## Oxfordshire Adult Palliative Care Guidelines

### Section 2: Symptoms other than Pain

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### Adapted From/Replaces:
Berkshire Adult Palliative Care Symptom Control Guidelines Paul Howard, Cathy Goddard

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2

### For distribution to:
All clinical staff providing palliative care to patients in primary and secondary care in Oxfordshire

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Related guidance

- Oxfordshire Adult Palliative Care Guidelines, Section 1: Pain
- Liverpool Care Pathway Prescribing Guidance describes:
  o End of life care symptom management
  o Prescribing syringe pumps and subcutaneous medication
- Syringe pump policy describes:
  o Administering medicines with syringe pumps
- Further medication guidance is available within local NHS trusts:
  o OUH Intranet palliative care site
  o OUH intranet pharmacy site
Who are these guidelines intended for?

Which patients?
- These palliative care guidelines are intended to help alleviate symptoms in adults with advanced life-limiting illnesses, including both malignant and non-malignant conditions.
- Whilst some of the principles of symptom control presented here are applicable to adults with potentially curable illnesses, there are often important differences. The likely causes, underlying pathophysiology and therapeutic aims may differ, making these guidelines inappropriate for use in the non-palliative setting.

Which healthcare professionals?
- These guidelines are aimed at all members of the multi-disciplinary healthcare team, regardless of specialty and profession, providing palliative care wherever it is required (in hospitals, nursing homes or the patient’s own home).
- They are designed to aid decision making by experienced professionals without specialist palliation training. Palliative Care Specialists sometimes recommend drugs or doses not described here. If in doubt, specialist palliative care advice is available 24 hours a day.
- They are not intended to discourage professionals from seeking specialist advice if they are uncertain or outside of their usual experience.

What knowledge, on the part of the professional, is assumed?
It is assumed that the professional using these guidelines understands the overall clinical context (for example, whether care is aimed at palliation or cure; the degree of urgency with which to act; the clinical questions posed in the guidelines).

Where medication is recommended, the usual skills of a prescriber are assumed, including that:
- They are familiar with disease states (e.g. renal impairment) and other concurrent medication that might affect the use or dose of the suggested medication. Details of these drug- and disease-interactions are found in the British National Formulary or Summary of Product Characteristics and not replicated here. It is assumed that prescribers are able to make appropriate adjustments to the doses suggested in these guidelines in the light of such circumstances. If in doubt, discuss with a pharmacist or palliative care specialist.
- They practice a shared decision making (concordance) approach to making treatment decisions, combining their own experience and clinical knowledge with the patient’s priorities and wishes.

In palliative care, medications are often used outside of their marketing authorisation (product licence). These guidelines are intended to give a clear indication of where such use is “generally accepted” and where use should be overseen by a specialist (“amber/red” drugs are listed at the end of each section).

Where to get advice and further information

<table>
<thead>
<tr>
<th>Patients location</th>
<th>Daytime weekdays advice</th>
<th>Out of hours advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxfordshire community setting</td>
<td>Sobell triage 0800 2761484 or 01865 857036</td>
<td>Sat/sun triage 0900-1600 otherwise as below</td>
</tr>
<tr>
<td>John Radcliffe, Churchill and NOC hospitals</td>
<td>JR 21741 Churchill/NOC 23585</td>
<td>Sobell ward 25870/3</td>
</tr>
<tr>
<td>Horton Hospital</td>
<td>24195 or bleep 374</td>
<td>Katharine House Hospice 01295 811866</td>
</tr>
</tbody>
</table>
1.1 Breathlessness

Key points

1. Treating the underlying cause offers the best relief
2. **In fitter patients** (e.g. walking, but with exertional breathlessness) the emphasis is on:
   - Optimising underlying disease control and concurrent contributors (e.g. anaemia)
   - Rehabilitation (attention to nutrition, encouraging exercise and coping strategies, use of formal programs such as the pulmonary rehabilitation program for COPD)
   - Treating co-existent anxiety or panic disorders (e.g. with SSRIs or benzodiazepines)
3. **In less fit patients** (e.g. breathless at rest or on minimal exertion):
   - Opioids are helpful
   - Co-existent anxiety and panic still requires separate treatment

Main options

1. **Opioids** – effective for breathlessness at rest/on minimal exertion. They do not improve exercise tolerance in fitter patients with exertional breathlessness
2. **Anxiolytics** – effective for co-existent anxiety and panic
   - Benzodiazepines where rapid onset needed (e.g. short prognosis or for p.r.n. treatment of panicky breathless attacks)
   - SSRIs where prognosis sufficient (delayed onset, but avoids the cognitive and falls risks of benzodiazepines).
3. **Oxygen** – helpful for hypoxic patients (not appropriate for non-hypoxic patients who usually obtain the same relief from increased airflow; advice to use electric fans/open windows in conjunction with breathing exercises. See below)
4. **Physiotherapy referral** – particularly facilitating rehabilitation in fitter patients (see above)

Overview of sections:

- Treatable causes
- Simple advice aimed at improving self-management
- Opioids for breathlessness
- Medication for secondary anxiety and panic
- Oxygen therapy in palliation
- Nebulisers in palliation

A. Treatable causes

Examination, with further investigations if appropriate (e.g. full blood count, chest X ray), may reveal treatable underlying contributors:

<table>
<thead>
<tr>
<th>In any patient</th>
<th>In patients with malignancy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>Pleural effusion (if well enough to consider drainage +/- pleurodesis, d/w a respiratory physician)</td>
</tr>
<tr>
<td>Bronchoconstriction</td>
<td>Superior vena cava obstruction (<strong>section 4.3</strong>)</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Lymphangitis carcinomatosa (d/w an oncologist)</td>
</tr>
<tr>
<td>Heart failure¹</td>
<td>Bronchial obstruction (<strong>section 4.4</strong>)</td>
</tr>
<tr>
<td>Lower respiratory tract infection</td>
<td>Pericardial effusion (d/w a cardiologist)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td></td>
</tr>
</tbody>
</table>

¹ Consider SC furosemide for those with problematic IV access: see ‘SC administration’ section of the LCP

Consider **multiple pulmonary emboli** in patients with breathlessness disproportionate to, or unexplained by, their underlying disease, chest examination and X ray:

- Out of hospital: request hospital investigation if appropriate
- In hospital: request a CT Pulmonary Angiogram: If in doubt, discuss with a respiratory physician or radiologist
B. Simple advice aimed at improving self-management

Breathlessness may respond to careful explanation and simple advice [Bredin 1999].

- **Breathing exercises** (nurse specialist or physiotherapy referral)
- **Increased airflow** (opening windows, electric fans)
- **Encourage exercise and good nutrition if appropriate**: In fitter patients, where muscular deconditioning is a contributor, advise gentle exercise until mildly tired and breathless with a view to gradually increasing exercise capacity over time
- **Optimising independence** by providing appropriate aids/assistance at home (e.g. by involving an occupational therapist)

C. Opioids for breathlessness

Opioids are effective for breathlessness at rest in both cancer and advanced non-cancer conditions (COPD, pulmonary fibrosis and heart failure) [Chua 1997, Jennings 2002, Johnson 2002, Abernethy 2003, Allen 2005, Viola 2008]. They can generally be used without detrimental effects on carbon dioxide levels or length of life [Kamal 2012], although additional caution is required in patients already retaining carbon dioxide – consider seeking advice from a respiratory or palliation specialist. Opioids do not improve exercise tolerance [Jennings 2002] and should generally not be used for exertional breathlessness.

For the palliation of breathlessness at rest:

- If opioid naïve: commence **morphine sulphate** liquid 2.5mg 4 hourly PO or morphine sulphate MR tablets 5mg b.d. PO
- If already on opioids and not toxic, increase dose of opioid as with pain titration
- Add **anxiolytic** (see below) if anxious/panicky, or if not responding to opioids alone

If unable to manage oral opioids (e.g. terminal breathlessness)

- If opioid naïve: give morphine sulphate 5-10mg over 24 hours via SC syringe pump plus 2.5mg p.r.n. 2-4 hrly SC
- If already on opioids, and not toxic, increase dose of opioid as with pain titration
- Add midazolam 5-15mg/24hours to the syringe pump if anxious/panicky, or if not responding to opioids alone.

D. Medication for secondary anxiety and panic

Where prognosis likely to be weeks: benzodiazepines (dependence risk is not relevant; prognosis is too short for benefit from an SSRI):

- E.g. **lorazepam** 0.5mg b.d. PO and/or p.r.n. PO or SL. Titrate as required
- Where the oral route is unavailable, consider **midazolam** 5-15mg over 24 hours via SC syringe pump plus 2.5-5mg p.r.n. SC 2-4 hourly. In patients with anxiety/panic and breathlessness, combine midazolam and morphine sulphate in a syringe pump.

Where prognosis likely to be months: SSRI (palliative care patients are vulnerable to the cognitive and balance problems of longer term benzodiazepine use)

- E.g. **citalopram** 10mg o.m. PO for 7 days then increase to 20mg o.m.
- Short term regular lorazepam may be helpful while awaiting onset of SSRI’s effect
- Lorazepam 0.5mg p.r.n. SL may be a useful adjunct for panicky breathless ‘attacks’

E. Oxygen therapy in palliation

Like any treatment, oxygen can have adverse effects (worsening dry mouth/nostrils, reinforced ‘sick role’, barrier to close contact with loved ones, hindering mobility). It should be reserved for patients most likely to benefit (especially hypoxic patients)

In hypoxic patients (oxygen saturation <92% [or presence of cyanosis if oximetry unavailable]):

- Oxygen therapy is often helpful and should usually be tried
- Start 24% or 2l/min and titrate until oxygen saturation >92% before deciding it’s unhelpful
- Safety aspects need to be discussed with patient and family (oxygen is not supplied to patients who are current smokers).
• Blood gas estimation is not usually required for optimising symptom control unless severe COPD is present (needed to detect CO₂ accumulation secondary to hypoxic drive)

In non-hypoxic patients (oxygen saturation >92%):
• Oxygen is generally not used in non-hypoxic patients. For breathlessness at rest use:
  o opioids [Kamal 2012] (Combine with anxiolytics if concomitant anxiety/panic)
• Consider palliative care team referral if relief from above measures is insufficient.

Ambulatory oxygen (i.e. portable oxygen for use during exercise and activities of daily living) is helpful for selected patients: It is accessed by referral to the respiratory team. Consider referring patients that desaturate during exercise (i.e. oxygen saturation fall of ≥4% to a value <90%). However, it is unhelpful for patients that do not desaturate or are confined to the house (conventional home oxygen equipment may be more appropriate) [Bruera 2003].

Obtaining oxygen
• All health care professionals can request a static oxygen concentrator or static cylinder by faxing Part A of a Home Oxygen Order Form (HOOF) to the oxygen supplier. For further advice: HOAS Home Oxygen Advisory Service as below or Respiratory Liaison Nursing Team

Inpatient Oxygen Assessment Service

Patient may need Oxygen to go home

Refer to Home Oxygen Assessment Service (HOAS) (8-4 Mon-Fri)
CH/JR – 25472 (Bleep 5119)
Horton – 29501
Urgent – 07768707921

HOAS Review

No Oxygen needed

Help/Advice to wean Oxygen & manage breathlessness

Oxygen Required

HOAS will complete oxygen forms & order home Oxygen

HOAS Support on discharge as needed

PLEASE THINK AHEAD & REFER YOUR PATIENTS EARLY–Service available Mon – Fri 8 – 4
F. Nebulisers in palliation

- Main place is for bronchodilators (though inhalers with good technique or spacers are more portable and less expensive)
- Nebulised sodium chloride 0.9% 5ml q.d.s. is sometimes helpful for breathlessness or to aid expectoration: limited evidence, but minimal risk other than financial cost and medicalisation
- A number of other nebulised drugs have been tried without success (opioids, lidocaine, furosemide) and have no place in the routine palliation of breathlessness.[Charles 2008, Wilcock 2008]

References

1.2 Cough and respiratory secretions

Main options

1. Can the underlying cause be treated?
   - Tumour-related: consider corticosteroids or discussion with an oncologist
   - Other common causes: infection, oesophageal reflux, aspiration, post-nasal drip

   - 1st line: simple linctus 5-10ml q.d.s.
   - 2nd line: codeine phosphate 15-30mg q.d.s. PO (go straight to 3rd line if already receiving opioids)
   - 3rd line: morphine 2.5-10mg 4 hourly PO if opioid naïve (if already on opioids and not toxic increase dose of opioid as with pain titration; see pain guidelines)

3. Productive cough
   - Aid expectoration with ‘huffing’ and sodium chloride 0.9% nebulisers 10ml q.d.s.
   - Consider a physiotherapy referral to teach ‘huffing’ and other techniques.
   - For viscous sputum refractory to these measures, consider carbocisteine
   - If dying and too weak to expectorate, treat as retained respiratory secretions (aim to dry secretions with hyoscine butylbromide: see LCP)

Overview of sections:
A. Treatable causes: Cancer related
B. Treatable causes: Other
C. Carbocisteine for reduction of sputum viscosity
D. Amber drugs: Refractory cough and secretions, and specialist referral

A. Treatable causes: cancer related
The commonest cancer cause is large airway irritation from mediastinal or hilar deposits. Consider:
   - Trial of dexamethasone 8mg o.m. PO for 5 days (or SC if oral route unavailable).
     - If effective, reduce by 2mg weekly down to minimum effective dose.
     - If ineffective, reduce to 2mg for 5 days then stop.
   - Discussion with an oncologist for radiotherapy or other anti-cancer treatments

Other cancer causes include:
   - Lymphangitis carcinomatosa (discuss with an oncologist)
   - Pleural effusion (if well enough to consider drainage +/- pleurodesis, discuss with a respiratory physician)
   - Haemoptysis (section 4.6)

B. Treatable causes: other
   - Respiratory tract infection
   - Bronchoconstriction: e.g. asthma, COPD
   - Pulmonary oedema
   - Recurrent aspiration
   - Gastro-oesophageal reflux: May be worse in recumbent position/at night [Zylicz 2004a]. Consider proton pump inhibitor (higher doses are generally used e.g. omeprazole 40mg o.m. PO). Benefit may take several weeks. If no improvement, consider adding a prokinetic (e.g. metoclopramide 10mg t.d.s. PO) or referral to gastroenterology. If improvement, consider reducing to minimum effective dose after 4-8 weeks. See also NICE guidance
   - Post-nasal drip: consider trial of a nasal corticosteroid spray, e.g. beclomethasone 100 micrograms (2 sprays) into each nostril twice daily
C. Carbocisteine for reduction of sputum viscosity

- **Indications:** viscous sputum refractory to physiotherapy and nebulised sodium chloride
- **Contra-indications:** active peptic ulceration (mucolytics can disrupt gastric mucosal barrier)
- **Dose:** 750mg t.d.s PO (subsequently reducing to b.d.). Available as capsules or liquid.

D. Amber drugs: refractory cough and secretions, and specialist referral

- **Green drugs:** the above are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs:** Other off-licence, infrequently used agents are amber for these indications (i.e. initiated after discussion with, or review by, a palliation specialist):
  - Paroxetine† (cough) [Zylicz 2004b]
  - Cromoglicate sodium†, inhaled (cough) [Moroni 1996]
  - Nebulised lidocaine† (cough) [Twycross 2001]
  - Erythromycin† (bronchorrhoea) [Marom 1991, Suga 1994, Yamaguchi 1995]
  - Nebulised furosemide† (bronchorrhoea) [Twycross 2001]
  - Nebulised indomethacin† (bronchorrhoea) [Homma 1999, Kawaguchi 1994, Ichiro 2000, Tamaoki 1992]. *The parenteral preparation of indomethacin requires pH correction before nebulisation: discuss with a pharmacist*

References

### 1.3 Hiccup

1st line options for persistent hiccup either:
- **Metoclopramide 10mg t.d.s. PO** *(gastric distension is the commonest treatable cause in palliative care patients (domperidone 10-20mg t.d.s. PO is an alternative)*
- **Haloperidol 1.5mg o.d.-t.d.s PO. or chlorpromazine 25mg t.d.s. PO (licensed for hiccup)*

2nd line:
- **Baclofen** 5mg b.d. PO, increasing as required to a maximum of 10mg t.d.s. (effective in case reports and a small clinical trial [Ramírez 1992, Prodigy 2005, Guelaud 1995])

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**Overview of sections:**

A. Treatable causes
B. Non-drug approaches for hiccups of short duration
C. Amber drugs: Refractory hiccup and specialist referral

#### A. Treatable causes [CKS Hiccups guidance 2008]

Gastric distension is the commonest treatable cause.
- **Clinical features:** hiccup, bloating, early satiety, nausea, vomiting
- **Predispositions:** constipation, antimuscarinic or opioid drugs, Ca pancreas, nerve dysfunction (diabetes, spinal cord compression, retroperitoneal disease)
- **Treatment:** prokinetics (metoclopramide or domperidone: see grey box) or facilitate belching (peppermint water/peppermint oil capsules or simeticone [e.g. Maalox Plus])

Other treatable causes
- **Gastro-oesophageal reflux** (proton pump inhibitor, e.g. omeprazole 20mg o.m. PO)
- **Metabolic disturbance** (e.g. uraemia, uncontrolled diabetes, hypokalaemia)
- **Drug-induced** (benzodiazepines and corticosteroids most commonly implicated. Benzodiazepines are reported to both worsen and improve hiccup)

#### B. Non-drug approaches for hiccups of short duration

- nasopharyngeal stimulation (e.g. touching the uvula with a cotton bud)
- respiratory interruption (e.g. breathing into a paper bag, breath holding): contra-indicated in patients with respiratory compromise

#### C. Amber drugs: Refractory hiccup and specialist referral

Where hiccup fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the specialist Palliative Care Team.
- **Green drugs:** the above are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs:** Other off-licence infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation specialist):
  - **Nifedipine** [Quigley 1997]
  - **Gabapentin** for neurogenic hiccup (e.g. post-stroke, cerebral metastasis) [Petroianu 2000, Porzio 2003, Moretti 2004, Hernandez 2005]

References

1. CKS Hiccups guidance 2008: http://www.cks.nhs.uk/hiccups
### 2.1 Nausea and vomiting

#### Choosing antiemetics

<table>
<thead>
<tr>
<th>Features of gastric stasis?</th>
<th>1st line options</th>
<th>If symptoms persist</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Large volume vomits</td>
<td><strong>Metoclopramide</strong> (or domperidone, if risk of Parkinsonian effects)</td>
<td></td>
</tr>
<tr>
<td>• Nausea eased by vomiting</td>
<td><strong>Consider:</strong> Dose increase, NG tube</td>
<td></td>
</tr>
<tr>
<td>• Bloating/distension/hiccup</td>
<td>Increase GI transit to ↓ stasis</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td><strong>Palliative Care Referral</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical/toxic cause?</th>
<th>2nd line options</th>
<th>If symptoms persist</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypercalcaemia, uraemia</td>
<td><strong>Haloperidol†</strong></td>
<td></td>
</tr>
<tr>
<td>• Some drugs</td>
<td><strong>Consider:</strong> Changing to:</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>• <strong>Levomepromazine†</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other situations</th>
<th>3rd line options</th>
<th>If symptoms persist</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cause unclear or:</td>
<td><strong>Cyclizine</strong></td>
<td></td>
</tr>
<tr>
<td>• Raised intracranial pressure</td>
<td>Act on N+V final common pathway, and on vestibular system</td>
<td></td>
</tr>
<tr>
<td>• Vestibular, others</td>
<td><strong>Palliative Care Referral</strong></td>
<td></td>
</tr>
</tbody>
</table>

#### Summary of antiemetic dose and use

<table>
<thead>
<tr>
<th></th>
<th>Oral dose</th>
<th>24hr syringe pump dose</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Starting</td>
<td>Usual max</td>
</tr>
<tr>
<td><strong>1st Line Agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclizine</td>
<td>50mg tds</td>
<td>50mg tds</td>
</tr>
<tr>
<td>Domperidone</td>
<td>10mg tds</td>
<td>20mg qds</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10mg tds</td>
<td>20mg qds</td>
</tr>
<tr>
<td><strong>Haloperidol†</strong> (licensing varies) [Buttner 2004, Critchley 2001] Licensed alternatives (e.g. prochlorperazine) not tolerated SC</td>
<td>0.5-1.5mg on</td>
<td>5mg bd</td>
</tr>
<tr>
<td>Acts on CTZ (chemo-receptor trigger zone), a ‘toxin detector’, so helpful for chemical/toxic causes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **2nd Line Agents**     |               |                        |          |          |
| Levomepromazine†        |               |                        |          |          |
| Broad spectrum 2nd line agent helpful in many situations [Kennett 2004, Eisenclias 2005] Sedation and postural hypotension problematic at higher doses | 6.25mg on | 25mg on | 6.25mg | 25mg |
| Ondansetron             |               |                        |          |          |
| Helpful for chemical/toxic or gastrointestinal irritation/distension (e.g. obstruction). Only licensed for post-op and chemotherapy | 4mg bd | 8mg tds | 8mg | 16mg |
| Dexamethasone†          |               |                        |          |          |
| Broad spectrum 3rd line agent [Glare 2004] Reduce slowly if helpful, quickly if not | 4-8mg | 16mg | Give 4-8mg SC bolus o.m. (or morning and lunch) |
| Lorazepam†              |               |                        |          |          |
| For anticipatory nausea[Roscoe 2011] or if anxiety a contributor | 0.5mg p.r.n. | 1mg bd | Replace with midazolam 5-10mg |

† = Off-label indication or route, # = unlicensed product

(N.B. Can the underlying cause be addressed?)

(1st line options)

If symptoms persist
Overview of sections:
- The three main groups of nausea/vomiting problems (summarised in flow diagram above):
  - A. Gastric stasis
  - B. Chemical/toxic causes
  - C. Other situations
- Difficult problems
  - D. Refractory nausea and vomiting: a checklist
  - E. Antiemetics for patients with Parkinsonism
- F. Amber treatments and specialist referral

Current consensus guidelines are largely derived from basic pharmacology [Twycross 1998, Glare 2004]. However, open-label audit suggests that this approach is effective [Bentley 2001] and some controlled studies lend support to selection based on mechanism [Glare 2004].

A. Gastric stasis
Address underlying causes where possible (e.g. constipation, some drugs: antimuscarinics [e.g. cyclizine, hyoscine], ondansetron)

Give a prokinetic antiemetic
- **Metoclopramide** 10mg t.d.s. PO (or 30-40mg/24hrs via SC syringe pump if marked vomiting or unable to manage oral route)
- Prescribe additional metoclopramide 10mg p.r.n. PO or SC (up to 3 extra in 24 hours)

If vomiting continues and still a gastric stasis pattern (large vomits with nausea relief post-vomits):
- Could intestinal obstruction be present? ([section 2.2](#))
- If the metoclopramide is PO, change to 30-40mg/24hrs via a SC syringe pump
- If there is no colic and no evidence of extrapyramidal adverse effects, increase the metoclopramide to 60mg/24hrs and monitor for these problems
- Alternatively, offer an NG (nasogastric) tube to allow aspiration of vomitus¹
- d/w Palliative Care Team

B. Chemical/toxic cause
Address underlying causes where possible (e.g. hypercalcaemia, uraemia, drugs such as opioids)

Give an antidopaminergic antiemetic
- **Haloperidol**† (licensing varies) 0.5-1.5mg nocte and p.r.n. (up to 3 extra in 24 hours) PO (or SC if marked vomiting or unable to manage oral route)
- Alternatives include buccal **prochlorperazine** (Buccastem) 3-6mg p.r.n. b.d.

If nausea or vomiting continue:
- Stop haloperidol and start **levomepromazine**† 6.25mg nocte and p.r.n. (up to 3 extra in 24 hours) PO (or SC if marked vomiting or unable to manage oral route)
- If p.r.n.’s needed and helpful, titrate regular dose (usually up to a maximum of 25mg/24hrs)
- If p.r.n.’s unhelpful or too sedating consider:
  - Adding **ondansetron** 4-8mg t.d.s. PO or 16mg/24hrs via SC syringe pump
  - Trial of **dexamethasone** 8mg o.m. PO or SC
  - Discussing with the Palliative Care Team

C. Other situations (e.g. vestibular irritation, raised intracranial pressure, gastritis, reflux or unknown cause)
Address underlying causes where possible

¹ Ensure that all involved in the patients care have appropriate competencies to understand the therapeutic aim and safe use of the tube.

† = Off-label indication or route, # = unlicensed product
Give an antihistaminergic antiemetic:

- **Cyclizine** 50mg t.d.s. PO (or 150mg/24hrs via SC syringe pump if marked vomiting or unable to manage oral route)
- If additional p.r.n. option desired give **haloperidol†** (licensing varies) 0.5-1.5mg p.r.n. (up to 3 doses in 24 hours): haloperidol and cyclizine have complementary sites of action

If nausea or vomiting continue:
- Has gastric stasis or a treatable underlying cause been missed?
- If gastritis or reflux are suspected, commence omepazole 20mg o.m. PO
- Discontinue both cyclizine and haloperidol and start **levomepromazine†** 6.25mg nocte and p.r.n. (up to 3 extra in 24 hours) PO (or SC if marked vomiting or unable to manage oral route)
- If p.r.n.’s unhelpful or too sedating consider:
  - Adding **ondansetron** 4-8mg t.d.s. PO or 16mg/24hrs via SC syringe pump SC
  - Trial of **dexamethasone** 8mg o.m. PO or SC
  - Discussing with the Palliative Care Team

**Difficult problems**

**D. Refractory nausea and vomiting: a checklist**

- **Right antiemetic?** E.g. cyclizine and ondansetron exacerbate gastric stasis, while metoclopramide has little effect on vestibular-irritation nausea. See flow diagram above
- **Right route?** In refractory situations, the antiemetic is usually needed IV or SC initially (e.g. an antiemetic SC syringe pump)
- **Sufficient time?** Decide on the appropriate choice (see flow diagram) and then give for 48 hours before changing (unless adverse effects occur)
- **Interacting drugs?** E.g. prokinetics (metoclopramide and domperidone) act via acetylcholine and are therefore less effective if antimuscarinics (e.g. hyoscine, cyclizine) given concurrently
- **Psychosocial distress?** Fear and anxiety can exacerbate nausea as well as pain
- **Anticipatory component?** A common response to protracted nausea. Consider relaxation therapies or lorazepam [Roscoe 2011]

**E. Antiemetics for patients with Parkinsonism**

Many antiemetics are antidopaminergics with the potential to exacerbate Parkinsonism
- Likely to be a problem: haloperidol, metoclopramide, prochlorperazine, levomepromazine
- Generally OK but problems occasionally occur: domperidone, ondansetron, cyclizine

<table>
<thead>
<tr>
<th>Situation</th>
<th>1st line</th>
<th>2nd line</th>
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<tbody>
<tr>
<td>Gastric stasis</td>
<td>Domperidone</td>
<td>d/w Palliative Care Team</td>
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<tr>
<td>Chemical/toxic cause</td>
<td>Domperidone</td>
<td>Ondansetron or dexamethasone</td>
</tr>
<tr>
<td>Other situations</td>
<td>Cyclizine</td>
<td>Ondansetron or dexamethasone</td>
</tr>
</tbody>
</table>

If in doubt, d/w Palliative Care Team

**F. Amber drugs: Refractory symptoms and specialist referral**

- Where nausea or vomiting fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the specialist **Palliative Care Team**.
- **Green drugs**: the above are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs**: Other off-license, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a **palliation specialist**):
  - **Erythromycin†** (PO; as prokinetic) [Maganti 2003, Sturm 1998]

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References

2.2 Gastrointestinal obstruction

The palliation of obstruction is particularly difficult.

<table>
<thead>
<tr>
<th>PARTIAL OBSTRUCTION WITHOUT COLIC</th>
<th>PARTIAL OBSTRUCTION WITH COLIC/ COMPLETE BOWEL OBSTRUCTION</th>
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</thead>
<tbody>
<tr>
<td><strong>Promoting resolution of obstruction</strong></td>
<td><strong>Promoting resolution of obstruction</strong></td>
</tr>
<tr>
<td>1st line (prokinetic drugs):&lt;br&gt;• Metoclopramide s/c– starting at 30-60mg over 24 hours, then increasing to a maximum of 100mg in 10-30mg increments.&lt;br&gt;• Reduce or stop if patient develops colic.&lt;br&gt;• Docusate up to 500mg in 24 hours.&lt;br&gt;• PR glycerine and bisacodyl suppository if indicated. (NB: avoid suppositories in patients with neutropenia or low platelets).&lt;br&gt;<strong>If no response after 24 hours:</strong>&lt;br&gt;• Add dexamethasone phosphate 8mg OD s/c or IV (may take up to 5 days to have effect)&lt;br&gt;<strong>Control of nausea and vomiting</strong></td>
<td><strong>Promoting resolution of obstruction</strong>&lt;br&gt;• Dexamethasone phosphate 8mg OD s/c or IV for 5 day trial.&lt;br&gt;• Docusate in partial obstruction with colic– maximum 100mg BD PO. Discuss with senior colleague re. use of laxative in complete bowel obstruction.&lt;br&gt;• Glycerine suppositories if PR intervention indicated. (NB: avoid suppositories in patients with neutropenia or low platelets).&lt;br&gt;<strong>Control of nausea and vomiting</strong>&lt;br&gt;• Stop metoclopramide as may add to colic&lt;br&gt;• 1st line: Cyclizine 150mg s/c over 24 hours in syringe-driver titrating up to 25mg.&lt;br&gt;• If metoclopramide is ineffective, stop and switch to s/c levomepromazine starting at 5mg nocte, titrating if indicated. If needing doses &gt;10mg place levomepromazine in 24 hour syringe-driver.&lt;br&gt;• Use PRN levomepromazine 2.5-5mg s/c for breakthrough nausea.&lt;br&gt;<strong>Control of pain and discomfort</strong>&lt;br&gt;• Stop metoclopramide as may add to colic&lt;br&gt;• 1st line: Cyclizine 150mg s/c over 24 hours in syringe-driver with PRN s/c haloperidol 0.5-1.5mg TDS. If necessary, haloperidol can be added to syringe driver at 1.5-5mg over 24 hours.&lt;br&gt;• 2nd line: Stop cyclizine and haloperidol and switch to s/c levomepromazine starting at 5mg nocte. If needing doses &gt;10mg place in 24 hour syringe-driver titrating up to 25mg.&lt;br&gt;<strong>If large volume vomits consider:</strong>&lt;br&gt;• Hyoscine butylbromide 60mg s/c over 24 hours, titrating to max of 120mg OR&lt;br&gt;• Octreotide (250-500 micrograms s/c over 24 hours up to a maximum of 750 micrograms)&lt;br&gt;• Consider ryles tube or venting gastrostomy.</td>
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<td><strong>Control of pain and discomfort</strong></td>
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| Hydration and Nutrition | Hydration and Nutrition<br>• IV hydration must be considered carefully on a case by case basis. If required, 1-1.5 litres/24 hours is often sufficient. Parenteral fluids may be a barrier to returning home and can increase gastric secretions.<br>• Regular mouth care, ice chips, water spray and saliva substitutes can provide symptomatic relief of dry mouth.<br>• May be appropriate to consider TPN if patient has a prolonged prognosis and/or is receiving active treatment (surgery/chemotherapy) that may reverse the underlying malignant cause. |

Adult Palliative Care Symptom Control Guidelines, Oxfordshire – February 2013
Gastric outflow obstruction

1. Consider bypass surgery and stenting: if in doubt discuss with surgeons.
2. If very distressed by vomiting, offer a nasogastric tube to allow aspiration while trying medication below.
3. Aim to re-establish transit through the pylorus (if imaging available and suggests complete occlusion, add steroids from the outset: metoclopramide only helps if obstruction is partial)
   - Trial of metoclopramide 30mg via 24 hour SC syringe pump
   - After 48hrs: if partial improvement, increase metoclopramide to 60mg (monitor for extrapyramidal problems and colic), otherwise add dexamethasone 8mg o.m. SC
4. If nauseous between vomits add levomepromazine 6.25mg o.d. SC (centrally acting antiemetics [e.g. cyclizine, levomepromazine, ondansetron] won’t affect the vomiting itself)

Overview of sections:
A. Bowel obstruction
B. Gastric outflow obstruction
C. Amber drugs: refractory obstruction and specialist referral

A. Bowel Obstruction

Consider disease modification
- Options include surgery, chemotherapy and stenting.
- Do not over-rely on prognostic indicators (e.g. single site of obstruction, absence of rapidly accumulating ascites): results are conflicting and based on mortality not symptom control [Feuer 2000]. If in doubt, discuss with surgeons and oncologists.
- Where disease modification is not possible, proceed to the options described below:

If there is no colicky pain, the aim is to ‘re-start’ the bowel by stimulating peristalsis:
- Stop/minimise anti-motility drugs (e.g. antimuscarinics, ondansetron)
- Commence metoclopramide†, sodium docusate and rectal measures (enemas), as described in flow diagram above:
  - Metoclopramide† aims to stimulate peristalsis. Its use is acceptable in obstruction where the aim is palliation [Twycross 2009, Isbister 1990] Discontinue if colic occurs
  - Sodium docusate aims to soften stool allowing movement through a narrowed lumen. Other softeners are avoided: they increase stool volume via osmosis and so worsen intestinal distension
  - Dexamethasone improves nausea and reduces peri-tumour oedema (increasing resolution rates from ~1/3 to ~2/3 [Feuer 1999])

If there is colicky pain, the aim is to ‘rest’ the bowel (colic implies peristalsis against an immovable obstruction. Stimulating further peristalsis would be ineffective and worsen the colic)
- Commence hyoscine butylbromide and levomepromazine as described in the flow diagram above. Individual drugs are titrated according to symptoms:
- It is important to distinguish nausea from vomiting:
  - Vomiting is controlled with hyoscine butylbromide and/or a nasogastric tube. Hyoscine butylbromide is as effective as octreotide (amber) in allowing good symptom

1. Ensure that all involved in the patients care have appropriate competencies to understand the therapeutic aim and safe use of the tube

† = Off-label indication or route, # = unlicensed product
control without the need for a nasogastric tube [Ripamonti 2000]. Neither reduces the vomiting of ingested food or drink: this can only be removed mechanically (i.e. by a nasogastric tube). Conventional antiemetics (e.g. cyclizine, ondansetron, prochlorperazine) will not help vomiting in a patient with obstruction

- **Nausea** in between vomits is controlled by levomepromazine. If nausea persists, consider adding dexamethasone or discussing with the Palliative Care Team.

- **Pain**
  - **Hyoscine butylbromide** also reduces *colicky pain* (by suppressing peristalsis)
  - Distinguish colic from continuous background pain (treated initially with opioids)

- **Resolution of obstruction.** The patient’s general condition, wishes and duration of obstruction affect the likelihood that the bowel can be ‘restarted’. Where this is the aim, use docusate +/- corticosteroids alongside the above measures. If in doubt, discuss with the Palliative Care Team
  - **Sodium docusate** aims to soften stool allowing movement through a narrowed lumen. Other softeners are avoided: they increase stool volume via osmosis and so worsen intestinal distension
  - **Dexamethasone** reduces peri-tumour oedema (increasing resolution rates from ~1/3 to ~2/3 [Feuer 1999])

**B. Gastric outflow obstruction**

- Consider surgical referral in all patients. Symptoms of high obstruction can be difficult to control pharmacologically. Options include bypass surgery and stenting
- It may be helpful to characterise the nature of the obstruction with a contrast swallow: prokinetics are unlikely to help if the obstruction is complete
- Use **metoclopramide +/- dexamethasone** as described in ‘key points’ above
- Centrally acting antiemetics (e.g. cyclizine, levomepromazine, ondansetron) are unhelpful for vomiting in this situation (but should be considered if prominent nausea between vomits)

**C. Amber drugs: Refractory obstruction and specialist referral**

- Where obstruction fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the specialist Palliative Care Team
- Where there is doubt about the place of active treatment, discuss with surgeons and/or oncologists
- **Green drugs:** the above are “accepted uses” and may be initiated by non-specialists for the indications described
- **Amber drugs and other approaches:** Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation specialist):
  - **Venting gastrostomy:** gastrostomies and jejunostomies can perform a similar function to a nasogastric tube. Successful palliation is described (though in teams with particular expertise in their placement and use) [Brooksbank 2002, Piccinni 2005]. Specialist evaluation is advised.
  - **Octreotide** [Ripamonti 2000]
  - **Long-acting octreotide:** Efficacy in bowel obstruction appears variable [Matulonis 2005]. Use under specialist guidance only in patients responding well to octreotide and not requiring a syringe pump for other medication, particularly if finding the pump especially limiting, or running out of sites for subcutaneous cannulation

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**References**

2.3 Mouth Problems

Management of oral symptoms

Principles of care:
People with advanced disease are very likely to experience oral symptoms.
Oral symptoms are a significant source of distress. Distress may be due to pain, discomfort when eating, swallowing or speaking, infection, halitosis, and the psychosocial impact of symptoms.

All patients should have enquiry about oral symptoms. Contributing factors to oral symptoms are many. They include: weakness, fatigue, depression and loss of ability to carry out own oral care; side effects of medicines; hyposalivation; use of oxygen; radiotherapy and chemotherapy; tumour in the mouth; co-morbidities such as diabetes.

The evidence base for management of oral symptoms is not conclusive. Management of symptoms is based on: patient's individual preference, clinical experience and guidance from recent studies; the following factors should also be taken into account: prognosis, whether patient carries out own care or needs nursing care, dental health, conscious level, and whether the patient can swallow safely.

All patients should have regular routine oral care. The aim of oral care is to maintain a moist, clean and comfortable mouth, and to identify and manage problems as they arise. Management of nausea may be required to help patients tolerate oral care.

In the last days/hours of life: regular oral care is important to maintain the comfort and dignity of the patient, and also has a role in reassuring family members that attentive care is continuing.

Products used in oral care which are not "medicines": in the in-patient setting it is suggested that products are prescribed on the medicine chart to indicate multi-disciplinary agreement and consistency regarding use.

Management of particular problems:

1. Dry mouth (xerostomia):
   - Review whether any medicines which cause dry mouth can be discontinued; consider humidification of oxygen if using.
   - Saliva stimulants (better to stimulate patient’s own saliva than substitute if possible): any food or drink stimulates salivation; drinks such as bitter lemon, or apple juice may be particularly helpful; proprietary pastilles (Salivix); sugar free chewing gum; pilocarpine 5-10mg tds if salivary glands are working - weigh benefit against side effects. Start with 5mg tds with meals. Can use eyedrops (4%) orally: 2-3 drops p.o tds.
   - Saliva substitutes: water – frequent sips, or other drinks; ice; artificial saliva spray p.r.n and prior to eating (be aware that Saliva Orthana contains porcine mucin; Glandosane is non-porcine but has lower pH so not good for teeth in longer term; Salivese is pH neutral, and non-porcine); artificial saliva gel (Biotene Oralbalance is pH neutral and non-porcine).
   - Protect and retain moisture in lips: use Vaseline/soft paraffin; if using oxygen, use water based gel eg KY, optilube.
   - Other measures: Moisten food with gravy/sauces. Acupuncture may have a role in longer prognosis, if there is access to complementary therapies.

2. Dirty mouth (coated tongue, debris on teeth):
   - Remove debris: regular mechanical cleaning by patient or carer (clean tongue, mucosa and teeth with toothbrush or foam sticks and toothpaste); vitamin C tablet ¼ on tongue qds (effervesces and lifts off coating); pineapple (contains ananase, a proteolytic enzyme which breaks down coating on tongue.)
   - Chlorhexidine: (anti-bacterial; prevents plaque building up on teeth and minimises gum disease); use twice daily diluted as a rinse (can be diluted in warm water to minimise stinging caused by alcohol component), or delivered on foam sticks, or as a gel.

3. Oral candida (may affect tongue, mucosa, palate and oesophagus):
   - Treatment: Fluconazole 50 mg od for 7 days then review and consider further 7 days; fluconazole 150 mg stat (useful option if patient has short prognosis and will soon lose ability to swallow); nystatin oral solution (1ml 4 or 5 times/day for 10 days) is second line treatment to fluconazole but can be useful if patient cannot swallow capsules or absorb from GI tract – but needs to be able to manage to rinse and hold nystatin in mouth; miconazole gel (Daktarin gel) if no gag reflex. Be aware that chlorhexidine de-activates nystatin.
   - Send swabs if candida persists: may be a different organism.
   - Scrub and soak dentures daily: soak overnight in chlorhexidine to ensure eradication of candida alongside oral treatment; rinse well to avoid deactivating nystatin in the patient’s mouth.
4. Painful mouth (ulcers or generalised soreness):
   - **Treatment of ulcers:** Hydrocortisone oromucosal tablets 2.5mg qds up to 5 days – place at the site of the ulcers (Corlan Pellets).
   - **Send swabs if ulcers persist:** consider if herpes or other organism present; a non-healing ulcer may be a tumour.
   - **Pain relief:** Benzydamine (Difflam) has an anti-inflammatory, analgesic and anti-microbial effect: available as a rinse or spray; rinse with dispersible diclofenac 50 mg tds, or dispersible paracetamol 1 g qds; Bonjela (choline salicylate) can be placed on ulcers to relieve pain. For generalised soreness consider if role for Dr. Venning’s solution (nystatin and lidocaine).
   - **Dentures:** pain and soreness may be related to specific problems with dentures – arrange review with dentist if prognosis allows.
   - **Other measures:** Take drinks via a straw to reduce contact of liquids with painful areas; avoid food and liquids which may sting – including oromorph which is alcohol based; alternatives to oramorph include oxynorm liquid which is not made with alcohol, or Sevredol (morphine) tablets.

5. Tumour in oral cavity:
   - **Mechanical removal of debris:** If not able to brush/clean with toothbrush or foamstick, rinse or irrigate regularly with saline rinse (may need to use oral syringe to rinse), or water, which may be warmed.
   - **Control of infection:** Metronidazole systemically controls anaerobic organisms, so reducing odour and exudate; other antibiotic treatment may be needed particularly if there is erosion of bone.
   - **Pain management:** Consider measures listed above; systemic management of pain may require strong opiates and neuropathic agents.

6. Stomatitis or oral mucositis (painful inflammation, ulceration, and vulnerability to infection caused by radiotherapy or chemotherapy):
   - **Keep clean and moist:** Regular and frequent rinses (warmed saline)
   - **Pain management:** Topical analgesia (see previous section); systemic analgesia including strong opioids via PCA or syringe driver.
   - **Coating agents:** Sucralfate coats and protects from some discomfort; not indicated if mucositis is severe; other coating agents are Orobase, and Gelclair (a rinse which forms a protective layer); patients undergoing DXT are advised to combine analgesia, mucosal protector and salivary stimulant.
   - **Seek specialist advice:** Radiotherapy, oncology, haematology and head and neck cancer departments will have specialist experience and will be able to advise.

7. Excessive salivation (feels uncomfortable, undignified and a cause of skin problems):
   - **Identify cause:** may be caused by lack of gag reflex/weak movements of mouth; some medicines (such as anti-convulsants) cause excessive salivation.
   - **Reduce saliva reduction:** anti-muscarinics reduce saliva production, such as amitriptyline 10-25mg nocte po, hyoscine hydrobromide 1mg/72 hrs transdermal patch, or hyoscine butylbromide 10mg tds po or 20 mg s/c (bioavailability s/c is better than po.)
   - **Review whether poorly fitting dentures are a contributing factor:** consider whether prognosis is long enough to have review by dentist, as poor fit may stimulate excessive salivation.
   - **Consider if role for DXT to salivary glands.

8. Alteration in taste:
   - **Discussion of what is palatable:** see Macmillan Cancer Support advice re managing taste change:
     http://www.macmillan.org.uk/Cancerinformation/Livingwithandaftercancer/Eatingwell/Eatingproblems/Tastechanges.aspx
   - **Experiment with temperature:** cold foods may be more palatable.
   - **Explore role of magnesium supplement:** see Macmillan Durham Cachexia Pack.
Sources:

Milton Keynes Hospital NHS Foundation Trust (2012) Recommended first-line symptom management for palliative care in the hospital setting
Royal Marsden Hospital Manual of Clinical Nursing Procedures 8th edition http://www.rmmonline.co.uk/rmm8/chapter/09/ss34
ORH NHS Trust Oxford Centre for Head and Neck Oncology (2010 version 7) A guide to the management of sore mouth or throat
2.4 Constipation

This section deals with aspects of management particular to/common in palliative care patients

Patients commencing opioids are also routinely started on laxatives (see Pain guidelines)

Key differences from usual care in debilitated patients

- Lifestyle advice (e.g. diet, fluid) is usually inadequate: laxatives are generally required
- Bulk forming agents (e.g ispaghula husk: "Fybogel") are avoided because they become constipating without adequate fluid intake (a common feature in such patients)
- Patients may assume that reduced dietary intake will reduce frequency of defaecation. Whilst volumes may alter, the aim is still to maintain a regular bowel habit

Colic with constipation

- Implies peristalsis against stool that won’t move (i.e. either hard stool or obstruction).
- Therefore treated by increasing the softener and reducing or dividing the stimulant.
- If severe, omit the stimulant for 48hrs and give hyoscine butylbromide 20mg q.d.s. PO (or 40-120mg/24hrs via SCut syringe pump) whilst softeners take effect

Overview of sections:

- A. Choice of laxatives
- B. Colicky pain and constipation
- C. Is fentanyl helpful in refractory constipation?
- D. Amber drugs for constipation (including opioid antagonists; e.g. methylnaltrexone)

A. Choice of laxatives

Choice is influenced by palatability, cost and familiarity. 1st line treatment is usually with:

- Senna 7.5-15mg (1-2 tablets or 5-10ml) b.d. PO and/or a softener if the stool is hard

Specific situations requiring a modified approach include:

- Faecal impaction: consider Laxido (+/-rectal measures) [Culbert 1998]
- Constipation with vomiting. Consider obstruction (see section 6.2); rectal intervention; and concurrent antiemetics (see section 6.1). If refractory to these, and if opioid-induced, consider methylnaltrexone non-formulary (see below)
- Constipation with colic. See section B below.
- Gastrointestinal obstruction: sodium docusate (200mg b.d. PO) is the laxative of choice because it softens without substantially increasing stool volume, causing a smaller increase in bowel distension than osmotic laxatives. See also section 6.2

Codanthramer and codanthrusate combine a stimulant (dantron) with a softener

- Use is confined to terminally ill patients (possible carcinogenic risk in rodent studies)
- Avoid with faecal incontinence (prolonged skin contact causes burns)
- Be cautious when switching between preparations: the quantity of dantron differs markedly
- Inform the patient that the urine may become harmlessly coloured red

B. Colicky pain and constipation

This is caused by peristalsis against stool that won’t move. Unless the patient is obstructed (section 2.2), the cause is hard stool. The aim is, therefore, to soften the stool. Temporarily reducing peristalsis will ease pain:

- Reduce or divide stimulant laxatives (e.g. change senna 20ml nocte to 10ml b.d.)
- Increase softeners, using rectal softeners initially, if required
- If colic is severe:
Discontinue stimulants and use **Laxido** alone
- Give **hyoscine butylbromide** 20mg p.r.n. q.d.s. SC or PO (or 60mg/24hrs via SC syringe pump) for 48hrs while the softeners take effect
- Use rectal measures (softeners initially e.g. glycerin suppositories, micralax enema or arachis oil enema [ask about peanut allergy])

**C. Is fentanyl helpful in refractory constipation?**

Patients do not experience less constipation with fentanyl than with morphine, provided laxatives are appropriately titrated, despite generally lower laxative doses [Radbruch 2000]. Factors other than opioids are usually responsible for intractable constipation in palliative care patients [Fallon 1999, Bennett 2003]. Therefore, changing to fentanyl is often ineffective and should only be considered when attempts at laxative titration have been unhelpful.

**D. Amber drugs for constipation**

- **Amber drugs**: Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a **palliation specialist**):
  - SC **methylnaltrexone** NON-FORMULARY; a staff information sheet is available describing its use for opioid-induced constipation refractory to usual measures
  - Oral **amidotrizoate** (Gastrografin) [Mercadante 2011]
- **Red drugs**
  - Parenteral parasympathomimetics (IV **neostigmine**) [Thomas 2003]
- **Drugs not currently recommended for routine use in palliative care**
  - Combined **naloxone-oxycodone** (Targinact NON-FORMULARY) (see Effective Prescribing Committee [policy 004])
  - **Prucalopride** NON-FORMULARY

**References**

### 2.5 Diarrhoea

#### Key points
Non-specific treatment should only be used after considering specific treatable causes:
- In any patient group (e.g. clostridium difficile, drug-induced, overflow [i.e. constipation])
- In malignancy (e.g. steatorrhoea, carcinoid syndrome, radiation-induced)

Main options for non-specific palliation of diarrhoea:
- 1\textsuperscript{st} line: Loperamide 2-4mg p.r.n. PO initially (less systemic effects and more potent than codeine) Consider b.d. regimen thereafter, with dose based on p.r.n. requirement. Usual maximum 16mg/24hrs (up to 32mg/24hrs occasionally used under specialist direction).
- 2\textsuperscript{nd} line options:
  - Hyoscine butylbromide\textsuperscript{†} 60mg/24hrs via subcutaneous syringe pump
  - Specialist referral: Specialist options include
    - Octreotide\textsuperscript{†} (AMBER: discuss with Palliative Care Team) 250-500micrograms/day via SC syringe pump if too unwell for colostomy
    - Colostomy formation (discuss with surgeons)

#### A. Specific treatable causes
(Assess fluid and electrolyte balance in all cases)

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<td>Where rapid control is required in the dying give dexamethasone 8mg o.m. SC</td>
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</tbody>
</table>
### Radiation-induced

<table>
<thead>
<tr>
<th>Radiation-induced</th>
<th>Usually within days/weeks of radiotherapy directly affecting bowel (e.g. treatment to spine or pelvis)</th>
<th>D/w an oncologist</th>
</tr>
</thead>
</table>

### B. Amber drugs

Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation specialist):
- **Octreotide**

### References

3.1 Lymphoedema

**Patient/carer education is the mainstay of management:**
1. Scrupulous skin care (emollients, avoiding skin trauma)
2. Exercise and movement advice
3. Compression hosiery
4. Seeking prompt treatment for infection (cellulitis, fungal infection)
5. Lymphatic drainage massage techniques (including by patients and carers themselves if they have been taught by lymphoedema specialist)

**Further considerations for healthcare professionals**
1. Minimise trauma to affected limbs (e.g. venepuncture, cannulae, blood pressure checks)
2. Avoid drugs that worsen fluid retention where possible (e.g. corticosteroids, NSAIDs, calcium antagonists)

**Managing complications – key points:**

**Worsening oedema.** Consider:
- Poor adherence (e.g. ill-fitting hosiery) - seek advice from lymphoedema team
- DVT
- Infection (acute or recurrent)
- Recently commenced medicines; e.g. gabapentin/pregabalin, NSAIDs, calcium channel blockers, corticosteroids [Keeley 2008]
- Worsening underlying disease (e.g. if malignancy-related, see ‘corticosteroids’ below)

**Cellulitis.** Prompt antibiotics for at least 2 weeks (choice as for conventional cellulitis) is essential because:
- The immune response in lymphoedematous areas is impaired
- Infection causes further permanent damage to lymphatic drainage
- Systemic flu-like symptoms can be severe (may precede visible skin changes)

**Pain.** Consider:
- Oedema itself (distension and myoligamentous strain): simple analgesics and general management of underlying lymphoedema
- Lymphoedema complication (e.g. DVT, infection): treat appropriately
- Underlying disease (e.g. consider axillary recurrence with new pain in a mastectomy-related lymphoedematous arm): urgent referral

**Lymphorrhoea (leaking):** Gentle bandaging - seek advice from the lymphoedema team

**Drug treatment**
1. **Diuretics** for mixed lympho-venous oedema (lymphoedema alone does not respond): measure limb circumference before and after a 1 week trial of furosemide 40mg o.m. PO, continuing if effective
2. **Corticosteroids** for severe malignancy-related lymphoedema: not usually for long-term maintenance. Helpful for lymphoedema in difficult (i.e. non-limb) areas or if lymphoedema is worsening despite the optimal use of non-drug measures (e.g. hosiery, massage)

**Overview of sections:**
- A. Introduction to lymphoedema (an overview for clinicians unfamiliar with its management)
- B. Patient and carer education
  - Promotion of skin integrity
  - Simple advice on exercise and hosiery
- C. Managing complications
  - Worsening oedema
  - Cellulitis in lymphoedema (management, prophylaxis)
  - Pain
  - Lymphorrhoea (leaking)
- D. Specialist services, referral criteria and links to professional and patient organisations
A. Introduction to lymphoedema

For further reading, search ‘lymphoedema’ at [http://learning.bmj.com/learning/home.html](http://learning.bmj.com/learning/home.html)

Lymphoedema is oedema due to reduced lymphatic drainage. It is subdivided as:

- **Primary** (no external cause identified: generally due to an inherited lymphatic abnormality, though may take years, or a traumatic/infective trigger, to become clinically apparent). A family history is not always present. It is usually clinically apparent by the 4th decade of life.
- **Secondary** (identifiable external cause: e.g. surgery, radiotherapy, lymphatic metastases, infection)

Venous oedema (oedema caused by increased fluid formation: e.g. post-thrombotic limb, congestive heart failure, venous stasis, dependency oedema) puts extra load on lymphatic drainage, eventually causing progressive lymphatic damage with features of lymphoedema (lympho-venous oedema)

The clinical features of lymphoedema change with time:

<table>
<thead>
<tr>
<th>Underlying process</th>
<th>Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial fluid formation</td>
<td>Pitting oedema that reduces on elevation</td>
</tr>
<tr>
<td>Subsequent secondary fibrosis</td>
<td>Non-pitting oedema with no reduction on elevation</td>
</tr>
<tr>
<td>Finally, secondary overlying skin changes occur</td>
<td>Hyperkeratosis (horny scale, with or without ‘furry’ appearance)</td>
</tr>
<tr>
<td></td>
<td>Papillomatosis (cobblestone, ‘warty’ appearance)</td>
</tr>
<tr>
<td></td>
<td>Lymphangiomas (‘blisters’ of dilated lymphatics)</td>
</tr>
</tbody>
</table>

The key aims of lymphoedema management are:

- **To minimise oedema** through:
  - Use of **hosiery**: firm garments (with higher compression than used for venous conditions), against which muscles contract improving movement-induced drainage. It is essential that they are well fitting: **ill-fitting hosiery is at best ineffective and at worst causes ischaemic limb injury**. There are different indications for various types of lymphoedema garments, and they should be fitted by a specialist physiotherapist or nurse with lymphoedema experience. Some can be prescribed on an FP10 form.
  - Encouraging **activity and regular (gentle) exercise** (especially while wearing hosiery). Care should be taken with vigorous, heavy or very repetitive activities that can sometimes exacerbate swelling.
    - Lymphatic drainage massage (broadly along lines of patent lymphatic drainage): Patients and carers can be taught **simple lymphatic drainage**, and specialists use a more comprehensive **manual lymphatic drainage**
    - If oedema is severe, **multi-layer bandaging** can sometimes be used to rapidly reduce volume before subsequently maintaining this reduction with hosiery. Multi-layer bandaging can be arduous and time consuming, requiring daily visits and the use of bulky bandaging (a particular concern if patients are fatigued or unsteady)

- **To avoid progressive lymphatic damage** (and consequently worsening oedema) through:
  - **Scrupulous skin care** (regular emollients: e.g. aqueous cream)
  - **Avoiding trauma** (blood pressure readings, venepuncture, venflons, BMs, sunburn, bites etc)
  - **Prompt treatment of cellulitis and fungal infections**

- **To provide supportive care**:
  - Self-help (advice on above techniques)
  - Advice on clothing and footwear
  - Analgesia and related symptom control
  - Psychosocial support (e.g. adapting to altered body-image or limb function)
B. Patient and carer education

Support this advice with the lymphoedema patient information leaflet and information about the lymphoedema support network (see links at the end)

Promotion of skin integrity

Good skin care improves comfort and reduces the risk of cellulitis:

- Avoid skin trauma / puncture:
  - Protecting skin from cuts, burns, bites, sunburn
  - Avoid medical procedures to affected limbs (blood pressure readings, venepuncture, venflons, BMs, injections etc)

- Regular emollients
  - Use a non-perfumed emollient (e.g. Diprobase, Cetroban or Oilatum cream) on intact skin once or twice daily
  - On very dry skin, switch to a greasier emollient (e.g. emulsifying ointment)
  - Consider aqueous cream as a soap substitute

- Prompt treatment for fungal or bacterial infections. Ensure patients are aware of the signs and the need to seek treatment promptly:
  - Warmth and redness
  - Increased pain or tenderness
  - Fever or flu-like symptoms

All members of the health care team should be aware of the above when dealing with patients with, or at risk of, lymphoedema.

Advice on exercise, positioning and diet

Normal activity and regular gentle exercise including use of the limb should be encouraged to increase the effect of the ‘muscle pump’ on lymphatic drainage.

- Continue specific exercises that have may been advised by a lymphoedema specialist
- If they have a compression garment, wear this whilst exercising
- Keeping Body Mass Index normal helps lymphatic drainage
- Do not restrict fluid intake. This will not affect the degree of oedema
- Elevation of a swollen arm to shoulder height, or swollen leg to hip height, when sitting can reduce oedema formation; discourage patients with leg oedema from sleeping in a chair.

N.B. Overexertion or sudden, strenuous or repetitive exercise can exacerbate swelling

Advice on hosiery

It is important that compression garments are well fitting; patients should be encouraged to ask for advice if the garments are not comfortable or are slipping.

- They should be renewed at least every 6 months if worn daily in order to maintain the appropriate compression
- Advice should be sought if patients are experiencing problems applying the hosiery

C. Managing complications

Worsening oedema

- Are they experiencing problems with their regular maintenance treatment? (e.g. exercise, use of hosiery, massage techniques): discuss with lymphoedema team
- Look for evidence of:
  - Infection (see ‘cellulitis’ below)
  - DVT (if present, refer for Doppler imaging and appropriate treatment)
  - Worsening underlying disease. If malignancy-related, look for lymphadenopathy. Worsening lymphoedema can be a sign of recurrence: consider oncology or surgical referral. If no active anti-cancer treatment available, consider a trial of corticosteroids (e.g. dexamethasone 8mg o.m. PO for 2 weeks and then reduce by 2mg per week to minimum effective dose)
  - Co-existent venous oedema (congestive cardiac failure, etc): treat as needed
Cellulitis in lymphoedema (management, prophylaxis)
The immune response in a lymphoedematous area is impaired. Management differs from that of standard cellulitis described in local antibiotic policies because:
- Onset may be faster (hours) or subacute (weeks)
- Systemic upset (fever, flu-like symptoms) is more frequent. It may precede skin changes
- Infection can further damage lymphatic drainage
Prompt treatment, for a minimum of 14 days, is therefore imperative

Acute attack
If afebrile, no systemic upset and otherwise healthy: commence oral antibiotics as per local policy, for example:
- **Flucloxacillin** 1g q.d.s. PO for 14 days unless
  - penicillin allergic [use: clindamycin 450mg tds. PO for 14 days]
  - MRSA likely [use: doxycycline 100mg b.d. PO for 14 days]
- Advise bed rest and elevation
- Decrease level of compression (garments or bandaging) during the acute attack
- Review 48 hrs after starting antibiotics: If no response or deterioration consider switching to IV antibiotics (i.e. referral to hospital if in the community) or discussion with a microbiologist
- Monitor rash and systemic upset (use additional monitoring with CRP / ESR / white cell count, and microbiology if appropriate)
- Continue antibiotics for not less than 14 days after clinical response to treatment

If febrile/systemic upset and/or unstable co-morbidities:
- If in the community, admit to hospital (likely to need IV antibiotics)
- Inpatients: Follow acute hospital cellulitis guidelines

Holiday supply of “if needed” antibiotics
The risk of further cellulitis in lymphoedema is high. It is recommended that patients who have had an attack of cellulitis should:
- Carry a 2 week supply of the above antibiotics if away from home for any length of time
- Start antibiotics immediately familiar symptoms occur, (but still seek medical review as soon as possible)

Prophylaxis to prevent recurrent cellulitis

<table>
<thead>
<tr>
<th>If ≥2 attacks per year:</th>
<th>Treat risk factors</th>
<th>Fungal infections, dermatitis (and skin care), open wounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start prophylaxis</td>
<td>First line</td>
<td>Phenoxyimethylenicillin (penicillin V) 500mg o.d. PO</td>
</tr>
<tr>
<td></td>
<td>Penicillin allergic</td>
<td>Clarithromycin 250mg o.d. PO</td>
</tr>
<tr>
<td>If breakthrough attacks occur</td>
<td>Increase frequency to b.d.</td>
<td></td>
</tr>
<tr>
<td>If prophylaxis successful</td>
<td>Halve dose after 1 year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stop after 2 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If relapse occurs, lifelong prophylaxis may be needed</td>
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</tbody>
</table>

Pain
Management depends on the cause:
- Oedema itself (distension and myoligamentous strain): analgesics and general management of underlying lymphoedema. Good emollient care may ease distension pain.
- Lymphoedema complication (e.g. cellulitis, DVT): analgesics while arranging appropriate treatment
- Underlying disease: in malignancy-associated lymphoedema, pain can be a feature of cancer recurrence, requiring urgent referral
In addition to broad-spectrum analgesia (e.g. paracetamol, opioids: see pain guidelines), look for:

- Neuropathic pain (e.g. due to lymphadenopathy). Neuropathic-like skin hypersensitivity also occurs in oedema: consider discussion with a specialist or trial of a neuropathic agent
- Secondary muscle imbalance and articular problems: seek advice from a physiotherapist
- Analgesic-induced fluid retention (e.g. NSAIDs, antiepileptic drugs)

**Lymphorrhoea (leaking)**

This is difficult to manage: seek advice from the Lymphoedema Team. In the interim:

- Be vigilant for infection; continue scrupulous skin care, moisturising, gentle exercise and elevation if comfort allows
- Cover leaking areas with absorbent dressing; skin fragility often precludes adhesive dressings
- Consider gentle bandaging
- In end of life care, if there is a single point source of leakage, cover with a stoma bag (not generally used in the longer term because of detrimental impact on skin integrity)

**D. Specialist services, referral criteria and links to professional and patient organisations**

Early diagnosis and prompt referral for treatment is vital – referrals by healthcare professionals can be made to the Lymphoedema Clinic on 25864 which is based on the renal Unit.

### Out of Area Lymphoedema Referrals

<table>
<thead>
<tr>
<th>St George's (adults or children)</th>
<th>Oxford (adults only)</th>
<th>Basingstoke (adults only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoedema Service</td>
<td>Transplant Ward</td>
<td>North Hampshire Hospital</td>
</tr>
<tr>
<td>St George's Hospital, Clinic B</td>
<td>Churchill Hospital</td>
<td>Aldermaston Road</td>
</tr>
<tr>
<td>Blackshaw Road,</td>
<td>Old Road, Headington</td>
<td>Basingstoke</td>
</tr>
<tr>
<td>London SW17 0QT</td>
<td>Oxford, OX3 7LJ</td>
<td>Hampshire</td>
</tr>
<tr>
<td>Tel: 020 8725 1857</td>
<td>Tel 01865 225864</td>
<td>Tel 01256 313564</td>
</tr>
<tr>
<td></td>
<td>Fax 01865 225473</td>
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### Links

**The British Lymphology Society** (for interested professionals):

- British Lymphology Society  Tel: 01452 790178
- Garth House Email: info@thebls.com
- Rushey Lock Website: [www.thebls.com/](http://www.thebls.com/)
- Tadpole Bridge
- Buckland Marsh
- Nr Faringdon
- Oxfordshire
- SN7 8RF

**The Lymphoedema Support Network** (patient support organisation):

- Lymphoedema Support Network  Tel: 020 7351 4480 (information and support)
- St. Luke's Crypt  Tel: 020 7351 0990 (Administration)
- Sydney Street Fax: 020 7349 9809
- London Email: adminlsn@lymphoedema.freeserve.co.uk
- SW3 6NH Website: [www.lymphoedema.org/lsn/](http://www.lymphoedema.org/lsn/)

[Return to contents page](#)
References

- Keeley 2008 Drugs that may exacerbate and those used to treat lymphoedema. Journal of lymphoedema 3:57-65
### 3.2 Itching

#### General measures

1. **Emollients**
2. **Lifestyle changes**
   - **Keep skin cool** (avoiding hot baths pre-bed, light clothes etc)
   - **Minimise excoriation** by keeping fingernails short. If desperate to scratch, rub in emollient rather than scratching with fingernails
3. **Sedative antihistamine-antipruritics** (less sedating alternatives may be unhelpful: see text)
   - **Chlorphenamine** 4mg q.d.s. PO or
   - **Doxepin†** 25-75mg o.n. PO

#### Address underlying cause

1. Cholestasis – biliary stent, corticosteroids
2. Uraemia – iron deficiency and phosphate level
3. Neuropathic itch (i.e. a symptom of nerve injury) – options similar to neuropathic pain
4. Drug-induced pruritus – consider an alternative (e.g. opioid switching; see pain guidelines)

#### Refractory itch

1. **SSRIs†** (e.g. sertraline† 50mg o.m.) appear beneficial for itch due to a variety of systemic illnesses [Zylicz 2003, Mayo 2007]
2. Specialist referral
   - To site-specific specialty if treatment of the underlying cause is likely to be possible
   - Otherwise, refer to the Palliative Care Team

#### Overview of sections:

- A. General measures
- B. Cause specific measures
  - Cholestasis
  - Uraemia
  - Haematological
    - Neuropathic itch (i.e. a symptom of nerve injury)
- C. SSRIs for itch
- D. Amber treatments and specialist referral

#### A. General measures

**Adequate skin hydration with emollients is essential** [Twycross 2003]:

- Regular emollients
  - Use a non-perfumed emollient (e.g. Diprobase, Cetroban or Oilatum cream) on intact skin once or twice daily. Some patients report greater benefit if kept in the fridge.
  - On very dry skin, switch to a greasier emollient (e.g. emulsifying ointment)
  - Consider aqueous cream as a soap substitute

**Sedative antihistamine-antipruritics (e.g. chlorphenamine, doxepin†)**

- The antihistamine action is of most relevance for dermatological causes of itch (e.g. urticaria, drug rashes, insect bites, etc). Less sedating alternatives (e.g. loratadine 10mg o.d. PO) may be as effective, and better tolerated, for such causes
- However, itch due to systemic metabolic disturbance (uraemia, cholestasis) is not mediated by histamine, and antihistamines' benefit lies mainly in their non-specific sedative action (especially for sleep disturbance). Less sedating alternatives are probably unhelpful
B. Cause specific measures

<table>
<thead>
<tr>
<th>Cause</th>
<th>Measures for underlying cause</th>
<th>Symptomatic options if general measures (emollients, antihistamines, etc) unhelpful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholestasis*</td>
<td>Is a biliary stent possible (discuss with gastroenterologists) Otherwise, consider a trial of dexamethasone 8mg o.m. PO for 2 weeks. If helpful, reduce by 2mg per week down to minimum effective dose</td>
<td>Sertraline† 50mg o.m. PO. increasing to 100mg after 2 weeks if needed [Mayo 2007]</td>
</tr>
<tr>
<td>Uraemia</td>
<td>Discuss with the renal team: optimise phosphate balance; treat iron deficiency; consider gabapentin† (dose as for neuropathic pain, noting dose reduction is required in renal impairment) [Gunal 2004, Naini 2007]</td>
<td></td>
</tr>
<tr>
<td>Haematological</td>
<td>Discuss with the haematologists: itch often responds to treatment of the underlying disease</td>
<td></td>
</tr>
<tr>
<td>Neuropathic itch</td>
<td>Treatment directed at the underlying cause of the lesion</td>
<td>Treat with antiepileptic drugs or tricyclic antidepressants as with neuropathic pain (e.g. gabapentin†: see pain guidelines)</td>
</tr>
<tr>
<td></td>
<td>*Cholestyramine is now rarely used in the palliation of cholestatic itch. The alternatives described here and below are more effective, better tolerated and have fewer drug interactions.</td>
<td></td>
</tr>
</tbody>
</table>

C. SSRIs† for itch

Serotonin is thought to be an important central nervous system mediator of itch, especially where caused by systemic illness. 2 small RCTs suggest benefit from sertraline [Cholestatic Itch: Mayo 2007] and paroxetine [Itch of Mixed Causes in Cancer Patients: Zylicz 2003]. A case series also describes benefit in polycythaemia vera [Tefferi 2002]. Onset of action is quicker than for depression (days rather than weeks [Zylicz 2003]).

Consider a trial of sertraline† (50mg o.m. PO. increasing to 100mg after 2 weeks if needed) if:
- General measures (emollients and lifestyle advice and antihistamines) are unhelpful and
- Treatment of the underlying cause is already optimal and
- Cautions/contra-indications of SSRIs allow

D. Amber drugs: Refractory itch and specialist referral

- Where itch fails to respond to the above measures, or where there is uncertainty about their use, consider referral to the specialist Palliative Care Team.
- Green drugs: the above are “accepted uses” and may be initiated by non-specialists for the indications described
- Amber drugs: Other off-licence, infrequently used agents are amber for this indication (i.e. initiated after discussion with, or review by, a palliation specialist):
  - Opioid antagonists and partial agonists (for this indication)†: The endogenous opioid system is also an important mediator of itch due to systemic illness, but severe reactions are sometimes seen when opioids antagonists are used for this purpose [Zylicz 2004]
  - Ondansetron†: Appears helpful in case series, but controlled trial results are conflicting [Zylicz 2004]
  - Rifampicin [Ghent 1988]
  - Mirtazapine [Zylicz 2004]
  - Androgens [Zylicz 2004]
  - UVB therapy (discuss appropriateness with the dermatologists)
References

D. Managing cancer-specific problems in the community

N.B. Refer to acute oncology guidelines in the acute inpatient setting

4.1 Hypercalcaemia of malignancy

| Recognition | • Drowsiness  
| • Confusion, agitation, hallucinations  
| • Nausea and vomiting  
| • Constipation  |

| Confirmation | Raised albumin-corrected serum calcium  |

| Community Management | If the patient is imminently dying, treat symptomatically only. However, patients with hypercalcaemia can appear to be extremely unwell and improve markedly with treatment: if in doubt, discuss with a palliative care physician  
  
Symptomatic management for nausea, agitation and/or hallucinations:  
• **Haloperidol** 0.5-1.5mg nocte and p.r.n. t.d.s. PO/SC (usual maximum 5mg/24hrs)  

Active management with IV bisphosphonates  
• **IV pamidronate up to 90mg** can be given. However, if the patient is unwell and dehydrated, they may require admission to allow IV rehydration with sodium chloride 0.9% before and after the IV pamidronate. If in doubt, discuss with a Palliative Care Physician.  
• Additional guidance is available for community clinicians involved in the prescribing or monitoring of IV pamidronate.  

Subsequently  
• Hypercalcaemia can be a feature of worsening disease. Consider the appropriateness of further investigation and/or anticancer treatment (discuss with the oncologists), and arrange for the patient to be given appropriate information by a senior clinician  
• If prognosis is anticipated to be ≥6 months (unusual with malignant hypercalcaemia outside of the context of breast cancer), and ongoing IV bisphosphonate treatment is anticipated, recommend dental review within the 1st month (the risk of osteonecrosis of the jaw with dental work during long term bisphosphonate treatment increases with time).  

4.2 Spinal Cord Compression and Cauda Equina Syndrome

| Recognition | The aim is to make the diagnosis before significant neurological signs are obvious  
| • Known, or high risk of, bone metastases (e.g. prostate, breast or lung cancer)  
| • Pain: back pain, neuropathic leg pain and/or radicular pain  
| • Motor changes: Unsteadiness or leg weakness, especially if rapidly evolving (over days) or incongruent with general condition  
| • Sensory alteration: sensory level  
| • Sphincter disturbance: urinary retention, urinary or faecal incontinence, or altered anal tone (these are late features: do not be reassured by normal sphincter function)  |

| Community Management | TVCN malignant SCC guidelines  
| Give **dexamethasone** 16mg one-off dose PO (or other available high dose corticosteroid) with **omeprazole** 20mg o.d. PO  

If active treatment is appropriate:  
• arrange same day admission to an acute hospital  
• do not admit to a Palliative Care Unit or hospice – these do not have MRI or radiotherapy facilities  

If in doubt, discuss with a Palliative Care Clinician
### 4.3 Superior vena cava obstruction (SVCO)

| Cause | • Extrinsic venous compression (mediastinal malignancy, most commonly from lung cancer, lymphoma or breast cancer)  
|       | • SVC thrombosis (e.g. secondary to indwelling lines) |
| Recognition | • Respiratory distress (breathlessness, cough, cyanosis)  
|            | • Upper body venous congestion (distended neck veins, facial plethora)  
|            | • Oedema of head, neck and upper limbs  
|            | • Cerebral dysfunction (confusion, seizures, coma)  
|            | • Other mediastinal symptoms (stridor, dysphagia, vocal cord paresis) |
| Community Management | Give **dexamethasone** 16mg one-off dose PO (or other available high dose corticosteroid) with **omeprazole** 20mg o.d. PO  
|            | If active treatment is appropriate:  
|            | • arrange same day admission – discuss with Oncologist or Palliative Care clinician |

### 4.4 Bronchial obstruction

| Recognition | Stridor in the context of mediastinal malignancy (e.g. from lung cancer, lymphoma, or breast cancer)  
|             | There may be other mediastinal symptoms (e.g. dysphagia, vocal cord paresis) |
| Community Management | If the patient is imminently dying give emergency symptomatic relief:  
|            | • **Morphine sulphate** 10mg SC (or slow IV bolus over 2 minutes) or a dose based on 1/6 of a regularly taken 24 hour opioid dose and  
|            | • **Midazolam:**  
|            |   o Intravenous: Dilute 20mg with sodium chloride 0.9% up to a volume of 10ml (dilution may not be required if using 10mg in 5ml strength). Give IV in 1ml (2mg) increments every 1-2 minutes until unconscious. Higher doses may be required if receiving regular benzodiazepines or patient is alcoholic  
|            |   o If the IV route is not available, give midazolam 10mg SC and repeat after 10 minutes if not unconscious  
|            | Otherwise give:  
|            | • Oxygen  
|            | • **Dexamethasone** phosphate 16mg one-off PO, SC or IV (followed by 8mg morning and lunchtime PO) and **omeprazole** 20mg o.d. PO. Check blood sugar daily (in view of high dose corticosteroids)  
|            | • Symptomatic relief:  
|            |   o **morphine sulphate** liquid 2.5mg 4 hourly PO (or an additional dose based on 1/6 of a regularly taken 24 hour opioid dose)  
|            |   o **lorazepam** 0.5mg t.d.s. p.r.n. SL if anxious or panicky  
|            | • See section 1.1 for more advice on the symptomatic management of breathlessness  
|            | Then:  
|            | • If appropriate to consider stenting or anti-cancer treatment, arrange urgent admission to an acute hospital – discuss with Oncologist / Respiratory Physician  
|            | • If the patient wishes to remain at home for end of life care, and understands the implications of not exploring active treatment, seek urgent advice from the palliative care team |
4.5 Malignant Ascites

Main options
- Anti-cancer treatment (e.g. endocrine therapy, systemic or intra-peritoneal chemotherapy)
- Drainage (paracentesis)
- Diuretics (spironolactone is the diuretic of choice)
- Symptomatic treatment (of nausea, breathlessness and distension pain)

General approach
- Tense ascites: paracentesis. Subsequently, reduce rate of re-accumulation with diuretics
- Symptomatic, but not tense, ascites: consider diuretics (especially for ascites due to liver metastases: see text)
- Rapidly re-accumulating ascites: if diuretics and/or anti-cancer treatment are ineffective or not possible, optimise symptomatic treatment and discuss with the Palliative Care Team

Paracentesis
Prior to the procedure, review medication and perform a Full Blood Count and Coagulation Screen looking for potentially increased bleeding/complications risk (e.g. INR>1.7, Platelets<50, neutrophils<1.5, hypotension, renal impairment).

When taking informed consent:
- The aim of fluid removal is symptom control. The majority of patients experience improvement in breathlessness, nausea, vomiting and distension-pain [McNamara 2000]
- The fluid will gradually re-accumulate. The rate varies, but drainage can be repeated if required
- The commonest adverse effect is short-lived discomfort afterwards, occurring in around a quarter of people [McNamara 2000]. Patients should also be informed of unusual complications: bleeding; infection; visceral perforation; low blood pressure; ongoing leak post procedure (and cutaneous seeding, if ascites is due to abdominal mesothelioma) [McNamara 2000, Stevenson 2002]

The procedure is done by an appropriately trained clinician. Ultrasound evaluation is used if there is diagnostic uncertainty or the procedure is likely to be difficult (e.g. loculated ascites, previously complicated paracentesis, bowel distension).

After the procedure:
- Leave the drain unclamped for the first 5 litres. At this point, if the patient is well and systolic blood pressure >100mmHg, the drain can continue to be left unclamped for a further 5 litres and reviewed again. There is no evidence to support the clamping of drains but experience suggests that in frail patients with advanced cachexia or liver failure controlled drainage is sometimes required. Patients do therefore need to be observed.
- If the patient appears more unwell at any stage, check their blood pressure. If hypotensive, clamp the drain and consider administering fluids (e.g. dextrose 5% 1 litre IV over 1 hour), then review
- Aim to remove the drain within as short a time as practicably possible. It is not always appropriate to drain to dryness. Symptomatic benefit is usually seen after the first few litres are removed: further drainage brings little extra benefit (except, possibly, with breathlessness) [McNamara 2000]. Drainage must therefore be tailored to the clinical situation
- Aseptically flushing the drain is only indicated if significant amounts of fluid appear to remain on clinical examination
- If there is diagnostic uncertainty, send fluid for appropriate laboratory investigation (e.g. cytology to establish the presence of peritoneal carcinomatosis)
**Diuretics for ascites**

**Who benefits from diuretics?**
Malignant ascites is usually caused by peritoneal carcinomatosis and/or portal hypertension (due to massive hepatic metastases). Patients with massive portal hypertension are the most likely to benefit from diuretics, though ascites from other causes does occasionally respond [Pockros 1992]. Where anti-cancer treatment is ineffective or not possible, and ascites is recurring rapidly after paracentesis, a trial of diuretics is sometimes reasonable whatever the suspected mechanism.

**Initiating treatment**
If baseline U+E and blood pressure are acceptable, commence **spironolactone** 100 mg o.m. PO. Check that amiloride (or co-amilofruse) is not being received concurrently.

If serum potassium is towards the upper limit of normal:
- Commence **furosemide** 40mg o.m. PO concurrently (furosemide alone is less effective for ascites). The combination reduces the risk of hyperkalaemia but increases the risk of dehydration [Fogel 1981]
- Stop or reduce other potassium-sparing medication if possible (e.g. ACE inhibitors, ATII antagonists)
- Monitor U+E more frequently (e.g. every 2-4 days)

**Monitoring**
- Re-check U+E after 5-7 days (or sooner if original results were abnormal)
- After 7 days, if the response is inadequate, increase spironolactone to 100 mg b.d. PO and consider adding in furosemide 40-80mg o.m. PO (partly depending on the serum potassium level).
- Consider further increases after 5-7 days. Monitor U+E after each increment: if abnormal, decrease the dose. Doses up to furosemide 80 mg b.d. and spironolactone 200 mg b.d. are occasionally used, but require frequent biochemical and clinical monitoring
- If the patient’s symptoms worsen, consider paracentesis and/or specialist referral

**Maintenance**
If diuretics are successful, patients should be maintained on the lowest doses possible, with U+E measured regularly (weekly initially; progressively less frequently once dose and U+E results are stable). Ensure that it is clear who is taking responsibility for this monitoring)

**Rapidly re-accumulating ascites refractory to diuretics**

1. **Reconsider anticancer treatments**
2. **Optimise symptomatic treatment:**
   - Metoclopramide for vomiting (see section 2.1)
   - Opioids and other measures for breathlessness (see section 1.1)
   - Analgesia and topical emollients (e.g. aqueous cream) for distension pain

3. **Consider a tunnelled peritoneal drainage catheter** where recurrent paracentesis is anticipated (placed by interventional radiologists as a ‘day case’ procedure). This allows regular drainage in the community setting without the need to wait for substantial volumes to accumulate.

   - Intra-peritoneal corticosteroids are an alternative if a tunnelled catheter is inappropriate† (amber for this indication- discuss with specialist). Approximately doubles the interval between paracentesis, but may risk bacterial peritonitis [Mackey 2000]. Once paracentesis is complete, **triamcinolone acetonide** † (8mg/Kg; up to a maximum of 520mg) is injected via the ascitic drain followed by 10ml of sodium chloride 0.9%. The drain is then removed. Other specialist-only interventions are rarely used and include:**Octreotide** † (in view of limited evidence base): Doses between 150 and 500micrograms/24 hours are reported to reduce ascitic accumulation in malignancy [Harvey 1996, Caims 1999]. Benefit is also reported for chylous ascites (in combination with fat-reduced diet) [Mincher 2005].
• **Peritoneo-Venous Shunts**: considered for recurrent ascites, refractory to diuretics and other treatment, in relatively well patients with an anticipated prognosis of at least 3 months [Parsons 1996, Gough 1993]

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4.6 Haemorrhage

Urgent management of major haemorrhage in the imminently dying

[If aim is to resuscitate - follow advanced life support guidelines]

Health professionals with experience of major haemorrhage at the end of life emphasise:
- Staying with the patient to support them and their family
- Using dark-coloured towels/sheets to camouflage blood
- That sedative medication often has little role because death frequently occurs before it can be administered.[Harris 2011]

If circumstances allow sedation to be used, give midazolam:
- Intravenously if possible: Dilute midazolam 20mg with sodium chloride 0.9% up to a volume of 10ml (dilution not required if using 10mg in 5ml strength). Give IV in 1ml (2mg) increments every 1-2 minutes until distress relieved or unconscious. Higher doses may be required if receiving regular benzodiazepines or patient is alcoholic
- If the IV route is not available, give midazolam 10mg SC and repeat after 10 minutes if appropriate
- Consider prescribing midazolam p.r.n. for use in the event of major haemorrhage if this is anticipated

Death from major haemorrhage is distressing for all involved.
- Arrange appropriate support and follow up for relatives (e.g. via the Palliative Care Team or chaplaincy)
- Consider the need for debriefing of the health care team. As with any other distressing event, also allow time to reflect yourself. Consider discussing with a colleague

Management of non-major haemorrhage

Treat any underlying bleeding diathesis:
- Correction of coagulopathies or platelet disorders (e.g. vitamin K [phytomenadione], fresh frozen plasma, platelet transfusion) - discuss with a haematologist
- Reversal/discontinuation of anticoagulation or antiplatelet agents (e.g. vitamin K [phytomenadione] - discuss with a haematologist or clinical pharmacist)

Local measures depend on site and cause (if in doubt, discuss with Palliative Care Team)
- Specific treatment (radiotherapy; chemotherapy; laser therapy; cryotherapy; embolisation)
- Local pressure and dressings [e.g. Kaltostat]. If insufficient, soak dressings in adrenaline† 1:1000 solution or tranexamic acid solution
- Nose bleeds: use ribbon gauze soaked in adrenaline† 1:10 000). If persistent, consider cocaine nasal spray (seek advice from an ENT surgeon)
- Oral cavity: tranexamic acid (1%) mouthwash# 10ml q.d.s. [Twycross 2007]

Systemic haemostatic agents
- Tranexamic acid 500mg-1g b.d.-q.d.s. PO. Generally avoided with urological bleeding: risk of ureteric obstruction in upper renal tract bleeding and of clot retention in any renal tract bleeding) [Twycross 2007]

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