breakthrough doses and divide into new dose.
- Divide 24-hour dose accordingly for oral syrup 4hrly (divide by 6) /slow release morphine administered 12hrly (divide by 2) /subcutaneous doses (continuous subcutaneous infusion – total dose over 24hr period).

#### Converting to slow release opioid

- For 12 hrly dosing, calculate the 24-hour dose of syrup and divide into two bd doses.
- Give the last dose of syrup together with first dose of slow release morphine to cover the few hours until slow release absorption has built up.
- Continue to give morphine syrup for breakthrough pain. A dose of morphine syrup of 50 – 100% of the 4-hourly dose equivalent may be taken for breakthrough pain.
- Remember to increase the dose of prn oral morphine proportionally if the dose of slow release morphine is increased.

#### Alternative routes of opioid administration

- IV bolus or infusion (acute severe pain or compromised oral route and in hospital setting). Parenteral boluses may be given 3 hourly.
- Subcutaneous:
  - If parenteral bolus dosing required and no IV access, SC route is preferred to IM route (less painful and equal efficacy).

- As a 24-hour infusion of morphine, using a syringe driver.
- 24-hour subcutaneous dose is 30 – 50 percent of 24-hour oral dose.
- Transdermal – Fentanyl patches deliver 12, 25, 50, 75 or 100 microgram/h over three days. Consult manufacture's instruction for conversion from morphine to fentanyl. It is advised that pain control is achieved by rapid release morphine before converting to slow release products as pain control can be achieved more quickly with rapid release morphine.
- Epidural or intrathecal (specialist only)
- Topical morphine: depending on size of wound, 4-20mg morphine sulphate mixed in an inert cream, can be applied to a chronic wound (limited evidence)

**NB: DO NOT USE PETHIDINE** in palliative care, as its analgesic effect only lasts for 2 hours. Continuous use may lead to neurotoxicity (myoclonic jerking, confusion and convulsions).

Despite the wide availability of additional strong opioids, morphine is the strong opioid of choice, as it is widely available, predictable and safe.

#### Consider combination analgesia treatment

Some patients experience refractory pain - pain that is difficult to control with opioid analgesics alone. If pain is difficult to control it may be that additional medication is required to supplement the use of an opioid analgesic and enhance pain control.

Examples of medication useful in combination with Step1, 2 and 3 analgesics are described in the table below.

Table 1. Examples of medication used in combination analgesia, together with their main indications follow:

Class	Main indications	Mechanism(s) of action	Examples	Typical regimen	Undesirable effects
Corticosteroids	Nerve compression Spinal cord compression Raised ICP Bone pain	Reduce peri-tumour oedema and inflammation	Prednisolone  Betamethasone	15-30mg daily 8-16mg daily	Include hyperglycaemia, anxiety, steroid psychosis, myopathy
Antidepressants	Nerve injury pain	Potentiation of two spinal descending inhibitory pathways	Amitriptyline  Duloxetine  Venlafaxine	25-150mg nocté  30-120mg daily 37.5-225mg daily	Antimuscarinic effects, drowsiness, postural hypotension.

Anti-convulsants	Nerve injury pain	GABA inhib. and sodium channel blockers  Ca channel $\alpha 2$ - $\delta$ ligands	Carbamazepine  Sodium valproate  Gabapentin  Pregabalin	100-200mg bd 400-1000mg nocté 100mg tds-600mg tds 50mg tds-100mg tds	Drowsiness and dizziness
NMDA-receptor channel blockers	Pain poorly responsive to morphine and other standard therapies  Severe neuropathic pain	Inhibits glutamate binding to NMDA receptor	Methadone  Ketamine	10-60mg bd 100-500mg /24hrs CSCI 10-20mg q6h PO	Drowsiness (methadone)  Dysphoria, hallucinations (ketamine)
Antispasmodics	Bowel colic, renal colic	Relax intestinal smooth muscle	Hyoscine Butylbromide	60-100mg/24h SC	Peripheral antimuscarinic effect
Muscle relaxants	Muscle spasm	Relax somatic muscle	Diazepam (EDL) Baclofen	5-10mg nocté 10mg tds	Drowsiness, ataxia
Bisphosphonates	Intractable metastatic bone pain	Block osteoclast activity	Zoledronic acid	4mg IV infusion every 4-8 weeks	Pyrexia, malaise 1-2 days (uncommon) Osteonecrosis of jaw

Review assessment and management regularly

If pain recurs or increases – reassess, if pain is due to disease progression, titrate dose of morphine to achieve pain control

Consider involving the interdisciplinary team at all stages of assessment and management

Support and counselling to address psychosocial and spiritual factors can significantly modify the perception of pain.

Referral to appropriate palliative care services such as hospice in patient unit, palliative care physician or pain specialist.



## 2. Bone Pain

Bone pain is usually caused by cancer metastases to bone (80% of which occur secondary to breast, prostate or lung cancer). Painful bone metastases frequently give rise to incident pain or pain on movement. Pain is described as dull, aching, constant and worse with movement and weight-bearing activities. It may be localised to the area of infiltration or referred pain if there is compression of nerves.

Pain frequently caused by pathologic fracture.

### Management

1. WHO step 1/2/3 analgesics
  - NSAIDs are considered first-line therapy for bone pain, if there are no contra-indications to these, although evidence for this practice is limited.
  - Opioids: since most patients experience moderate to severe pain, opioid analgesics are frequently needed.
  - Additional doses of opioid ( $\pm$  15% of total daily dose) are frequently required for incident pain caused by bone metastases.
2. Radiotherapy is effective and recommended therapy for symptomatic bone metastases
  - 41-90% patients experience partial relief of bone pain, following radiotherapy, with 25-50% having complete relief.
  - The full extent of pain relief, however, can take 3-4 weeks.
  - Single fraction radiotherapy is well-tolerated and convenient. Multiple fractions may sometimes be indicated. Half-body radiation is used for disseminated bone metastases, but has significant side effects.
  - Not indicated in patients who are very weak or who have very limited life expectancy.
3. Surgical interventions
  - Stabilisation of osteolytic lesions by fixation with pins and plates, injection of bone cements and fusion of vertebrae
  - Laminectomy to relieve pressure on spinal nerves
4. Chemotherapy and hormone therapy, specific for the malignancy resulting in the bone metastases (in conjunction with oncologist).
5. Bisphosphonates (osteoclast inhibitors)
  - Pamidronate 90mg IV infusion (diluted in 500ml normal saline) and infused over 2-4 hours or Zoledronic acid 4mg IV infusion over 15 minutes.
  - Can be used as part of a long term strategy to reduce skeletal complications, including pain from bone metastases. In this case, bisphosphonates are initiated at first diagnosis of bone metastases (irrespective of symptoms) and administered every 3-4 weeks.
  - Also indicated to relieve metastatic bone pain as an adjunct to analgesics, radiotherapy or surgery.
    - i. Bisphosphonate analgesic effect within 14 days
    - ii. If no response, can repeat after 2 weeks
    - iii. Failure to respond after 2 treatments makes further treatment inappropriate

- iv. If good response, consider regular bisphosphonates every 3-4 weeks
  - Prolonged bisphosphonate therapy may be complicated by osteonecrosis of the jaw, which is difficult to treat. This occurs especially in patients with poor oral dentition. Patients should be advised to maintain good oral hygiene and have regular dental check-ups, while on this therapy.
  - Use with caution in patients with renal impairment.
6. Corticosteroids
- Not used routinely.
  - May be used in patients with diffuse bone pain with an inadequate response to analgesics and other treatment modalities.
  - Especially useful in patients with neurological symptoms due to spinal cord compression
7. Muscle relaxants for associated muscle spasm. Baclofen is preferred to diazepam and dantrolene, which have more side effects.
8. Radio isotope therapy for disseminated bone metastases – not widely used.

### 3. Neuropathic pain

The International Association of the Study of Pain defines Neuropathic pain (NeuP) as pain that arises as a “direct consequence of a lesion or disease affecting the somatosensory system”. It is caused by damage or disease affecting the central or peripheral nervous system, for example:

- 1) Peripheral nerve damage (injury) (HIV, surgery, radiotherapy, chemotherapy and other neurotoxic drugs);
- 2) Nerve compression or infiltration (peripheral nerve, spinal nerve root, brachial- and lumbosacral plexus)
- 3) Central pain (post stroke, myelopathy, spinal cord compression)

Neuropathic pain has different causes and mechanisms of pain and different treatment to nociceptive pain. Patients suffering from neuropathic pain require careful assessment, regular review of response to treatment and may require changes in treatment to achieve optimal pain control. Most of the evidence for treatment of neuropathic pain comes from studies of Diabetic peripheral Neuropathy (DPN) or Post-Herpetic Neuropathy (PHN).

#### Assessment of pain:

Patients with neuropathic pain experience symptoms in an area of altered sensations. Typical symptoms of NeuP include burning pain, pins and needles, numbness, allodynia (pain produced by a non-noxious stimulus) and hyperalgesia when a normally painful stimulus (e.g. pinprick) evokes a heightened pain sensation. The painful symptoms include spontaneous pain (i.e. occurs with no apparent stimulation), which can be continuous or paroxysmal.

Patients may have a mixed pain picture and frequently a neuropathic pain component is diagnosed, rather than pure neuropathic pain.

In assessing the patient's pain experience it is important to document the somatosensory abnormalities in the affected area. There are a number of screening tools to help identify NeuP. These include *Douleur Neuropathique en 4 questions* DN4 and Leeds Assessment of Neuropathic Symptoms and Signs LANSS.

A simple examination-based way to identify NeuP and differentiate from nociceptive pain is the “3L” approach: **Listen, Locate and Look** (Table I).

**Listen** to the verbal description of pain and any non-painful symptoms in the same area as the pain. **Locate** the region of pain and document with a pain drawing, created either by the patient or by the physician. Any abnormal sensations may also be highlighted on the same illustration.

**Look** for sensory abnormalities and recognise the distribution pattern. A careful inspection of the painful body area should be carried and any differences in colour, texture, temperature etc. should be noted. A simple bedside examination of somatosensory functions is recommended, including touch, cold, warmth and pain sensibility (table 1) The aim is to identify altered sensation in the painful area, and hence responses should be compared with a non-painful adjacent area.

**Table I. 3L approach to differential diagnosis of Neuropathic pain**

	Listen	Locate	Look
Neuropathic pain	Common descriptors: Shooting, electric shock, burning, tingling, itching, numbness	The painful region may not necessarily be the same as the site of injury. Pain occurs in the neurological territory of the affected structure (nerve, root, spinal cord, brain)	Apply bedside sensory tests Conduct aetiology-specific tests if appropriate
Nociceptive pain	Common descriptors: Aching, throbbing, stiffness	Painful region is typically localised at the site of injury	Physical manipulation causes pain in site of injury

*Modified from Haanpaa et al.<sup>59</sup>*

#### Explanation to patient and family:

Patients need to understand that neuropathic pain is challenging to treat, may need several different analgesic strategies and that response to treatment may take several days or weeks. Realistic expectations should be discussed. An explanation of the different drugs and why they are used is important. Patients need to know why they are taking “epilepsy” and “depression” medication for pain. Neuropathic pain is associated with additional problems such as insomnia, depression as well as psychosocial problems affecting a person’s ability to work and interact socially. It is important to involve the interdisciplinary team early to help a person with neuropathic pain.

#### Correct reversible factors:

In patients who are HIV positive experiencing distal sensory neuropathy respond to appropriate antiretroviral medication avoiding stavudine and didanosine. It is important to treat the patient’s pain while waiting for the ARVs to take effect in controlling peripheral neuropathy. Patients with peripheral neuropathy assessed as being caused by ARVs should be changed to a regimen without this side effect.

#### Disease specific palliative therapy:

HAART in patients with HIV/AIDS – prolonged use of any regimen has been shown to decrease the pain severity of HIV associated peripheral neuropathy.

Palliative radiotherapy or chemotherapy to reduce the size of the tumour mass causing the nerve pain may be appropriate.

#### Non-pharmacological interventions:

Good sleep hygiene and graded physical activity. Physiotherapy can reduce myofascial components that commonly exacerbate neuropathic pain.

#### Pharmacological management:

There is substantial individual variation in the response to the medications used to treat neuropathic pain. Therefore a trial of different medications or combinations of these may be required.

#### Mechanism of action of analgesics used in the management of Neuropathic Pain:

##### First-line treatment:

- 1) Tricyclic antidepressants – act on descending inhibitory serotonergic and noradrenergic pathways. The analgesic effect of tricyclic antidepressants is independent of the antidepressant effect. Starting doses are low 10-25mg amitriptyline at night with titration to 100mg nocte. Combination of low dose amitriptyline with low dose tramadol or morphine has been used successfully in managing peripheral neuropathy in HIV patients treated in SA hospices. The analgesic effect is independent of the antidepressant effect, and occurs at a lower dose. Therefore, low-dose TCA are not the neuropathic pain treatment of choice in patients with co-morbid depression. TCAs are associated with cardiac toxicity and hence amitriptyline is contraindicated in patients who have ischemic heart disease or an increased risk of sudden cardiac death
- 2) Pregabalin and gabapentin act on calcium channels in the dorsal horn of the spinal cord. Gabapentin –start 100mg tds, titrate to maximum 600mg tds (decrease if impaired renal function) Pregabalin start at 50 mg tds titrate up to 100mg tds. Caution in patients with renal insufficiency.
- 3) selective serotonin/noradrenaline reuptake inhibitors (SNRIs) also act on descending inhibitory serotonergic and noradrenergic pathways. Duloxetine – initiate treatment at 30 mg/day and titrate after one week to 60 mg/day. Venlafaxine – start with 37,5mg/d, titrate to maximum dose of 225mg/d; Venlafaxine should be tapered when treatment is being discontinued as a withdrawal syndrome has been described Both duloxetine and venlafaxine are approved for the treatment of major depression disorder (MDD) and generalised anxiety disorder (GAD) and hence are the treatment of choice in NeuP patients with these co-morbid conditions. Duloxetine is contraindicated in patients with hepatic impairment. Venlafaxine should be prescribed with caution in patients with cardiac disease.
- 4) carbamazepine and lidocaine target sodium channel in the peripheral nerve
- 5) Tramadol and opioid medications are recommended as first line for patients with acute neuropathic pain, neuropathic pain due to cancer, and episodic exacerbations of severe neuropathic pain, usually in combination with one of the above medications

Combination analgesia is often required in patients with neuropathic pain, often as first line therapy

To date, no single pharmacological agent has been conclusively shown to improve the outcome of pain due to HIV peripheral neuropathy. Symptomatic treatment is therefore based on medication shown to be effective for other similar neuropathic pain states.

#### Second-line treatment

Corticosteroids are used as adjuvant treatment if neuropathic pain is suspected to be due to nerve compression e.g. by tumour or inflammation

Betamethasone – 8mg daily

Prednisone – 40-60mg daily

NMDA receptor antagonists: Ketamine (if poor response to first-line options) – 0,25-0,5 mg /kg tds PO/SC/IV

A trial of ketamine is appropriate in patients with severe refractory neuropathic pain and should be reserved for pain and palliative care specialist use.

Local application of Capsaicin cream (0,75%) (if poor response to first-line options) applied 5x daily.

Burning skin pain following application can cause significant distress

(SSRIs and NSAIDs are not recommended for the treatment of neuropathic pain).

Review management: Pharmacological therapy for neuropathic pain requires adequate time to demonstrate maximum efficacy – usually several weeks although there will be an indication of decreasing pain levels as the medication takes effect. The patient and family will need encouragement and to set realistic goals to improving pain levels.

Always consider involvement of the interdisciplinary team or referral to a pain specialist or multidisciplinary pain centre.

<b>DN4 Questionnaire PATIENT INTERVIEW</b>
QUESTION 1: Does the pain have any of the following characteristics?
1. Burning
2. Painful sensation of cold
3. Electric shocks
QUESTION 2: Is the pain associated with any of the following symptoms in the same area?
4. Tingling
5. Pins and needles
6. Numbness
7. Itching
PATIENT EXAMINATION
QUESTION 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?
8. Hypoesthesia to touch
9. Hypoesthesia to prick
QUESTION 4: In the painful area, can the pain be caused or increased by:
10. Brushing
YES = 1 point
NO = 0 points
Patient's score: ____/10
If the patient's score is $\geq 4$ , the test is positive. (Sensitivity: 82.9%; Specificity: 89.9%)

Reprinted from Bouhassira D, *et al.*

### 3. Incident Pain

Incident pain is one type of breakthrough pain, which can be determined as a transient exacerbation of pain that occurs in patients with otherwise stable and adequately controlled baseline pain.

Incident pain is frequently movement-related. It may be:

- Volitional (due to voluntary act) e.g. walking
- Non-volitional (due to involuntary act) e.g. coughing
- Procedural (due to therapeutic intervention) e.g. wound dressing.

Incident pain is usually frequent in occurrence (several times per day), acute in onset, short in duration (median time is 30 minutes) and moderate to severe in intensity.

#### MANAGEMENT

Assessment of incident pain requires a detailed pain history. A patient diary, when appropriate, is useful.

Where possible, the cause of the incident pain should be identified, as well as precipitating factors and the pattern of pain.

Explanation and discussion should include the establishment of realistic treatment goals, with outcomes that are useful or meaningful to the patient e.g. complete pain relief may not be a realistic expectation, but being able to walk without excruciating pain would be achievable.

Underlying cause of incident pain should be treated where appropriate e.g. radiotherapy for bone pain.

#### Lifestyle changes and non-pharmacological interventions

1. Correcting poor posture
2. Warming up and stretching
3. Adjustment of bending or lifting techniques
4. Limiting or pacing physical activities (undertake tasks in small segments, instead of all at once)

#### Pharmacological interventions

- Optimise (sometimes increase) baseline opioid dose, aiming for a balance between maximal patient activity level and acceptable analgesic side effect profile
- Short-acting opioids, used on an as-needed basis, are the primary treatment of incident pain.

The problem is that the onset of action of oral short-acting morphine is 30 minutes and duration of action is 4 hours, which lags behind the time course of many episodes of incident pain.

Therefore, short-acting oral opioids are most effective for predictable incident pain – should be used 30- 60 minutes before a scheduled activity.

- Dose of short-acting opioid determined by individual titration and does not necessarily depend on dose of opioid used for background pain.
- Treatment of unpredictable incident pain is challenging.

Lipophilic opioids with transmucosal absorption allow for a more rapid onset of action.

Oral transmucosal Fentanyl citrate (OTFC) fits this profile, but is not yet available in South Africa.

Fentanyl buccal and sublingual tablets are being investigated and have produced positive results.

- Parenteral opioids may sometimes be considered to enable faster onset of action (15-20 minutes for IM or SC morphine, 10-15 minutes for IV morphine)
- Specific drugs such as antitussives, laxatives or anti-spasmodics for non-volitional incident pain
- Inhaled nitrous oxide, ketamine and midazolam may be considered in certain cases of incident pain, although limited evidence is available to support their use.

Reassessment of outcomes is necessary to monitor efficiency and tolerability of treatment. Physiotherapy and occupational therapy can assist with lifestyle and physical adjustments. Difficult-to-manage pain problems should be referred to a pain or palliative care specialist, where possible.

#### **4. Muscle spasm(cramp) myoclonus and dystonia**

##### **MUSCLE SPASM OR CRAMP**

**Muscle spasm or cramp** is a painful muscular contraction lasting generally from a few seconds to minutes, but some may persist for many hours. Cramp most often occurs in a single muscle of the foot or calf. Cramps are thought to be due to hyper-excitability of the intramuscular portion of the motor nerve. Muscle cramps may be followed by residual tenderness. They can occur spontaneously, after minor muscle movement or after forceful contraction.

##### Appropriate assessment to identify cause and severity of symptoms

Cramps can be idiopathic e.g. occurring after or during exercise  
e.g. nocturnal cramps

In the Palliative Care setting cramps are often pathological.

##### **Pathological causes of cramp include:**

##### **Metabolic dysfunction**

- Acute dehydration e.g. due to diarrhoea, vomiting or sweating
- Hypocalcaemia
- Hypomagnesaemia
- Uraemia

##### **Neuromuscular problems**

- Nerve root damage or compression e.g. caused by tumour or radiotherapy
- Part of a paraneoplastic syndrome
- Peripheral neuropathy
- Painful bone metastases or pathological fractures (often associated with muscle spasm which serves to protect and splint the area)
- Meningeal metastases
- Disease or damage to the brain or spinal cord can cause spasticity in the limbs which may be associated with painful muscle spasms.

Note: In patients with advanced cancer cramps in the upper arm/s should alert the healthcare provider to a possible underlying neurological cause.

## **Drugs**

- Diuretics with fluid loss
- Prednisone
- Amitriptyline
- B stimulants e.g. salbutamol
- Medroxyprogesterone
- Amphotericin
- Cimetidine
- Chemotherapeutics e.g. vincristine, cisplatin

## **Emotional causes**

### Explanation to patient and family

Explain to the patient and the family that cramp is a universal experience, but common in the Palliative Care setting and is treatable. Discuss probable underlying causes and contributing factors to the cramp/spasm and treatment options.

### Correct reversible factors

- Correct metabolic abnormality
- If possible stop or reduce dose of drug/s contributing to the cramps
- If there is an associated neurological condition, treatment should be aimed at the underlying cause e.g. nerve compression. If possible treat nerve infiltration or compression.
- Treat any associated bone metastases e.g. radiation therapy
- Reverse any dehydration and manage any cause of acute fluid loss
- Correct electrolyte imbalances

### Non-pharmacological interventions

- Forced dorsiflexion of the foot for 5-10 seconds stretches both the calf and foot muscles. This can be repeated as needed
- If possible the patient should try to stretch their own muscles against a wall or using a "theraband". Stretch the affected muscle regularly (both passive and active stretching) once or twice a day
- Massage and relaxation therapy
- Refer to physiotherapist if necessary

## **Pharmacological interventions**

### First line therapy

- Diazepam 5-10 mg nocte for nocturnal or resistant cramp
- Baclofen 10-20 mg bd-tds
- Phenytoin or carbamazepine

### Second line therapy

- Dantrolene 25 mg od – 100 mg qid. Start at 25 mg od and increase by 25 mg



increments to max 100 mg qid. This can be used in conjunction with diazepam or baclofen. It acts peripherally and so causes less drowsiness.

- Quinine sulphate 200-300 mg nocte for nocturnal foot and calf cramps
- Corticosteroids may be useful for neuropathic syndromes
- Other options include: Calcium channel blockers e.g. diltiazem, Vit B Complex, diphenhydramine

#### Involvement of the interdisciplinary team

- Cramp can be exacerbated or caused by anxiety. If diazepam alone does not reduce anxiety, refer for counselling.
- Consider breathing relaxation and retraining if hyperventilating
- Physiotherapy for myofascial trigger release

### **MYOCLONUS**

**Myoclonus** is random sudden brief involuntary jerking of a single muscle or group of muscles. Myoclonus occurs more frequently when asleep than awake. It can be a normal physiological occurrence and is not necessarily pathological e.g. muscle jerk experiences on falling asleep or “sleepstarts”.

Myoclonus in the palliative care setting can range from mild twitching to severe jerking. It is frequently seen in the last days of life and can progress to full blown seizures if left untreated. Myoclonus can be focal (single muscle) or regional or multifocal (generalised). It can be unilateral or bilateral.

**Multifocal Myoclonus** is a central pre-epileptiform phenomenon which can be seen in the terminal phase. It can occur after high doses of *any* opioid but especially with pethidine given in repeated doses parenterally. (e.g. over 250 mg/24 hrs) Multifocal Myoclonus is not to be ignored as it can lead to full blown seizures.

#### Appropriate assessment to identify cause and severity of symptoms

#### **Causes of myoclonus**

Myoclonus can be primary (essential) or secondary to metabolic dysfunction, drug toxicity, chemical toxicity and neurological disorders. Myoclonus can be part of the terminal restlessness syndrome. Myoclonus is associated with high doses of any opioid but is a particular problem even in low doses with Pethidine. Pethidine is not recommended for pain management in Palliative Care or any chronic pain condition requiring ongoing analgesia.

#### **.Metabolic dysfunction**

- Hypoglycaemia
- Renal failure
- Encephalopathy due to hepatic failure
- Severe hyponatraemia
- Hypocalcaemia
- Hypoxia

## **Neurological disorders**

- Brain damage
- Viral infection of the CNS
- Neurological degenerative disease e.g. MND
- Cerebral oedema

## **Drug toxicity**

- All opioid analgesics, especially Pethidine  
(Myoclonus is rarely seen in morphine use unless high doses are given repeatedly, especially intrathecally)
- Dopamine antagonists e.g. haloperidol
- Neuroleptics e.g. chlorpromazine
- Metoclopramide
- Gabapentin (gabapentin induced myoclonus is relatively frequent but is usually mild and most patients choose to continue treatment. Gabapentin increases the risk of myoclonus in end stage renal disease.)

## **Drug withdrawal**

- Benzodiazepines
- Alcohol
- Anticonvulsants
- Barbiturates

## Explanation to patient and family

Reassure the patient that the myoclonic jerks are not seizures and not life threatening. Discuss the patient's concerns about the myoclonus. There may be specific implications for the patient e.g. effect on sleep, worsening of bone pain from painful bone metastasis. The cosmetic appearance in public may be very bothersome to the patient and family.

Explain the possible cause/s of myoclonus in the patient. Explain that many of the treatments cause sedation and decide whether to treat the myoclonus or not. Most patients are satisfied with the explanation of its aetiology and elect for no treatment of this symptom.

Multifocal myoclonus may be part of pre-terminal restlessness and can be very distressing for relatives to witness. Careful explanation and reassurance is required for family and carers.

## Correct reversible factors

- As with muscle spasms and cramps, any reversible causes should be addressed and managed appropriately. Review drugs, reduce doses or switch to an alternative opioid.(Opioid rotation) Consider using an alternative analgesic e.g. NSAID.
- Treat hypoxia and hypoglycemia. Restore electrolyte imbalance and manage encephalopathy if feasible.
- Take a careful history to ascertain any possible drug/alcohol withdrawal.
- Exclude renal failure. Worsening myoclonus may herald the onset of renal failure, and measures to improve renal output should be considered.
- In a patient with terminal restlessness and deteriorating renal function the dose of opioid analgesic needs to be reviewed as it may cause or aggravate myoclonus.

### Non-pharmacological interventions

- Where possible use non-pharmacological measures to control pain such as palliative radiation, acupuncture, physiotherapy, TENS, peripheral nerve block etc in order to reduce the doses of opioid required.
- Give oxygen if needed
- Rehydrate patient

### First line therapy

- Clonazepam 0.5 mg nocté is usually effective
- Alternatively Lorazepam 1 mg stat, repeat as needed bd-tds

#### **If part of pre-terminal restlessness:**

- Diazepam 5-10 mg pr hourly until settled, then 10 mg pr once daily – bd. or
- Midazolam 5-10 mg S/C stat hourly until settled, then 10-30 mg/24 hrs via CSCI or
- Clonazepam 0.5 mg S/C hourly until settled, then 1-2 mg/24 hrs via CSCI

Adjust doses up or down as needed.

### Second line therapy

- Flunitrazepam
- Phenobarbitone

### Involvement of the interdisciplinary team

- Involve the pharmacist in reviewing the many drugs that are used in Palliative Care which could cause or exacerbate myoclonus.
- Physiotherapist
- Refer to a specialist if needed e.g. if there is a neurological complication or radiation needed
- Relaxation therapy, counselling.

## **DYSTONIA**

**Dystonia** is a sustained muscle contraction causing twisting and repetitive movements or abnormal postures. Examples include torticollis and facial spasms, trismus of the jaw, grimacing, gaping, tongue protrusion, oculogyric crisis and opisthotonus. Dystonia is often associated with anxiety.

**Tardive dyskinesia** is a form of dystonia caused by the long term effects of drugs that block dopamine receptors. It manifests as involuntary repetitive purposeless body movements such as grimacing, tongue protrusion, lip smacking, puckering of lips and rapid eye blinking. Tardive dyskinesia can unfortunately be a *permanent* adverse effect of neuroleptics (e.g. chlorpromazine), dopamine antagonists (e.g. haloperidol) and metoclopramide.

## Appropriate assessment to identify cause and severity of symptoms

### **Causes of dystonia**

In Palliative Care dystonias are often related to the extra-pyramidal side effects of commonly used drugs such as the phenothiazines e.g. chlorpromazine, metoclopramide and dopamine antagonists e.g. haloperidol.

Acute dystonias occur in up to 10% of patients on neuroleptic drugs. They develop abruptly within days of starting oral treatment and within minutes of an intravenous injection.

Dystonias can also be caused by brain damage, infection, chemical imbalances, toxins and poisoning.

Primary dystonias also occur in the general population.

### Explanation to patient and family

Acute onset of dystonia can be very distressing for the patient and family. Explanation as to the nature and possible causes of dystonia will help reduce fear and anxiety. Unfortunately some drug-induced dystonias e.g. tardive dyskinesia are irreversible (especially in the elderly) and the patient/family need to be prepared for this possibility. Explain that the causative drug will be reduced or stopped and that everything possible will be done to alleviate the symptom. Ensure that the family/patient are aware that the treatments are often sedating and are often unsatisfactory.

### Correct reversible factors

Discontinue causal drug. Substitute if necessary, e.g. use domperidone rather than metoclopramide. Always be vigilant when prescribing neuroleptic drugs in palliative care especially when combined with anti-emetics, metoclopramide or haloperidol. Do not combine metoclopramide with haloperidol!

### Institute non-pharmacological interventions by involvement of the interdisciplinary team

Dystonia is often accompanied by anxiety and involvement of the psychosocial team should be considered.

Consult with the pharmacist involved if necessary to discuss drug doses and interactions as well as alternative drugs.

Acupuncture has been effective in the treatment of some dystonias.

Consider physiotherapy with tactile pressure and massage.

### Pharmacological interventions

- Benzodiazepines e.g. clonazepam 0.5 mg po bd (alternately lorazepam 1mg po tds or diazepam 10 mg nocte)
- Baclofen 10-20 mg bd-tds
- Diphenhydramine 20-50 mg iv/im for acute severe dystonia, repeat after 20-30 minutes if necessary. Then 25-50 mg po bd-qid

Start all drugs at a low dose and slowly increase until symptom is controlled or intolerable adverse effects occur. Results are often poor or inconsistent.

### Consider adjuvant/second line treatment

- Anti-parkinson's drugs e.g. carbidopa/levodopa, ropinirole
- Injection of Botulinus toxin Type A into the dystonic muscles in specific cases e.g. blepharospasm, torticollis, hemifacial spasm and other focal dystonias (this is only to be administered by an experienced practitioner)

**Involve the interdisciplinary team and refer if necessary to a pain specialist or hospice service.**

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## Management of Respiratory Symptoms

### 1. Breathlessness

### 2. Cough

### 3. Hiccup

### 4. Oxygen therapy

#### 1. Breathlessness

Definition of breathlessness or Dyspnoea

Dyspnoea is defined as a subjective experience of breathing discomfort, not necessarily related to exertion, that compels an individual to increase his ventilation or reduce his activity.

#### Assessment and Severity

Grading of dyspnoea gives the health professional an objective framework to assess a patient but breathlessness is multi-dimensional and does not necessarily correlate with a lung function test.

The important questions to ask are:

- How does the patient experience his/her shortness of breath?
- Is this a first occasion of shortness of breath? Has there been a sudden or gradual onset?
- Precipitating factors? What makes it better? What makes it worse?
- Precipitating conditions e.g. heart failure
- Concurrent symptoms e.g. cough, haemoptysis, fatigue, loss of concentration, loss of appetite, pain and insomnia.
- Associated unpleasant emotions.
- Impact on daily functions.
- Impact on social well being

Physical Assessment:

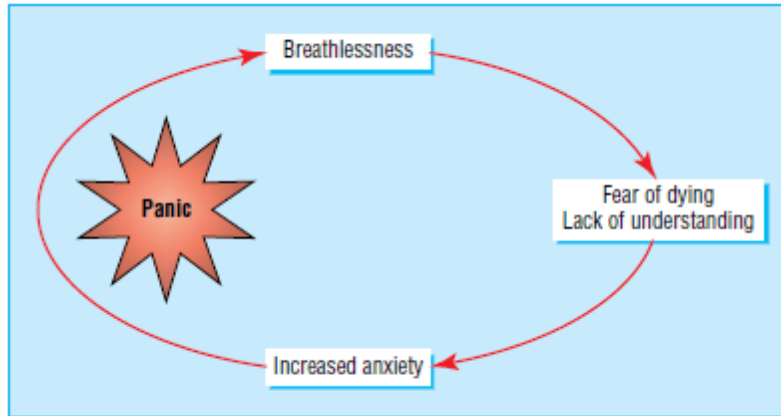
- Assess for pallor or central and peripheral cyanosis, clubbing, oedema, venous engorgement and palpable nodes
- Chest examination
- Abdominal assessment (ascites and masses)
- Cardiac examination

Investigations (will depend on the most likely cause determined clinically)

- Haemoglobin
- Temperature
- Sputum if infection suspected
- If possible:
  - CXR
  - FBC

Recognise the role of anxiety in dyspnoea and the cycle of increasing anxiety and dyspnoea that needs to be addressed:





#### Explanation to family

Reassure the patient and family where possible. Explain the probable cause in terms they can understand and describe the plan of action and how therapies will assist the physical &/or emotional distress.

Describe and encourage the use of distraction and relaxation techniques as appropriate.

#### Reversible factors and specific therapy

Lung Tumour	Review for further RT or chemotherapy. Discuss with oncologist
Bronchospasm	Bronchodilators and corticosteroids
Infections	Bacterial: antibiotics Tuberculosis: TB drugs PCP: Bactrim
Effusions	<u>Pleural</u> : pleural tap and / or pleurodesis Pericardial effusions: Refer specialist
Ascites	Paracentesis
Lymphangitis carcinomatosis	Corticosteroids (high dose) Bronchodilators Diuretics?
Large airway obstruction	High dose corticosteroids Refer/ manage as an emergency if airway not patent Refer to oncologist
SVC obstruction	High dose corticosteroids Refer for emergency RT
Anaemia	Blood Transfusions, Iron, Erythropoetin
Cardiac failure	Diuretics and disease specific treatment
Pneumothorax	Intercostal drain and refer
Pulmonary Embolism	Anticoagulants and refer

### Non-pharmacological interventions

#### Relaxation Techniques:

- Try to stay calm
- Purse your lips
- Relax shoulders, back, neck and arms
- Concentrate on breathing out slowly
- Visualisation
- Soothing music

#### Physiotherapy

Increasing airflow across the face by means of a fan or open window

Calm and containing environment

Positioning in bed in a upright position

Adaption to daily living

### First line treatment

Nebulised medication (to be used if there is an element of reversible bronchospasm)

- Salbutamol 2.5mg-5mg q6h or 2 puffs q 6h
- Ipratropium bromide 250-50mcg q6h or 2 puffs q 6h

Benzodiazepines (Panic with hyperventilation and fear of suffocation may worsen breathlessness)

- Lorazepam 0.5mg -2 mg SL
- Midazolam 2,5mg q 6h SC or IM

Opioids (Morphine reduces inappropriate and excessive respiratory drive and substantially reduces the ventilatory response to hypoxia and hypercapnia. By slowing respiration, breathing may be made more efficient, and the sensation of breathlessness reduced)

- Mist Morphine
- For opioid naive patients: 2,5mg q4h

### **Oxygen Therapy:**

Oxygen may help breathlessness in patients who are hypoxic. A trial of oxygen should be considered if available.

### Second line treatment

Theophyllines sustained release tablets 200mg-300mg b.d. (if there is an element of reversible bronchospasm)

Diazepam 2-5mg b.d.

Regular standard dose inhaled corticosteroids plus regular long-acting inhaled B<sub>2</sub>-stimulants (salmeterol 50 mcg b.d)

### Review assessment and management

Review within an hour.

Have we achieved our goals to control and relieve dyspnoea?

Is the cause of the dyspnoea more evident to us?

Have plans been put in place to treat reversible causes?

Has second line treatment been considered?

## Interdisciplinary Team

At all stages consider interdisciplinary team involvement including referral to specialised palliative care service.

## **2. Cough**

Involuntary cough is initiated by rapidly adapting 'irritant' receptors (RAR) that transmit through vagal fibres. The most sensitive sites for cough induction are the larynx, main carina and the branching points of the tracheobronchial tree. Cough has two main functions: to prevent foreign material entering the lower respiratory tract and to clear secretions from the lungs and bronchial tree. Excessive cough can impair QOL by preventing sleep, interrupting communication and causing social embarrassment. It can also cause haemodynamic changes, ruptured vessels, urinary incontinence, hernias, neurological problems, lung barotrauma, and rib fractures.

### Assessment and Severity

History:

- Duration: cough for more than 3 weeks is considered chronic
- Course: constant, worsening, intermittent, diurnal variation
- Dry or productive (nature and volume)
- Other:
  - Shortness of breath
  - Associated with pain
  - Wheeze or tightness of chest
  - Loss of weight
  - Fever and night sweats

Physical Examination:

- General: distress, fever, sweating, loss of weight, cyanosis and clubbing
- Respiratory: Respiratory rate, hyperinflation, dullness, crackles, wheeze, bronchial breathing, pleural rub.

Investigations: will depend on the most likely cause determined clinically. It is important to note that due to the high incidence of TB in South Africa, PTB should be excluded in all patients who have a chronic cough or any other symptoms of PTB.

### **Causes and Therapy**

<b>Non-malignant</b>	<b>Treatment</b>
Upper respiratory viral infection	Support; but consider prophylactic antibiotics
<b>Bronchopneumonia</b>	Antibiotics
<b>Asthma</b>	Bronchodilators and corticosteroids
Chronic obstructive pulmonary disease	Bronchodilators, trial of steroids, trial of oxygen and physiotherapy
Foreign body	Removal
Cigarette smoke	Avoidance
Oesophageal reflux	Proton pump inhibitors
Left ventricular failure	Cardiac drugs

Bronchiectasis	Postural drainage and antibiotics if needed
Motor neurone disease	See palliative care guidelines
Multiple sclerosis	See palliative care guidelines
Angiotensin converting enzyme inhibitors	Convert to other hypertension drugs
Inhaled drugs	Avoidance
Post nasal drip	Decongestants and antibiotics
Cystic fibrosis	
Interstitial fibrosis	
<b>Malignant</b>	
Endobronchial disease	Steroids
Pleural Effusion	Tap and pleurodesis
Mesothelioma	Refer to oncology
Lymphangitis	Steroids
Multiple pulmonary metastases	Steroids
Radiation pneumonitis	Steroids
Hilar tumour or lymphadenopathy	Consider palliative radiotherapy

#### Explanation to patient and family

- Discuss the most probable cause and planned management.
- Persistent cough can precipitate vomiting, exhaustion, pain and insomnia.
- Continued coughing at night can keep a household awake and it is therefore important for the family to be counselled.
- Avoid smoke and fumes
- If an infection is suspected e.g. TB, family members must be tested and infection control should be put into place.
- Atmospheric humidification

#### Non-pharmacological interventions

- Steam inhalation can help for tenacious sputum.
- A combination of lemon and honey and hot water can have a soothing effect
- Physiotherapy for standard vibration, percussion and postural drainage
- Suctioning in the patient who is unable to cough with loose secretions

#### First line treatment

Productive cough in patient who can cough effectively:

Tenacious sputum:

- Nebulised saline (0.9 percent) 2.5 ml q 6 h and prn
- Simple linctus: Currently none on state code, but with private patients:
  - Acetylcysteine 200mg tds
  - Bromhexine 10mg tds
  - Carbocisteine 750mg tds
- Bronchospasm must be treated with nebulised salbutamol

- Cough suppressant can be considered in the exhausted patient and to prevent further physical trauma.

#### Purulent sputum

- Antibiotics specific to cause
- Cough suppressants can be considered in the exhausted patient.

#### Loose secretions but unable to cough:

- Hyoscine butylbromide
- Inhalations with Ipratropium bromide 250-50mcg q 6h
- Morphine through a CSCI (It is the most effective antitussive agent and acts on the central cough centre)

#### Dry cough

- Saline inhalations 2.5ml q 6h
- Codeine Phosphate 30-60mg 4-6 hourly
- Morphine 5mg q 4h
- Pholcodine 5-10mg 3-4 times daily

#### Second line treatment

#### Loose secretions but unable too cough:

- Corticosteroids
- Macrolide antibiotics
- Nebulised furosemide

#### Dry cough:

- Methadone 2mg 3-4hourly
- Nebulised local anaesthetics
  - This must be done with great care.
  - The patient must be NPO for an hour after nebulisation
  - Bronchodilators must be on standby
  - Use lignocaine 5ml 2% solution every 6 hours or bupivacaine 5ml of a 0.25% solution every 8 hours

#### Review assessment and management

If no response to initial antibiotics, repeat an MC&S and a TB AFB and culture.

#### At all stages consider the involvement of the interdisciplinary team

The physiotherapist has a key role to play in managing respiratory problems

#### Referral

If cause remains unknown refer to a pulmonologist or referring oncologist.

### 3. Hiccup

Hiccups are diaphragmatic spasms caused by diaphragmatic irritation, which is associated with gastric distension, phrenic nerve irritation, uraemia, infection and central nervous system tumour.

#### Assessment and Severity

The severity of hiccups is subjective for each individual patient. However, if the hiccups are causing patients to have difficulty talking, eating and sleeping, causes weight loss, anxiety or depression, reversible causes must be sought.

The assessment should therefore consider:

- Are the hiccups troublesome to the patient?
- Know the current extent of disease to help identify pressure effects or nerve damage
- Are signs and symptoms of dyspepsia, reflux or epigastric fullness present?
- Are there signs of infection?
  - Do a chest examination
  - Test the patient's urine
- Test for faecal occult blood to exclude upper GIT bleeding
- Do appropriate biochemistry to exclude reversible symptoms (U&E and creatinine, corrected calcium and albumin)
- If a myocardial infarction is suspected do appropriate tests.

#### **Causes mediated:**

Via vagus nerve:

Gastric distension  
Gastro-oesophageal reflux  
Hepatic tumours  
Ascites/abdominal distension/intestinal obstruction

Via phrenic nerve

Diaphragmatic tumour involvement  
Mediastinal tumour  
CNS  
Intracranial tumour  
Meningeal infiltration of tumour

Systemic

Renal failure  
Hyponatraemia

Drugs

Corticosteroids  
(If hiccups occur shortly after starting new drug, a therapeutic trial of stopping the drug is worthwhile)

#### Correct reversible factors

Where appropriate and possible correct renal function or any other reversible factors e.g. for abdominal distension try peppermint water and metachlopramide.

### Non-pharmacological interventions

Many interventions are described but none have been clinically proven to help. Most interventions attempt pharyngeal stimulation.

- Massage the soft palate
- Hold your breath
- Eat dry granulated sugar
- Re-breathe into a bag

### First line treatment

Reduce gastric distension:

- Metaclopramide 10mg tds po
- Antacid combination such as aluminium hydroxide, magnesium hydroxide and simeticone

Relax smooth muscle

- Baclofen 5mg tds po

### Second line treatment

Suppress central hiccup in intractable cases:

- Chlorpromazine 25mg po (causes sedation and hypotension)

Suppress central irritation from intracranial tumour:

- Corticosteroids in high doses (can cause hiccups, consider stopping if recently started)
- Phenytoin 200mg -300mg nocte

## **4. Oxygen Therapy**

### **Indications:**

In the hospice setting oxygen use will take place under the following conditions;

- Long-term oxygen therapy(LTOT)(>15 hours/day)
  - **Indications**
    - All patients assessed and diagnosed with COPD found to be in need of LTOT by a pulmonologist or a physician
    - FEV<sub>1</sub> of less than 1, 5 litre and FEV<sub>1</sub>% in conjunction with FEV<sub>1</sub>/FVC ratio of less than 70.
    - Oxygen saturation level less than 90%
- Short term oxygen therapy
  - High concentration oxygen (60%)
    - **Indications**
      - Pneumonia, pulmonary embolism, fibrosing alveolitis, asthma, myocardial infarction

- Low concentration oxygen (<28%) (**to improve the breathlessness caused by hypoxia without worsening pre-existing CO2 drive**)
  - **Indication**
    - COPD, interstitial lung disease, heart failure

#### **Administration:**

Oxygen can be delivered via:

##### **Nasal Cannula**

- A Nasal Cannula provides low flow oxygen to a patient who can breathe spontaneously
- Percentage inspired oxygen depends on the flow rate and the patient's tidal volume
- At 1litre/min it provides 24% Oxygen
- Increasing the oxygen flow by 1 litre/minute will increase the oxygen by approximately 4%. (Max 44% at 6 litres)

##### **Simple Face mask**

- This provides 40-60% oxygen at a flow rate of 6-10 litre/min

##### **Face mask with oxygen reservoir**

- This will provide 60-100% oxygen at a flow rate of 6-10 litre/ min

##### **Venturi Mask**

- The flow rate at percentage oxygen delivered is indicated on the mask
- This provides accurate control.

Oxygen can be supplied via:

#### **Oxygen cylinders**

Can supply oxygen for up to 28 hours  
Heavy and a fire hazard  
Need no electricity

#### **Portable oxygen cylinders**

Supply only 2-4 hours of oxygen  
Ideal for transporting patients

#### **Oxygen concentrators**

Safer and more portable  
Patient has to pay for the electricity

#### **Patient advice:**

- The patient has to stop smoking
- Oxygen is a fire hazard
- Cannulas and prongs must be cleaned daily with soap and water
- If oxygen concentrators are used, the cost of the electricity should be remembered

#### **Oxygen use in the breathless patient:**

Oxygen may help the breathless patient who is hypoxic, however most breathless cancer patient are not hypoxic and will not benefit from it physiologically. A trial of oxygen can be given for 15-30 min and the situation can be reassessed.



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## Management of Gastro-intestinal symptoms

1. **Dysphagia**
2. **Nausea and vomiting**
3. **Intestinal obstruction**
4. **Ascites**
5. **Diarrhoea**
6. **Constipation**

### Introduction

In Palliative Care the primary aim of treatment is not to prolong life but to make life that remains as comfortable and meaningful for the patient as possible. Appropriate treatment for an acutely ill patient such as nasogastric tubes, IV infusion, cardiac resuscitation may not be appropriate measures in a patient with far advanced disease. Efficient, good quality and holistic care is called for; bearing in mind the patient's biological prospects, therapeutic aim of treatment and the need to die with dignity.

The gastrointestinal tract provides two important functions:

It gives pleasure from a personal and a communal aspect and also provides nutrition and hydration and elimination of waste. For most people eating is an important aspect of life and sharing meals an important social activity. Nausea, vomiting, dysphagia, intestinal obstruction and constipation or diarrhoea can be disturbing and difficult symptoms to manage in advanced disease. The evaluation and management of symptoms will lead to the most appropriate care for a patient with far advanced disease.

### 1. DYSPHAGIA

Definitions:

**Dysphagia** is a subjective awareness of difficulty in swallowing.

**Odynophagia** means painful swallowing.

Swallowing is a complex phenomenon involving the brain stem, the cranial nerves and the skeletal muscles. Swallowing is dependent upon the normal functioning of the buccal cavity, pharynx, upper oesophageal (crico-pharyngeal) sphincter, the body of oesophagus, lower sphincter of the oesophagus and the neurological pathways that supply them.

Appropriate assessment to identify cause and severity of symptoms

### Associated problems

Coughing whilst eating, dribbling, aspirational pneumonia, poor oral intake, hunger and thirst, weight loss and dehydration.

### CAUSES OF DYSPHAGIA

#### Box 1.1

<ul style="list-style-type: none"><li>• Mouth problems<ul style="list-style-type: none"><li>- Dry mouth</li><li>- Radiation induced mucositis</li><li>- Candidiasis</li></ul></li></ul>	<ul style="list-style-type: none"><li>• Peripheral nerve<ul style="list-style-type: none"><li>- Mononeuritis multiplex</li><li>- Diabetic neuropathy</li></ul></li></ul>
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<ul style="list-style-type: none"> <li>- Herpes</li> <li>- Sore mouth</li> </ul>	
<ul style="list-style-type: none"> <li>• Infection <ul style="list-style-type: none"> <li>- Candidiasis</li> <li>- Herpes simplex</li> <li>- CMV(Cytomegalovirus)</li> <li>- Pharyngeal abscess</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Myopathies <ul style="list-style-type: none"> <li>- Polymyositis</li> <li>- Dermatomyositis</li> <li>- Muscular dystrophies</li> <li>- Thyroid myopathy</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>• Neurological <ul style="list-style-type: none"> <li>- Cerebral tumour</li> <li>- MND</li> <li>- Multiple sclerosis</li> <li>- Huntington's Chorea</li> <li>- CVA</li> <li>- Parkinson's disease</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Obstructive <ul style="list-style-type: none"> <li>- Oro-pharyngeal malignancies</li> <li>- Malignant lymphadenopathy</li> <li>- Surgical resection / radiation induced</li> <li>- Oesophageal/gastric neoplasm</li> <li>- Bronchial carcinoma</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>• Inflammation <ul style="list-style-type: none"> <li>- Reflux</li> <li>- Radiation induced mucositis</li> <li>- NSAID</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Psychogenic</li> </ul>

#### Explanation to patient and family at all stages

Explain the causes of difficulty in swallowing. Providing food to one's family is an essential part of nurturing those we love and when a patient cannot eat and/or refuses food it is very distressing for family members. The palliative care team will attempt to reverse those causes that are reversible; but towards the end of life the desire for food and the need for food diminishes and this needs to be explained to the family so that it does not become a source of conflict.

Correct reversible factors: such as candidiasis, infections, drug-induced oesophagitis/gastritis – stop NSAIDs

#### Consider disease-specific palliative therapy:

Radiation for tumour impinging on oesophagus

#### Institute non-pharmacological interventions

##### **Dietary advice:**

- Recommend suitable soft food
- Use of liquidizer / blender
- Add cream to soup (high calorie content)
- Offer general advice about managing mealtimes, frequent small meals rather than large meals at set times

#### Prescribe appropriate first-line treatment

Apart from disease specific treatment eg to control infections, there may not be appropriate first-line treatment

#### Consider adjuvant/second-line treatment

- Trial of dexamethasone (4-8mg / 24 hourly) if it is likely that oedema surrounding a tumour is aggravating problems of dysphagia
- Endoscopic dilation or stent
- Radiotherapy

- PEG tube as an alternate method of feeding. This will depend on the patient's health, general condition and on agreement with the patient and family.
- If a patient is not able to swallow medication these can be administered via alternate routes such as a syringe driver.

Review assessment and management regularly

At all stages of management consider:

Involvement of interdisciplinary team

Referral to appropriate service/more experienced clinician

## 2. NAUSEA AND VOMITING

**Vomiting:** Forceful expulsion of gastric contents through the mouth.

**Nausea:** Unpleasant feeling of the need to vomit, often accompanied by autonomic symptoms eg. pallor, cold, sweating, tachycardia and fear.

**Retching:** Rhythmic, laboured spasmodic contractions of the diaphragm and abdominal muscles. It is essentially an effort to vomit that fails to expel gastric contents. Nausea is usually present and retching often ends in vomiting.

40-60% of patients with advanced cancer suffer from nausea. Vomiting is present in 30% of these patients.

Appropriate assessment to identify cause and severity of symptoms

Assessment to identify probable cause and mechanism of nausea and vomiting (NB more than 1 may play a role) There are generally 3 pathophysiological mechanisms that cause nausea and vomiting:

- Mechanical – gastric stasis, intestinal obstruction, excessive coughing, drug action on GIT, gastritis, ascites (increased intra-abdominal pressure), squashed stomach syndrome, Post surgery; eg. gastrectomy, resection of large tumour, constipation
- “Toxic” mediated through chemo-emetic trigger zone – drugs, chemotherapy, infection, renal failure, hypercalcaemia, hyponatraemia, toxins from tumour breakdown.
- Central mediated through vomiting centre- brain metastases & raised ICP, anxiety, pain, radiotherapy, vagal stimulation (mechanoreceptors in GIT and chemoreceptors in GIT, sensory stimulus eg smell, sight)

An understanding of the emetic process and the main neurotransmitters involved is helpful in assessing and treating patients who are vomiting because anti-emetic drugs are predominantly neurotransmitter blocking agents. They are effective at different receptor sites and therefore treat different causes of vomiting.

Vomiting is a complex reflex process. The vomiting centre lies in the medulla and has both histamine and muscarinic cholinergic receptors.

Stimulation of the vomiting centre occurs:

- From the chemoreceptor trigger zone (CTZ) where dopamine receptors are concentrated.
- From vagal afferents from the gastrointestinal tract.
- From the vestibular centre. This, like the vomiting centre, contains both histamine and muscarine cholinergic receptors.
- Directly, from raised intracranial pressure.
- From psychological causes.

#### Explanation to patient and family at all stages

Nausea is an extremely distressing and debilitating symptom. The goal of treatment should be to control nausea. It may not be possible to eliminate vomiting, particularly in patients with malignant intestinal obstruction. Most patients will tolerate one or two episodes of vomiting when they understand the reason for this and when the symptom of nausea is controlled. Continuous nasogastric drainage is seldom necessary. Some colleagues are using intermittent nasogastric drainage under sedation using low doses of midazolam for unresponsive vomiting in bowel obstruction that is not considered for surgery.

#### Correct reversible factors

Consider surgery for intestinal obstruction, treat hypercalcaemia, drain ascites, stop unnecessary medications, antacids PPI (proton pump inhibitor) for gastritis, manage constipation

#### Consider disease-specific palliative therapy

Surgery, chemotherapy, radiotherapy for cerebral tumour

Dexamethasone for raised intracranial pressure for inoperable cerebral tumour

#### Institute non-pharmacological interventions

- Adjust environment away from sight and smell of food/cooking
- Avoidance of cooking smells and unpleasant odours
- Arrange for someone else to prepare the food
- Offer small portions
- Cold food is often more palatable than hot food
- Patient preference is more important than nutritionally correct diet
- Positioning after meals (sit up ½ hour)
- Eliminate odours from wounds through thorough wound care and other management eg antibiotic for infection, crushed metronidazole tablets applied to wound
- Ensure good mouth care

#### Prescribe appropriate first-line treatment

Choose an anti-emetic based on the most likely cause of nausea and vomiting. If first choice drug is only partially successful after 24 hours, increase dose or use different anti-emetic

#### **Metoclopramide eg. Maxolon**

Metoclopramide is useful for most causes of nausea and vomiting, except labyrinthine causes such as motion sickness. It is one of the most commonly used first-line anti-emetics in palliative care. It is particularly useful for mechanical causes of nausea and vomiting (except for complete intestinal obstruction) – metoclopramide 10 mg 6 hrly by mouth or 40-100mg/24 h by continuous subcutaneous infusion (CSCI).

- Dopamine (D<sub>2</sub>) antagonist
- Serotonin (5-HT<sub>3</sub>) antagonist in high doses

- Serotonin (5-HT<sub>4</sub>) agonist in the gut, hence gastrokinetic effect
- Extra pyramidal effects more common in young patients; Hyperprolactinaemia is possible

### **Cyclizine eg. Valoid**

Cyclizine is a useful first-line anti-emetic with a central action such as raised intracranial pressure and is used in managing the nausea of complete intestinal obstruction (vomiting will still occur)  
cyclizine 50 mg 8 hrly by mouth, 100 mg rectally 8 hrly

- Histamine (H<sub>1</sub>) antagonist
- Some anti-muscarinic activity

### **Haloperidol: eg Serenace**

Haloperidol is particularly useful for drug-associated or metabolic nausea. Much lower doses are used to control nausea than in psychiatric practice haloperidol 1.5mg-5mg by mouth or by CSCI

- Butrophenone neuroleptic
- Dopamine (D<sub>2</sub>) antagonist
- Sedating
- Extra-pyramidal side-effects especially in patients who are HIV positive
- Use with caution in epilepsy, liver disease, thyroid dysfunction

Consider adjuvant/second-line treatment

### **Anti-Emetics for specific syndrome**

#### **Box 2.2**

	<b>1<sup>st</sup> CHOICE</b>	<b>2<sup>ND</sup> CHOICE</b>
<b>Metabolic</b>	Haloperidol	Ondansetron
<b>Drug-induced</b>	Haloperidol	Metoclopramide, Ondansetron
<b>Radiotherapy, Chemotherapy</b>	Ondansetron, Dexamethasone	Metoclopramide, Haloperidol
<b>Raised Intracranial Pressure</b>	Cyclizine	+ Dexamethasone
<b>Bowel Obstruction</b>	Cyclizine, Hyoscine, Dexamethasone	Octreotide, Ondansetron
<b>Delayed Gastric Emptying</b>	Metoclopramide	Domperidone

If using more than one anti-emetic drug, metoclopramide can be combined with haloperidol. Cyclizine and haloperidol also form an effective combination. Cyclizine may antagonise the prokinetic effects of metoclopramide and they should not usually be administered together. Metoclopramide and hyoscine are also not a good combination.

Vomiting is usually treated with oral drugs but in severe vomiting alternate methods will be used. An anti-emetic injection is suitable to control a single episode. Preferably anti-emetics are given as a suppository rectally or subcutaneously using a syringe driver.

### **Indications for SC Infusions**

- Persistent nausea and vomiting refractory to tablets
- Dysphagia
- Intestinal obstruction
- Semi-comatose or comatose states
- Profound weakness
- Poor absorption of drugs in the G-I tract

Review assessment and management regularly

At all stages of management consider:

Involvement of interdisciplinary team

Referral to appropriate service/more experienced clinician

### **3. INTESTINAL OBSTRUCTION**

Intestinal obstruction is caused by an occlusion to the lumen of the bowel or a lack of normal propulsion, preventing or delaying intestinal contents from passing along the gastrointestinal tract. Obstruction may be the presenting symptom of cancer problem, but more commonly develops during the course of the disease<sup>4</sup>. Any site in the bowel may be involved, from the gastro duodenal junction to the rectum and anus.

The incidence in cancer patients is 3%. The incident increases to 25-40% in advanced ovarian cancer.

Obstruction can be functional (paralytic) or organic (mechanical), or both<sup>5</sup>.

It can also be:

- partial or incomplete
- transient (acute) or persistent (chronic).

Appropriate assessment to identify cause and severity of symptoms

**SYMPTOMS:** Colicky pain, nausea and vomiting, abdominal distension, constipation

**CAUSES:**

- Primary tumours of the large bowel,
- Previous treatment eg. adhesions, post radiation, ischaemic fibrosis,
- Extra mural compression by tumour masses
- An unrelated benign condition eg. a strangulated hernia

Confirm obstruction with abdominal X-ray and exclude pseudo-obstruction – faecal impaction/ileus

#### Explanation to patient and family at all stages

Explain goals of treatment, including the fact that vomiting may not be eliminated particularly with complete intestinal obstruction. A discussion about the possibility of surgery or the fact that surgery is not appropriate and the fact that this means the prognosis is poor should be held in a sensitive and compassionate way.

#### Correct reversible factors

Surgery may be indicated in a younger patient, relatively fit, single site of obstruction, no ascites, previous good response to chemotherapy.

In many patients surgery is not indicated because of multiple sites of obstruction, advanced disease with relatively short prognosis to death, additional problems such as ascites or obstructive nephropathy.

#### Consider disease-specific palliative therapy

In few patients, further chemotherapy may be an option but in general intestinal obstruction is a manifestation of advanced disease unlikely to improve with chemotherapy.

#### Institute non-pharmacological interventions

Good mouth care is essential. Patients eat and drink as they choose and there are no special diets. With adequate oral fluids, thirst is not usually a problem and the occasional dry mouth is treated with local measures such as crushed ice to suck. Nasogastric intubation is not appropriate unless surgery is planned.

#### Prescribe appropriate first-line treatment

Subcutaneous infusion of a combination of drugs is the preferred treatment. Nasogastric tube and IV fluids are rarely used. The preferred route of drug administration is by subcutaneous infusion using a syringe driver. The three major symptoms of intestinal obstruction are colic, abdominal pain and vomiting.

#### **DRUGS USED IN SYMPTOM CONTROL:**

<b>Symptom</b>	<b>Drug</b>	<b>Dose</b>	<b>Comment</b>
Intestinal colic	<ul style="list-style-type: none"><li>• Morphine</li><li>• Hyoscine butylbromide</li></ul>	As required 40-60mg	Add antispasmodics Avoid gastrokinetic drugs eg. metoclopramide
Continuous abdominal pain	<ul style="list-style-type: none"><li>• Morphine</li></ul>	As required	Anti-emetic or antispasmodic



Nausea and vomiting	<ul style="list-style-type: none"> <li>• Haloperidol</li> <li>• Cyclizine</li> <li>• Hyoscine butylbromide</li> <li>• Octreotide</li> </ul>	5-15mg 100-200mg  40-60mg  0.3-0.6mg	May cause sedation May crystallise in syringe driver Reduces gastrointestinal secretions and mobility A somatostatin analogue (0.1mg – 0.6mg/day) Reduces gastrointestinal secretions and vomiting
Intestinal Obstruction	<ul style="list-style-type: none"> <li>• Dexamethasone may be added</li> </ul>	8-16mg	To reduce peritumoural oedema

Avoid stimulant drugs such as metoclopramide and senna as these drugs may increase colic and pain.

#### Consider adjuvant/second-line treatment

Corticosteroids may be used for an anti-inflammatory effect, reducing oedema with resultant symptom relief.

Review regularly. If the patient is terminally ill, within 1 or 2 days of death, sedation may be necessary. Midazolam – 15-45mg / 24 hourly can be added to the syringe driver.

#### Review assessment and management regularly

Most patients with intestinal obstruction can be made reasonably comfortable for most of the time using a combination of a continuous infusion of appropriate drugs, careful mouth care and frequent small sips of water. Some patients may choose to take some food and fluids by mouth recognising that vomiting will occur. In few cases, it may be appropriate to perform a venting gastrostomy.

#### At all stages of management consider:

Involvement of interdisciplinary team

Referral to appropriate service/more experienced clinician

### **4. ASCITES**

**DEFINITION:** Ascites is an abnormal accumulation of fluid in the abdomen. Malignant ascites accounts for 10% of all causes of ascites. It is associated with cancer of the ovary, breast, stomach, pancreas, colon and lymphoma. Cardiac failure, liver failure and renal failure are common causes of non-malignant ascites.

#### Appropriate assessment to identify cause and severity of symptoms

#### **SYMPTOMS:**

- Abdominal distension, discomfort and pain
- Dyspnoea
- Nausea and vomiting mainly due to squashed stomach syndrome
- Oesophageal reflux
- Leg oedema

## **CAUSES:**

- Peritoneal metastasis
- Subphrenic lymphatics blocked by tumour infiltration
- Increased peritoneal permeability
- Liver metastasis leading to hypo-albuminaemia and sometimes portal hypertension

Explanation to patient and family at all stages  
Correct reversible factors  
Consider disease-specific palliative therapy  
Institute non-pharmacological interventions  
Prescribe appropriate first-line treatment  
Consider adjuvant/second-line treatment  
Review assessment and management  
At all stages of management consider:  
Involvement of interdisciplinary team  
Referral to appropriate service/more experienced clinician

## **MANAGEMENT:**

- Chemotherapy
- Diuretics
- Paracentesis

Spironolactone is the drug of choice. Doses from 100-300mg orally. For rapid results 40mg of lasix (frusemide) which is a loop diuretic, can be added. Serum electrolytes should be monitored

Paracentesis is appropriate for patients with a tense distended abdomen and for whom there is no relief from diuretics. Paracentesis can be repeated if diuretics do not prevent re-accumulation of fluids and can be carried out in any setting including the patient's home. Patients with advanced disease, who accumulate fluid very quickly, could have a catheter type shunt put in which they can drain themselves.

## **5. DIARRHOEA**

Diarrhoea is an increase in the frequency of defaecation and/or fluidity of the faeces. If severe, it may manifest as faecal incontinence. In palliative care diarrhoea can be acute (less than 14 days) or chronic (lasting more than 2 weeks). In HIV diarrhoea may be due to the HIV infection itself and a causative organism of infective diarrhoea may not be evident.

### Appropriate assessment to identify cause and severity of symptoms

The presence of fever or blood in the stools are indications for microscopy to identify an infective cause of diarrhoea. Depending on the duration and severity of the diarrhoea, a limited non-invasive diagnostic workout is appropriate eg. stools for culture and sensitivity, acid-fast bacilli, ova, parasites, clostridium difficile toxin. CMV should be considered in patients with CD4 count less than 50.

It is important to assess for signs of dehydration.

## CAUSES

### Box 4.1

<ul style="list-style-type: none"><li>• Laxative overdose</li><li>• Faecal impaction with overflow</li><li>• Partial obstruction</li><li>• Radiation enteritis</li><li>• Steatorrhoea</li><li>• Drugs including some HAART drugs</li></ul>	<ul style="list-style-type: none"><li>• Antibiotics</li><li>• Gastro-enteritis, mainly viral</li><li>• Infections: salmonella, giardia, campylobacter, clostridiumdifficile, cytomegalovirus, cryptosporidium and microsporidium</li></ul>
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#### Explanation to patient and family at all stages

Explain the cause of the diarrhoea and the importance of maintain good hydration

#### Correct reversible factors

Appropriate antibiotics for infective diarrhoea.

If inappropriate laxatives have been used adjust laxative treatment accordingly.

#### Consider disease-specific palliative therapy

HAART for patients who are HIV positive.

#### Institute non-pharmacological interventions

Review diet. Improve hydration for home-based care patients. Boil one litre of water, add 8 level teaspoons of sugar and half-teaspoon salt. Allow the mixture to cool and give a cup full of the mixture every time the patient has diarrhoea.

Patients who have undergone a colectomy continue to experience diarrhoea and will require an extra 1 litre of fluid daily, additional salt, vitamin and iron supplements.

#### Prescribe appropriate first-line treatment

Loperamide 4mg stat and 2mg after each loose stool (do not exceed 16 mg in 24 hours).

In severe chronic diarrhoea in seriously ill patients use codeine phos 60mg tds or morphine suspension 5-10mg 4 hourly.

Monitor the patients especially when fluid intake is inadequate.

Octreotide (sandostatin) is a synthetic somatostatin analogue that is approved for the treatment of profuse diarrhoea and is effective in treating diarrhoea in HIV patients. The disadvantage is the high cost and it has to be administered subcutaneously.

For pancreatic deficiency, pancreatin may help; preparation of choice is creon.

## **Drugs for treating diarrhoea**

### **Box 4.2**

<b>DISEASE</b>	<b>TREATMENT</b>
<u>Acute radiation enteritis</u>	NSAID Octreotide
Steatorrhoea	Pancreatin supplements
Cholegenic diarrhoea	Colestyramine (an anion exchange resin)
Pseudomembranous colitis	Metronidazole Vancomycin
Ulcerative colitis	Sulfasalazine Corticosteroids
Infection	Appropriate antibiotic
CMV(Cytomegalovirus)	Ganciclovir/cytovene Foscarnet/foscavir Cidofovir/visitide Valganciclovir/valcyte

<b>NON-SPECIFIC TREATMENT</b>	
Absorbents	Hydrophilic bulking agents Pectins
Adsorbents	Kaolin Chalk Activated charcoal
Mucosal PG inhibitors	Aspirin Bismuth subsalicylate
Opioids	Codeine Morphine Diphenoxylate Loperamide
Somatostatin analogues	Octreotide

Review assessment and management regularly

At all stages of management consider:

Involvement of interdisciplinary team including dietician  
Referral to appropriate service/more experienced clinician

## 6. CONSTIPATION

**DEFINITION:** Passage of small hard stools passed infrequently and with difficulty.

Appropriate assessment to identify cause and severity of symptoms

**Associated symptoms :** Flatulence, abdominal pain, bloating.

**Symptoms of complications:** Anorexia, overflow diarrhoea, confusion, nausea and vomiting, urinary dysfunction

Investigations are rarely needed. Abdominal x-rays may be done to differentiate between intestinal obstruction and constipation. Abdominal examination and PR are vital

### CAUSES

#### Box 5.1

Diminished food and fibre intake; old age, anorexia, oral candidiasis	<b>Side effects of drugs including:</b>
Inactivity- lack of exercise	Opioids (morphine, codeine), cyclizine, NSAIDS, anti cholinergics, (hyoscine), some anti-depressants (amitriptyline), anticonvulsants, iron tablets.
Dehydration – vomiting, fever, poor fluid intake	Hypokalaemia, hypercalcaemia, spinal cord compression.
Weakness – too weak, inability to reach toilet when urged to defaecate	Haemorrhoids, Anal fissure,
Lack of privacy	Endocrine dysfunction, hypothyroidism
Positioning – best to sit upright not to be lying on bedpan	Idiopathic

#### Explanation to patient and family at all stages

Explain goals of treatment i.e. soft bowel movement every 3 days or less, not necessarily a DAILY bowel movement.

(If more than 3 days pass without a bowel movement, notify palliative care provider) Educate patient and family re need for bowel movement despite minimal intake of food. If the patient is on any opioid (weak/strong), it is essential that laxatives be used on a daily basis irrespective of bowel movement

#### Correct reversible factors

Review medication

Treat GIT disorder, hypercalcaemia, correct metabolic disorder

### Institute non-pharmacological interventions

Anticipate this common problem, enquire about bowel function regularly, encourage increase in fluid intake if possible, encourage increased mobility, avoid bedpans, provide toilet privacy and adjust toilet seat if necessary.

Increased fibre intake of benefit in early disease (ie patient with normal oral intake) but may not be appropriate in patients with advanced disease and poor appetite/reduced oral intake of food

### Prescribe appropriate first-line treatment

The **aim of laxative therapy** is comfortable defecation. They are divided into three groups:

- i. Bulking agents
- ii. Stool softeners
- iii. Stimulants

Bulking agents need to be taken with large volumes of water and are not effective for severe constipation and are not appropriate for routine use in palliative care particularly when the disease is far advanced and the patient is debilitated.

- Choose a combination of a stool softener and a stimulant laxative
- Stool softener – lactulose 15ml bd po/30mg d po, Sorbitol 15ml bd po/30mg d po
- Stimulant laxative – Senna 2-4 tabs nocte po, Bisacodyl 2 tabs nocte po
- A cost effective combination is magnesium hydroxide and liquid paraffin combination in 3:1 ratio

## **SOFTENING LAXATIVES**

### **Box 5.2**

	<b>Mode of action</b>	<b>Usual dose range</b>	<b>Comments</b>
Lactulose	Osmotic agent: (retains water in gut lumen)	15-40 mls BD-TDS	Active in the small bowel. Latency of action 1-2 days C/I: too sweet, flatulence, bloating
Magnesium Sulphate	Osmotic agent	2-4g daily	Acts throughout the bowel. Latency of action 1-6hr(dose dependent)
Liquid paraffin	Lubricant	-	Increases water retention, does soften stools. Latency 1-3 days C/I: weak contact stimulant
Glycerine Suppositories	Lubricant	1-3PRN	May also have an irritant action that provokes expulsion of stools.

## STIMULANT LAXATIVES

### Box 5.3

	<b>Mode of Action</b>	<b>Dose range</b>	<b>Comments</b>
Senna	All these stimulant laxatives have the same actions. <ul style="list-style-type: none"><li>• Stimulation of myenteric nerves</li><li>• Increased gut mobility</li><li>• Soften motion by reduced absorption of water from gut.</li></ul>	7.5-30mg bd	Anthraquinone family
Bisacodyl sodium picosulphate tablets	Cause colonic peristalsis.	10-20mg bd 5-50mg bd	Polyphenolic family Latency of action 6-12hr
Bisacodyl sodium picosulphate suppositories	Cause colonic peristalsis. Rapid action of 1 hour	10-20mg	Latency of action 1 hour C/I: Colic

### Consider adjuvant/second-line treatment

Many patients may need a combination of laxatives. Most patients prefer oral to rectal laxatives. Have an approach to the choice between rectal and oral laxatives and between softeners and stimulant drugs

- NB: Continue with first line drug therapy
- If no bowel movement for 3 days or patient very uncomfortable before 3 days do PR. If rectum empty, exclude bowel obstruction, increase dose of first-line laxatives
- If rectum full: hard stool - glycerine suppositories, or Olive oil/Arachis oil/ Sunflower oil retention enema (+/- 100ml PR),  
Soft stool - bisacodyl suppositories, if no result give sodium phosphate enema or sorbitol micro-enema
- If no result refer for manual removal under sedation Midazolam 15mg IV, or warm saline rectal lavage

### **Points to remember**

- Colostomies are managed in the same way.
- Paraplegic patients may require manual evacuation or rectal suppositories routinely every third day.
- Diarrhoea may be as a complication of constipation
- Be aware of faecal impaction.
- Severe constipation occasionally presents with symptoms of intestinal obstruction.
- A laxative should always be started with opioid analgesia unless diarrhoea is a pre-existing problem.
- If intestinal obstruction is a possibility – use only laxatives with a predominantly softening action eg. lactulose, sorbitol to avoid colic.

- If there is rectal impaction with hard faeces, soften the faecal mass using glycerine suppositories, or an oil enema retained overnight. If spontaneous evacuation remains impossible, a manual evacuation may be necessary.
- If there is rectal loading with soft faeces, a peristaltic stimulant eg. senna will be effective.
- If there is little or no stool in rectum – use a stimulant/softener combination.
- Constipation in AIDS is usually drug induced.

Review assessment and management regularly to attain regular comfortable bowel movement

At all stages of management consider:

Involvement of interdisciplinary team, including dietician  
Referral to appropriate service/more experienced clinician

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## Constitutional Symptoms

1. Anorexia, Asthenia and Cachexia
2. Fever and Sweating

### 1. Anorexia, Asthenia and Cachexia

#### Definitions:

Anorexia is the loss of desire to eat. In cancer patients anorexia & cachexia are interrelated and described as the anorexia-cachexia syndrome.

Cachexia is the ongoing, involuntary loss of body mass (with or without anorexia), declining muscle strength and inflammation (G. Hanks *et al* 2010). Cachexia is now recognized as a spectrum ranging from pre-clinical to late (irreversible) cachexia. The primary metabolic anorexia-cachexia syndrome is a complex, multidimensional process, with ongoing research into the sequelae and interactions between inflammation-catabolism, anorexia and anabolic dysbalance. Secondary anorexia-cachexia may result from starvation, deconditioning or infections.

Asthenia, or fatigue, can be caused by cancer and its treatment. As with cachexia, there are complex interactions between the cancer and host which are thought to play a role in fatigue. Many patients suffer from fatigue and cachexia simultaneously. However, there are numerous cases where patients with cachexia may not suffer from fatigue and *vice versa*. The pathophysiology of fatigue is also multifactorial with numerous possible causes as listed below.

Note that *"In the terminal phase of progressive illness there is virtually always a profound loss of appetite (and therefore an absence of hunger). The literature is clear that the body cannot use calories to become stronger or to gain weight. Instead, it breaks down its own energy stores (muscle, fat, carbohydrates) regardless of caloric intake. Efforts to improve caloric intake by enteral or parenteral means have no role in addressing comfort, functional status, or survival in such end-of-life scenarios"*. (Harlos M, 2010)

#### Brief Descriptions:

Asthenia:

- Generalized weakness
- Physical fatigue
- Mental fatigue

Anorexia:

- Loss of appetite

Cachexia:

- Loss of weight, including adipose and muscle tissue
  - Catabolic processes
  - Poor appetite

#### Aetiology

- Tumour-related anorexia and cachexia
  - Gastrointestinal tumours

- Catabolic metabolism mediated by cytokines increases basal metabolic rate with lipolysis, glucose intolerance and hepatic gluconeogenesis using proteins.
- Cachexia, due to tumour factors, may occur without anorexia
- Tumour-related asthenia
  - Chemical mediators related to the tumour
  - Raised intracranial pressure
  - Asthenia may occur independent of anorexia and cachexia
- Indirect causes of anorexia, cachexia and/or asthenia
  - Treatment-related e.g. chemotherapy, radiation therapy, surgery, drug side effects
  - Nausea and vomiting
  - Dysphagia for any reason e.g. dry mouth, stomatitis
  - Infections
  - Anaemia
  - Respiratory distress
  - Sleep disturbances or overexertion
  - Psychological problems and emotional state
- Non Cancer causes
  - Chronic obstructive pulmonary disease
  - Cardiac cachexia in cardiac failure
  - HIV/AIDS and related complications
  - Other co-morbid diseases/illnesses

#### Assessment:

Detailed history including; history of illness, and treatments, other chronic illnesses, psychosocial and spiritual assessments and the extent of patient and family distress related to the problems of loss of appetite, weight loss and fatigue. Carry out meticulous examination to identify any causes as listed above and to check for complications of anorexia-cachexia or asthenia. Conduct appropriate investigations to identify any reversible causes.

### **Management**

#### Correct Reversible Causes

- Nausea and vomiting
- Constipation
- Dysphagia
- Anaemia
- Depression and anxiety
- Stop or reduce causative drugs
- Reverse or treat possible medical or endocrine complications
- Hypercalcaemia
- Treat hypoxia
- Treat and control pain
- Antibiotics for infection
- Vitamin supplements as required
- Aberrant sleep patterns

### Explanation to patient and Family

- Be open and honest, explain the disease process and reassure and support the patient and family
- Discuss causes for declining appetite and nutritional requirements to attempt to alleviate anxiety over mealtimes
- Explain declining activity and discuss ways to alleviate boredom
- If the patient is in the terminal phase explain that the body can no longer use the calories provided in food (or through artificial nutrition) and that feeding the patient does not improve his comfort, that it is more important to ensure good mouth care than to insist on feeding.

### Non-Pharmacological interventions

- Advice to family :
  - Encourage eating little and often, and when hungry
  - Offer foods that patient enjoys
  - Plan meals, offer variety
  - Make food easily chewable
  - Make mealtimes emotionally light and enjoyable
- Consider nutritional supplements; discuss with a dietician
- Encourage and maintain appropriate mobility
  - Role of exercise in addressing anorexia/cachexia
    - It appears that physical exercise may be a feasible intervention for fatigue in cases where muscle deconditioning is a contributing factor. (G. Hanks *et al*, 2010)
    - A physiotherapist may be involved to devise a suitable exercise routine.
  - Occupational therapists to help maintain independence and mobility as long as possible
  - Aids to mobility; walking, continence, mobility in and out of bed
  - Pressure area care
  - Foot care
- Counselling regarding adaptation to declining function and how to avoid over-exertion exacerbating fatigue
- Be aware of depression and assess regularly, offering continued psychosocial support

### Pharmacological Interventions

:

- Progestogens: Megestrol acetate 80-160mg daily, can increase up to 800mg daily, or medroxyprogesterone acetate 400 – 960mg daily
  - Consider if prognosis is weeks to months
  - May increase appetite and cause weight gain, however slower onset than steroids but beneficial effects may last longer
  - More expensive than steroids
  - Side effects such as hypertension, oedema and insomnia may limit use
- Megestrol acetate is preferred for asthenia without anorexia-cachexia Periactin (cyproheptadine) 4mg tds PO; an antihistamine, which may be considered as an appetite stimulant, does not significantly stimulate appetite in advanced malignancy.
- Steroids: Dexamethasone 2-4mg daily, or prednisone 10-20 mg daily, to increase appetite and energy

- May increase appetite as well as cause weight gain. Also reduces fatigue. Effects last 2-4 weeks.
- If clear benefit after a few days, reduce dose to minimum required to maintain benefit. If no benefit, stop steroids.
- Side effects may limit use
- Review regularly whether benefit outweighs risk. Once there is no further beneficial response (usually after a few weeks), wean off the steroids.
- Eicosapentanoic Acid (EPA)
  - Current clinical reviews are inconclusive but a recent large study showed a non-significant but clinically relevant effect on lean body mass of 2g EPA/ day. (G Hanks, *et al* 2010).

#### Asthenia

- There is increasing evidence supporting the use of methylphenidate for cancer- related fatigue as well as the possibility of treating opioid related sedation and depression. Starting dose: Methylphenidate 2.5-5mg daily or bd PO, increase every few days to a maximum of 40-60mg per day. Usually doses of not more than 30mg a day are required. Side effects include anorexia (usually transient), insomnia and euphoria although it may paradoxically improve anorexia and insomnia. Insomnia is more common at the beginning of treatment and may be improved by reducing the doses. Contra-indications include anxiety, agitation, concurrent antipsychotic medications and cardiac arrhythmias. Methylphenidate potentiates the effects of TCAs and antagonizes the neuroleptic action of phenytoin.

#### Other Medical Non-pharmacological Interventions

- Total parenteral nutrition or nasogastric feeding is generally not encouraged in palliative care unless the patient is expected to have a favourable outcome with a good prognosis, such as before or after surgery. It may result in short-term weight gain, however is not advisable in patients with a poor prognosis as it does not significantly improve comfort or survival. Patients with a good prognosis, but with upper GIT obstructions or problems swallowing may benefit from a percutaneous gastrostomy tube. Family should be counselled about reducing feeds and fluids as the patient becomes terminal.
- Hydration of a dying patient is often an emotional issue to be resolved with the family. Over-hydration at this time often causes unnecessary complications such as respiratory secretions. The family needs to be well counselled with regard to fluid requirements and the risks of over-hydration. A dry mouth is managed with good mouth care. In some difficult situations, hypodermoclysis (subcutaneous fluid administration) may be considered.

#### Review assessment and management

Regularly re-assess the patient. Always consider the risk/benefit of any intervention. Review interventions as the patient's condition changes and progresses. Be aware of and try to anticipate new complications that may arise in the course of the illness.

#### Involve interdisciplinary team

Anorexia, cachexia and asthenia are multifactorial problems. Psychosocial and emotional issues often play a role both in the cause as well as the effects of these symptoms. It is important to involve all members of the team as required; the social worker, spiritual counsellor, physiotherapist, occupational therapist, dietician.

### Referral to appropriate Services

Consider surgical consultation for patients, who may benefit from surgical interventions such as relieving obstruction or for placement of feeding tubes, e.g. percutaneous gastrostomy tube.

## **2. Fever and Sweating**

### **Fever**

Normal body temperature ranges from 36,1°C - 37,4°C, maintained by thermoregulatory mechanisms. High temperatures are a result of either hyperthermia or fever. Hyperthermia is due to abnormal thermoregulation, whereas fever occurs with normal thermoregulation but with an abnormal hypothalamic set point.

Causes of fever:

- Infection, especially important in neutropenic patients
- Tumour (paraneoplastic syndrome)
- Blood transfusion
- Drugs, e.g. some chemotherapy drugs and some antibiotics e.g., vancomycin and amphotericin
- Drug withdrawal – opioids, benzodiazepines
- Neuroleptic malignant syndrome – rare but may be fatal. Occurs with neuroleptic drugs and presents with fever, rigidity, confusion and autonomic instability.

### **Sweating**

Sweating is very important component of thermoregulation in humans. It is most commonly the excessive sweating that is most distressing to patient, and may result in fatigue, drowsiness and confusion. Patients may complain of generalised or localised sweating

Causes of Generalised Sweating:

- Non-disease states
  - Warm environment
  - Exercise
  - Menopause
- Disease States, including co-morbidities
  - Fever from various causes as listed above
  - Tumour related, e.g., Hodgkin's Lymphoma, tumours with liver metastases, pheochromocytoma, functional neuroendocrine tumours
  - Endocrine disorders such as diabetes mellitus or insipidus, thyrotoxicosis and pituitary disorders
  - Ischaemic Heart Disease
  - Primary disorders of sweating
  - Surgical or chemical female menopause, e.g., androgen treatment, radiation, chemotherapy
  - Male menopause due to orchidectomy, GNRH or oestrogen use
  - Drugs: tamoxifen, aromatase inhibitors, opioids, TCAs and steroids

### Causes of Localised Sweating

- Spinal cord lesion
- Cerebrovascular Accident
- Intrathoracic mass
- Peripheral Neuropathy

### Assessment:

Detailed history including:

- history of current illness,
- other chronic illnesses,
- medications and other treatments,
- physical symptoms, especially extent and location of sweating,
- impact on patient's quality of living.

Meticulous examination

- All body systems
- Any sites of foreign bodies

Investigations

- Urine, sputum and blood cultures as required
- CXR, if necessary

### Management:

#### Disease Specific palliative therapy:

- Fever
  - Infection – treat appropriately with antibiotics. Even at end of life, infections may be treated as a palliative measure, relieving not only fever but associated symptoms, e.g., pain or cough. However this decision must be individualised for each patient.
  - Paraneoplastic Fever – is best managed by antineoplastic treatment. However this may not be possible, then use antipyretics.
  - Blood Transfusion – manage according to guideline on blood transfusion.
  - Drug-related – ideally withdraw the drug, however if not possible, manage with antipyretics (see below).
  - Neuroleptic Malignant Syndrome – stop the neuroleptic and supportive treatment.
  - Co-morbid causes, e.g. endocrine; treat underlying cause.
- Sweating
  - Fever – treat the cause
  - Tumour – antineoplastic treatment, if possible
- Endocrine and other co-morbid causes – treat the cause
- Hot flushes
  - for biological or induced postmenopausal states in women, oestrogen therapy is very effective, however some women have relative or absolute contraindications to oestrogen therapy. For women with ovarian failure for any reason and in men who have had androgen ablation therapy, megestrol acetate 40mg daily may provide relief. Full effect takes place after 2 -3 weeks. It may be necessary to titrate up monthly in increments of 10mg- 20mg to achieve the lowest effective dose.
  - Other non-hormone therapies for hot flushes have demonstrated efficacy in reducing discomfort between 40-60%. These include SSRIs, SSNRIs, gabapentin, and alpha adrenergic agonists :

- Venlafaxine extended release 75mg daily, start with 37,5mg daily
- Paroxetine CR 12,5mg daily or Paroxetine 10mg daily
- Gabapentin up to 300mg tds
- Fluoxetine 20mg daily
- Clonidine 0,1mg daily is associated with troubling side effects

If one medication is not effective in reducing hot flushes, it is possible to switch to another. It is important to note that paroxetine should not be used with tamoxifen due to detrimental drug interactions. Hot flushes in men appear to respond to the agents listed above, except clonidine. They may also respond to the anti-androgen, cyproterone acetate.

### **Explanation to patient and Family:**

Once an assessment is made, explain the cause of the sweating to the patient and the family. Discuss possible treatment options and non-pharmacological interventions, which could alleviate the patient's discomfort. It may not be possible to alleviate the sweating completely, however a reduction of 40-50% is often tolerated.

### **Non-pharmacological interventions:**

- Encourage patient to wear loose fitting, cotton clothing
- Provide a fan for cooling
- Tepid sponging and regular washing
- For hot flushes, relaxation techniques and deep breathing may reduce intensity by 40-50%
- Encourage oral fluids to prevent dehydration

### **General Pharmacological Interventions:**

- Paracetamol and non-aspirin containing NSAIDs, such as naproxen may be effective in reducing fever and sweating. However some patients are relatively asymptomatic with the fever and experience sweating during defervescence. It may then be necessary to discontinue the antipyretics.
- High dose steroids may have a role in chronic lymphatic leukaemia
- Clinical experience has shown benefit from cimetidine 400mg-800mg bd, in idiopathic and malignancy-related sweating.

### **Review assessment and management**

Regularly review the patient's condition and response to interventions. Consider changing medication such as NSAIDS, if the current formulation is no longer effective

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## **Infective symptoms**

### **3. Immune reconstitution inflammatory syndrome**

### **4. Neutropaenic sepsis**

### **1. Immune reconstitution inflammatory syndrome**

#### Definition

IRIS results from a pathological inflammatory response, driven by the recovering immune system after ARV therapy is initiated, causing clinical deterioration.

#### Appropriate assessment to identify cause and severity of symptoms

- The immune reconstitution inflammatory syndrome [IRIS] is a frequent early complication of antiretroviral [ARV] therapy, especially in patients who start ARV therapy with low CD4 counts and established opportunistic infections.
- Infective forms of IRIS may manifest either as an 'unmasking' of a previously untreated infection, or as a paradoxical clinical deterioration of an infective process for which the patient is on appropriate antimicrobial therapy.
- Most cases occur within three months of ARV initiation during early rapid immune recovery.
- IRIS may also occur when a failing ARV regimen is switched to a suppressive regimen or when ARV therapy is resumed after an interruption.

#### **Common causes of IRIS seen in southern Africa**

- Tuberculosis
- Cryptococcosis
- Acne
- Molluscum contagiosum
- Warts
- Herpes simplex and Zoster
- Hepatitis B
- Cytomegalovirus uveitis
- Kaposi's sarcoma

#### **Paradoxical TB IRIS**

- Paradoxical TB IRIS occurs in 8-43% of patients who are started on ARV therapy while on TB treatment, typically one to four weeks after ARV therapy is initiated.
- Common manifestations are the return of TB symptoms, fever, lymph node enlargement with inflammatory features, worsening radiographic pulmonary infiltrates, and the accumulation of serous effusions or sterile abscesses. A minority of patients may develop life-threatening meningitis.
- Most cases are self limiting within a few weeks, but a minority can persist for many months, especially sterile abscesses.

### **Paradoxical cryptococcal IRIS**

- Paradoxical cryptococcal IRIS occurs in patients who have had a diagnosis of cryptococcosis prior to starting ARV therapy, and are improving on antifungal therapy.
- Typically after starting ARV therapy they develop recurrent meningitis symptoms that may be associated with raised intracranial pressure.

### **Other manifestations of IRIS**

- A range of skin conditions can occur, recur or worsen with IRIS. These include;
  - HSV 1 and 2,
  - Herpes Zoster
  - Warts
  - Papular pruritic eruption
  - Acne
  - Molluscum contagiosum
- Patients with chronic hepatitis B and C may present with a flare of their hepatitis due to IRIS.
- A minority of Kaposi Sarcoma [KS] patients may develop KS IRIS after starting ARV therapy.

#### Explanation to patient and family

- This is probably the most important intervention.
- The patient and family need to know that the deteriorating symptoms are not due to the ARV therapy.
- An explanation needs to be given appropriate to the patient and family's education and understanding, that the body is getting stronger because of the ARV therapy and that a battle is going on in the body, causing the symptoms.
- They must be encouraged at all costs to continue with the ARV therapy and the TB therapy (for example). They must be encouraged to 'ride the storm' and be reassured that it will improve.

#### Institute non-pharmacological interventions

- A patient with severe symptoms of shortness of breath or high fever, or signs and symptoms of raised intracranial pressure may need to be admitted to an in patient unit.
- All patients with recurrent meningitis should have a lumbar puncture to measure and if necessary, reduce raised intracranial pressure [serial lumbar punctures may be needed to exclude alternate diagnoses].
- Patients may need tepid sponging or oxygen therapy to relieve symptoms.

#### Prescribe appropriate first line treatment

- Continue with ARV therapy.
- Prescribe analgesics according to WHO ladder if needed.
- In patients with unmasking IRIS, ARV therapy should be continued, and effective treatment for the condition started. For example, in the case of TB, not having been diagnosed prior to starting ARV therapy, TB treatment would now need to be started.
- In paradoxical IRIS, ARV therapy and effective OI treatment should be continued.
- In severe cases especially those with CNS involvement, corticosteroids [e.g. prednisone 2mg/kg, duration depending on response] should be considered in consultation with a specialist.
- In rare cases when the reaction is life threatening and not responding to corticosteroids, it may be necessary to interrupt ARV therapy.

### Review assessment and management

- Follow up the patient on a regular basis, monitoring all signs and symptoms.
- It may be necessary to drain sterile TB abscesses repeatedly.
- Serial lumbar punctures may be necessary.
- Continue to reassure the patient and family

## **2. Neutropaenic Sepsis**

### Introduction

More and more patients undergo chemotherapy and radiotherapy from home. All Palliative Care professionals need to be aware of the risks of lowered immune response, typically in the second week after chemotherapy.

### Appropriate assessment to identify cause and severity of symptoms

Manifestation of sepsis in a patient who is undergoing oncology treatment can be minimal, but it must be recognised. All clinical staff should be acutely aware of the serious risk and potential rapid fatality of patients who have become neutropaenic and febrile. The routine signs of a raised temperature, a fast pulse, sweating, etc, may be absent.

Without such vigilance, patients may suddenly deteriorate and become septicaemic which, for a significant proportion, will be fatal.

### Appropriate first-line treatment: Referral to acute oncology service

Contact the appropriate oncology unit urgently if sepsis in a patient undergoing oncology treatment is suspected. Such patients should be transferred to the care of the specialised in-patient oncology unit for definitive investigation and management, where essential investigations can be rapidly carried out and intravenous therapy commenced with suitable monitoring. Not all Hospices are able to offer this level of care, but some large academic hospices have the facilities to treat and monitor patients with neutropaenic sepsis. Close collaboration with the attending oncologist is imperative.

Empirical treatment of a febrile neutropaenic patient should be instigated and an appropriate antibiotic regime commenced in consultation with a local bacteriologist and the oncologist involved. Antibiotic regimes vary from region to region.

Treatment is intravenous and for a minimum of seven days until the neutrophil count is  $>0.5 \times 10^9$  g/l.

### Explanation to patient and family

The patient and their family members need to be involved in all decision making. They should be adequately educated about the seriousness of the situation and the potential risks involved. At times patients who have already been admitted to a Hospice may develop Neutropaenic Sepsis. Some patients may refuse transfer to an oncology unit and prefer to take the risk of remaining in

the Hospice setting. Again this should be discussed at length with the patient to be sure that they are making an informed decision, and with their oncologist, who will advise on treatment options.

### **Key Points**

- ✓ Be aware of the seriousness of this risk for patients who have recently undergone oncological treatments, particularly chemotherapy
- ✓ Contact the appropriate oncology department urgently if sepsis is suspected
- ✓ Transfer to specialised in-patient oncology unit for definitive investigation and management

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## Management of Neuro-psychiatric symptoms

1. Delirium
2. Anxiety
3. Depression
4. Insomnia
5. Convulsions

### Management of Delirium (acute confusional state)

#### Definition:

Delirium is an altered state of mind characterised by confusion of recent onset and variable severity. It is a collective term for the various causes of acute confusion rather than a specific diagnosis.

There are **4 key features** of delirium that need to be present to make the diagnosis:

(1) **A changed level of consciousness.** The patient has difficulty focusing, sustaining or shifting their attention. The patient may be agitated and restless or may be abnormally drowsy. Disorientation may be present but is not an essential feature in making the diagnosis.

(2) **A disturbance of the process of thinking** (cognition). The patient has short term memory loss, disorganized thinking, speaking and problem solving. (Exclude pre-existing dementia.) Hallucinations and delusions may be present but are not essential features in making the diagnosis.

(3) The above changes are of **recent onset** and may **fluctuate** over a period of hours.

(4) There is definite clinical evidence that the disturbance is caused by the abnormal physiology of an underlying **general medical condition**.

#### Types of delirium:

There are 3 clinical sub-types of delirium

- a) **Hyperactive delirium:** The patient is restless, irritable, agitated and may become aggressive or inappropriate in their behavior.
- b) **Hypoactive delirium:** The patient is inactive, disinterested and incoherent.
- c) **Mixed delirium:** The patient fluctuates between hypo- and hyperactive delirium. This is the most common sub-type (>50%).

Delirium may be present on admission or it may develop later. Risk factors for delirium include advanced age, poor vision, deafness, existing cognitive impairment/dementia, liver and brain metastases, use of benzodiazepines (Daily dose equivalent (DDE) >2mg lorazepam), opioids (DDE>90 mg morphine) and cortisone (DDE>15 mg dexamethasone)

#### Screening for delirium

The Confusion Assessment Method (CAM) is a simple way of screening for delirium. The following table has been developed from the CAM by the Institute for Palliative Medicine at San

Diego Hospice, California (used with permission). The CAM's sensitivity is 94-100% and its specificity is 90-95%.

Appropriate assessment to identify cause and severity of symptoms

Patients with advanced, life threatening illnesses may suddenly begin behaving strangely.

- They may become agitated, demanding or respond in an irrational way.
- They may appear anxious, tearful or depressed.
- They may become restless and try to get out of bed.

Initially it may be difficult to understand what is causing the problem and they may even be thought of as being difficult or unco-operative. In such a situation it is important to consider **delirium** as this is the most common reason for this pattern of behaviour.

DELIRIUM SCREENING GUIDELINE	
<p><b>Confusion Assessment Method (CAM)</b> A diagnosis of delirium is suggested if question 1 &amp; 2 are YES with either YES from 3 OR anything other than alert in 4.</p>	
<p><b>1. ACUTE ONSET</b> Is there sudden onset of confusion (hrs-days)?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p><b>3. DISORGANISED THINKING</b> Is the patient's thinking disorganised or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, unpredictable switching from subject to subject?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>
<p><b>2. INATTENTION</b> Does the patient have difficulty focusing attention, for example, easily distracted, or has difficulty keeping track of what is being said?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p><b>4. ALTERED LEVEL OF CONSCIOUSNESS</b> Overall how would you rate this patient's level of consciousness?</p> <p><input type="checkbox"/> Alert <input type="checkbox"/> Vigilant (hyper-alert, overly sensitive to stimuli) <input type="checkbox"/> Lethargic (drowsy, easily aroused) <input type="checkbox"/> Stupor (difficult to arouse) <input type="checkbox"/> Coma (unarousable) <input type="checkbox"/> Uncertain</p>

### Differential diagnosis

Delirium should be differentiated from depression, dementia and major psychotic illness.

The following table may help to do so:

	Delirium	Depression	Dementia	Psychosis
Alertness	Abnormal	Normal	Normal	Normal
Onset	Sudden and recent	Gradual	Gradual	Gradual
Course	Fluctuates frequently	May vary slightly and be worse in morning	Progressive, may be slightly worse in evening ("Sundowning")	No fluctuation

Elderly patients with dementia can develop delirium on top of their dementia. Establish from the main care giver what the person's baseline function was previously and how they appear in comparison during this examination.

### The importance of recognizing delirium

Delirium is distressing to the patient and the family; it disrupts effective patient care and may even lead to injuries. Early intervention is necessary to identify possible reversible causes and to take effective action to prevent the problem from getting out of hand.

### Prevalence:

Delirium is common in a palliative care setting. About 30-40% of admissions are due to sudden confusion and more than 80% will develop some degree of delirium during the terminal phase of their illness.

### Correct reversible factors

### Underlying causes

The underlying mechanism for delirium is thought to an imbalance of neurotransmitters ( a deficiency of acetylcholine and an excess of dopamine). The cause of this imbalance is multifactorial. The following are some of the risk factors that may lead to delirium:

- advanced age,
- dehydration,
- psycho-active medication,
- infection,
- liver, bone and brain metastases,
- underlying dementia,
- head trauma,
- impaired vision and hearing.
- 

Most delirious patients will have 3 or more contributing causes.

For those who like mnemonics: "DIMTOP"

**D**rugs e.g. opioids, anticholinergics, benzodiazepines, regular drugs (esp. alcohol) omitted

**I**nfection e.g. UTI, chest, meningitis or wound

**M**etabolic e.g. hypo/hypernatraemia, hypercalcaemia

**T**rauma e.g. hypoperfusion, fat embolism (fractures)

**O**xygen lack/hypercarbia

**P**ressure (intracranial) psychiatric, pain, poisons

### Special Investigations

Delirium can often be adequately assessed and managed without any special investigations. In selected cases where resources are available, appropriate investigations may be helpful. It is, however, inappropriate to blindly screen for every possible abnormality "just in case." Empirical treatment for common causes is appropriate where resources are limited.

### Reversibility

While some studies have shown that up to 50% of episodes of delirium may be reversible, reversibility is dependent on a number of interrelated factors. The prognosis is poorer in the presence of advanced age, severe cognitive impairment and poor vital organ function. There is no easy way of predicting reversibility. *"It remains prudent to treat all cases of delirium as potentially reversible while remaining sensitive to the needs of patients that have actively entered the final 24-48 h of life where the balance between minimising risk factors for delirium versus achieving optimal levels of comfort requires careful consideration."*

### Consider disease-specific palliative therapy

- a. Where appropriate rehydrate patients (orally or by hypodermoclysis).
- b. Review all medications, stop or reduce the dosage of all non-essential drugs and recheck for previous excessive alcohol or illicit drug use.
- c. A trial of steroids for suspected brain metastases.
  - Further options include confirmation by scanning if the patient's general performance status is good and if the patient is keen on further treatment.
  - Solitary, accessible metastases may benefit from surgery. (Less than a third of cerebral metastases are single.)
  - Whole brain irradiation could be considered for multiple metastases for the relief of severe headache. Whole brain irradiation does not improve survival. It should not be considered if there are metastases in other organs and if the patient's performance status is poor.
  - Chemotherapy could be considered for certain lymphomas, small cell lung cancer and germ cell tumours.
- d. Most infections should be appropriately treated unless the patient has signs of impending death (within 24-48 hrs).
- e. Consider using rehydration and bisphosphonates for hypercalcaemia.

### Explanation to patient and family

This is a particularly stressful time for the family. Arrange a family meeting and facilitate a clear understanding of what is going on and what can be done. Here are some suggestions:

- Allow the family to explain how they see things and what their chief fears are



- Ask the family to help you get to know their loved one as a person. This helps them refocus on the person and not just the drama of the current events.
- Explain that their loved one is not mad or being difficult – their behaviour is as a result of their illness which has caused a temporary disturbance of brain's function.
- Ask about previous mental and physical status
- Explain the nature of delirium, its causes and its significance
- Discuss the management options available and the likely outcomes.
- Ask about family and patient preferences
- Review goals of care: The need for care and safety as well as a focus on comfort.
- Clarify the role of the family and the roles of the health professionals
- Give a rough estimate of expected prognosis acknowledging the uncertainty of the future.
- Allow the family to share something special about the delirious person. This helps the discussion to end on a positive note.

#### Institute non-pharmacological interventions

- a. Calm reassurance of the delirious patient
- b. Regular orientation for time and place
- c. Presence of a family member. Limit visitors.
- d. Identify and maintain care giver consistency where possible
- e. Familiar personal objects or photos
- f. Encourage walking, or if bedridden, range of motion exercises
- g. Appropriate lighting at night
- h. Soothing music
- i. Gentle back massage and a glass of warm milk rather than a sleeping tablet
- j. Noise reduction as far as possible
- k. Optimise vision and hearing (check hearing aid)

NB: Physical restraints are not necessary. They may aggravate the situation and cause injury. Effective calming and if necessary, sedation is possible by means of appropriate medication at effective dosages.

#### Prescribe appropriate first-line treatment

Mild delirium without agitation			
Drug	Dose	Frequency	Comment
Haloperidol (Serenace)	0.5 - 2mg PO	Every hr p.r.n. x3 (Notify Dr if 3 doses not effective. This allows a review of the situation so that the dose can be adjusted if needed)	Usual effective dose is 0.5 -2mg/day Maintenance: Previous day's total used given as a single daily dose & the same p.r.n. dose for break through symptoms NB: Medication is not always needed but as agitation may occur unexpectedly in a new environment consider its use for a short period.

Delirium with mild agitation but no aggression:			
Drug	Dose	Frequency	Comment
Haloperidol (Serenace)	1-2 mg SC	Every 30 min p.r.n. x3 (Notify Dr if 3 doses not effective.)	Usual effective dose is 6-12mg/day Maximum 100mg/day Maintenance: Previous day's total used given as a single or divided dose plus the same p.r.n. dose for break through symptoms

Delirium with agitation, restlessness and aggression			
Drug	Dose	Frequency	Comment
Haloperidol (Serenace)	3-5mg SC, IM or IV	Every 30 min p.r.n. x3 (Notify Dr if 3 doses not effective.)	Up to 1200mg IV per day has been safely used. Occasionally prolongation of the Q-T interval may occur. An aggressive delirious patient may be dangerous and calming the patient must be an urgent priority for all staff. (See second line drugs)

NB: Benzodiazepines such as lorazepam (Ativan) or diazepam (Valium) should not be used alone as first line treatment as they may result in increasing confusion, disinhibition and falls. They are however, useful when sedation is needed in patients with delirium due to alcohol withdrawal.

Alternative first line drug:

Drug	Dose	Frequency	Comment
Chlorpromazine (Largactil)	12.5 – 50 mg PO, IM or IV	Every 2-4 hours p.r.n. x3 (Notify Dr if 3 doses not effective.)	More sedating than haloperidol. May cause hypotension

Consider additional second-line treatment where sedation is needed

Drug	Dose	Frequency	Comment
Lorazepam (Ativan)	1-2 mg PO, SL, IV	Every hr p.r.n.x3 (Notify Dr if 3 doses not effective.)	
Midazolam (Dormicum)	3-5mg SC or IV		For rapid sedation
	1mg Continuous SC infusion	Per hour	Titrate the dose according to effect. Max 10mg/hour
Promethazine (Phenergan)	50 mg PO,IM, IV	8 hourly	Very sedating but helpful as an adjunct to other drugs.

#### Review assessment and management

The CAM is useful for screening for delirium but it does not measure the severity of the delirium nor does it assess the degree of change in response to treatment or to the worsening of the patient's condition. In severely ill patients it may be unduly burdensome to carry out time consuming assessments of mental state. However, in some patients it may be helpful to objectively measure improvement or deterioration.

A test that is relatively simple and quick to perform is the Clock Drawing Test (CDT). First, the patient is asked to draw a clock with all the numbers on it. Then the patient is asked to put the hands on the clock to make it read 2:45. The instructions can be repeated but no

further directions are given. The drawing is scored according to the correct sequence and spacing of the numbers and the correct placement of the hands. The CDT assesses comprehension, visuo-spatial abilities, concentration, numerical knowledge, visual memory and executive function. It also provides a visual record of changes in cognitive ability.

Care and routine observations should be non burdensome. The dose of the drugs being used to control the delirium can be reduced as soon as the patient is no longer agitated. Where there is refractory agitated delirium, proportionate sedation may need to be continued until the patient dies.

At all stages of management consider:

Involvement of interdisciplinary team:

Managing a delirious patient requires a well functioning team. Clear notes setting out the goals of care, progress and reasons for new decisions will help to keep everyone up to date and working towards the same end. The family needs to be supported and to be kept involved in the decision making as much as possible.

Referral to appropriate service/more experienced clinician:

Delirium presents many complex clinical and ethical problems. If the degree of uncertainty about the diagnosis and management is interfering with proper care, the advice of a more experienced palliative care clinician needs to be sought.

## **2. Anxiety**

### Definition

Anxiety is defined as a feeling of apprehension and fear characterized by physical symptoms such as palpitations, sweating, and feelings of stress.

It is normal to be anxious in certain circumstances, especially in the Palliative Care setting. The spectrum of anxiety ranges from “normal” anxiety through to persistent and severe anxiety. Anxiety becomes a problem when its duration and severity exceed normal expectations and it interferes with normal functioning. Anxiety may be acute or chronic.

Anxiety is common in the terminally ill for a variety of reasons such as the fear of uncontrolled symptoms, fear of dying or being left alone to die.

### Appropriate assessment to identify cause and severity of symptoms

### **Symptoms of anxiety**

#### **Core features**

- Persistently tense and unable to relax
- Worry
- More than normal mood variation

- Cannot distract self

### **Key symptoms**

- Poor concentration
- Indecisiveness
- Insomnia
- Irritability
- Sweating, tremor, nausea
- Panic attacks

### Assessment to identify cause and severity

- Is it severe?
- Is it long-standing?
- Is it alcohol withdrawal?
- Is it situational?
- Is it related to a specific fear?
- Are the family anxious?

### **Causes of anxiety in Palliative Care**

<b>Situational causes</b>	<b>Caused by drugs</b>	<b>Organic causes</b>	<b>Related to the person's inner world</b>	<b>Psychiatric causes</b>
Adjustment disorder	Corticosteroids	Severe pain	Thoughts about the past, regrets, guilt	Panic attacks
Fear of hospital, hospice, chemo/radioRx	Neuroleptics	Insomnia	Thoughts about the future	Phobia
Worry about illness, family, finances	Benzodiazepine/ alcohol withdrawal	Dyspnoea	Fear of pain	Depression
Persecutory fantasies		Nausea	Fear of incontinence	Delirium (50% experience anxiety)
		Hypoglycaemia	Fear of mental impairment	
		Brain tumour	Fear of loss of independence	
		Secondary mental disorders	Thoughts about life after death	

### Explanation to the patient and family

It is normal to feel anxious when faced with the realities of serious illness. Anxiety can be exhausting and is not helpful in managing the problems faced. It helps to know the facts of the illness so that we are not anxious about imagined things and to talk through our anxieties. Distraction and relaxation also help to control anxiety. If anxiety is severe and interferes with your activities, your doctor can prescribe medication to reduce the feeling of anxiety.

### Correct reversible factors

Management involves assessing the patient for any reversible factors, such as pain or unfounded worries. Stimulant drugs, excessive alcohol or withdrawal of drugs or alcohol may exacerbate anxiety and need to be monitored.

### Non-pharmacological intervention

It is necessary to provide the time and opportunity for patients to express their worries and concerns, and for these concerns to be addressed, honestly and clearly. Relaxation techniques and various complementary therapies may help, as may the controlled safe atmosphere of a hospice with professional carers. Professional counselling is a key intervention in management of anxiety. It is important for all members of the palliative care team to be aware of the “infectious” nature of anxiety, and for the team to avoid being driven to management extremes because of the anxiety of the patient, or their family.

Anxiety can also be a problem for the palliative care team itself, particularly where individual team members feel unsupported in their work and are confronted with stressful situations for which they perceive their options to be very limited. No team is immune from anxiety and strategies need to be devised to provide ongoing support for team members, where such issues can be talked over and dealt with more concertedly where necessary.

### **Psychological methods for managing anxiety and/or pain**

Distraction	Behavioural therapy	Creative activity	Cognitive therapy
Art therapy	Imagery	Relaxation	Music therapy
Biofeedback	Psychodynamic therapies	Hypnosis	

### Pharmacological intervention

**Benzodiazepines** - These very useful drugs have received a bad press because of their addictive potential. They are traditionally divided between compounds which have more sedating effects and those which have more anxiolytic actions. However, there is considerable overlap on the anxiety/sedating spectrum.

They are useful to break the anxiety cycle, to restore sleep and to reduce the suffering of the situation where a patient feels they are “*losing control*”. **They are not a substitute** for taking the time to allow a patient to discuss their fears and anxieties.

Benzodiazepine	Dosage	Description
Diazepam	1 to 5 mg p.r.n., p.o.	Diazepam has a long half-life and may therefore accumulate and be sedative. It should be possible to give it once a day, at night, although initially it can be given tds (three times a day).
Lorazepam	1 to 2 mg p.r.n., p.o. or SL	Lorazepam is short-acting, rapidly anxiolytic and less sedating than diazepam. It may be more addictive on a longer-term basis.
Midazolam	5 to 10 mg p.r.n., SC or 15 to 60 mg per 24 hours CSCI	Useful for emergency sedation. Useful in syringe driver (continuous subcutaneous morphine). Can be used with other medication such as morphine, haloperidol.
Alprazolam	0.5-2mg prn or tds	Less sedating so helpful for daytime use, and anxiety associated with depression

### Antidepressants for anxiety

Tricyclic antidepressants, such as amitriptyline, may be useful as anxiolytics, often in “*sub-antidepressant*” dosages. Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants, such as paroxetine and citalopram, are more expensive alternatives, but have fewer reported side-effects. Care must be taken to avoid enervating SSRIs, such as fluoxetine, which can initially *increase* anxiety.

### Antipsychotics for anxiety

Risperidone	From 0.25 mg, daily, b.d.	In patients with associated agitation, risperidone may be helpful.
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At all stages consider referral to specialist care

Complex anxiety states with depression and psychosis may be more suitably treated with neuroleptics. The help of a psychiatric team may be needed.

## 3. Depression

### Introduction

Definition:

Depression is defined by the World Health Organisation as a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration.

All Palliative Care patients should be assessed for depression as it is strongly and consistently associated with poor quality of life. It causes more reduction in role and social functioning than could be attributed to the physical illness alone. Depression reduces physical functioning and is often associated with symptoms that are difficult to control. Depression also has a major impact on the patient's family and carers.

Estimates of the prevalence of depression in patients vary but at least 25% may develop a significant mood disorder when suffering from advanced cancer.

Certain types of cancers are associated with an increased incidence of depression. A spectrum ranging from sadness to adjustment disorder to depressive illness is recognised. There is concern that depression may be under-diagnosed as patient, family members and clinicians may attribute the emotional signs and symptoms of depression to natural sadness and the physical features to the progressive illness. Other confounding factors may be the patient's presentation with overriding anxiety or a slow worsening of personality traits, such as attention seeking, which may go unnoticed.

**Depression in HIV/AIDS patients** – the diagnosis and treatment of mood disorders is essential to the well-being of a patient infected with HIV. Depression is very common and often under-diagnosed and under-treated in HIV/ AIDS. Depression often increases over the course of the illness, especially after the onset of AIDS.

**Risk factors: for depression:**

- Personal or family history of depression.
- Concurrent life stresses.
- Absence of social support.
- Depression is more common in oropharyngeal, pancreatic, breast and lung cancers

Appropriate assessment to identify cause and severity of symptoms

Physical symptoms commonly associated with depression are also features of physical illness or treatment so are less helpful in making a diagnosis such as:

- Weight/appetite change
- Insomnia
- Loss of energy
- Fatigue
- Psychomotor slowing
- Loss of libido

These biological features are not reliable as features of depression in patients with late stage illness and greater emphasis must be placed on psychological and behavioural features.

**Depressive symptoms in palliative care patients include:**

- Greater severity of dysphoric mood.
- Excessive feelings of hopelessness, guilt, worthlessness.
- Social withdrawal; loss of pleasure in daily activities.
- A wish for earlier death (or suicidal thoughts).

- A positive response to the question “Do you feel depressed?”

#### **Atypical presentation of depression** (More common in the Palliative Care setting)

- Irritability
- Agitation
- Anxiety
- Histrionic behavior
- Hypochondriasis
- Psychotic features (delusions, paranoia) with depressed mood

#### **Assessment tools:**

- In primary care, the PHQ-9 is used as a screening tool. (Patient Health Questionnaire)
- The HADS (The Hospital Anxiety and Depression scale) and the BECKS Depression Inventory have been used most commonly in Palliative Care but have not been altogether satisfactory as they rely on physical symptoms.
- The Brief Edinburgh Depression Scale is more suited to palliative care patients.

#### Explanation to patient and family

As always in the Palliative Care setting it is essential to take time to explain the signs, symptoms and causes of depression, as well to discuss treatment options with both patient and family/carers. Witnessing a loved one becoming depressed can result in considerable stress and burden on the family and they should be offered counseling and supportive care. Patients and families need to understand that depression in patients with serious illness is still treatable and should not be accepted as “normal”. It is never appropriate to assume that a psychiatric symptom is simply an ‘understandable’ reaction to the situation.

#### Correct reversible factors

Ensure that any reversible causative factors such as distressing physical symptoms are eliminated. Adequate pain control may improve depressive symptoms significantly

#### Institute non-pharmacological interventions by involvement of the interdisciplinary team

Ensure adequate emotional support and counselling is available so that fears and concerns can be explored and channelled appropriately. In mild depression, psychological support can be as effective as medication.

Spiritual distress may be a component of depression, or distinct from it.

Recommend supportive psychotherapy or cognitive behavioral therapy as appropriate.

#### Pharmacological interventions

There is little difference in efficacy between antidepressants.

Consider side effects and any co-morbid illnesses. Check for drug interactions.

A current or previously effective antidepressant should be used unless contra-indicated.

*Treatment of depression can significantly improve quality of life and is as effective in palliative care as in other situations.*



**Antidepressants** – there is little information concerning the effectiveness of antidepressant medication in terminally ill patients. There is, however, a body of evidence showing that undertreatment of depression is common and that patients are often not prescribed antidepressants within the final six weeks of life. Further, psycho-stimulants are very rarely used in this terminal situation despite some evidence of benefit.

<b>Tricyclics</b>	e.g.	Amitriptyline	10-150 mg nocte
		Imipramine	10-150 mg per day
		Lofepramine	70-210 mg per day

Tricyclic antidepressants may take several weeks to lift depression. Amitriptyline has a greater sedative effect in comparison with imipramine and lofepramine. They all have antimuscarinic properties to greater or lesser degrees, and therefore may be associated with symptoms such as hypotension, dry mouth and difficulty in micturition. Doses should gradually be increased to avoid unnecessary side effects.

#### **Selective serotonin re-uptake inhibitors (SSRIs),**

e.g.	Paroxetine	20 mg mane
	Fluoxetine	20 mg mane
	Citalopram	20 mg mane

These drugs are less sedative than tricyclic antidepressants and have few antimuscarinic effects, low cardio-toxicity and may have a faster onset of action than the tricyclics. Gastrointestinal side effects such as nausea are dose-related. Fluoxetine in particular may cause restlessness and anxiety and should be used with caution. There is some evidence of an increased incidence of gastrointestinal bleeding in combination with NSAIDs or aspirin.

#### **Serotonin and noradrenaline re-uptake inhibitors (SNRIs)**

e.g. Venlafaxine 37.5 mg b.d. increased to 75 mg b.d  
These have fewer adverse effects than SSRIs. Slow release capsules are preferable. (75mg and 150 mg given once daily)

#### **Noradrenergic and specific serotonergic agents (NaSSA)**

e.g.	Mirtazapine	15-45 mg nocte
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Consider adjuvant/second line treatment

#### **Other agents**

Corticosteroids	e.g.	Dexamethasone 2-4 mg daily
Psychostimulants	e.g.	Methylphenidate (Ritalin) from 10 mg daily
Sulpiride (Eglonyl®)		150-300 mg tds

At the end-of-life stage, when a patient has a prognosis of only a few weeks, it may be more appropriate to try a low dose of psycho-stimulant or corticosteroid to increase cognitive function and to lift a patient's mood. Sulpiride does not have a delayed effect like other antidepressants so can be useful when prognosis is limited.

These agents can also be used for a few weeks when waiting for the antidepressant medication to set in.

### **Key notes to remember when prescribing antidepressants**

“Start low, go slow”

Antidepressants should not be stopped abruptly if at all possible but withdrawn gradually.

### Referral to appropriate service/more experienced clinician

Patients with severe, prolonged or resistant depression and/or suicidal ideation are uncommon, but should be referred to a psychiatrist for assessment and medication.

## **4. Insomnia**

### Definition

The inability to fall asleep or to remain asleep for an adequate length of time

### Appropriate assessment to identify cause and severity of symptoms

It is important to get a thorough history of the patient's sleep pattern now and before he/she started to have problems.

Establish the patient's understanding about insomnia and their expectations.

Identify possible medications that the patient is taking that could be causing the insomnia.

Identify possible emotional stresses that could be causing the insomnia.

Identify possible symptoms such as pain that may be causing the insomnia.

### Explanation to patient and family

Explain the possible causes of insomnia.

Reassure patient and family that condition is being taken seriously.

Discuss management options with patient and family.

### Correct reversible factors

Identify and treat the primary condition; eg pain.

Eliminate disturbance and noise.

### Consider disease-specific palliative therapy

Treat insomnia with a holistic approach.

Consider physical, psychosocial and spiritual causes and management options.

### Institute non-pharmacological interventions

Avoid alcohol and stimulants in the evening

Relaxation techniques

Massage  
Warm milk/herbal tea at night  
Cognitive-behavioural therapy  
Progressive muscle relaxation therapy  
Biofeedback  
Hypnotherapy  
Sleep hygiene.

#### Prescribe appropriate first-line treatment

Benzodiazepines have been successfully used for short term insomnia, although there are no systematic studies on long-term use and rare studies in palliative care.

- Nitrazepam 5-10 mg nocte
- Oxazepam 10- 15 mg nocte

#### Review assessment and management

Review treatment after first night and adjust treatment accordingly.  
Advise patient to inform the healthcare team if treatment stops being effective.

#### **At all stages of management consider:**

##### Involvement of interdisciplinary team

Management of insomnia in palliative care patients is a holistic process and the participation of the interdisciplinary team will ensure this.

Insomnia has a large psychosocial element which should be explored and addressed for optimal treatment results.

##### Referral to appropriate service/more experienced clinician

Referral to sleep clinics is an option, but is rarely appropriate or necessary for palliative care patients.

## **5. Convulsions**

Definition: An involuntary contraction of the muscles producing contortion of the body and limbs.

#### Appropriate assessment to identify cause and severity of symptom

Assess the following:

- Duration and severity of the seizure.
- The circumstances before the seizure.
- Point of origin of seizure.
- The parts of the body that are involved.
- The type of movements in the part of the body involved in the seizure.
- Size of and changes in pupils.
- Presence of automatism.
- Changes in consciousness.
- Incontinence of urine or faeces.
- Any residual symptoms post seizure: paralysis or weakness, inability to speak, confusion, sleep, etc.

- Once seizure is over, monitor blood pressure, pulse, respiration and temperature.
- Take blood samples to eliminate metabolic disorder or chemical imbalance that may be causing the convulsions.

#### Explanation to patient and family

It is important to realise that seizures are very traumatic for the patient and the family. It is important to reassure them and to make the patient as comfortable as possible and maintain the patient's dignity.

- Explain what is happening.
- Explain possible causes
- Explain immediate and long-term management.

#### Correct reversible factors

- Treat pyrexia if present.
- Treat any other conditions that may have caused seizures.
- If brain tumour is the cause, consider steroid therapy to reduce inflammation around it which may reduce seizures. Also consider palliative radiation and/or chemotherapy to shrink the tumour so as to reduce seizures.

#### Consider disease-specific palliative therapy

If the patient's condition is imminently terminal, sedation may be appropriate to reduce distress and discomfort.

#### Institute non-pharmacological interventions

- Clear airway
- Put patient into the recovery position and secure the environment to prevent injury.

#### Prescribe appropriate first-line treatment

Give appropriate medications:

- Diazepam 10mg PR (repeat after 15 and 30 min PRN)
- OR*
- Lorazepam 2-4mg SL, SC or IV (repeat after 15 and 30 min PRN)
- OR*
- Midazolam 5-10mg SC or IV (repeat after 15 min PRN)

#### Consider adjuvant/second-line treatment

- Consider doubling the dose of diazepam or midazolam
- OR*
- Phenobarbital 100-200mg SC or IV (slowly by IV over 30 min with 100cc of saline)  
Repeat PRN. Follow with 100mg TDS SC.

#### **Prophylactic management of seizures:**

Seizure prophylaxis with anticonvulsants has only been proven useful in patients with brain metastasis due to malignant melanoma and in patients with brain metastases from other cancers who have already had a seizure.

- Anticonvulsants:
  - Phenytoin 300mg PO followed by 100-200mg PO TDS
  - Carbamazepine 100mg PO BD
  - Valproate 200mg PO BD
  - Other anticonvulsants appropriate to the situation may also be used.
  - **Drug interactions!** Be mindful of possible drug interactions with existing medication regimes.
- Corticosteroids are helpful in the prevention and management of seizures which are secondary to brain metastases, by decreasing the oedema surrounding the tumour mass. Be mindful and monitor the dose and duration of treatment, especially when used for more than 4 weeks.
- Radiation can be helpful in preventing seizures in patients with metastatic brain disease.
- Opioid rotation. Opioids rarely cause seizures, but some are known to do so; switching to another opioid can be helpful.

#### Review assessment and management

Regular assessment of treatment and management is necessary to ensure optimal management.

#### **At all stages of management consider:**

##### Involvement of interdisciplinary team

As with all palliative care issues; the management of the patient who is experiencing seizures is best accomplished by an interdisciplinary team approach. The physical, psychosocial and spiritual components of care all need to be addressed. The doctor, pharmacist, nurse, social worker and/or psychologist and the spiritual practitioner all need to be involved, and if residual physical or neurological symptoms persist, an occupational or physiotherapist will also be needed.

##### Referral to appropriate service/more experienced clinician

Depending on the patient's wishes and the stage of disease, it may be appropriate to refer the patient to a neurologist for further investigation and management.

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## Management of Urinary Symptoms

1. Incontinence
2. Urinary Tract Infection
3. Urinary haemorrhage
4. Bladder and ureteric spasm

### 1. Incontinence

**Definition:** The involuntary loss of urine, which may cause hygienic, physical and/or social problems

#### Assessment

Urinary Incontinence is a common and distressing symptom at the end of life, affecting the patients' lives physically, psychosocially, socially and sexually. Thus, leading to isolation from family and friends as they try to maintain their own personal hygiene and fear losing their dignity in public.

Continence difficulties may be:

- Caused by an underlying condition
- Triggered by medication
- Associated with reduced mobility or cognitive decline
- Present before the onset of the disease

It is essential to determine the cause and identify those patients where the incontinence is due to an inability to reach the toilet in time.

- i. **Urge incontinence signs and symptoms:** sudden, strong desire to void, frequency, loss of moderate to large volume of urine, may be unable to reach the toilet in time, nocturia and/or enuresis usually present. Timed voiding and anticholinergics may be helpful.
- ii. **Stress incontinence signs and symptoms:** leakage with physical activity (coughing, laughing, lifting etc.), small volume of urine, intermittent dribbling, unable to reach toilet following urge to void. Common in multiparous women with poor urethral support and reduced pelvic floor tone. Support prosthesis such as a ring pessary or urethral inserts may be useful.
- iii. **Overflow incontinence:** urethral overactivity (anatomical obstruction e.g. BPH (Benign Prostatic Hyperplasia), neoplasm) , bladder underactivity (neuropathy – sacral plexus damage or spinal cord/cauda equina compression, opioids), strain to void, sense of incomplete emptying, lower abdominal pain/fullness. Clinically able to distinguish the distended palpable bladder much more easily than the floppy large bladder. Permanent catheterization is probably unavoidable, however in less terminal patients, intermittent catheterization, urethral stenting or surgical interventions should be explored. Referral to a urologist is essential in this instance.
- iv. **Functional incontinence:** inability to reach the toilet in time due to physical, psychological or environmental impediment.
  - **Fistula:** (abnormal communication between two hollow viscera or viscera and skin) causes relate commonly to radiotherapy, colonic malignancy/local tumour invasion or diverticulitis/inflammatory bowel disease. Cystoscopy, contrast cystography or intestinal barium studies will demonstrate the fistula. The following options should be explored: surgical removal of bowel section/excision and repair, bypass surgery



or urinary diversion. The advantages and disadvantages of these interventions should be discussed with the patient.

- Vesicoenteric or rectal: common symptoms are pneumaturia, foul urine odour, fecal matter in the urine and recurrent urinary tract infection (UTI). Treatment options depend on the patient's fitness and willingness to live with a stoma.
  - Vesicovaginal: continuous leakage of urine from the bladder into the vagina and must be distinguished from total urethral incontinence.
- v. **Total urethral incontinence:** local incompetence of the urethral sphincter (direct tumour invasion or surgery) or central loss of sphincter control (confusion and dementia) leads to uncontrollable loss of urine. Regular toileting, a female urethral catheter or a male sheath catheter in men, may be tried.

#### Explanation to patient and family

Incontinence is a devastating blow to dignity and should therefore be managed with great sensitivity. Inability to maintain personal hygiene and malodour will lead to social isolation and this will need appropriate discussion. Continence care is usually aimed at promoting continence but the approach may change in end-of-life care. Care should be based on the patient's wishes and preferences and aimed at maintaining comfort and dignity and relieving symptoms.

#### Correct reversible factors

- Diet (excessive volume of liquid late in the day, caffeinated drinks, alcohol)
- Medical conditions (delirium, infection, restricted mobility, impaction, diabetes)
- Medication (carbamazepine, diuretics, lithium, opioids (overflow))
- Physical/environmental barriers
- Odour: Metronidazole 400mg tds may reduce odour from anaerobic infections. Buchu douching or cleansing is found to be useful. Charcoal dressings and masking the smell is not always effective.

Consider disease-specific palliative therapy: - discussed in relation to the identified problems, as management is varied.

#### Institute non-pharmacological interventions

- Patient education (fluid restriction in the afternoon and evening)
- Lifestyle modification (e.g. commode, decreased caffeine)
- Behavioural modification: timed voiding
- Invasive devices (e.g. catheter, stent) FG 16 is the smallest useful size for adults, sialastic catheters are most appropriate and should be changed 6 weekly.
- External collection of urine (nappies, Paul's tubing) – meticulous skin protection with barrier creams such as zinc and castor oil is mandatory.
- Intermittent self-catheterisation used together with an absorbent pad

#### Prescribe appropriate first-line treatment

- Infection: MCS and appropriate antibiotic
- Barrier preparation to protect the skin (Zinc and castor oil/ Vaseline/ Fissan paste)
- Relieve constipation (see GIT guidelines)
- Review medication for medicines which may be exacerbating the problem.

#### Consider adjuvant/second-line treatment

- Desmopressin (EDL secondary list) 10-40 micrograms intranasally or 100-400micrograms orally at night. (contraindicated in cardiac insufficiency, peripheral or cerebral vascular disease, hypertension, renal impairment)
- Palliative surgery, chemo- or radiotherapy to relieve spinal cord compression or reduce size of local mass.

#### Review assessment and management

#### **At all stages of management consider:**

##### Involvement of interdisciplinary team

Sensitive counselling is important, physiotherapy may provide some relief from incontinence especially in the early stages

##### Referral to appropriate service/more experienced clinician

Urologist or gynaecologist.

## **2. Urinary Tract Infection**

#### Appropriate assessment to identify cause and severity of symptoms

Differentiate between complicated and uncomplicated UTI. In palliative care most UTIs will be complicated as the following risk factors are often associated: indwelling catheter, diabetes, structural abnormalities (congenital, tumour, fistula), low output (dehydration), immune impairment, spinal cord injury, previous urologic surgery, atrophic vaginitis, renal calculi

The clinical picture may vary from asymptomatic to severe symptoms to septicaemia.

History: dysuria, frequency, incontinence, urinary retention, pyuria, haematuria, supra-pubic pain, loin pain, fever (PUO), rigors

Examination: pyrexia, confusion, tender supra pubic area, loin area

Investigation: bedside test for urinary blood, protein, leucocytes, nitrates (any or all may be positive)

MCS for men, children, complicated cases, structural abnormalities, upper UTIs (e.g. pyelonephritis)

If dipstick is negative, but UTI symptoms are present, consider yeasts (candida)

#### Explanation to patient and family

UTI can cause considerable morbidity in terminal disease and should therefore be managed with the necessary empathy and rapid response to needs.

Relieve anxiety around urinary incontinence and request support from family members.

The patient will be helped by;

- close proximity to the toilet
- ready availability of a commode, urinal or bottle
- a rapid response for help by family members

#### Correct reversible factors

- Rehydrate if appropriate (especially in hypercalcaemia, septicaemia)
- Check on catheter hygiene – do not treat asymptomatic bacteriological colonization in catheterized patients

- Local oestrogen therapy for severe atrophic vaginitis
- Distinguish and treat related symptoms due to STI infections such as gonorrhoea, Chlamydia or genital herpes

Consider disease-specific palliative therapy. UTIs are most commonly caused by E Coli/ other gram neg. Bacilli – resistance common and increasing, therefore:

- i. Acute, uncomplicated bacterial cystitis
  - trimethoprim-sulphamethoxazole (160mg trimethoprim-800mg sulphamethoxazole i.e 1 DS or 2 SS tablets) or trimethoprim 200mg twice daily for 3 days;
  - ciprofloxacin 250 – 500 mg twice daily for 3 days
  - nitrofurantoin 50-100mg 4 times daily for 7 days/nitrofurantoin monohydrate 100mg twice daily for 7 days
  - Cefuroxime 250 – 500mg bd

More severe cases

- Cefuroxime 750 mg IVI 8 hourly ( Zinacef )
  - Ceftiraxone ( Rocephin) 1-2 g daily IMI/IVI
  - Gentamycin 80 mg IVI/IMI daily
- ii. Extend to 7 days if diabetic, symptoms > 7 days, >65 years old or change regime according to MSU result which should be taken in any complicated UTI prior to starting antibiotics;
  - iii. If UTI is due to a fungal infection found upon culture of a midstream specimen, it is usually a systemic infection (yeasts - candida sp) Rx: Fluconazole 400mg/day X14 days . Exclude asymptomatic commensal from the GIT tract, which does not require treatment;
  - iv. For frequent recurrences of lower UTI, prophylaxis required with once daily treatment Trimethoprim 200mg, or Nitrofurantoin 50 – 100 mg

### Institute non-pharmacological interventions

General:

- Supporting the patient with adequate fluid intake, especially cranberry/blueberry juice 180 ml bd could be beneficial as a preventative measure in recurrent infections. The juice contains a large polymer which inhibits bacterial adherence to the bladder mucosa. Avoid if on Warfarin.
- Abstaining from caffeine and alcohol is beneficial
- Regular voiding – every 3 hours.

Catheterized patients:

- bladder washouts with 100mls 0.9% Saline or with continuous bladder irrigation;
- change indwelling catheter – ensure that antibiotics are given for 48 hours prior to decatheterization;
- revert to intermittent catheterization 4-6 hourly

### Prescribe appropriate first-line treatment

Treat the infection with the necessary antibiotic and provide antibiotic prophylaxis in recurrent infections as above.

### Consider adjuvant/second-line treatment

1 Treat bladder spasms and pain symptomatically with the following treatment options:

- Hyoscine Butylbromide 10-20 mg po, IVI, IMI or S/C tds. Maximum of 100mg per day
- WHO pain ladder
- Intravesical morphine and bupivacaine tds (morphine 10-20mg and 0.5% bupivacaine 10ml diluted in 0.9% saline to 20 ml), instil through an indwelling catheter and clamp for 30 min.
- Spinal analgesia, e.g. epidural morphine and 0.5% bupivacaine

2 Treatment of urgency and frequency

- Tricyclic antidepressants ( Amitriptyline and imipramine 25-50 mg nocte) for nocturnal enuresis
- Anti-inflammatories (NSAID) such as Naproxen 250-500 mg bd
- Desmopressin Oxybutinin 5mg bd/tds 200-400µg po or spray 20-40µg intranasally as a last resort for refractory troublesome nocturia

### Review assessment and management

It is mandatory that refractory treatment and resistance to antibiotics causing unabated symptoms need careful review of antibiotic regime. Consider prophylactic antibiotics where successful treatment of UTI is followed by repeated infections.

#### **At all stages of management consider:**

Involvement of interdisciplinary team – ensure that appropriate treatment regimes for pain management are adhered to and involve the nursing staff to assist in adherence support.

Referral to appropriate service/more experienced clinician – refer to Urologists where necessary for additional interventions such as dilatation of urinary stricture, retention, complicated pyelonephritis and enlarged prostate. The following tests may be required to confirm diagnosis: MSU, Ultrasound, CT scan and MRI if contrast contra-indicated.

### 3. Urinary haemorrhage

#### Appropriate assessment to identify cause and severity of symptoms

- Haematuria is a frequent presentation in urological disease and should be explored as abnormal, ranging from microscopic haematuria, detected by urinalysis, to clearly visible frank haematuria or passage of clots. Identify the cause:
- Tumour: renal, ureteric, bladder, prostate,
- UTI
- Drug-induced: Warfarin and NSAIDs causing bleeding tendency; Cyclophosphamide causing haemorrhagic cystitis

#### Explanation to patient and family

Patients and families alike are often perturbed by the discoloration of urine, thinking that red urine necessarily means haemorrhaging. Discuss the relevant cause and relieve the related anxiety, as common changes relate to the following:

- Red/pink: haematuria, beetroot, rhubarb, danthron
- Dark: Metronidazole

Purple Urinary Bag: caused by the breakdown of dietary triptophan metabolites by bacteria in the urine.

#### Correct reversible factors

Complete evacuation of clots (irrigation with water or saline through large bore urethral catheter

Cystourethroscopy for diagnosis and cautery if patient fit enough

If haemorrhage is mild it may be appropriate to reassure patient and family alike and treat the infection if needed, reporting back if haemorrhage persists or increases..

More severe haemorrhage: consider referral to assess whether it is appropriate to use Tranexamic acid 1 g qid po or IVI recognising the risk of clot formation and obstruction.

Severe haemorrhage:

- Cauterization
- Arterial embolisation
- This may be a terminal event – stabilize – blood transfusion if needed

Other: Bladder instillations and irrigation

- Alum 50ml 1% instilled through a catheter and retained for 1 hour – repeat bd as needed

Clot retention:

Evacuate clots as a non-distended bladder bleeds far less. A large bore (22Fr) catheter to be inserted. It is necessary for a urologist to assist if a 3-lumen catheter is to be inserted. Cystoscopic bladder irrigations may be needed. Percutaneous insertion of a suprapubic catheter is contraindicated – the lumen is too small for irrigation and seeding of bladder tumour may occur.

Irrigate with:

Saline 0,9%	Continuous irrigation until urine clear	
Alum 1%	Continuous irrigation until urine clear. Anaesthesia may be required	
Silver Nitrate 0,5-	Installation, retain 10-20	

1.0%	min Anaesthesia required	
Formalin 3%	Installation, retain 20-30 min Anaesthesia required	
Phenol 100%	Installation, retain 1 min Only in refractory cases	

Consider disease-specific palliative therapy

Palliative radiotherapy

Involve the urologist early in managing this problem

#### **4. Bladder and ureteric spasm/pain**

Appropriate assessment to identify cause and severity of symptoms

**Bladder spasms:** transient, often excruciating sensations felt in the suprapubic region and urethra. They are generally secondary to irritation or hyperexcitability of the trigone. It often relates to local cancer, radiation fibrosis, infective cystitis, indwelling catheter or anxiety.

**Bladder pain:** more constant pain, from a dull ache in UTI to acute disabling pain and may be a sign of obstruction and retention.

Correct reversible factors

Reassess the indwelling catheter where applicable as mechanical irritation can be caused by the catheter balloon - change catheter/ reduce volume of the balloon

Catheter sludging with partial retention – bladder washouts or continuous bladder irrigation as described in the UTI section

Blood clots/haematuria: relating to bladder cancer/ chronic radiation cystitis

Consider disease-specific palliative therapy

- Treat UTI
- Relieve obstruction/instability – especially related to catheter
- Tumour ablation
- Remove foreign body (catheter or stones) if obstructing bladder outlet
- Inflammatory causes

Explanation to patient and family

Explain the cause of the spasms and pain and the steps the care team will be taking to manage this distressing symptom

Institute non-pharmacological interventions

- Regular toileting
- Good fluid intake if possible
- Avoiding caffeine and alcohol
- Cranberry juice

### Prescribe appropriate first-line treatment

Treat bladder spasms and pain symptomatically with the following treatment options:

- Hyoscine Butylbromide 10-20 mg po, IVI, IMI or S/C tds. Maximum of 100mg per day – avoid if in retention
- WHO pain ladder

### Consider adjuvant/second-line treatment

Intravesical morphine and bupivacaine tds (morphine 10-20mg and 0.5% bupivacaine 10ml diluted in 0.9% saline to 20 ml), instil through an indwelling catheter and clamp for 30 min.

Spinal analgesia, e.g. epidural morphine and 0.5% bupivacaine

### Review assessment and management

Review catheter care, assess for possible infection, obstruction and retention

### **At all stages of management consider:**

Involvement of interdisciplinary team – ensure that appropriate treatment regimes for pain management are adhered to and involve the nursing staff to assist in adherence support. Relieve patient anxiety through support from counsellors and social worker involvement.

Referral to appropriate service/more experienced clinician – refer to Urologists where necessary for additional interventions such as dilatation of urinary stricture, retention, complicated pyelonephritis and enlarged prostate. The following tests may be required to confirm diagnosis: MSU, Ultrasound, CT scan and MRI if contrast contra-indicated

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## **Guidelines for Pressure Care and Wound Care**

### **1. Pressure Care**

### **2. Wound Care**

#### **1. Pressure care**

Pressure sores (decubitus ulcers) are ulcers of the skin which can extend into the subcutaneous tissue caused by ischaemia secondary to extrinsic pressure and shearing forces.

Tissue ischaemia is caused by external pressure that is greater than capillary pressure (25mm Hg). Pressure for periods of 1-2hrs can cause cell death and ulceration.

When sitting, pressure over ischial tuberosity is about 300mm Hg; when lying, pressure on heels is about 160mm Hg on foam mattress. (Twycross, 1997)

There are a number of risk factors that increase the likelihood of a patient developing pressure sores in the bed-bound patient including general debility, malnutrition, cachexia, dehydration, anaemia, incontinence, neurological deficit, reduced mobility, restlessness, coma, infection, poor hygiene.

It is essential that professional and non-professional health care workers are aware of the causes and risk of pressure sores and the imperative to prevent pressure sores where possible.

The following measures will assist in the prevention of pressure sores:

- Vigilance of nursing staff
  - Inspect the skin every time the patient is moved
- Care of the skin and pressure areas
  - The skin should be washed and dried regularly, including bed bath for bed bound patient
  - Maintain suppleness of skin by regular massage with skin lotion
  - Avoid trauma – no restraints, lift patients do not drag them to move them in the bed
- Regular positional change, if patient is not able to lift and shift their weight 3-4 times an hour, family or hospice/hospital carers should assist in changing the patients position every 2-4hrs depending on patient's risk factors
- Special mattress to distribute body weight more evenly
- Keep the bed linen dry and free from creases
- Keep the patient well nourished and well hydrated

The most vulnerable areas are elbows, shoulder blades, spine, buttocks and heels. If the patient is more comfortable lying on his/her side, then special attention should be given to ears, shoulders, hips and knees.

Periods of contact with the patient are valuable to the HCW. Regular position chnges also serve to keep joints supple and add to patient's comfort. Using cushions to support joints helps the patient relax and prevent ligaments from being overstretched.



## 2. Guidelines for Wound Care

In palliative care we mainly deal with chronic wounds. Chronic wounds are characterised by ischaemia, lengthened inflammatory processes, increased protease concentration and reduced level of growth factor activity.

### Appropriate assessment

A comprehensive history and physical examination should be performed keeping in mind the local and systemic factors that influence wound healing.

#### 1. **Assess systemic factors:**

- Nutrition –
  - Deficiency in the following macro-nutrients may delay healing: albumin, carbohydrates, fats and dehydration.
  - Deficiency in the following micro-nutrients may delay healing: Vitamins A, B, C, E, K, Copper, Iron and Zinc.
- Medication –
  - Steroids inhibit wound closure
  - NSAIDs – may delay healing
- Chemotherapeutic agents slow wound healing
- Immunosuppressive drugs impair the inflammatory phase of healing, inhibit immune response and predispose to infection
- Other: Beta blockers, anticoagulants and phenytoin may delay healing.
- Radiotherapy depletes dermal fibroblasts locally and total body irradiation depresses bone marrow which causes minimising of wound macrophages.
- Drug and Alcohol abuse cause vascular injury and reduce the immune response.

#### 2. **Assess Body Systems:**

- Respiratory system – decreased blood oxygen supply.
- Circulatory system – poor circulation at wound site or anaemia causing a reduction in the oxygen carrying capacity of the blood
- Endocrine system – diabetes causes circulatory impairment, peripheral neuropathy, impaired inflammatory response and an increased risk of infection.
- Digestive system – malabsorption may lead to deficiencies in macro and micro-nutrients.
- Renal system – incontinence and/or renal failure may cause skin irritation, increased susceptibility to infection.
- Central nervous system – impaired sensation results in no pain signals to warn of tissue damage, impaired movement facilitates pressure ulcers.

#### 3. **Assess psycho-social circumstances**

Giving accurate information and explanation will lessen the sense of isolation and enhance confidence and morale in patients

4. **Assess pain:** Ensure that pain is caused neither by infection nor the dressing itself! Limit the frequency of dressing changes.

5. **Assess wound:**

- Classification
  - Mechanical (surgical)
  - Burns and chemical (thermal, radiological)
  - Chronic ulcerative wounds (pressure sores, leg ulcers, radiotherapy or malignancies)
  - Post-operative
- Location:
  - Pressure sores commonly on heel, sacrum and buttocks
  - Peripheral areas with poor local circulation
  - Position affects vascularity e.g. wounds over joint areas tend to heal slower.
- Wound circumference and depth – ruler based measurement
- Wound margins – redness could indicate infection, red/grey could be the result of undermining, white typifies maceration (excess moisture)
- Exudate –
  - Amount: A sudden increase may indicate infection but the presence of exudates is a necessary part of the healing process and varies during the different phases.
  - Appearance: serous, haemo serous, sanguineous, purulent
- Odour – an offensive odour usually indicates the presence of high levels of bacteria.
- Wound base –
  - Dry and necrotic
  - Moist and sloughy
  - Granulating
  - Epithelialising

Explain to patient and family

1. Involve patients in all the decisions
2. When working through the assessment, pinpoint factors which may be detrimental to the care of the wound.
3. Set realistic goals aimed at quality of life.

Treat reversible factors

The focus in palliative care is quality of life for the patient. Reversible factors include oedema, malnutrition, anaemia, diabetes and medication. Treatment of these factors may involve hospitalisation, transfusion of blood and withdrawing medication which may benefit the patient as far as other symptoms are concerned. A balance is needed between reversing systemic factors and improving wound healing in palliative care patients.

Wound specific treatment

- Remove Necrotic Tissue
  - surgical – tweezers, scissors or a scalpel
  - enzymatic debridement – in dressings
  - autolytic debridement – hydrogel dressings can be used for this method
- Bleeding

Match the treatment objective to the appropriate dressing

- Gauze soaked in adrenaline 1:1000 or kaltostat may be used
- Gentle removal of dressing with normal saline spray or irrigation using a syringe containing warm NS 0.9% to prevent trauma at dressing changes.
- Odour
  - See below guidelines on malodorous wounds
- Infection
  - Irrigate wound with warm NS 0.9% or under running water.
  - Use antibiotics if there is spreading inflammation, not just a red rim.
  - Fucloxacillin or trimethoprim or erythromycin should cover most common infections.
- Choosing a dressing
  - To maintain moisture - films, hydrocolloids, hydrogel sheets
  - to add moisture (no or low exudates) - hydrogels
  - to absorb moisture - foams, alginates, superabsorbents
  - protect wound surface - contact layers, impregnated gauzes, Bactigras
  - control bacteria - silver sulphadiazine cream, ichthammol glycerine, activated charcoal ± silver dressings
  - control odour - activated charcoal, see separate guidelines below

#### Choosing a dressing

<b>Type of dressing</b>	<b>Wound care goal</b>	<b>Advantages</b>	<b>Disadvantages</b>
Films (Opsite, Tegaderm)	Protection Not for exuding wounds As cover dressing	Permit visibility, Good secondary dressing, conformable to contours, can promote autolytic debridement	No absorbency, may be difficult to apply or remove, can cause skin tears, may adhere to new epithelium
Foam dressings (Allervyn, BiatainColoplast) adhesive & non-adhesive	Moist wound healing via absorption, protection As cover dressing	Highly absorbent, remove drainage from wound surface, provide cushioning	May not conform well to wounds with depth, could potentially dry out the wound and adhere to surface
TIELLE hydropolymer adhesive dressing	For low to moderate exuding wounds, including pressure sores and venous ulcers	Provides moist wound healing environment, easy to handle, can be left on wound for up to 7 days, waterproof, moisture and gas permeable, skin friendly adhesive, can be used under compression bandage, reduces leakage and odour	
Hydrocolloid dressings (Comfeel Plus, Granuflex, Replicare Ultra)	Moist wound healing for minimally to moderately exuding wounds, protection,	Minimally absorbent, can adhere to moist skin, stay in place for long periods, can promote autolytic debridement	Can macerate wound edges, may promote hypergranulation, may not conform to

	debridement		depth, sticky edges
Amorphous hydrogels (Intrasite Gel) hydrogel + hydrocolloid (Granugel)	Debridement via rehydration, use in minimally exuding wounds, fill in dead space	Add moisture to a dry wound, can assist in autolytic debridement, can maintain moisture longer than saline	Can macerate wound edges, should only coat the wound surface, not fill up a wound
Hydrogel with Alginate (NuGel)	Sloughy and necrotic wounds and to create a moist wound healing environment	Effective rehydration of necrotic and sloughy wounds, ideal moist wound healing environment, maintains consistency, easy to use, non-traumatic	

Remember that the aim is to contain problems and improve quality of life. Be prepared to change and experiment. The simplest products may be the best and the most cost effective.

Re-evaluate: Continually re-evaluate. The criteria are comfort, acceptability, and availability.

Refer to a nurse with specialist experience of wound management.

## Malodorous wounds

The wounds seen in palliative care patients are often a result of their advanced illness and/or poor physical or social state. Wound malodour can be a significant and distressing symptom for the patient, his/her family and care givers. Patients may experience embarrassment, disgust, guilt and shame, which can lead to social isolation and relationship problems.

### Appropriate assessment

The wound itself may be a small part of the problem for patients with cancer, HIV or other chronic illnesses. Accurate assessment includes:

- Nutritional assessment
- Medication (corticosteroids slow rate of epithelialisation)
- Cytotoxic chemotherapy and radiotherapy reduce wound strength
- Diabetes control
- Immune system assessment (HIV, Leukaemia, treatments)
- Find out what the patient perceives as the major problem.

Assessing the wound: (for complete assessment see guidelines on 'wound care')

- Surface area – size
- Base of the wound – slough, pus, necrosis
- Discharge – amount, colour, odour
- Pain

#### PRINCIPLES OF PALLIATIVE WOUND MANAGEMENT (Naylor 2005)

1. Prevent wound development and/or deterioration
2. Correct or treat underlying cause
3. Control wound-related symptoms (pain, malodour, bleeding, discharge)
4. Utilise patient self-assessment
5. Provide psychosocial support
6. Promote independence
7. Improve quality of life

#### Correct reversible factors

Malodour is often caused by anaerobic bacterial infection of the necrotic tissue within a fungating wound. Metronidazole has been shown to be effective.

#### Consider disease-specific treatment

Treatment of lesions depends on the stage of the wound, size and the patient's general health:

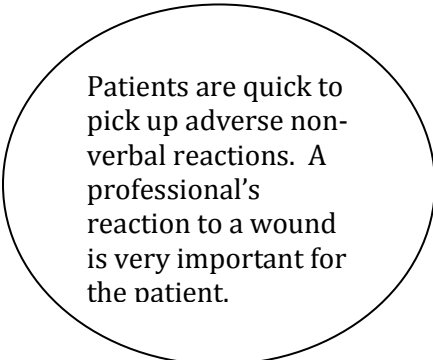
- Surgery (debulking) of large fungating tumours
- Chemotherapy
- Palliative radiotherapy
- Hormone therapy for responsive tumours

#### Explain to patient and family

Involve patients in all the decisions

When working through the assessment, pinpoint factors which may be detrimental to the care of the wound.

Set realistic goals aimed at quality of life. Healing may be an unrealistic goal, but getting rid of the odour can be achieved.



Patients are quick to pick up adverse non-verbal reactions. A professional's reaction to a wound is very important for the patient.

#### Non-pharmacological treatment of malodour

1. Good hygiene:
  - Regular wound cleaning
  - Regular bedding and clothing changes
  - Adequate disposal of soiled dressings
  - Adequate ventilation
2. Dressings:
  - Use highly absorbent dressings to contain a high level of exudate to control odour.
  - Preferably use non-adherent dressings (to make regular changing less painful)
3. Debridement:
  - Mechanical/surgical (only if physical condition allows)
  - Chemical
  - Auto-debridement (hydrocolloid, hydrogel dressings provide suitable environment)
  - Burning candles/incense

- Vanilla or lavender sprigs in room

*The use of perfumes and air fresheners does not always help to reduce smell and may result in their fragrance being thereafter associated with the odour.*

### Pharmacological treatment of malodour in wounds

TOPICAL (For mildly infected wounds without cellulitis):

- Metronidazole solution for cleaning a wound: 2l saline + 13 (400mg) crushed metronidazole tablets
- Metronidazole gel: KY jelly or intrasite gel mixed with crushed metronidazole tablets applied to the wound
- Metronidazole cream: aqueous cream mixed with crushed metronidazole tablets
- Metronidazole powder: crushed metronidazole tablets applied directly on to the wound
- Silver sulphadiazine (flamazine)
- Bacitracin, Fucidin or antifungal ointments where appropriate
- Charcoal dressings
- Honey and yoghurt

SYSTEMIC antibiotics for significant infections (preferably after obtaining a wound swab if possible)

- Metronidazole 400mg b.d PO until good effect is obtained. (Side-effects: nausea and alcohol intolerance)
- Other antibiotics: amoxycillin, erythromycin, trimethoprim sulphamethoxazole

PAIN: Treat pain appropriately

### Involve the Interdisciplinary team

The psychosocial impact of malodour is significant and may cause patients to withdraw from social contact, fear the stigma associated with cancer or AIDS and have an altered body image. It is important for the IDT to be the social support for such a patient alongside family and friends.

### Review

Refer to a wound care specialist in the area if you are not happy with the progress or if you are unsure.

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## **The Terminal Phase**

### Definition

The terminal phase occurs when inevitable and irreversible decline in normal function sets in just prior to death. It may come on gradually or it may happen suddenly and unexpectedly. Death usually occurs within 48 hours.

### Assessment

Clinical features include:

- being bedbound,
- cyanosis,
- irregular or noisy breathing,
- delirium and increasing drowsiness,
- reluctance to eat or drink,
- oliguria
- hypotension

While there may sometimes be a degree of clinical uncertainty, it is usually possible to “diagnose dying”. Diagnosing dying is important to do as it greatly assists in proper care planning by shifting the focus to preparing for the end.

### Explanation to patient and family

Each family has its own internal dynamic and pattern of communication. A meeting with the family gives the hospice staff an opportunity to help everyone understand the situation. By showing sensitivity and flexibility it is usually possible to get everyone to focus on “comfort” as the main goal of care. All future care options can then be weighed up against this goal. It is important that families understand that the decision must be based on what the dying person would have chosen if it was possible for them to talk.

### Correct reversible factors

When an unexpected deterioration occurs, first consider if it could be due to side effects of the patient’s current medication. Other possibilities include dehydration, metabolic disturbances or infection.

**NB:** A full bladder and an impacted rectum can contribute to restlessness.

### Consider appropriate options

While stopping medication may be easy, correcting complex abnormalities or treating hypostatic pneumonia is usually not appropriate. By clarifying the main goal of care, one can usually reach consensus about the most appropriate course of action.

### Institute non-pharmacological interventions

- The immediate family should be allowed “free” access to visiting. Most other visitors should be restricted, apart from persons involved in pastoral care.
- Mouth and pressure care are continued.



- Food and fluids may be offered but should not be forced.
- Intravenous fluids and indwelling catheters are usually not necessary.
- Occasionally, in the pre-terminal phase when there is repeated vomiting, parenteral fluids via a subcutaneous infusion (hypodermoclysis) may be considered. One, to one and a half litres of normal saline can be run in over a 12 hour period by means of a subcutaneous butterfly needle. Any suitable site can be used. Commonly the thigh, abdomen, upper chest or suprascapular area are used. If run in during the night, it can be discontinued during the day so that the patient can be more mobile during the day.

*“In the terminal phase of progressive illness there is virtually always a profound loss of appetite (and therefore an absence of hunger). The literature is clear that the body cannot use calories to become stronger or to gain weight. Instead, it breaks down its own energy stores (muscle, fat, carbohydrates) regardless of caloric intake. Efforts to improve caloric intake by enteral or parenteral means have no role in addressing comfort, functional status, or survival in such end-of-life scenarios”. (Harlos M, 2010)*

- Routine checking of vital signs may be discontinued.
- Laboratory investigations and monitoring oxygen levels are not required.
- Psychosocial support by palliative care professionals facilitates the patient and family’s expression of emotional pain, fear or anger; assists in the containment of these emotions and allows end of life tasks to be completed. It has been described that there are important messages that need to be conveyed at the end of life.

These are:

Forgive me  
I forgive you,  
Thank you,  
I love you,  
Goodbye.

#### Prescribe appropriate first-line treatment

- Adequate analgesia must be continued. If the patient can no longer swallow, switch to a syringe driver, regular intermittent subcutaneous injections or a transdermal fentanyl patch. Special care needs to be taken when changing drugs and the dosages need to be frequently re-evaluated.
- When a patient remains distressed (pain, dyspnoea or agitation), the appropriate drug (an opioid or sedative) needs to be given and repeated until the patient is comfortable. The time between doses should be guided by the route of administration. The IV route should be effective within 10 minutes, while the effect of a drug given sublingually or by subcutaneous injection may take up to 30 minutes. If there is no improvement by that time, the drug needs to be repeated until the desired response is obtained. This must be regarded as an emergency and be handled as such.
- Sedation is essential if the patient is agitated and restless. Not only is this distressing to everyone, including the patient, but the patient and the nursing staff may be injured if the patient becomes aggressive. It is an essential duty of the

doctor to provide adequate sedation in such situations. There needs to be zero tolerance of the inadequate management of agitation.

NB: Physical restraints should never be used.

- Continuous sedation may be indicated for refractory symptoms. This is a complex topic that needs careful consideration. Consult an experienced palliative care physician for advice.
- Drugs that may be used for sedation:

	<b>Drug</b>	<b>Bolus dose</b>	<b>Dosage for continuous administration</b>
<b>Step 1</b>	<b>Midazolam</b>	5-10 mg iv or sci	15-60 mg/24 hours by continuous subcutaneous infusion pump.
<b>Step 2</b>	<b>Haloperidol</b>	5 mg iv or sci	5-15 mg/24 hours by continuous subcutaneous infusion pump. (Can be combined with midazolam in the same syringe.)
<b>Step 3</b>	<b>Phenobarbital</b>	100-200 mg iv or sci	400-900 mg/24 hours by continuous subcutaneous infusion pump. (Step 3 replaces steps 1 & 2)

Alternative drugs that may be used if the above are not available:

- Step 1: Lorazepam 1-4 mg sublingually, repeated every 30 minutes till effective, then repeated 4 hourly.  
or Diazepam 10 mg – may be given rectally (using a syringe without the needle), repeat every hour till effective, then 40-60 mg per 24 hours.  
or Clonazepam 1-2.5 mg sublingually, repeated every 30 minutes till effective, then repeated 6 hourly.
- Step 2: Chlorpromazine 12.5 mg iv/im, followed by 25-100 mg 12 hourly per rectum.
- Most other drugs can be discontinued.

#### Consider adjuvant/second-line treatment

- Noisy breathing may be distressing to the watching family. It occurs when dying patients are no longer able to cough or are aware of the need to. Secretions collecting in the upper airways result in the rattling sound. This process must be explained to the family.  
Suctioning is not effective and should not be tried as it causes more secretions to accumulate.  
It may help to reposition the patient – head up or down at about 30°.  
Drugs such as **hyoscine butylbromide** 20-40 mg sci or glycopyrrolate 0.2-0.4 mg sci 4 hourly may be tried, but are seldom very effective unless started as soon as possible after the onset of noisy breathing.

### Review assessment and management

The patient's condition and medication must be carefully reviewed on a regular basis. Families need to be informed of any changes and their concerns should be adequately addressed. Helping families along what has been aptly described as "the path of least regret" greatly eases their current pain and their future grief.

### Involvement of interdisciplinary team

Good care for dying patients requires adequate time and staff. This is only possible if everyone, including the family, participate appropriately. It is imperative that the senior staff members ensure that the whole team functions effectively. When the dying process is prolonged, special care needs to be taken that there is effective communication and support for all involved.

### **Resuscitation**

During the terminal phase, CPR is inappropriate. It will not restore cardio-pulmonary function for any significant period of time. It merely prolongs the dying process and is distressing for the family. There is no ethical obligation to discuss CPR with most palliative care patients.

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## **Vascular and haematological disorders**

- 1. Anaemia and blood transfusions**
- 2. Lymphoedema**
- 3. Thromboembolism**

### **Anaemia and Blood Transfusions**

The aetiology of anaemia in palliative care patients may be multifactorial and can result in significant distressing symptoms, such as:

- Dyspnoea
- Postural hypotension
- Oedema
- Anorexia
- Headache
- Fatigue
- Exacerbation of angina
- Impaired concentration
- Low mood
- Loss of libido

Major causes of anaemia in the palliative care setting include:

- Anaemia of chronic disorders
- Malnutrition or malabsorption
- Acute and chronic haemorrhage
- Marrow failure or suppression
- Haemolysis (may be encountered with chronic lymphocytic leukaemias, non – Hodgkin's lymphoma and various adenocarcinomas)
- Congenital anaemia

### Assessment

Take a detailed history including:

- history of current illness,
- other chronic illnesses,
- any symptoms, related to the cause or effects of anaemia

Examination:

- to assess for possible causes of anaemia
- to assess clinical severity of anaemia

Investigations:

- should be considered in the light of the most likely cause of anaemia
- should be appropriate for the patient's condition
- should be undertaken to guide the most appropriate management
- May include; full blood count, iron studies, vitamin B12, folate, Coomb's test, and rarely, bone marrow studies.

### Explanation to patient and family

Explain the likely causes of tiredness and the options for treatment. Involve the patient and family in decisions regarding treatment, in particular the options to administer a blood transfusion, explaining the likely benefits and burdens of the transfusion and the probable time that it will provide relief of symptoms. Repeated blood transfusions may become a burden to the patient, may not be providing benefit and may not be appropriate for the stage of illness

## **Management**

### Correct reversible causes:

- Chronic haemorrhage:
  - Control bleeding if possible
  - Limit drawing of blood to only necessary blood tests that will improve management
  - Consider iron supplements if haemorrhage has led to iron deficiency
  - Consider blood transfusion for symptomatic anaemia
- Acute Haemorrhage:
  - Consider the patient's stage of illness and prognosis
  - After assessment, if appropriate, resuscitate
  - Institute appropriate measures to prevent recurrence
  - If the haemorrhage is considered a terminal event, manage the patient's and family's distress appropriately - non-pharmacological and pharmacological)
- Marrow Failure
  - Consider blood transfusions, while these are still of clinical benefit to the patient.
- Chronic Haemolysis
  - Immune haemolysis may respond to steroids (e.g., prednisone 0,5 – 1,0 mg/kg)
  - Microangiopathic, haemolytic anaemia responds poorly to any treatment unless the tumour can be removed
  - Hypersplenism may be treated by surgical resection or radiation to the spleen
- Keep the patient and family informed. Involve them in the decision-making process. Carefully explain the cause of the anaemia and go through the therapies available and the advantages and disadvantages of interventions.

## **Blood Transfusion**

- Blood transfusion should be considered in a patient who has distressing symptoms attributable to anaemia, in whom no other treatment is feasible, and for whom a favourable outcome of the transfusion is expected. A transfusion may not be indicated if the patient's poor functional status is due to the worsening illness as a transfusion will not improve these symptoms. Typically these patients have a very limited prognosis and symptomatic support is required.
- Each unit of packed cells should raise the Hb in adults by 1g/dl.
- In treating anaemia in palliative care, packed cells are preferable to whole blood.
- Complications include:
  - Volume overload
  - Febrile Non-haemolytic Transfusion Reaction
  - Mild allergic Reaction
  - Acute Haemolytic Transfusion Reaction/ ABO Incompatibility
  - Hypersensitivity/Anaphylaxis
  - Transfusion related acute lung injury (TRALI)

- Bacterial contamination
- Iron overload as a long term complication of numerous blood transfusions as may be required in marrow failure

Iron overload is not a problem until about 50 to 75 units have been transfused, so this complication is rarely seen in the palliative care setting.

Transmission of infections through blood transfusion is minimal, due to careful screening of blood to be used for transfusion. In the palliative care setting, the advantages usually outweigh this risk.

### Review Assessment and Management

It is important to regularly review the patient's status and responses to interventions such as blood transfusions. At some stage in the progression of terminal illness, the blood transfusions will no longer achieve the desired effects of alleviating symptoms. It will then be necessary to explain to this to the patient and family.

Other interventions; such as steroids or haematinics, may become redundant as the patient's condition deteriorates and should be stopped if there is no benefit. It is always important to discuss this with the family first

### Involve the Interdisciplinary Team

All members of the team are available to support the family and the patient, through each phase of the illness. It is especially important, when transfusions are no longer effective. The patient and family need to know that the team is not "giving up". The treatment is being tailored to the patient's condition and care is always being given.

### Referral to Appropriate Services

Refer patients for a surgical consult if surgical treatment to prevent anaemia is appropriate.

Referral or consultation as required for any of the severe acute blood transfusion reactions.

## **2. Lymphoedema**

In palliative care, lymphoedema is usually due to blockage of lymphatic vessels and glands in cases of malignancy or fibrosis as a result of previous radiotherapy or surgery. There is often a latent period that averages 18-24 months from lymphatic damage to manifestation of oedema.

Lymphoedema differs from other forms of chronic oedema in that the swelling is not due to fluid accumulation alone.

### Appropriate assessment

- Chronic condition – usually affecting limbs (can affect trunk, head, genitalia)
- Symptoms – discomfort, heaviness, tightness, bursting feeling, pain
- Signs – generally a combination of non-pitting and pitting oedema.

**Oedema** that does not reduce significantly after overnight elevation is likely to be lymphatic in origin.

- Progressive changes – grossly swollen, coarseness, folding and distortion of skin, elephantiasis (which differs from all other forms of oedema)
- **Stemmer's sign:** thickened skin folds of the toes prevent pinching of the skin, particularly at the base of the second toe.
- Risk factors –
  - Obesity,
  - Lack of physical exercise.
- Exclude other causes of oedema in a unilateral swollen limb:
  - e.g. Venous outflow obstruction in breast cancer: dilated collateral veins around shoulder and chest wall, skin that appears mottled or cyanosed.
  - Lack of movement in limb which limits the activation of the muscle pump, which in turn helps with lymph and venous drainage.
  - Neurological deficit causing reduced mobility. Progressive neurological signs may be the first clue to recurrence of tumour by infiltration or compression.
  - Hypo-albuminaemia
  - DVT

#### Causes

Primary lymphoedema – congenital

Secondary lymphoedema (damage to lymphatic system)

- Cancer
- Treatment of cancer (surgery and radiotherapy)
- Trauma
- Infection – post cellulitis, filariasis in tropical countries
- Chronic venous disease
  - Deep vein thrombosis (DVT)
  - Venous insufficiency

#### Explanation to patient and family

The aim of lymphoedema treatments is to encourage lymph transport by means of physical therapies, to prevent complications, to achieve maximum improvement and long-term control. Success requires full patient cooperation and the ultimate aim is to make the patient feel more comfortable.

#### Consider disease specific treatment

Decrease tumour bulk if possible, by radio- or chemotherapy

Treat cellulitis promptly

#### Non Pharmacological management

Regular reassessment is needed to adjust treatment as the condition progresses.

#### Four main principles of treatment:

##### SKIN CARE

1. Scrupulous skin care to prevent dryness, cracking and infection.
2. Avoid trauma, exposure to heat, venepuncture, acupuncture or vaccinations in the affected limb to minimise risk of infection.
3. Avoid insect bites

##### EXTERNAL SUPPORT/COMPRESSION

1. Compression bandaging: **when the aim is to re-shape the limb and decrease the swelling:** multilayer lymphoedema bandaging (MLLB) – this is used daily in the intensive phase of treatment to increase the lymph drainage when the limb is exercised. It's left in place and re-applied every 24hrs. (First a tubular stocking is applied as protection against chafing, next a layer of padding to protect the joint flexures and to even out distortion in the shape of the limb, finally high-compression bandages are applied to give graduating pressure)
2. External support: **when reduction of limb size is not anticipated or necessarily desirable:** These garments are used during the maintenance phase to prevent increased swelling. They require specialist measurement and fitting and should be replaced on a regular basis. They provide graduated external pressure and are not the same as anti-embolism stockings which do not offer graduated pressure.
3. Compression pumps have been used but may cause problems with skin integrity and misdirect oedema into unwanted areas.

##### MASSAGE

1. The aim is to move lymph from a congested area towards an area where the lymphatics are functioning normally.
2. Manual lymphatic drainage (MLD) is the use of specific massage techniques by a qualified therapist.
3. Simple lymphatic drainage: modified form of MLD; should only be enough to move the skin and tissues beneath the hand; it should not cause the skin to redden; involves stroking the surface of the body more than a massage; the skin should be free of oils, creams or powder when massaging; can be performed by the patient or carer in the maintenance phase of treatment

##### MOVEMENT

1. Exercises in the form of gentle movements to improve or simply preserve movement in the swollen limb and prevent joint stiffness.
2. Exercise programme may be provided.
3. There is no need to elevate the limb beyond the horizontal.
4. Avoid sitting or standing for prolonged periods.
5. Movement is better than elevation



### Specific problems

#### LYMPHORRHOEA

Clean the limb, apply thick sterile pad to the leakage area, bandage in usual way, maintain pressure for 24 to 48 hours

#### TUMOUR IN THE ABDOMEN OR PELVIS

- If chemo- or radiotherapy have not been able to decrease the size of a pelvic tumour, which may cause obstruction to venous or lymph flow, high dose steroids may bring some relief by reducing the peritumour oedema of a tumour. If used in large doses over a long period, steroids may cause more fluid retention and lead to muscle wasting.

### Pharmacological management

1. Cellulitis (streptococcal infections are the most common) should be treated promptly: Penicillin V 250 mg qid or erythromycin 250mg gid or amoxycillin 250- 500 mg tds.
2. Patients who have had 2 or more episodes of cellulitis should have prophylactic antibiotics. Penicillin V 250 mg bd or erythromycin 250 mg bd.
3. Diuretics are of very limited use in treating lymphoedema. The longterm use of diuretics is contra-indicated. They may be useful in palliative care where oedema may be very tense and prognosis is short.
4. Benzopyrone group of drugs which may promote breakdown of fibrous tissue have been used in some centres to treat lymphoedema, but concerns regarding hepato-toxicity remain and they are not indicated for routine use.

### Conclusion

Conservative physical treatments are the mainstay of therapy and need to be initiated early and perhaps even prophylactically.

### Involve the Interdisciplinary team

Once lymphoedema is established, it is incurable. Therefore the whole team is involved when patients suffer from lymphoedema for support and motivation in empowering the patient and family to help prevent complications. Some patients are unable to assume their duties because the lymphoedematous limb has restricted movement, is heavy and at risk for developing infection, especially when in frequent contact with water or chemicals. The psychological condition of the patient should be evaluated. Studies have shown that emotional distress, psychosocial maladjustment and psychological morbidity are all significantly higher in women with lymphoedema. They experience more anxiety, depression, sexual dysfunction, disturbance of body image and social avoidance than those who do not develop lymphoedema.

### Consider referral to specialist care

There may be a lymphoedema clinic/service available

### 3. Thromboembolism

Venous thromboembolism (VTE) comprising deep venous thrombosis (DVT) and pulmonary embolism (PE) is a leading cause of death after admission to hospital. VTE is commonly seen in patients with disseminated malignancies and is therefore a frequent problem in the palliative care setting. Studies have suggested that the incidence of DVT may be 52% in palliative care. DVT is also at least 10 times higher in HIV-infected patients, especially when their CD4 count is less than 200 cells/ $\mu$ l.

#### Appropriate assessment

Patients at risk include:

- Previous episodes of VTE
- Malignancy
- Dehydration
- Age > 60 years
- Major surgical procedures
- Hormone replacement therapy

#### **Virchow's triad:** (risk in cancer)

1. **Stasis:** immobility due to weakness; compression of vessels by tumour; extrinsic compression from oedematous legs
2. **Endothelial perturbation:** recent surgery; central venous access; direct tumour invasion of vessel.
3. **Hypercoagulable state:** dehydration; tissue factor/tumour procoagulant release; increased platelet activation; DIC; cytokine-related thrombotic changes; prothrombotic changes from certain chemotherapeutic agents.

Symptoms and signs:

- Painful leg
- Swollen leg
- Unexplained chest pain and
- Sudden onset dyspnoea (indicating PE)

Diagnosis:

- High index of suspicion
- Best achieved at acute care facility
- Duplex doppler studies
- V/Q scan of lungs if suspecting PE
- D-dimer blood test

#### Explain to patient and family

Explain risks and benefits of treatment to patient and family.

Discuss preventative measures such as exercising the lower calf muscles, keep active and move if possible, walking, lifestyle changes including stop smoking, lose weight, control blood pressure if these are a problem; it may be appropriate to wear compression stockings on your doctor's advice.

### Correct reversible factors

VTE is a treatable and largely preventable disease. For most terminally ill patients whose prognosis exceeds a few days and who have significant symptoms of a DVT, anticoagulation should be offered.

**Major contraindications** include active gastrointestinal haemorrhage, active bleeding from any other site, an intracranial neoplasm and uncontrolled hypertension.

### Consider disease-specific treatment

- Treat specific causes
- Assess patients for prophylaxis according to:
  - Their individual VTE risk
  - Their clinical condition
  - Their risk of bleeding
  - The appropriateness of the prophylaxis for the individual patient

Prophylaxis is indicated for high risk patients being hospitalised for major surgery and for long periods of bedrest.

- Low molecular weight heparin (LMWH) and graduated compression stockings (GCS) for hospitalised patients.
- GCS for home-based care patients.
- Aspirin may have, at best, only a weak protective effect against development of DVT and is not generally recommended for this purpose.

### Pharmacological intervention for DVT

**Initiation of anticoagulation:** LMWH offers definite advantages over unfractionated heparin in terms of convenient dosing, no need for monitoring and the possibility of outpatient management. It may also result in a reduced risk of recurrence.

- Enoxaparin sodium (Clexane®) 1mg/kg s.c. bd (in renal impairment 1mg/kg s.c. daily) or dalteparin sodium (Fragmin®) 2500U -5000U/day
- Warfarin should be started at a dose of 5 mg po daily from day 2 of anticoagulation.
- The INR should be measured 2-3 days after starting Warfarin and then daily with dose adjustments to achieve a therapeutic range of 2-3 (for most indications)
- LMWH must be given for at least 7 days even if the INR has reached therapeutic level
- LMWH can be discontinued once the INR has been in the therapeutic range for two consecutive days.
- For massive thrombosis or pulmonary embolism LMWH should be given for at least ten days.
- For massive PE, thrombolytic therapy should be initiated.

**Duration of oral anticoagulation:** This needs to be individualised according to the patient's thrombo-embolic risk level and only basic recommendations are given.

- Patients with reversible or time-limited risk factors should be treated for at least 3 months.
- Patients with idiopathic DVT and all patients with PE should be treated for at least 6 months.
- Patients with recurrent idiopathic VTE, continuing risk factors, life-threatening event or thrombosis in an unusual site will probably benefit from longer duration anticoagulation,

probably life-long in some patients. However, this needs to be individualised and consideration should be given to the ability of both the prescribing physician and the patient to maintain a stable INR.

- For most terminally patients anticoagulation should be ongoing.

**Outpatient management:** management of VTE in the outpatient setting is safe and cost-effective provided that:

- The patient is able to understand and administer therapy him/herself.
- The patient is able to attend regular follow-up.
- There are no complicating factors, e.g. an increased bleeding risk.
- There is adequate compression treatment (with graduated compression stockings)

**Management of non-therapeutic INRs:** The following are general guidelines.

- INR >3<5, no significant bleeding
  - Omit warfarin
  - Re-start lower dose once the INR is in the therapeutic range
- INR >5<10 no significant bleeding
  - Omit warfarin
  - Monitor INR daily until back in the therapeutic range
  - Restart Warfarin at a lower dose
  - Consider low-dose oral vitamin K if INR remains prolonged
- INR >10 no significant bleeding
  - Stop Warfarin
  - Give vitamin K 2mg orally
  - Monitor INR daily until in the therapeutic range (repeat vitamin K as required)
  - Restart Warfarin at a lower dose
- Patients with significant bleeding
  - Stop Warfarin
  - Give fresh-frozen plasma (FFP) at a dose of 15ml/kg or prothrombin complex concentrate (if the bleeding is life-threatening)
  - Give vitamin K 1 mg slowly IV

Special caution should be exercised when reversing anticoagulation in patients with prosthetic heart valves and should be done in consultation with the cardiologist.

### **Monitoring of INRs**

- The INR should be monitored weekly at
  - The local clinic or
  - Private pathology laboratory

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## **Annexure 1**

### **Managing Complications of Blood Transfusion**

#### **Fluid Overload/ Acute Left Ventricular Failure**

- Anticipate volume overload by giving furosemide 20mg IVI slowly with each unit of blood and transfuse slowly over 4-6 hours. Aim to give not more than 2 units per day.
- Symptoms and signs include: breathlessness, basal crepitations, tachycardia, initial hypertension, possible raised JVP
- Stop transfusion
- High concentration oxygen
- Furosemide 40mg IVI
- Once patient has been stabilised, can reconsider transfusing at a later stage, very slowly with furosemide (as above)

#### **Febrile Non-haemolytic Transfusion Reaction**

- Mild fever, temperature rise < 1,5° C, possibly shivering and general discomfort
- Usually towards end of transfusion or up to 2 hours after completed
- Patient otherwise stable
- Give paracetamol
- Reduce transfusion rate
- Observe more frequently

#### **Mild Allergic Reaction**

- Quite common, especially if large volumes of plasma, e.g. FFP, platelets
- Urticaria with / without itch within minutes of starting transfusion
- Patient otherwise stable
- Give antihistamine, e.g. chlorpheniramine 10mg slow IV or IMI if not thrombocytopenic
- Stop transfusion
- If no progression after 30min, may continue at slower rate

#### **Acute Haemolytic Transfusion Reaction**

- Infusion of ABO incompatible blood
- Reaction most severe if group A red cells infused to group O
- A few millilitres of blood will usually cause symptoms within minutes

- Before transfusing, always check patient and donor details and that correct blood has been issued.
- Acute onset – within minutes of starting transfusion:
  - Pain with oozing at venepuncture site, chest pain, hypotension or hypertension, tachycardia
  - Stop transfusion (keep all units to send back to blood bank)
  - Keep line open with 0.9% saline and resuscitate as required
  - Consider inotrope support for prolonged hypotension
  - Monitor vital signs, temperature and urine output
  - Manage patient according to clinical developments
  - If possible, admit to ICU

#### Hypersensitivity/ Anaphylaxis

- Rare but life-threatening
- More common with rapid infusion of plasma e.g., FFP and Platelets
- Symptoms and signs, usually in early part of transfusion:
  - Hypotension, chest pain, breathlessness, signs of bronchospasm
  - periorbital and laryngeal oedema, urticaria, erythema and conjunctivitis
  - nausea, vomiting, abdominal pain,
- Stop transfusion
- Maintain IV access
- Administer high concentration oxygen
- Chlorpheniramine 10-20mg IVI over 1-2 minutes
- Hydrocortisone 100-200 mg IVI
- Adrenaline 0.5-1 mg (0.5-1 ml of 1/1000) IMI
- Salbutamol 2.5-5 mg by nebuliser

#### Transfusion-related Acute Lung Injury

- Usually within 6 hours of transfusion
- Develops breathlessness and non-productive cough
- Hypotension with shock is common
- May have fever/chills and may develop monocytopenia or neutropenia
- CXR – bilateral nodular infiltrates in batwing pattern, typical of ARDS
- Resuscitate, avoid diuretics, steroids of uncertain benefit
- Refer to critical care unit, haematology advice

#### Bacterial Contamination

- Rare, but more likely with platelets than with red cells
- Acute, severe reaction
- Hypertension/ hypotension, rigors, collapse
- Treat as for acute haemolytic reaction, i.e. resuscitation
- Start antibiotics immediately, either obtain microbiology consult or if necessary, start with broad spectrum cover, e.g.:
  - Ceftriaxone 1g IV daily (2g if very severe infection) – gram -
  - Teicoplanin 400mg IV bd x 2 doses, then daily – gram +
- Send blood for microbiology

## **Palliative Care Emergencies**

- 1. Haemorrhage**
- 2. Hypercalcaemia**
- 3. Spinal cord compression**
- 4. Superior Vena Cava obstruction**

### **1. Haemorrhage**

#### Introduction

#### Appropriate assessment to identify cause and severity of symptoms

Haemorrhage occurs in about 20% of patients with advanced cancer and may contribute to death in 5%. Bleeding may be directly from the cancer itself or caused indirectly e.g. by medication causing gastric erosion or thrombocytopaenia. A generalised clotting deficiency seen in thrombocytopaenia, hepatic insufficiency or anti-coagulation with warfarin, are also contributory factors, particularly in patients with cancer.

Common types of haemorrhage include haemoptysis, haematemesis, erosion of major vessels, rectal bleeding, vaginal bleeding, haematuria, gum and/or oral mucosal bleeding, epistaxis, intracerebral haemorrhage, bleeding into skin/muscle.

#### Explanation to patient and family

Do not alarm the family unless really necessary. Bleeds are often feared but seldom occur. Tell the patient and family what they need to know in small steps according to what they want to know. One needs to be careful not to raise fears of unlikely complications which are terrifying and about which little can be done.

#### **Non-acute haemorrhage**

#### Correct reversible factors

- H<sub>2</sub> receptor blockers, e.g. ranitidine 150 mg bd or proton pump inhibitors e.g. lansoprazole 30 mg daily. Sucralfate may act as a local astringent to stop stomach mucosal bleeding but inhibits absorption of other medications such as proton pump inhibitors.
- Check INR and adjust warfarin doses. Vitamin K may be needed.
- Stop anticoagulants, NSAIDs, aspirin. (COX-2 Inhibitors are safe)
- Correct any platelet abnormality if appropriate
- Treat infection as infection exacerbates bleeding
- If the haemorrhage is not immediately fatal, such as with a haematemesis or bleeding from the rectum, vagina or superficially ulcerated wound, the aim of treatment is local control if possible and sedation of a shocked, frightened patient.

#### Consider disease-specific palliative therapy

- Palliative radiotherapy is very useful for superficial tumours and those of the bronchus and genito-urinary tract.

#### Prescribe appropriate first-line treatment

- If radiotherapy is not appropriate, coagulation should be enhanced with oral tranexamic acid 500-1000 mg tds. po or i/v but caution is necessary with haematuria since clots may form in the bladder resulting in further problems.
- Local measures such as topical tranexamic acid or adrenaline (1:1000) soaks, calcium alginate dressings, e.g. Kaltostat, may be useful.

#### **Acute terminal haemorrhage**

- Erosion of a major artery may be catastrophic and rapidly fatal within minutes
- It is usually associated with tumour erosion into a major artery such as the femoral or carotid artery (causing external haemorrhage) or the aorta or pulmonary artery (causing haematemesis or haemoptysis).
- The main aim of treatment is to comfort the patient and support the family

#### Institute non-pharmacological interventions

- If a major haemorrhage is anticipated it is best to be prepared. Major haemorrhages might be preceded by smaller bleeds.
- Warn family members of the possibility of a bleed and prepare them for what needs to be done.
- If the patient is in an in hospital or hospice inpatient facility, move the patient to a side ward or private room so as not to distress other patients. Have a senior staff member stay with the patient at all times, if possible, and attempt to comfort and reassure the patient and family
- Have aprons and gloves ready and dark towels on hand for mopping up and reducing the visual impact of the haemorrhage (dark green or blue or red blankets and towels)
- Apply towels to the bleeding site for pressure and to absorb blood
- Apply gentle suctioning to the mouth and trachea if needed

#### Prescribe appropriate first-line treatment

- Have medication ready on hand in case of a bleed. In the event of a bleed, the aim of treatment is to sedate the patient to relieve distress from what will be the terminal event of his/her life.
- Give medication ideally intravenously or by deep intramuscular injection. Subcutaneous drugs are poorly absorbed when in shock
- Midazolam 5-10 mg SC, i/v or S/L via buccal mucosa. (Use higher doses in patients who are already on benzodiazepines or heavy alcohol drinkers)
- Lorazepam 1 mg S/L stat
- Morphine 10 mg SC OR i/v
- Rectal diazepam is another option and can be administered by a family member if the patient is at home
- Repeat drugs every 10-15 minutes if needed.



### Consider Second-line treatment

- Ketamine 150-200 mg i/v stat will rapidly sedate a patient dying from a terminal bleed. If i/m route is used then a higher dose of 500mg is required.

### Explanation to patient and family

- Bleeds are often feared but seldom occur. Tell the patient and family what they need to know in small steps according to what they want to know. One needs to be careful not to raise fears of unlikely complications which are terrifying and about which little can be done.
- The palliative care team needs to balance the anxiety of alerting the family to the possibility of an acute bleed, with the likelihood of such an event occurring and the need for the family to be prepared. If the patient chooses to be looked after at home, the issues of managing acute haemorrhage need to be discussed with the family and the home care team and a clear plan worked out. Are there any special circumstances such as children in the house who might be especially traumatised by witnessing a severe bleed?
- An Emergency Kit containing any of the following is helpful: Syringes, needles, adrenaline, Caltostat®, tranexamic acid, morphine, S/L lorazepam and or midazolam.
- **After the event:** The visual impact of such an event is enormous and anyone present will need support
- Debrief the family, carers, staff, domestic workers and anyone who witnessed the trauma. Offer them counselling at Hospice or direct them to their usual support network. Offer a follow up meeting to answer any questions they might have. Extensive counselling immediately after such a traumatic event can do more harm than good.

## **2. Hypercalcaemia**

### **Introduction**

Hypercalcaemia is a paraneoplastic condition associated with advanced cancer. It describes a raised level of corrected calcium in the blood. Total plasma calcium is the combination of free, ionised calcium and protein-bound calcium. If the albumin level is low, protein bound calcium is low. This may mask a high concentration of free, ionised calcium. Calcium is, therefore, 'corrected' for albumin level.

Hypercalcaemia occurs as a result of increased osteoclastic activity (which releases calcium from bone) and decreased excretion of urinary calcium. This is attributed to locally active substances produced by bone metastases or by factors such as ectopic parathyroid hormone-related protein (PTHrP) or cytokines produced by some tumours and occurs in 10% of the cancer population.

### **Incidence**

- 10-20% of all cancer patients
- 20-40% of patients with cancer of the bronchus, breast or myeloma will have hypercalcaemia

### **Cancers producing hypercalcaemia**

- Multiple myeloma is the most likely tumour to produce hypercalcaemia
- Lymphoma

- Carcinoma of lung and breast account for over half of the cases seen, e.g. squamous cell carcinoma of the bronchus.
- Other squamous cell tumours of breast, bronchus, head and neck
- Renal and genito-urinary cancers.

Hypercalcaemia from carcinoma of the prostate is surprisingly rare.

### **Significance of hypercalcaemia**

Hypercalcaemia from malignancy is caused by the secretion of a PTH-like substance by the tumour. Contrary to popular belief, it can occur in the absence of bone metastases. Conversely, patients can have widespread bone metastases and remain normocalcaemic.

Hypercalcaemia usually indicates disseminated disease (74%). 95% of patients with breast cancer and hypercalcaemia have disseminated disease. 61% of patients with lung cancer and hypercalcaemia have disseminated disease. Hypercalcaemia usually means a very poor prognosis – 4 out of 5 patients die within a year.

### Appropriate assessment to identify cause and severity of symptoms

A corrected plasma calcium concentration above 2.6 mmol/l defines hypercalcaemia. It is often mild and asymptomatic and significant symptoms usually only develop with levels above 3.0 mmol/l, although some patients may have significant symptoms at lower levels. It is probable that the rate of rise determines symptoms. Levels of 4.0 mmol/l and above will cause death in a few days if left untreated. 80% of hypercalcaemic patients with cancer survive less than one year.

### Common symptoms and signs

- Thirst
- Polyuria, polydipsia, dehydration
- Nausea and vomiting
- Worsening pain (usually bone) that is difficult to control (Hypercalcaemia lowers the pain threshold)
- Constipation
- Drowsiness and lethargy
- Muscle weakness
- Confusion
- Coma

### Management

Treatment is only necessary if there are symptoms or there is a high likelihood of symptoms developing. Treatment may be unnecessary if the patient is very near to death.

Treatment is aimed at improving well-being and symptoms for symptomatic patients for weeks or even months.

Before treatment, the following issues need to be considered:

- Is the patient symptomatic or is the serum corrected calcium >3mmol/l? Symptoms are only likely if the corrected calcium is >2.8 mmol/l.

- Is this the first episode? If so, an oncology opinion is warranted. A change in anti-tumour therapy may be indicated
- Is the patient's quality of life good (in their opinion)? Is the patient willing to undergo IV therapy/blood tests?
- Will the treatment work? (What response was there to previous treatment?)

#### Explanation to patient and family

The symptoms experienced are due the spread of cancer to the bones and calcium from the bones in the blood stream. Fluids and medication can reduce the calcium levels and improve the patient's symptoms. Additional medication may be required at intervals to prevent this from happening again

#### Institute non-pharmacological interventions

- Fluid replacement – patients are often dehydrated and need adequate fluid replacement. A high oral intake of fluid is essential if this is possible. Extra fluid intravenously is necessary especially if the patient is significantly dehydrated, which is likely. Give 0.9% saline ivi, 1 litre every 6 hours before bisphosphonates if calcium is >3.5 or patient is clinically dehydrated. Continue 0.9% saline 1 litre every 6-8 hours for a further 48 hours after bisphosphonates, if the patient is able to tolerate fluids and as clinically indicated. Fluid replacement alone improves symptoms but rarely achieves total control.
- Control associated symptoms – such as pain, confusion and constipation

#### Prescribe appropriate first-line treatment

- The treatment of choice is an intravenous bisphosphonate infusion: Pamidronate or Zoledronic acid.
- Bisphosphonates inhibit osteoclast activity and thereby inhibit bone resorption. Because of poor alimentary absorption, they are usually given intravenously initially. Bisphosphonates are effective in 70-80% of patients for an average of 2-3 weeks.

Treatment is usually simple and well tolerated. Sometimes transient flu-like symptoms occur which respond to paracetamol. A typical dosing schedule is given below:

- Disodium pamidronate      60-90 mg in sodium chloride 0.9%, 500 ml over 2-4 hours
- Zoledronic acid              4 mg in 100 ml sodium chloride 0.9% over 15 minutes ivi, has a longer (4 week) period of action and a short (15 minute) period of administration

#### **Guideline to use of Pamidronate**

<b>Corrected serum calcium mmol/l</b>	<b>Pamidronate dose (mg)</b>
3	15-30 mg
3-3.5	30-60 mg
3.5-4	60-90 mg
>4	90 mg

### Review assessment and management

A single infusion will usually maintain normocalcaemia for three weeks. Hypercalcaemia tends to recur. Consider monitoring the serum calcium every 2 weeks or monthly and ensure the patient and family know the symptoms to watch for. Pamidronate infusions can be repeated every 3-4 weeks according to the serum calcium.

Plasma calcium levels start to fall after 48 hours and fall progressively for the next 6 days. The dose can be repeated after a week if the initial response is inadequate. If calcium remains high or rises again shortly following a bisphosphonate infusion, it may be useful to try an alternative bisphosphonate. If it is not possible to reduce the calcium levels, attention should be paid as always to the management of symptoms particularly pain, confusion and constipation. Check U&E before giving Zoledronic acid, if creatinine >400 µmol/l it is not recommended.

- Check calcium after 3-4 days if symptoms have not significantly improved
  - Normocalcaemia should be achieved in 3-7 days
  - If calcium is not falling, repeat dose of bisphosphonate or try a different bisphosphonate
- Be aware that the mean length of response is 2-4 weeks for Pamidronate and 4-6 weeks for Zoledronic acid.
- Arrange for serum calcium to be checked every 2 weeks or monthly.
- If symptoms of hypercalcaemia recur, or there is a general deterioration in the patient's condition after a few weeks, recheck serum calcium.
- Institute maintenance therapy after two episodes of hypercalcaemia.

### **Maintenance treatment to prevent recurrence**

- Pamidronate 90 mg IV every 4 weeks, or
- Zoledronic acid 4 mg IV every 4 weeks, or
- Ibandronic acid IV or PO

### **Treatment – resistant Hypercalcaemia**

Pamidronate may be progressively less effective when hypercalcaemia recurs (90% response to first treatment, 15% to third treatment). This is observed mainly in patients with hypercalcaemia of humoral origin, i.e. usually without bone metastases or tumours other than breast. The usefulness of pursuing further therapy has been questioned, although resistance can sometimes be overcome by the use of increasing doses of Pamidronate or by a more potent bisphosphonate, e.g. Zoledronic acid.

### 3. Spinal Cord Compression

#### Introduction

Spinal cord compression (SCC) occurs in 3-5% of patients with cancer. 10% of patients with spinal metastases develop spinal cord compression, the frequency being highest in multiple myeloma and cancers of the prostate, breast and bronchus.

#### **Cancers with the highest frequency of SCC**

- Multiple myeloma
- Breast
- Prostate
- Bronchus
- Renal cell
- Lymphoma

#### **The site of the compression**

- Thoracic 70%
- Lumbosacral 20%
- Cervical 10%

80% of cases are caused by extradural deposits due to direct extension from the vertebral body into the anterior epidural space. Lesions above L1 (lower end of spinal cord) may produce upper motor neurone signs and a sensory level, whereas lesions below L1 may produce lower motor neurone signs and peri-anal numbness (cauda equina syndrome)

#### Appropriate assessment to identify cause and severity of symptoms

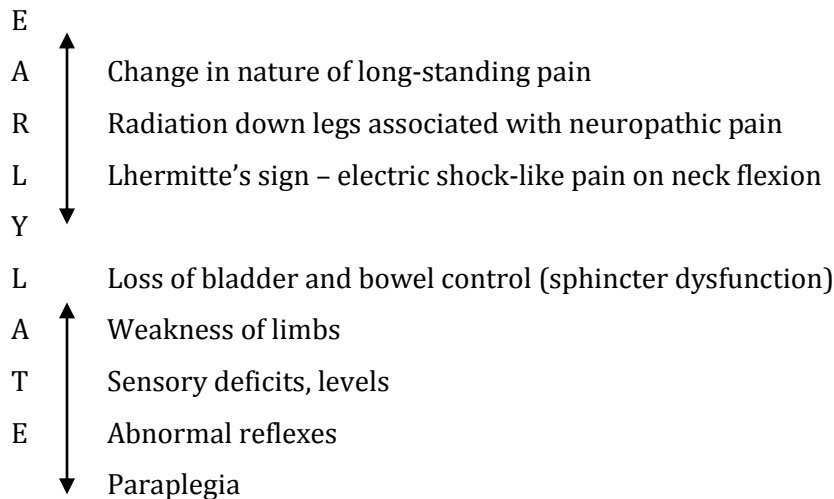
Those looking after such patients should always be vigilant in checking for early signs and symptoms of spinal cord compression.

It is important for all health professionals to have a high index of suspicion for possible spinal cord compression because of the catastrophic consequences of a delay in diagnosis, such as paraplegia and urinary and faecal incontinence.

#### **Symptoms and signs of spinal cord compression –**

- Back pain 90% (Central back pain aggravated by movement, coughing, straining, lying down, leg raising.)
- Weak legs
- Absent and hyperactive reflexes
- Sensory level
- Urinary hesitancy or retention
- Back pain, a sensation of weakness in the legs and often vague sensory symptoms may be early manifestations. Patients may complain of a band-like pain, particularly on coughing and sneezing.
- For those presenting with profound weakness, a sensory 'level' and bladder and anal sphincter disturbance, which are relatively **late features**, the outcome is poor and the compression is much less likely to be reversible.

## Early and late clinical signs



Deciding whether a course of treatment is appropriate for a particular patient involves an overall assessment. Spinal cord compression is an **emergency** and two questions need to be answered urgently.

### 1. Does this patient have a reasonable likelihood of having spinal cord compression?

Even the most skilled clinician is unable to diagnose early spinal cord compression with absolute certainty. Often by the time clinical signs are 'classical' the damage is irreversible. Once the compression has fully developed, treatment outcome is very poor. Thus, if intervention to prevent paraplegia is to be meaningful, spinal cord compression needs to be diagnosed early.

#### Checklist –

- ☐ Does this patient have back pain? Indicate site, severity and tenderness on body chart.
- ☐ Does the patient have muscle weakness/paraplegia? Indicate areas of weakness on body chart.
- ☐ Does the patient have altered or loss of sensation? Indicate areas on dermatome chart.
- ☐ Is there a new sphincter problem?
 

Urinary retention	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
Urinary incontinence	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
Hesitancy/frequency	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
Constipation	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>
Faecal incontinence	Yes	<input type="checkbox"/>	No	<input type="checkbox"/>

**Note** – check anal tone and saddle area sensation. Indicate on body chart.

### 2. Would this patient benefit from instituting emergency investigation and treatment? –

once the possibility of spinal cord compression has been raised, the patient may now be committed to a course of management that will include urgent transfer to a specialised unit,

where an MRI scan can be carried out and radiotherapy or other compression-relieving procedure performed.

- Consider the patient's overall condition and prognosis.
- Consider the patient's goals and wishes.
- An urgent multidisciplinary management decision is ideally needed to decide on appropriate treatment options.

The keys to diagnosing spinal cord compression include –

- ✓ Having a high index of suspicion in patients with spinal metastases, particularly those with multiple myeloma, breast, lung and prostate cancer.
- ✓ Taking patient's complaints about back pain, difficulty in walking and in passing urine, seriously.

#### Explanation to patient and family

Patients at risk of developing SCC should be encouraged to report any new or worsening symptoms. If spinal cord compression is suspected the patient needs to know the urgency associated with the referral to radiation oncology for further assessment and treatment.

#### Prescribe appropriate first-line treatment

- If the patient is still walking, emergency treatment gives a 1 in 3 chance of regaining leg strength and **treatment should be started immediately with high dose Dexamethasone**, while arrangements are made for **urgent transfer** to oncology centre.
- Dexamethasone 8-16 mg stat. (Give oral or by injection SC or i/v if patient vomiting.) Give i/v if symptoms have developed rapidly in past 48 hours (8 mg po bd) Note – do not delay urgent referral in order to obtain dexamethasone.
- Treat pain and other symptoms whilst awaiting further treatment

#### Referral to appropriate service: acute Oncology centre

- Any patient suspected of having a SCC or being at risk of having a SCC must be discussed with the patient's oncologist or the palliative care specialist on an emergency basis.
- Where suspicion of spinal cord compression is high, it is quickest to involve the oncology team who have been managing the patient and who will be able to co-ordinate the necessary scans and appropriate treatment rapidly. Investigations include an MRI scan (the investigation of choice) and /or a myelogram.

#### **Consider disease-specific palliative therapy**

- Radiotherapy
- Occasionally – chemotherapy
- Rarely – surgical decompression

### **Indications for radiotherapy**

- Radiosensitive tumour
- Multiple levels of compression
- Unfit for major surgery
- Patient choice

### **Indications for surgical decompression**

- Uncertain cause – to obtain histology
- Radiotherapy has not been effective or symptoms persist or worsen despite radiotherapy
- Radio-resistant tumour, e.g. melanoma, sarcoma
- Unstable spine
- Major structural compression
- Cervical cord lesion
- Solitary vertebral metastasis

### Review assessment and management

- Although the overall outcome from treatment is not good, the potential difference that successful treatment can make to a patient's quality of life is enormous. Treatment outcome is better, the earlier it is started
- Corticosteroids alone may be appropriate for some patients with very advanced cancer, especially if their mobility or performance status was already poor. Nevertheless, making an urgent appropriate management decision is the emergency.
- Overall, 30% of patients with spinal cord compression may survive for one year. Function will be retained in 70% of patients who were ambulant prior to treatment, but will return in only 5% of those who were paraplegic at the outset.
- Return of motor function is better in those with an incomplete block and particularly with partial lesions of the cauda equina. Loss of sphincter function is a bad prognostic sign.
- In practice, most patients with an established diagnosis are relatively unwell and have multiple metastases and will be referred for radiotherapy, achieving similar results to those of surgery.

### Explanation to patient and family

As always in Palliative care, involvement of the patients and their family is a vital component of the management of a patient with a Spinal Cord Compression. This potentially devastating complication has many issues that need attention, including loss of control, loss of mobility and loss of independence. Not surprisingly patients with paralysis resulting from SCC often feel hopeless, helpless and depressed. Thorough explanation and repeated reassurances are required as well as the involvement of a counselling social worker and/or psychologist.

### Involvement of interdisciplinary team

Such patients provide great challenges to the multidisciplinary team. These challenges include –

- Mobility management, within the limits considered safe for the compromised spinal cord. Physiotherapy. Occupational therapy.



- Skin care in a patient confined to bed
- Bowel interventions
- Urinary system management
- Psychological and social support

#### 4. Superior Vena Cava Obstruction

##### Introduction

Superior Vena Cava Obstruction (SVCO) is due to compression, invasion and /or thrombosis of the Superior Vena Cava by mediastinal lymph nodes or tumour in the region of the right main bronchus. It is caused by:

- Carcinoma of the bronchus 75% (most common)
- Lymphoma 15%
- Breast )
- Colon ) 10%
- Oesophagus )
- Testis )

##### Appropriate assessment to identify cause and severity of symptoms

- **Symptoms** – are those of venous hypertension and include breathlessness (due to laryngeal oedema, tracheal or bronchial obstruction), headache (due to cerebral oedema), visual changes, dizziness and swelling of the face, neck and arms.
- **Signs** – include engorged conjunctivae, peri-orbital oedema, non-pulsatile dilated neck veins and dilated collateral veins (chest and arms). Papilloedema is a late feature.

SVCO can present acutely, causing very distressing symptoms. In the Palliative Care setting the diagnosis e.g. Ca Bronchus is usually already known and so a high index of suspicion is required.

##### Explanation to patient and family

Without treatment SVCO can progress over several days resulting in death. In patients presenting with advanced SVCO, the prognosis is poor even with treatment, unless the primary cancer is responsive to either radiotherapy or chemotherapy. The prognosis depends on the prognosis of the cancer. Hospice staff will need to inform the patient and family of the seriousness of the situation and the urgency of seeking treatment while also providing the ongoing support and security they will need at this time.

Management: Emergency treatment (needed for advanced, acute SVCO)

##### Referral to appropriate service: acute oncology service

Contact specialist oncology centre as a priority. If possible the patient should be transferred to an oncology centre for management.

### Institute non-pharmacological interventions

Sit patient upright and give 60% oxygen.

### Prescribe appropriate first-line treatment

Dexamethasone – 8-16 mg p.o. or i/v or SC.

Furosemide – 40 mg p.o. or i/v (maximum rate 4 mg/min)

Consider prophylactic anti-convulsant.

### **Disease-specific palliative therapy**

Emergency radiotherapy or chemotherapy (Small Cell Carcinoma of Bronchus, Lymphoma or Testicular Cancer) is given with steroid cover, e.g. dexamethasone

16 mg daily. Survival may be prolonged for several months but a recurrence may be more difficult to control.

### Consider second-line treatment

Intra-luminal stents can be inserted via the femoral vein into the SVC in patients whose SVCO has recurred after standard treatment. It may also be used as a first line treatment to control symptoms.

Thrombosis in the SVC may be an added problem and should be managed accordingly using the appropriate thrombolytic agent.

### Involvement of interdisciplinary team

Due to the prognostic implications of SVCO, the interdisciplinary team should be involved in support and counselling for the patients and/or family and carers.

### Review assessment and management

Regular follow-up is required which may involve close communication with the oncologist involved if the patient has been transferred to an oncology centre. Patients may be on a high dose of steroids and will require close monitoring. Many patients will need In Patient Unit admission for daily assessments by a Palliative Care doctor and monitoring by the interdisciplinary team.

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Swish Adult Palliative Care Guidance

## **General Guidelines for Mouth Care**

### **General Guidelines for Mouth Care**

The mouth has important functions: eating, drinking, taste, communication, breathing and defence. It is the most convenient route for medication administration.

Oral health problems are common in palliative care patients, impacting severely on quality of life.

Poor dental hygiene encourages oral infections.

Oral infection, inflammation or ulceration can be very painful, compromising eating, drinking, speaking and causing embarrassing halitosis.

Patients are at risk for dehydration, malnutrition, systemic infections, haemorrhage, distress and depression.

Even mild oral discomfort can cause difficulty in speaking and eating, aggravating problems of nutrition, anorexia and cachexia.

Dry mouth affects 90% of hospice in-patients to varying degrees.

**Patients seldom report oral problems. Symptoms need to be enquired about and signs regularly assessed.**

Oral problems in palliative care include:

- Infections - fungal (Candidiasis, Aspergillus); viral (HSV, CMV) or bacterial (Staphylococcus and anaerobic).
- Dry mouth (Xerostomia).
- Ulceration: Stomatitis (Apthous Ulcers) and Mucositis.
- Pain
- Halitosis
- Taste alterations.
- Drooling (hypersalivation).
- Dental caries, gingivitis and periodontitis.

Oral health depends on the patient's immune status and is thus an important consideration in HIV/AIDS patients. Oral lesions may herald worsening immune suppression and disease progression. Oral manifestations of HIV infection include fungal, viral and bacterial infections and opportunistic cancers.

### **Risk factors for oral problems in palliative care patients:**

- Factors compromising secretion of saliva:
  - *Medication* that decreases salivary secretions or predisposes the patient to opportunistic infections:
    - Antibiotics and Anti-retrovirals.
    - Excessive antiseptic mouthwash use (especially alcohol-based preparations).
    - Diuretics and opioids.
    - Drugs with anticholinergic side effects: antidepressants, antispasmodics (hyoscine), antihistamines, neuroleptics (phenothiazines) and anticonvulsants.
    - Immunosuppressant drugs – cortisone, chemotherapy.
    - Oxygen therapy (drying of mouth).
  - Decreased oral intake (weakness, dehydration).
  - Chemotherapy and radiotherapy (especially local).

- Local tumour.
- Factors affecting oral self-care (debility, neurological impairment, coma).
- Mouth breathing
- Immune-deficiency
- Chronic diseases: respiratory and cardiac pathology, diabetes mellitus, epilepsy, kidney disease, inflammatory bowel conditions and cranio-facial abnormalities.
- Denture-related trauma and hygiene problems.

**Objectives of good mouth care are:**

- Early detection and prompt treatment of oral problems to preserve functionality, maintain quality of life and prevent progression of minor problems.
- Control of associated unpleasant symptoms and signs of dry mouth, pain, infections, halitosis and altered taste.
- Active management of pain is an integral part of oral pathology treatment.

**Oral assessment**

Simple interventions prevent or relieve many problems:

- *Ask specifically about oral problems* (pain, dry mouth, taste alterations).
- Examine the oral cavity thoroughly at each visit for mucosal changes, growths and signs of infection.
  - Explain the procedure to patient and family.
- Educate patients and caregivers about mouth, teeth and denture care assessment.
- Use an oral assessment protocol (see Oral Assessment Guide below), gloves and a good torch.
- Assess need for assistance with effective oral care.
- Denture-bearing surfaces need careful assessment.
- Be alert for oral candidiasis in all palliative care patients.
- Oral lesions and pain associated with fever suggest possible bacterial infection.
- Assess and document pain associated with each lesion.

Oral Assessment Guide			
	<b><u>Healthy</u></b>	<b>Mild - Moderate Dysfunction</b>	<b>Severe Dysfunction (compromised mucosa or loss of function)</b>
<b><u>Saliva</u></b>	Watery	Thick, reduced, altered taste	Absent (or excessive)
<b>Mucosa</b>	Moist, pink, intact, comfortable	Dry, inflamed, white-coated, and painful. (No ulceration)	Shiny, red, ulcerated, painful, with or without bleeding
<b>Tongue</b>	Pink, moist, and papillae present	Dry, reddened or white-coated, loss of papillae	Dry, white-coated, ulcerated or cracked
<b>Lips</b>	Moist, pink, smooth	Dry, cracked, uncomfortable	Dry, cracked, ulcerated or bleeding
<b>Teeth or denture bearing areas</b>	Clean, free of debris. Dentures comfortable	Dull (plaque), localised debris, sensitive areas. Intermittent pain	Generalised debris or plaque along gum line or denture-bearing area. Can't wear dentures. Frequent pain

<b>Voice</b>	Normal	Deep or hoarse	Difficulty or pain on speaking
<b>Swallowing</b>	Normal	Painful or difficult	Not able to swallow

Based on Gibson,L and the Singapore MOH guidelines

**Explanation to patient and family:**

Give reassurance and education about the importance of regular, diligent mouth care.  
Involve the family with mouth care, where appropriate.

**Correct reversible Factors:**

- Disease-specific intervention is often possible. Identify possible underlying causes (diabetes mellitus, HIV infection, dental or periodontal disease).
- Review medications that may (cumulatively) contribute to dry mouth (anticholinergics, diuretics, etc).
- Consider possible interactions between topically administered oral preparations and allow appropriate intervals between treatments.
- Encourage meticulous oral care.
- Rehydrate if appropriate.
- Humidify oxygen.

**Non-pharmacological intervention:**

**Tools for Oral Care:**

- **Toothbrushes:** small-headed (baby), soft, rounded nylon bristles. Change 3-monthly. Soak regularly (mouthwash or salt/bicarbonate solution). Rinse before use. Brush gently, especially if mucosa is fragile.
- An electric toothbrush (rotating) may be more effective and easier to use.
- *Foam sponges/sticks:* for removal of debris when mucositis or bleeding prevents brushing. Not effective in plaque removal.
- *Glycerine-lemon swabs:* less effective for oral cleaning and exacerbate oral dryness.
- **Toothpaste:** fluoride; low abrasive.
- Use water if toothpaste cannot be tolerated.
- **Mouthwashes:**
  - Water or saline rinses as often as desired.
  - Saline – a teaspoon of salt in 500 ml of boiled, cooled water.
  - Saline–sodium bicarbonate mouth rinse. A teaspoon each of salt and baking powder in 500 ml of boiled cooled water.
  - A teaspoon of vinegar or lemon juice in one litre of water.
  - Equal parts of cider mixed with soda water.
- **Lip Care:**
  - Vaseline/paraffin ointment (Lip Ice®): soothes dry lips; retains moisture.

**Principles of Oral Care**

Regular care: 6-12 hourly (2-4 hourly in at-risk patients - dry mouth or severe infections).

- Chewing pineapple (fresh or unsweetened tinned) helps to keep the mouth clean due to the action of the enzyme ananase.
  - Avoid if sores or ulcers are present.
- **Teeth:**
  - Brush and floss regularly (after meals and at night).
  - Use a soft sponge, cotton buds or gloved finger/spatula wrapped with gauze if pain or bleeding prevents tooth brushing.
  - Remove debris and plaque without damaging gingivae.
  - If brushing is not possible use gauze wipes to remove debris and clean teeth with foam sponge/stick.
  - Regular dental checks and removal of established plaque.
- **Dentures** may become reservoirs of infection:
  - Brush/clean after meals to remove food particles and plaque.
  - Remove at night. Brush with mild soap/commercial denture cleaner and denture brush. Do not boil.
  - Soak dentures overnight:
    - *Metal dentures* in a chlorhexidine solution;
    - *Plastic dentures* in dilute sodium hypochlorite (Miltons®).
  - Rinse well with water before replacing.
  - Ill-fitting dentures may be able to be relined if soft tissue or facial muscle wasting or xerostomia cause discomfort.
  - Clean denture-bearing areas.
- **Regular mouthwash rinses** after meals and at night to remove debris; keep mouth clean and prevent halitosis.
- Increase frequency if high risk of mouth problems (e.g. head & neck radiotherapy, chemotherapy).
  - Water rinses p.r.n.
  - Homemade saline mouthwash (see above) p.r.n.
  - If oral infection present use:
    - Chlorhexidine (Paroex®, Corsadyl®), Dentyt pH® or povidone iodine (1%) (Betadine®) – 15 ml b.d. / t.d.s. to assist with bacterial and fungal control. (Discussed below)
- In very ill patients mouthwash-soaked sponge sticks can be used.  
*Frequency of mechanical cleaning is more important than the antiseptic qualities of different mouthwashes.*
- **Tongue:**
  - Clean a coated tongue gently with a soft toothbrush, sponge or gauze swab moistened with salt/sodium bicarbonate solution.
  - Sucking effervescent vitamin C (250 mg) q.d.s. helps with furred tongue.
  - In advanced disease, KY jelly applied to the tongue and oral cavity is a cost-effective means of oral cavity moistening and lubrication.
- Halitosis: see Specific Problems in Oral Care
  - Avoid acidic or spicy foods if these trigger pain.
  - Avoid alcohol, caffeine and tobacco (drying and irritation).
  - For relief of dry mouth see: Dry Mouth/Xerostomia.
  - Treat pain according to WHO pain guidelines.

### **Mouth Care in the comatose patient:**

- Brush teeth with toothpaste and soft toothbrush. Remove excess toothpaste with a moistening swab on a stick.
- Clean Oral mucosa with water or vitamin C solution.
- Moisten mouth: water-soluble lubricating jelly on foam stick, or water sprays.
- Lip care with paraffin jelly (Vaseline).

### **Pharmacological interventions:**

- Treat as appropriate (See: Oral Pain, Bleeding, Drooling, Dry Mouth, Mouth Ulcers and Oral Candidiasis sections).
- If oral disease is present, rinse mouth regularly with topical antiseptics to assist with bacterial and fungal control:
  - Chlorhexidine, Dentyl pH® or povidone iodine (1%) 15 mL b.d./ t.d.s.
- Artificial saliva products may provide relief for a dry mouth (see below), but are expensive, short acting and less effective than saliva stimulants (Pilocarpine or Bethanecol).
- Treat pain according to WHO pain guidelines using topical or systemic medications, or combinations, as appropriate (Oral Pain).
- **Antibiotics:**
  - Antimicrobial mouthwashes: (see below).
  - Treat specific infections.
- Antivirals: oral and systemic: see Appendix - Herpes.
- Antifungals: oral and systemic: see Appendix - Candidiasis.
  - **Miracle Mouth Rinse/Paint** (Uganda):
    - A mixture of:
      - **aciclovir** (200 mg tab)
      - **metronidazole** 2x200 mg crushed tabs
      - 5 ml nystatin (Mycostatin®) (500 000 U)
      - Use as mouthwash or paint on to ulcers.
      - *A 15 mg amp of **morphine** can be added to this mixture.*
- Metronidazole gel/rinses can be made by mixing crushed **metronidazole** tablets with KY gel or mouthwash (approximately one 400mg tablet per 5 ml volume). Useful for malignant ulcers.
- A 1% topical metronidazole paste can be made with UEA cream and **metronidazole** (as above).
- Consider systemic **metronidazole** to control foul-smelling anaerobic infections and associated halitosis: 500 mg p.o. q.12.h. or 1g P.R.
- Tetracycline mouthwash for resistant ulcers (250 mg in 15 ml water). Hold in mouth t.d.s for 2-3 min. Avoid swallowing. May stain teeth (children!). Probably treats superimposed infections.
- Persistent, severe ulcers may respond to thalidomide 50-100 mg nocte. Use under specialist guidance.
- Apply dressings of an appropriate absorbent and odour controlling nature.
- Treat secondary infection promptly and appropriately.
  - Oral bacterial infections may be mixed – consider use of broad-spectrum antibiotics. Use a **penicillin** and **metronidazole** combination to cover anaerobic infections.
- Don't delay antibiotic treatment if carious teeth are associated with an abscess (swelling, pain).



## **Mouthwashes:**

### ***Antibacterial Rinses:***

Bactericidal or bacteriostatic, with substantivity (retention ability)

Chlorhexidine gluconate (CHX) (Corsadyl®) is a bis-biguanide – most researched and consistently effective in management of oral infections. Use 15 ml of 0.12% or 10 ml 0.2% after meals, twice daily. Observe nil per mouth for 15 minutes after rinsing and preferably wait 30 minutes after teeth brushing (or rinse thoroughly with water before CHX rinse). Gauze around a tongue depressor can be soaked in CHX and used to remove dried mucus and oral debris.

Cetylpyridinium chloride (Cepacol®), a quaternary ammonium compound, and Hexatidine (Oraldine®) are less effective oral antimicrobials but have fewer side effects.

Povidone-iodine (1%) (Betadine®) solution: rinse b.d. with 10 ml for 30 seconds and spit out. May discolour teeth.

### ***Analgesic mouthwashes:***

Used in ulcerative conditions. Benzocaine (combined with 0.2% CHX (Orochlor®). Numbs mouth. Rinse and expel 15 ml t.d.s.

### ***Anti-inflammatory mouthwashes:***

Useful for primary or secondary inflammation, analgesic benefit

Andolex® (benzylamine hydrochloride alone or in combination with CHX as Andolex-C® is best known.

Benzylamine stabilises cell membranes, preventing arachidonate release, and inhibits cyclo-oxygenase.

Rinse and expel 15 ml t.d.s.

### ***Breath freshening mouthwashes:***

Essential oils (Listerine®) are useful for gingivitis and halitosis, but >20% alcohol content precludes use in ulcerative conditions.

Dentyl pH®, a two-phase mouthwash has recently become popular. It combines two antibacterial substances (cetylpyridinium chloride and triclosan) with oil that binds bacteria. Alcohol-free and contains fluoride.

### ***Fluoride mouthwashes:***

Protect permanent dentition against caries. Oro-NaF® 0.05% is alcohol free.

### ***Alcohol-containing mouthwashes: (5-27%).***

No correlation with increased risk of oropharyngeal cancer.

Acetaldehyde concentrations comparable with alcoholic beverages have been reported in saliva. Restrict to short-term use.

*The drying action of mouthwashes with high alcohol content exacerbates xerostomia. Avoid during local radiotherapy, if severe mucositis or ulceration is present.*

### ***Covering (protective) agents:***

Useful in ulcerative conditions to protect damaged mucosa and facilitate healing.

- Sucralfate (Ulsanic®) – mixed results in mouth care. 15-30 ml q.4.h. Rinse and expel.
- Carmellose paste (Orabase®). Apply p.r.n.
- Diphenhydramine elixir-kapectate (1:1). Rinse and expel q.4.h with 15-30 ml.
- Rinse and expel using a solution of equal parts of diphenhydramine elixir, aluminium hydroxide antacid and viscous 2% lidocaine: 15-30 ml, 2-4 hourly.

- Gelclair (Alocclair®) improves pain management in mucositis. Available in SA in spray/mouthwash form. Alcohol-free. Apply p.r.n.

#### **Analgaesics agents (topical):**

*Topical pain control is generally short-acting (< 2 hours). Apply frequently or consider systemic analgaesia.*

#### **Mouthwashes and sprays:**

*Topical anaesthetic agents may interfere with swallowing and epiglottic reflexes. Avoid eating for an hour after treatment.*

- Benzocaine:  
Rinse: rinse and expel with 15-30 ml q.4.h. Dilute 1:1 if stings.  
Lozenges: (Cepacaine®) 1-2 t.d.s.  
Gel: Rinse and expel 15 ml t.d.s.  
Sprays: if available, 2-3 q.3.h.
- **Lidocaine** (Lignocaine®):  
2% **viscous**: 15 ml q.4.h. Rinse and expel  
10% **spray**: 2 sprays, 2-3 hourly to affected areas  
**Gel** (Remicaine®): apply to affected areas p.r.n.  
Tetracaine (Dynexan®): apply p.r.n. to affected areas.

#### **Morphine mouth rinse:**

15 ml of 2% **morphine**; or add a 15 mg amp of **morphine** sulphate to saline/other mouth washes/Magic Mouth Rinse/Paste.

Rinse for 2 min, 5-6 times daily. Don't swallow.

#### **Corticosteroids:** (painful aphthous ulceration).

- Dexamethasone gargle (0.5mg /20 ml normal saline).
- Paediatric corticosteroid syrup, rinse and expel b.d.

#### **Topical Salicylates:**

- Soluble **aspirin**, unless contraindicated, 300-600 mg q.d.s.
- Choline-salicylate gel (Teejel®, Bonjela®).  
Apply q.6.h, with gentle massage.

#### **Salivary substitutes:**

Used in Xerostomia to facilitate speech, eating and swallowing

Carboxymethylcellulose (CMC)-based. Provide relief for dry mouth, but are expensive, short-acting and less effective than saliva stimulants. Acid content may predispose patient to caries and oral candidiasis. Products should be pH neutral, with electrolyte composition approximating that of saliva. Use as required.

- Betaine® alleviates xerostomia and protects mucosa from irritant substances.
- Biotene® and Xerostom® (betaine-olive oil base, alcohol-free).

#### **Saliva stimulation:**

Parasympathomimetic salivary stimulants used before meals.

- Pilocarpine eye drop solution (4%), 2-3 drops in juice p.o. t.d.s.  
Will cause sweating, avoid if there is cardiac disease, bowel obstruction, glaucoma, asthma, or COPD.
- Bethanecol (start with 10 mg t.d.s. with meals). Fewer side effects.

#### **Review assessment and management:**

- Regular and thorough assessment.
- Be alert for new complications e.g. secondary infections.

**Involve the Multidisciplinary Team:**

- Nursing care, family education and involvement.
- Diet and nutritional assistance.
- Psycho-social support, especially if lesions are disfiguring.

**Referral:**

Dietetic, ENT, dental or periodontal where appropriate.

- Refer timeously for specialist assistance.
- ART, as appropriate, in HIV/AIDS.

**SPECIFIC ASPECTS OF ORAL CARE**

**Oral care is one of the least understood and worst managed areas in general medical treatment – amongst healthcare staff, patients and their families. This is particularly relevant in palliative care (home care and in-patient). Education of all involved about meticulous oral mindfulness and management is an important component in quality end-of-life care.**

1. Dry Mouth (Xerostomia)
2. Oral Pain
3. Specific Problems in Oral Care:
  - 3.1 Bleeding
  - 3.2 Drooling
  - 3.3 Halitosis
  - 3.4 Taste Disturbances
  - 3.5 Mouth Ulcers - General
  - 3.6 Oral Problems in HIV/AIDS and Immune-compromised Patients:
    - CMV & EBV Infections
    - Gingivitis, Periodontitis
    - Kaposi's Sarcoma
    - Non-Hodgkin's Lymphoma
4. Oral Candidiasis
5. Oral Herpes Simplex
6. Oral Stomatitis (Apthous Ulcers)

**1. Dry Mouth (Xerostomia)****Definition:**

Dry mouth is a subjective multifactorial sensation associated with thirst, discomfort, taste alteration, infections, and difficulty with chewing, swallowing or speaking. It is common in advanced cancer. It is caused by decrease in saliva secretion, altered saliva composition or combinations of these, producing viscous saliva.

Saliva comprises mucin and fluid. Mucin actions include antibacterial activity. Adults normally produce about 1.5 litres of saliva daily that helps to protect and keep the mouth, teeth and gums

healthy. Salivary buffers maintain a neutral oral pH and ions ( $\text{Ca}^{++}$ ) assist in the remineralisation of teeth.

Saliva production is often decreased in patients who are unwell. Ninety percent of hospice in-patients experience dry mouth to a varying extent.

A persistent dry mouth may lead to a burning or scalded sensation and taste changes.

A severely dry mouth can compromise appetite, nutrition and self-esteem; and predisposes to dental complications such as caries and periodontal disease.

*Patients and clinicians frequently disregard the symptoms of a dry mouth as 'not serious enough to mention'.*

**Risk factors for dry mouth in palliative care patients include:**

- Medication (common!):
  - Anticholinergic drugs reduce saliva production: tricyclic antidepressants, antihistamines, some antipsychotics, antispasmodics (hyoscine), anticonvulsants.
  - Beta blockers opioids and diuretics.
- HIV infection and antiretroviral treatment (indinavir).
- Local tumour effects, surgery and head/neck irradiation may damage salivary glands.
- Chemotherapy predisposes to mucositis and xerostomia for 2-3 weeks after treatment.
- Local radiotherapy usually causes early mucositis and xerostomia, lasting 6-8 weeks.
- Infections: including Candidiasis, Aphthous Ulcers, Herpes simplex.
- Mouth breathing.
- Aggravation by oxygen therapy (non-humidified).
- Decreased oral fluid intake and dehydration.
- Debility: decreased chewing and inability to care for own oral hygiene.
- Anxiety and depression reduce salivary flow.
- Underlying diabetes mellitus.
- Sjogren's Syndrome (arthritis, dry eyes, decreased salivary output).

**Oral assessment:**

As per Oral Assessment Guide

Assess also for pain

**Explanation to patient and family:**

Explain the importance of regular, good mouth care and describe the role that family can play in assisting with management and care

**Correct reversible factors:**

Consider and treat appropriately any underlying causes:

- Review possible medication-related causes.
- Treat infections such as Candidiasis, Herpes simplex.
- Manage anxiety.
- Humidify oxygen.

**Non-pharmacological intervention:**

Maintain good oral and dental hygiene to prevent infection:

- Routine oral care (2-4 hourly with severe stomatitis). (Mouth Care).
- Assistance with brushing teeth/dentures if necessary.
- Use fluoride toothpaste/supplements.

- Water, saline or saline-sodium bicarbonate mouthwashes as required.
- Cleaning of the tongue and application of lubricating gel to tongue and oral cavity.
- Frequent sips of cool water (or sugar-free liquid) are an effective saliva substitute.
- Sucking ice chips, frozen tonic water/dilute fruit juice (lemon or pineapple).
- Pineapple chunks (fresh or canned) to suck chew or rubbed on the lips of patients unable to swallow or suck relieves the sensation of dryness. Ananase in pineapple has antibacterial properties and assists with mouth cleaning. Avoid if open mouth lesions.
- Oral water sprays or wet sponge sticks if patient very weak.
- Keep lips clean, soft and moistened with soft paraffin jelly (Vaseline)
- Encourage natural saliva stimulants: sucking vitamin C tablets, sugar-free lemon flavoured or sour sweets and chewing sugar free gum.

#### Avoidance/prevention strategies:

- Soften food with milk, broth, gravy or margarine or prepare as purees.
- Lubricate mouth with margarine or salad oil before eating.
- Avoid dry or sticky foods.
- Avoid alcohol, caffeine and tobacco.
- Humidify room air if air very dry.
- Non-pharmacological management of anxiety (relaxation, distraction).
- Good dental care to prevent caries

There is little evidence that rehydration relieves xerostomia.

Glycerine-based products or hydrogen peroxide are not recommended for mouth care.

#### **Pharmacological interventions.**

- Prevent infection:
  - Regular mouth washes to assist with bacterial and fungal control: Chlorhexidine, Dentyt pH® or povidone iodine (1%)  
10-15 ml b.d.–t.d.s. (Avoid alcohol or phenol products)
  - Fluoride rinses assist with caries control.
- Artificial saliva products:
  - Betaine®, Biotene® and Xerostom® - use p.r.n. if helpful.
- Saliva stimulation:
  - Pilocarpine and Bethanecol.
- Topical pain management as appropriate (see Mouth Care, Oral Pain).
- Treat pain according to the WHO Pain Ladder and consider Total Pain.

#### **Review assessment and management:**

- Mouth care should be assessed and reviewed daily.
- Regularly review requirements for and side effects of opioid, phenothiazine, diuretic, anticholinergic medication.

#### **Involve the Multidisciplinary Team:**

- Educate patients and all caregivers concerning oral care and dry mouth.
- Consider patient preferences and encourage participation in all management.

#### **Referral**

- Referral for oral hygiene or dental assistance where appropriate.
- Local radiotherapy for tumour effects.

## 2. Oral Pain

### **Definitions:**

*Stomatitis* refers to painful, inflammatory and ulcerative conditions of the oral mucosa.

*Mucositis* describes similar changes associated with chemotherapy or radiotherapy. Forty percent of chemotherapy and 75% of bone marrow transplant patients develop mucositis.

Most patients receiving head and neck radiotherapy will develop a degree of mucositis.

Oral pain can be severe and, depending on extent of tissue damage, can be a pain emergency. It compromises nutrition and communication and can cause severe distress.

Due to the complex structure of the mouth, multiple pathologies and different pain types may be present. Oral pain may thus be both localised and generalised.

### **Risk Factors:**

- Infections: candidiasis, apthous ulceration, ulcers caused by CMV, herpes simplex and EBV infections; mycobacterial infections (typical and atypical).
- Mucositis: a common complication during and after chemotherapy and local radiotherapy.
- Medication induced stomatitis (ART).
- Salivary gland disease.
- Dentures or surgically induced tissue trauma.
- Tumours and local spread.
- Opportunistic malignancies: Kaposi's sarcoma, Non Hodgkins Lymphoma.
- Dental caries and abscesses.
- Gingival and periodontal disease.
- Radiotherapy causes inflammation, swelling and crusting of oral mucosa.
- Chemotherapy results in thinning of oral mucosa, surface tissue sloughing and ulcer formation.

### **Oral assessment:**

As per Oral Assessment Guide

- Consider recent contributory cancer intervention therapies.
- Check for ulceration, infection and bleeding.
  - Mucositis appears as red, burn-like sores. It appears 4-5 days after chemotherapy, peaking at 1-2 weeks and resolving by 2-3 weeks. After radiotherapy it appears after about 2 weeks and may last 6-8 weeks.
- Identify all lesions, their nature and possible causes.
- Assess also for pain
- Chart and rate each pain. Pain diaries are useful.
- Oral pain may be severe.

### **Explanation to patient and family:**

- Acknowledge pain and reassure the patient and family.
- Set goals for pain management.
- Education for patient and caregivers about appropriate and regular mouth care.
- Encourage appropriate family assistance and describe how to provide oral care

### **Correct reversible factors:**

- Treat underlying causes, e.g. infection.
- Treat mucositis – as below, same for all causes.

- Eliminate/reduce irritant factors.
- Severe treatment-related mucositis may require temporary suspension of chemo or radiotherapy.

#### **Non-pharmacological intervention:**

- Modify measures according to pain and tolerance.
- Maintain meticulous oral care and plaque control to reduce the risk and severity of infection and dry mouth (xerostomia) during cancer therapies.
- Clean mouth 2-4 hourly, according to severity.
- Use a soft bristle toothbrush or foam stick.
- Rinse frequently with water or bland (saline) rinses to moisten and soothe mucosa and help prevent crust formation.
- Drink plenty of fluids (about 3 litres per day).
- Avoid citrus or spicy foods that trigger pain.
- Soft/liquid-based diet.
- Eat food cooled or warm – not hot.
- Avoid alcohol and tobacco.
- Lubricate the mouth with a water-soluble gel.
- Pain management techniques (relaxation, distraction).

#### **Pharmacological interventions:**

##### **Generalised Oral Pain:**

- Coating and protection:
  - Sucralfate suspension (Ulsanic®) 15-30 ml, q.4.h. Rinse and expel.
- Mouthwashes:
  - *Mouthwashes containing alcohol or phenol may cause pain or further tissue damage.*
  - Regular mouth washes to assist with bacterial and fungal control: Chlorhexidine, Dentyl pH®, povidone iodine(1%): 10-15 ml b.d. /t.d.s
  - Orochlor® 15 ml t.d.s.
  - **Miracle Mouth Rinse/Paint** (Uganda). A mixture of **acyclovir** (200 mg tab), **Metronidazole** 2x200 mg crushed tabs, 5 mL **nystatin** (500 000 U). Use as mouthwash or paint onto ulcers. A 15 mg amp of **morphine** can be added to the mixture.
- Analgesic mouthwashes and sprays:
  - Benzocaine, **Lidocaine** (Lignocaine®) rinse, spray or gel,
  - Tetracaine (Dynexan®): apply p.r.n. to affected areas.
- Topical anaesthetic agents may interfere with swallowing and epiglottic reflexes. Avoid eating for an hour after treatment.
- Non Steroidal anti-inflammatory mouthwashes:
  - Benzydamine solution (0.15%) (Andolex®) or Andolex-C®).
  - Rinse and expel with 15 ml t.d.s.
- Corticosteroids: (if painful aphthous ulceration).
  - Dexamethasone gargle (0.5mg /20 ml N/S).
  - Paediatric corticosteroid syrup, rinse and expel b.d.
- Morphine mouth rinse:
  - Rinse for 2 min, 5-6 times daily. Don't swallow.
- **Localised Oral Pain:** as above plus:

- Coating and protection:
  - Carmellose paste (Orabase®). Gelclair (Alocclair®)
  - Apply protective paste p.r.n.
- Topical Analgesia:
- *Topical anaesthetic sprays may interfere with swallowing and epiglottic reflexes. Avoid eating for an hour after treatment.*
  - **Lidocaine** or benzocaine spray/gel p.r.n. to affected area.
- NSAIDs:
  - Benzydamine ointment (Andolex®). Apply t.d.s. as required.
- Salicylates:
  - Soluble **aspirin**, unless contraindicated, 300-600 mg q.d.s.
  - Choline-salicylate gel (Teejel®, Bonjela®). Apply q.6.h, with gentle massage.
- Corticosteroids: (painful Aphthous ulceration).
  - *Caution: Steroids exacerbate CMV/Herpes ulceration.*
  - Triamcinolone acetate 0.1% (Kenalog/orobase®):
  - Apply paste to ulcer t.d.s. for 5 days.
  - **Prednisone:** 5mg dissolve half a tablet on affected area, b.d.
  - Beclomethasone spray, 1-2 puffs b.d. onto ulcer.
  - Dexamethasone gargle (0.5mg /20 ml normal saline).
  - Consider oral prednisone if lesions are very large or there is oesophageal involvement.
- **Miracle Mouth Paint/Paste** (Uganda). See above. Apply locally.

*Topical pain control is generally short-acting (< 2 hours). Apply frequently or consider systemic analgesia.*

#### **Systemic Analgesia:**

- Treat according to WHO Pain Ladder:
- Severe pain not responding to paracetamol or NSAIDS requires addition of appropriate opioid analgesics.
- Consider ketamine for persistent neuropathic pain. (Specialist guidance).
- *Give analgesia parenterally, transdermally or rectally if swallowing is not possible.*

Treat secondary infection, including anaerobe cover if appropriate.

#### **Review assessment and management:**

- Evaluate effectiveness of pain management regularly.
- Monitor for new symptoms and treat appropriately.
- Treat secondary infections appropriately.
- Severe mucositis may require temporary suspension of chemo or radiation therapy.

#### **Involve the Multidisciplinary Team:**

To manage Total Pain, (physical, psychosocial and spiritual aspects) and to support patient, family and all caregivers.

#### **Referral:**

Dental, ENT, Oncology, Anaesthetic, Dietetic



### 3. Specific Problems in Oral Care

(Bleeding, Drooling, Halitosis, Mouth Ulcers, Oral Problems in Immune-compromised Patients, Taste Disturbances).

#### 3.1 Bleeding

Mouth bleeding is a distressing symptom, common in patients with advanced leukaemia or platelet counts  $<50000$  cells/mm<sup>3</sup>.

Risk factors include: infection, radiotherapy, chemotherapy, Xerostomia (Dry Mouth), local malignancy/tumour infiltration, mucosal ulceration due to physical trauma (ill-fitting dentures) or deficiencies of iron (angular stomatitis/glossitis) or Vitamin C (gingivitis).

Exclude coagulopathies (hepatic failure, excessive warfarin therapy).

#### Treatment:

##### Non-pharmacological:

- Consider and treat reversible causes
- Reassurance and support
- Avoid tooth brushing. Use gentle swabbing instead.

##### Pharmacological:

- Calcium impregnated gauze can be applied with pressure
- **Vit K<sub>1</sub>** (Konakion®): 1-2.5 mg IM/IV prn, or 5mg daily, p.o.) Monitor INR daily.
- **Tranexamic** (Cyklokapron®) acid mouthwash (50 mg/ml: 1g effervescent tab in 20 ml water).
- Systemic **tranexamic acid** (Cyklokapron®) 1g p.o. q.i.d.
  - Platelet transfusions (Requires repeating every few days)

#### 3.2 Drooling

Drooling is caused by overproduction of saliva (sialorrhoea) and/or inability to swallow normal amounts of saliva.

#### Associated with:

- Neuromuscular disease (CVA, cerebral palsy, MND, Parkinson's disease).
- Head and neck cancers (especially naso-pharyngeal).
- Oral factors (ill-fitting dentures or surgical deformity).
- Medication side effects (cholinergic agents, lithium, cholinesterase inhibitors).

#### Treatment:

- Consider and treat reversible causes (review medication; attend to denture-related problems).

##### Non-pharmacological:

- Reassurance and explanation for patient and family.
- Positioning of head to allow drainage.
- Suctioning, as appropriate.
- Consider PEG tube for feeding and medication if unable to swallow.

##### Pharmacological:

- Antimuscarinic drugs decrease saliva production:
  - **Amitriptyline** 25 mg nocte p.o.
  - **Propantheline** 15 mg t.d.s. (Marked anticholinergic side effects)

### 3.3 Halitosis

Halitosis (offensive breath odour) may be physiological or pathological. The mouth becomes malodorous due to bacterial putrefaction of food, blood or epithelial cells, particularly in oral cancer with anaerobic infection. It is commonly related to poor oral health or local pathology, (85% of halitosis has an intra-oral aetiology, often micro organism-associated). Sinus/throat infections, lung abscess, gastric stasis and metabolic problems have also been implicated.

#### **Treatment:**

- Treat any underlying disease, if appropriate (periodontal disease, caries, tongue coatings, food impaction, oral thrush, infection and xerostomia).
- Multifactorial treatment aims to reduce accumulation of food debris and micro-organisms and includes dental/periodontal intervention. Check regularly for red/swollen gum tissue and ask about loose teeth or bleeding gums.
- Mechanical care: flossing; tongue cleaning; cleaning and scaling of teeth; cleaning/scraping of the tongue.
- Rinse mouth with saline/bicarbonate solutions.
- Rinse mouth with chlorhexidine, Dentyl pH® or povidone iodine (1%) to reduce bacterial load.
- Listerine® mouthwash is effective for halitosis, but alcohol content can burn oral mucosa. Dentyl pH® also has breath-freshening properties.
- Chemical odour control with zinc salts (mouthwash, toothpaste or chewing gum).
- Herbal products, e.g. black tea.
- Dietary modification.

### 3.4 Taste Disturbances

Taste alterations are a common problem in oral disease.

Risk factors include: poor oral hygiene, dry mouth, mouthwashes, antibiotics, chemotherapy, denture problems and the malignancies themselves.

#### **Management:**

- Reduced with good oral care.
- Eat preferred foods.
- Enhance taste with sugar and acceptable salts, spices and flavourings.
- Pay attention to smell, consistency, presentation and preferred quantity and temperature of food.
- Zinc supplements may assist (possible deficiency).
- Avoid allowing decreased appetite and altered food taste/temperature preferences to become social issues.
- Reassure and educate patient and family.

### 3.5 Mouth Ulcers General

#### **Aphthous ulcers**

Aphthous ulcers are common, painful lesions occurring anywhere in the mouth. They affect at least 20% of the population at some stage of their lives. Women may be more susceptible

Minor (<10 mm) or Major lesions; round, with a grey central pseudomembrane and a raised, circumscribed, erythematous border. They may be multiple and recurrent and can occur on keratinised tissue in HIV patients.

**Risk Factors**

- Cause unknown.
- Genetic/endocrine factors and iron or vitamin (B12, folate) deficiencies have been implicated.
- Occur in immune-competent and immune-compromised patients. Larger in the latter group.
- May be related to stress of chronic illness, especially in HIV/AIDS.
- Local trauma may play a significant role.

**Oral assessment:**

- As per Oral Assessment Guide
- Assess also for pain, oral pain may be severe

Characteristic lesions (differentiate from Herpes ulcers – below)..

**Management:** see Ulcer management, below.

**Non-pharmacological intervention:**

- Regular oral care (See Mouth Care) Use a soft toothbrush.
- Soft, lubricated diet.
- Avoid spicy or salty foods and acidic/citrus fruit drinks.
- Use a straw to drink *cool* fluids, to bypass lesions in the front of the mouth.
- Pain management techniques.
- Water/saline mouth rinses p.r.n.

**Pharmacological interventions:**

**Protection:**

Sucralfate suspension (Ulsanic®) 15-30 ml, q.4.h. Rinse and expel.

**Mouthwashes:**

- Water/saline mouthwashes as required.
- Regular mouth washes to assist with bacterial and fungal control: Chlorhexidine or povidone iodine (1%) *Do not rinse mouth at same time as antibiotics or topical steroids are applied.*

**Analgaesia:** (see also Oral Pain)

Topical: (transient benefits!)

- Anaesthetic mouth rinse/spray: Benzocaine / Lidocaine: 15 mL, q.4.h.
- Anaesthetic gel: 2% lidocaine, p.r.n.
- NSAID mouth rinses: benzydamine (Andolex®/Andolex-C®) have analgaesic and anti-inflammatory actions. Rinse with 15 mL, t.d.s.
- Choline-salicylate gels: Teejel®, Bonjela® p.r.n.

Systemic:

- Treat pain as per WHO Pain ladder (**morphine** if severe).

**Steroids:**

Steroid lozenges can reduce pain and promote healing.

*Exclude CMV/Herpes ulceration as steroids exacerbate these.*

- Triamcinolone acetate 0.1% (Kenalog/orobase®). Apply paste to ulcer t.d.s. for 5 days.
- Prednisone 5 mg tabs. Dissolve half a tablet on affected area, b.d.
- Beclomethasone spray: 1-2 puffs b.d on lesion.
- Dexamethasone gargle (0.5mg /20 mL N/S) b.d.
- Oral prednisone if lesions large or there is oesophageal involvement.

**Antibiotics:**

- Antimicrobial mouthwashes: (see above)
- Miracle Mouth Paint (Uganda).  
Use as mouthwash or paint onto ulcers.  
Can add an amp of morphine (15 mg) or lidocaine if pain is severe.
- Tetracycline mouthwash for resistant ulcers (250 mg in 15 mL water). Hold in mouth t.d.s for 2-3 min. Avoid swallowing. May stain teeth (children!). Probably treats superimposed infections
- Persistent, severe ulcers may respond to colchicine or thalidomide 50-100 mg nocte.  
Use under specialised guidance.

Treat secondary infection promptly and appropriately

#### **Review assessment and management:**

- Assess and review mouth care regularly.
- Pain control.

### **Oral Candidiasis**

#### **Definition:**

Candida albicans is normally commensal in the healthy human mouth. Overgrowth infections of oral candidiasis are common in palliative care, occurring in about 80% of patients with metastatic cancer and almost all HIV/AIDS patients.

Infection may be asymptomatic, but usually presents with white patches on mucous membranes; pain, burning, altered taste and loss of appetite. Local spread may cause oropharyngeal or oesophageal candidiasis. Systemic infection may also occur.

Prompt diagnosis and treatment is important.

Topical treatment may be inadequate, requiring systemic azole therapy.

#### **Risk Factors:**

- Poor oral hygiene.
- Decreased salivary flow (Dry Mouth).
- Immune suppression: medication (corticosteroids, broad-spectrum antibiotics and chemotherapy) and HIV disease.
- Poor nutritional status.
- Ill-fitting, unclean dentures.
- Diabetes mellitus.

#### **Key areas for assessment:**

- Dry mouth.
- Tongue: red and smooth or furred and coated. Central fissuring may occur.
- Oral mucosa or tongue may have white adherent plaques lesions.
- Angular cheilitis (reddening at corners of mouth).
- Pain or burning.
- Taste alterations.
- Dysphagia (oropharyngeal/oesophageal candidiasis).

#### **Non-pharmacological intervention:**

- Regular oral care, after meals and at night.
- Remove and soak dentures overnight in Milton. Check fit.
- Dietary modifications, as required.
- Water/saline mouth rinse p.r.n.

### **Pharmacological interventions:**

- Treat early!
- Remove dentures before treatment.
- **Mouth care:**
- Paint mouth with Gentian violet 0.5% aqueous solution t.d.s.
- Regular mouth washes to assist with bacterial and fungal control: Chlorhexidine or povidone iodine (1%) 10-15 ml, b.d. – t.d.s.
- **Antibiotics:**
  - Topical:
    - Nystatin (Mycostatin®) suspension 100 000U/mL, 2.5-5 ml q.4.h. p.o. Swish and swallow. *Don't apply within an hour of using Chlorhexidine mouthwash.*
    - Clotrimazole pessaries (500 mg) can be sucked as “lozenges” once daily for 5 days.
    - Miconazole 2% oral gel (Daktarin®). Apply b.d./t.d.s. for 10 days.
    - Apply miconazole gel/clotrimazole cream (1%) t.d.s. to angles of mouth for angular cheilitis.
    - Itraconazole suspension, 100-200 mg daily as swish and swallow.
    - Amphotericin B lozenges (Fungizone®), 10 mg, q.6.h. for 10 days.

#### **Systemic:**

- Consider if no response after 1-2 weeks of topical treatment; possible resistance; poor topical compliance or widespread disease.
- **Fluconazole** tabs/suspension, 50-100 mg p.o. daily for 7 days. (Start with 100-200 mg stat in severe cases). For systemic candidiasis use 150–200 mg daily.
- Itraconazole tabs 100-200 mg p.o. daily for 7 days.
- Ketoconazole tabs/suspension, 200-400 mg p.o. daily for 7days.
- Recurrent candidiasis in HIV/AIDS may require prophylactic treatment with fluconazole 50 mg daily p.o.
- *Azoles are CYP 450 inhibitors. Drug interactions may occur in ART.*
- *Overuse of azole drugs may result in drug resistance.*
- *In children under 2 years of age, topical anti-fungals, especially miconazole gel, should be the first-line of approach.*
- **Analgesia:**
  - Use NSAID-containing rinse (Andolex®/Andolex C®) 15 ml, t.d.s., or morphine rinse if pain severe - rinse for 2 min, 5-6 times daily. Don't swallow). (See **Mouth Care**).
  - Treat pain systemically according to the WHO Pain Ladder.

### **Review assessment and management:**

- Assess and review mouth care regularly.

### **Oral Herpes Simplex**

Common oral viral infection usually caused by HSV-1. Herpes Simplex infection is often more severe and complicated in immune-compromised patients (HIV, leukaemia and after chemotherapy or head/neck radiation therapy).

Reactivation of latent infection is common.

Lesions are usually painful and may be associated with an early tingling sensation and a viral prodromal phase of malaise, fever and debilitation. Vesicles form within about 24 hours and subsequently rupture, ulcerate and scab. They may coalesce. Lesions resolve in a couple of weeks,

but may persist and progress locally in immune-compromised patients. Extensive mucocutaneous involvement may compromise eating, nutrition and patient morale. Secondary bacterial infection may occur.

Common sites for lesions are the gums, hard palate, borders of the lips and adjacent skin. Herpes labialis ("cold sores" on the lips) can usually be managed symptomatically in immune-competent patients.

**Risk Factors**

- Xerostomia.
- Immune-compromised patients.

**Key areas for assessment:**

- Clinical features of HSV infection (*prodrome and ulcers preceded by vesicles*).
- The prodrome may be masked in debilitated patients
- Pain
- Nutritional status.

**Management:** see Ulcer management, below.

- Aciclovir cream applied early (vesicular stage) to lesions.
- If non-resolving, use oral antivirals:
  - **Aciclovir** 200 mg q.i.d for 5 days.
  - **Famciclovir** 250 mg t.d.s. for 5 days.

Intravenous antivirals may be required for infections not responding to oral treatment

**Review assessment and management:**

- Assess and review mouth care regularly.

**Malignant Ulcers**

Local tumour spread and invasion, metastatic spread of tumours or secondary malignancies.

- Debilitating and distressing.
- May be malodorous, especially if infected.
- Interfere with activities of daily living (speech, eating, swallowing).
- Socially isolating (appearance, drooling, odours).
- Pain may be severe, with many different physical components, and psycho-social factors.

**Key areas for assessment:**

- Interference with activities of daily living.
- Nutritional status and diet.
- Oral hygiene.
- Wound care.
- Pain.
- Psycho-social implications.

**Management:** see Ulcer management, below.

- Apply appropriate absorptive and protective dressings.
- Pay attention to wound odour management (regular cleaning and dressings of an appropriate absorbent and odour controlling nature).
- Total care with multidisciplinary support is essential.

**General Principles of Management of Mouth Ulcers:**

### **Explanation to patient and family:**

- Acknowledgement of pain.
- Reassurance.
- Stress the importance of regular, good oral care and management of lesions.

### **Correct reversible factors:**

- Encourage good oral hygiene.
- Act promptly to control pain, prevent secondary infections and speech/swallowing complications.
- HAART for HIV positive patients.

### **Non-pharmacological intervention:**

- Regular oral care
- Management of dry mouth (Dry Mouth/ Xerostomia).
- Soft, lubricated diet.
- Avoid acidic or citrus food/drink.
- Saline or saline-sodium bicarbonate mouth rinses p.r.n.
- Pain management techniques (relaxation, distraction techniques).
- Regular cleaning and dressing of ulcers, as appropriate.
- Dressings of an appropriate absorbent and odour controlling nature.

### **Pharmacological interventions**

Principles – for pain management details see section on Oral Pain, above.

- Protection (coating):
  - Rinse and expel q.4.h. with:
    - Sucralfate suspension (Ulsanic®) 15-30 ml, q.4.h.
    - Diphenhydramine elixir-kapectate (1:1).
    - Equal parts of diphenhydramine elixir, aluminium hydroxide antacid and viscous 2% lidocaine.
    - Carmellose paste, Sucralfate, Gelclair (Alocclair®), apply p.r.n.
- Mouthwashes:
  - Use water/saline rinses as required.
  - Chlorhexidine, Dentyt pH® or povidone iodine (1%) (Betadine®) mouthwashes 10-15 ml b.d., after meals.
  - Dilute with water if severe pain.
- Analgesia: (see Mouth Care, Oral Pain).
  - Topical:
    - Mouth rinse/spray/gel: Benzocaine or 2% lidocaine, p.r.n.
    - NSAID mouth rinses: benzydamine (Andolex®), 15 ml t.d.s.
    - Choline-salicylate gels: Teejel®, Bonjela®) apply p.r.n.
    - Morphine mouth wash: (rinse, don't swallow), p.r.n.
    - Miracle Mouth Paint/Paste (Uganda). Can add an amp of morphine sulphate(15 mg) and /or lidocaine, if required.
  - Systemic:
    - Treat pain as per WHO Pain ladder (**morphine** if severe).
- Steroids:

*Caution: Steroids exacerbate CMV/Herpes ulceration.*

  - Triamcinolone acetate 0.1% (Kenalog/orobase®), p.r.n.
  - Prednisone: dissolve a 2.5 mg tab on affected area, b.d.

- Beclomethasone spray: 1-2 puffs b.d on lesion.
- Dexamethasone gargle (0.5mg /20 ml normal saline).
- Oral prednisone if lesions are very large or there is oesophageal involvement.
- **Antibiotics:**
  - Antimicrobial mouthwashes: (see above)
  - Antivirals (**Herpes**):
- Aciclovir cream applied early (vesicular stage) to lesions.
- If non-resolving, use oral antivirals:
  - **Aciclovir** 200 mg q.i.d for 5 days.
  - Famciclovir 250 mg t.d.s. for 5 days.

Intravenous antivirals may be required for infections not responding to oral treatment.
- Miracle Mouth Paint (Uganda)
  - Use as mouthwash or paint onto ulcers. Can add an amp (15 mg) of morphine.
- Metronidazole gel/rinses can be made by mixing crushed **metronidazole** tablets with KY gel or mouthwash (approximately one 400mg tablet per 5 ml volume). Useful for malignant ulcers.
- 1% topical metronidazole paste. Make own with UEA cream and **metronidazole** (as above). Useful with absorbent wound dressings for malodorous ulcers and wounds.
- Tetracycline mouthwash for resistant ulcers.
- Consider systemic **metronidazole** to control foul-smelling anaerobic infections and associated halitosis: 500 mg q.12.h. or 1g P.R.
- Persistent, severe ulcers may respond to thalidomide 50-100 mg nocte. Use under specialist guidance.
- Treat secondary infection promptly and appropriately.

#### **Systemic Analgesia:**

- Treat according to WHO Pain Ladder: Severe pain not responding to paracetamol or NSAIDS requires addition of appropriate opioid analgesics.
  - *Give analgesia parenterally, transdermally or rectally if swallowing is not possible.*
  - Consider ketamine for persistent neuropathic pain. (Specialist guidance).

#### **Review assessment and management:**

- Assess and review mouth care regularly.
- Ensure adequate pain control.
- Treat secondary infections promptly and appropriately.

#### **Involve the Multidisciplinary Team**

- Nursing care, family education and involvement.
- Deal with Total Pain.
- Dietary and nutritional advice.

#### **Referral**

- Oral hygiene and dental care where appropriate.
- For ART where appropriate.

### **3.6 Oral Problems of HIV / AIDS and Immune-compromised Patients:**



Oral manifestations include fungal, viral and bacterial infections and opportunistic cancers. Oral candidiasis is common.

**Cytomegalovirus Infection:**

HIV patients with CD4 counts <50-100/ml are at risk for reactivation of latent CMV infection. Oral CMV infection presents as large erythematous ulcers and gingivitis.

**Management:**

- HAART as appropriate, in HIV patients.
- Consider ganciclovir treatment (for life - specialist guidance).

**Epstein - Barr virus (EBV) Infection: (oral hairy leucoplakia)**

Oral infection associated with immunosuppression (low CD4 count), presenting as oral hairy leucoplakia, with vertically corrugated white hyperkeratotic lesions on the lateral border of the tongue, are asymptomatic and cannot be wiped off. Lesions may disappear, especially with HAART.

**Management:**

- HAART, as appropriate, in HIV patients.
- **Cotrimoxazole** prophylaxis to prevent other opportunistic infections.
- **Tretinoin gel** (0.025-0.05%) applied b.d. to exfoliate lesions.
- **Aciclovir** 800 mg q.i.d. for 10 days, if cosmetically bothersome.

**Necrotising Ulcerative Periodontitis**

Localised or generalised destruction of the alveolar bone and periodontal tissues supporting the teeth in severely immune-compromised patients. Associated with rapid bone loss, deep-seated pain, erythematous and bleeding gingivae, halitosis and tooth mobility. Recurrences are common.

**Management:**

*N.B. Systemic antibiotics and dental care are required - mouthwashes alone are insufficient.*

**Non-Pharmacological:**

- Brush teeth with soft toothbrush. Floss well.
- Saline mouthwashes after meals.
- Chlorhexidine or Dentyl pH® mouthwashes: 10-15 ml b.d.-t.d.s.
- Urgent referral for dental curettage and debridement of necrotic tissue, plaque removal and splinting of mobile teeth,
- Regular dental monitoring (2-3 weekly),

**Pharmacological:**

- Systemic antibiotics: **metronidazole** 400 mg t.d.s. for 5 days or **co-amoxiclav** (375 mg t.d.s. for 5 days).
- Topical and systemic analgesia as required (WHO Pain Ladder).

**Necrotising Ulcerative Gingivitis**

Infection-related, localised or generalised destruction or necrosis of inter-dental papillae. A whitish pseudomembrane outlines the affected area. Ulceration and sloughing may occur, together with bleeding and halitosis. Bone is not involved.

**Management:**

- Antimicrobial mouthwashes (Paroex, Corsadyl or Dentyl pH), 10-15 ml, t.d.s.
- Systemic antibiotics:
  - **Metronidazole** - 400 mg t.d.s. for 5 days.
  - **Co-amoxiclav** - 375 mg t.d.s. for 5 days.
- Appropriate topical and systemic analgesia (WHO Pain Ladder).

- Urgent dental and periodontal referral (infection can progress rapidly).

### **Linear Gingival Erythema**

Atypical gingivitis, occurring in immune-compromised patients. Manifests as localised erythema, with pronounced 2-3 mm red bands in the marginal gingiva around the teeth. Lesions are usually asymptomatic. Spontaneous bleeding may occur. May be associated oral candidiasis.

#### **Management:**

- Antimicrobial mouth washes (Chlorhexidine or Dentyl pH®) 10-15 ml, t.d.s.
- Andolex-C® is an NSAID mouthwash option if inflammation is present, 15 ml t.d.s.
- Topical antifungal therapy.
- ART as appropriate, in HIV patients.
- Dental scaling.

### **Kaposi's sarcoma:**

Angiosarcomas with red-bluish macular/nodular gingival or palatal lesions that do not blanch with pressure, occurring commonly as an opportunistic neoplasm in HIV/AIDS patients with severe immunosuppression. Lesions are usually asymptomatic, but may enlarge resulting in ulceration, bleeding, super-infection and pain.

#### **Management:**

- Consider and treat reversible causes.
- HAART may promote tumour regression.

#### **Non-pharmacological:**

- Good oral hygiene - prevent super-infection.
- Water/saline mouth rinses as required.
- Plaque control.
- Radiotherapy.
- Surgical or laser excision.

### **Pharmacological:**

- Regular mouth washes to assist with bacterial and fungal control: Chlorhexidine (Paroex®, Corsadyl®), Dentyl pH® or povidone iodine (1%) (Betadine®) – 10-15 ml, b.d. – t.d.s.
- Topical and systemic analgesia as required (WHO Pain Ladder).
- Intra-lesional chemotherapy (vinblastine).  
Systemic chemotherapy and/or interferon, if disseminated (oncology referral).

### **Non-Hodgkin's Lymphoma**

Oral presentation: rapidly growing soft, tumour-like masses causing pain and interference with eating and speaking.

Associated with severe immune-suppression in end stage HIV disease. Biopsy confirms the diagnosis.

#### **Management:**

- Regular mouth washes to assist with bacterial and fungal control: Chlorhexidine (Paroex®, Corsadyl®), Dentyl pH® or povidone iodine (1%) (Betadine®): 10-15 ml, b.d. – t.d.s.
- Radiotherapy.
- Chemotherapy.
- Topical and systemic analgesia as required (WHO Pain Ladder).

- Surgical referral and reduction.

**At all stages of management consider the involvement of the interdisciplinary team to mitigate the impact of oral problems on social life, nutrition, quality of life and general health.**

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