Isle of Wight
Palliative Medicine Symptom Advice Guidelines

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This book has drawn significantly from the “Wessex Specialist Palliative Care Handbook: Advice on Clinical Management” with modifications to reflect local practices and service design.

The authors also greatly appreciate the comments and suggestions from Dr Teena Silakong, Dr Mil Chan, Dr David Isaac, Dr Alaisdair Gove, Dr Jenny Collier, Sandra Clawson, Liz Harrison, Tracey Green, Odran Farrell, Dr David Grove and Dr Nicole Grove, and from colleagues in other specialties relevant to specific symptoms.

This guideline is also available as an app and a paper pocketbook:
- Android, i-OS, WP8 and Windows 8 apps available via their respective app stores
- Paper pocketbook (available to all IoW clinical staff) – ask your palliative care CNS
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Introductory Comments

“There is a time for everything, and a season for every activity under the heavens: a time to be born and a
time to die, a time to plant and a time to uproot, a time to kill and a time to heal, a time to tear down and a
time to build, a time to weep and a time to laugh, a time to mourn and a time to dance, a time to scatter
stones and a time to gather them, a time to embrace and a time to refrain from embracing, a time to
search and a time to give up…”  - Ecclesiastes 1

This guideline is intended to support symptom management for all patients receiving palliative care

Palliative care is the care of patients who have an advanced, progressive illness that is not curable, and in
general, will probably result in death within weeks or months (as opposed to many years). As such there is
an emphasis on quality of life and symptom control. At times there will also be a focus on active
interventions to reverse acute complications of illness and, in doing so, prolong a person’s life. At other
times there will be a focus on maintaining comfort and so avoiding interventions and instead allowing a
natural death. Palliative care extends past the physical and into the care of a person’s emotional and
psychological well-being. Good palliative care also takes note of the well-being of a dying person’s family
and friends. It is an art as well a science.

This book is intended for use by primary and
secondary care clinicians throughout the Isle of
Wight

It is not meant to be a replacement of other
textbooks – how could a book this small ever do
that! Nor is it intended as a set of strict protocols
that should always be followed. Rather, this book
is intended for health professionals who have a
good background knowledge of general medicine
and pharmacology and can use that background
knowledge and their experience in conjunction
with the advice found on these pages.

Roles and responsibilities

The treatments suggested in this book will not be
appropriate in all circumstances. It supplements,
but doesn’t replace, other sources (e.g. the BNF
and SPC; education and training; seeking advice
from the palliative care team). Medication
adverse effects, contra-indications and drug-drug
interactions are not discussed in any significant
detail in this book. This means that the usual
competencies of clinicians and prescribers are
assumed: users of this book need to use their
clinical judgement with regards to the
appropriateness of any suggestions, and if in
doubt, seek advice from other sources.

Getting advice from the Palliative Care Service

For patients at St Mary’s Hospital

To ask a palliative care nurse or doctor for advice,
to review, or to transfer a patient to the hospice:

- Fax a referral form to extension 4265
- If urgent, please also call extension 4177
- If you wish to speak to the palliative care nurse
  about a patient call extension 4177

For patients in the community

To ask a palliative care nurse or doctor for advice,
to review, or to admit a patient to the hospice:

- For a new referral, download a referral form
  from the EMH website and fax it to 535 314
- For a patient known to the EMH team, call 533
  331 and ask to speak to the patient’s
  community nurse

To speak specifically to a palliative care doctor:
Call 529 511 and ask to speak to a senior palliative
care doctor
Further Reading and Guidelines

The following sources give additional guidance and information on palliative illnesses, their treatment and specific medications:

- Palliative Medicine Handbooks
  - The Oxford Handbook of Palliative Medicine by Max Watson, Caroline Lucas, Andrew Hoy and Jo Wells

- Palliative Medicine Textbooks
  - Palliative Medicine edited by Declan Walsh
  - The Oxford Textbook of Palliative Medicine edited by Geoffrey Hanks, Nathan Cherny, Nicholas Christakis, Marie Fallon, Stein Kaasa and Russell Portenoy

- Palliative Care Medication Books
  - Palliative Care Formulary by Robert Twycross and Andrew Wilcock
  - The Syringe Driver: Continuous Subcutaneous Infusions in Palliative Care by Andrew Dickman and Jennifer Schneider

- Online Sources
  - UpToDate at www.uptodate.com (available to NHS staff via their OpenAthens login)

Abbreviations and Symbols Used

Abbreviations are not used frequently in this book, but where they are used, they are consistent with ones in common usage (e.g. DVT stands for deep venous thrombosis). The following abbreviations and symbols are relatively frequent in this book:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Stands For</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSCI</td>
<td>Continuous subcutaneous infusion</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>PRN</td>
<td>As required</td>
</tr>
<tr>
<td>SC</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>†</td>
<td>Off-label route or use</td>
</tr>
<tr>
<td>††</td>
<td>Unlicensed ‘special’</td>
</tr>
<tr>
<td>#</td>
<td>Specialist-initiated for this indication</td>
</tr>
</tbody>
</table>

References, process and approval used in creating this guidance

The palliative care service used the following reference sources in compiling this guidance:

- The Palliative Care Formulary 5th edition (in press)
- The Electronic Medicines Compendium
- NICE clinical guidelines 140 (opioids) and 173 (neuropathic pain)
- The Oxford Textbook of Palliative Medicine (4th edition)

We gratefully acknowledge the advice and suggestions from primary and secondary care colleagues at all stages of consultation and development, with final approval from the Isle of Wight NHS trust’s Clinical Standards Group.
Care in the Last Few Days of Life

This page, used with the “Just-in-Case Drugs” sheet, is intended to offer advice and help to doctors and health professionals providing care for people who they believe are in their last few days of life and a decision has been made that the clear focus of care is ensuring patient comfort and family support.

- It is usually very hard to be 100% sure that a person is dying, especially in non-cancer patients with multiple general medical co-morbidities
- Remain flexible. Sometimes it is reasonable to be giving basic ward treatments whilst also giving palliative-type symptom control medications
- Communicate clearly with the family about the expected prognosis and any uncertainty and document both your thoughts on prognosis and the contents of any discussion with family.
- Anticipate symptoms and write up PRN medications before they are needed (see “Just in Case Drugs” sheet). Ensure all PRN medications have a clear indication documented on the drug chart. Seek advice if 2 or more doses are ineffective, or if benefit lasts less than 1 hour.

### Analgesia

- For opioid naïve patients, dose is age dependent.
  - For the elderly – half the dose
  - For young adults – increase dose by 50%
- In renal failure, consider avoiding morphine
  - Use oxycodone in mild renal impairment
  - Use fentanyl in severe renal impairment

<table>
<thead>
<tr>
<th>Initial doses for opioid-naïve patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine 5mg hourly SC PRN - 1st line</td>
</tr>
<tr>
<td>OR Oxycodone 2.5-5mg hourly SC PRN – if morphine intolerant</td>
</tr>
<tr>
<td>OR †Fentanyl 25-50micrograms hourly SC PRN – if severe renal impairment</td>
</tr>
</tbody>
</table>

In opioid tolerant patients, these doses will be inadequate. In these patients, change oral background opioids to CSCI pump and ensure appropriate SC PRN doses (pages 9-11)

### Restlessness and Agitation (see also page 21)

- Relieve reversible causes (e.g. urinary retention with catheterization)
- Benzodiazepines are ideal for anxiety and restlessness
- Anti-psychotics are ideal for hallucinations
- In refractory terminal restlessness, specialist-initiated options include #phenobarbital (see page 30 - seek advice)

### Respiratory Secretions

- Can be very distressing for relatives although unlikely to distress drowsy patients
- Once too weak to expectorate, give †hyoscine butylbromide (Buscopan) 20 mg SC 4-hourly PRN and 60mg via CSCI over 24 hours
- Persisting noisy secretions can be treated with a regular dose +/- PRN doses

### Nausea and Vomiting

- If already on an effective anti-emetic, continue this SC if possible (see page 5)
- Otherwise, †haloperidol is a good first line option

|†Haloperidol 1mg hourly SC PRN (up to 5mg/day) |

† = off-label route or use  †† = unlicensed ‘special’  # = specialist-initiated
Dyspnoea

- Dyspnoea often improves with opioids
- Benzodiazepines also help dyspnoea, especially when anxiety plays a role

Options for dyspnoea include:

† Morphine 2.5-5 mg hourly SC PRN
AND/OR †† Midazolam 2.5-5 mg hourly SC PRN
Adjust opioid dose if already opioid tolerant (page 10)

Starting and Using a Continuous Subcutaneous Infusion (CSCI or Syringe Pump): see pages 6 and 11

Nutrition and Fluids

- Allow an awake patient to take sips of fluids and small mouthfuls of food if the patient requests it
- Keeping the mouth moist is believed to minimize thirst
- Parenteral fluids are usually ineffective for thirst and may worsen distressing respiratory secretions. Reserve for severe thirst refractory to optimal mouth care, or where oral route is lost before the desire to drink has reduced (e.g. due to an occluding oesophageal tumour)
- Taper any supplemental nutrition (e.g. via a PEG) as this is usually inappropriate

Long-term Medications

- Long-term medications (e.g. oral hypoglycaemic drugs) should usually be ceased unless they reduce symptoms (e.g. a GTN patch)
- To reduce seizure risk in patients with epilepsy, give midazolam 20mg over 24 hours via CSCI
- For patients with type I diabetes, to reduce symptoms of diabetic ketoacidosis, give half the previous total daily dose of insulin as a single daily dose of glargine insulin, checking blood glucose levels once daily, and modifying glargine insulin dose to maintain glucose levels between 6 and 15 mmol/l
- Steroids should be continued if used for symptom control. Dexamethasone can be given subcutaneously (3.3mg SC dexamethasone ≈ 4mg oral dexamethasone ≈ 30mg oral prednisolone)
- Continue anti-Parkinsonians until oral route lost. In the imminently dying, use midazolam 10mg over 24 hours via CSCI for rigidity. If it is desirable to avoid midazolam’s sedating effects, alternatives include continuing existing medications via a PEG or NG (in hospital only) or transdermal rotigotine (but seek specialist advice: can exacerbate delirium and hallucinations)

Implanted Cardiac Defibrillators (ICDs)

- If a patient has one, implanted cardiac defibrillators should be turned off if this has not already been done: call the Cardiology Unit at St Mary’s Hospital (552 182) to arrange switching the ICD off.
- In urgent situations, a strong magnet placed on the chest over the defibrillator temporarily deactivates the defibrillator (once the magnet is removed, the defibrillator will be active again): magnets are kept in the Earl Mountbatten Hospice and St Mary’s CCU Resus Trolleys or can be loaned from the Community Palliative Care Team Office (533 331).

Place of Care

- Asking about wishes ahead of time allows plans and preparations to be made. Record them using the island-wide Adastra advance care plan
- If a patient is not where they want to be cared for, or you need help coordinating their care, speak to the palliative care team
- The hospice will always endeavour to admit people in their last days of life if they wish to die there but is not able to offer long term placement as an alternative to nursing homes. Promising hospice admission when no bed is available can cause further distress - if in doubt, please seek advice first.
The injectable preparations of the following medicines can be given subcutaneously (SC). Many are only licensed for IV or IM use and thus the ampoule will be labelled ‘for IV or IM use only’. Note that syrups or solutions intended for oral use cannot be given by injection.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Comparative dosing</th>
<th>Diluent/Flush*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfentanil</td>
<td>N/A</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td>50mcg oral ≈ 50mcg SC</td>
<td>NaCl</td>
<td></td>
</tr>
<tr>
<td>Cyclizine</td>
<td>50mg oral = 50mg SC</td>
<td>WFI</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>4mg oral ≈ 3.3mg SC</td>
<td>WFI/NaCl</td>
<td>Generally given as a stat morning dose rather than via CSCI to avoid sleep disturbance</td>
</tr>
<tr>
<td>Diamorphine</td>
<td>N/A</td>
<td>WFI/NaCl</td>
<td>Morphine sulphate is generally preferred</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>150mg oral ≈ 75mg SC</td>
<td>NaCl</td>
<td>By SC infusion only (i.e. via CSCI). Do not give stat SC injections (tissue necrosis reported)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>N/A</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td>40mg oral ≈ 20mg SC</td>
<td>WFI/NaCl</td>
<td>Either SC infusion or stat SC injection (but the overnight diuresis from CSCI can be problematic unless catheterized)</td>
</tr>
<tr>
<td>Glycopyrronium</td>
<td>Seek advice</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Granisetron</td>
<td>2mg oral ≈ 1mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>2mg oral ≈ 1mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>3mg oral ≈ 1 mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Hyoscine butylbromide</td>
<td>20mg oral = 20mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Hyoscine hydrobromide</td>
<td>N/A</td>
<td>WFI/NaCl</td>
<td>Hyoscine butylbromide is generally preferred</td>
</tr>
<tr>
<td>Ketamine</td>
<td>10mg oral = 10mg SC</td>
<td>NaCl</td>
<td></td>
</tr>
<tr>
<td>Ketorolac</td>
<td>10mg oral = 10mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>250mg oral = 250mg SC</td>
<td>WFI</td>
<td>By SC infusion only (i.e. CSCI) diluting IV preparation with water</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>25mg oral = 12.5mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Lidocaine</td>
<td>N/A</td>
<td>NaCl</td>
<td>See page 27 for CSCI administration†</td>
</tr>
<tr>
<td>Methadone</td>
<td>10mg oral = 5mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10mg oral = 10mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>N/A</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Morphine sulphate</td>
<td>10mg oral = 5mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Octreotide</td>
<td>N/A</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>8mg oral = 4mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>10mg oral = 5mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>100mg oral = 100mg SC</td>
<td>WFI</td>
<td>By SC infusion only (i.e. CSCI). Bolus doses are given undiluted IM. Do not give stat SC injections (tissue necrosis reported) see p30</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>100mg oral = 50mg SC</td>
<td>WFI/NaCl</td>
<td></td>
</tr>
<tr>
<td>Valproate</td>
<td>200mg oral = 200mg SC</td>
<td>WFI</td>
<td>By SC infusion only (i.e. CSCI) diluting IV preparation with 30ml water. Do not give stat SC injections.</td>
</tr>
</tbody>
</table>

* WFI = water for injections; NaCl = sodium chloride 0.9%

† = off-label route or use †† = unlicensed ‘special’ # = specialist-initiated
Subcutaneous Infusions and Medication Compatibilities

Mixing medications in subcutaneous infusions can cause problems if there are drug incompatibilities that cause reactions. Always use caution when mixing medications looking especially for crystallization. The following small table lists some compatible combinations - it is not an exhaustive list. If unsure about a combination, speak to a palliative care pharmacist, physician or nurse specialist.

<table>
<thead>
<tr>
<th>Compatible combinations</th>
<th>Diluent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclizine (avoid if oxycodone dose &gt;100mg – may precipitate)</td>
<td>Water</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Water</td>
</tr>
<tr>
<td>Hyoscine butylbromide</td>
<td>Water</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Water</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Water</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Water</td>
</tr>
<tr>
<td>Cyclizine and haloperidol</td>
<td>Water</td>
</tr>
<tr>
<td>Cyclizine and midazolam</td>
<td>Water</td>
</tr>
<tr>
<td>Haloperidol and hyoscine butylbromide</td>
<td>Water</td>
</tr>
<tr>
<td>Haloperidol and midazolam</td>
<td>Water</td>
</tr>
<tr>
<td>Haloperidol and octreotide</td>
<td>Sodium chloride 0.9%</td>
</tr>
<tr>
<td>Midazolam and hyoscine butylbromide</td>
<td>Water</td>
</tr>
<tr>
<td>Midazolam and levomepromazine</td>
<td>Water</td>
</tr>
<tr>
<td>Midazolam and metoclopramide</td>
<td>Water</td>
</tr>
<tr>
<td>Midazolam and octreotide</td>
<td>Sodium chloride 0.9%</td>
</tr>
<tr>
<td>Levomepromazine and hyoscine butylbromide</td>
<td>Water</td>
</tr>
<tr>
<td>Levomepromazine and ondansetron</td>
<td>Sodium chloride 0.9%</td>
</tr>
<tr>
<td>Haloperidol and midazolam and hyoscine butylbromide</td>
<td>Water</td>
</tr>
<tr>
<td>Levomepromazine and midazolam and hyoscine butylbromide</td>
<td>Water</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Either MORPHINE or OXYCODONE with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>FENTANYL with:</strong></td>
</tr>
<tr>
<td>Haloperidol</td>
</tr>
<tr>
<td>Hyoscine butylbromide</td>
</tr>
<tr>
<td>Levomepromazine</td>
</tr>
<tr>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Midazolam</td>
</tr>
<tr>
<td>Haloperidol and midazolam</td>
</tr>
<tr>
<td>Levomepromazine and metoclopramide</td>
</tr>
<tr>
<td>Levomepromazine and midazolam</td>
</tr>
<tr>
<td>Haloperidol and hyoscine butylbromide and midazolam</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OPIOID-FREE combinations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levomepromazine and ondansetron</td>
</tr>
<tr>
<td>Haloperidol and ondansetron</td>
</tr>
<tr>
<td>Haloperidol and hyoscine butylbromide and octreotide and ranitidine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specialist-initiated medicines:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine – see page 28 for compatible combinations</td>
</tr>
<tr>
<td>Methadone – see page 26 for compatible combinations</td>
</tr>
</tbody>
</table>

| Ketorolac is compatible with ranitidine and/or oxycodone | Sodium chloride 0.9% |

**The following drugs cannot be combined in the same syringe with other drugs**

<table>
<thead>
<tr>
<th>Diclofenac</th>
<th>Furosemide</th>
<th>Levetiracetam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>Lidocaine</td>
<td>Valproate</td>
</tr>
</tbody>
</table>

† = off-label route or use †† = unlicensed ‘special’ # = specialist-initiated
Prognostication

Predicting life expectancy is not easy and it is as much an art as a science. Of course none of us know the future and so it is not helpful to be too definite about a patient’s prognosis. None-the-less, being able to make a reasonable, educated guess about a patient’s illness trajectory and the likely prognosis is important because:

- Some patients (and their relatives) want to know this (although it is equally true that some do not)
- It helps inform decisions regarding how aggressively to treat complications as they arise

If discussing prognosis and life expectancy with a patient, be sensitive, compassionate and honest in your approach. Do not be afraid to be unsure and to defer to other doctors and specialists who have more experience in treating the patient’s particular illness.

A key element to determining prognosis is to understand the natural history of the particular disease that the patient suffers from. It is helpful to remember that new treatments are changing the trajectory and course of many illnesses.

The following information boxes, tools and rules of thumb may be helpful in determining prognosis. None of them is perfect, however, so use them in conjunction with common sense.

**Patients gradually declining with advanced, metastatic cancer**

Palliative Prognostic Index (PPI)

- If the PPI > 6 → death is likely within a month

Specific complications and scenarios

- If a patient develops acute renal failure with anuria due to obstructive uropathy and this is not relieved via stenting → creatinine will typically rise 50-100µmol/l daily with death likely within weeks, especially once creatinine passes 1,000µmol/l
- If a patient develops bile duct obstruction due to tumour and this is not relieved via stenting → bilirubin will typically rise 15-30µmol/l daily with death is likely within weeks, especially once bilirubin passes 400µmol/l
- If a patient has a rapidly rising white cell count and a short doubling time of a few days in the context of untreated acute myeloid leukaemia → death likely within weeks, especially once the total white cell count passes 400 x 10^9/L

<table>
<thead>
<tr>
<th>Palliative Performance Score (PPS)</th>
<th>Palliative Prognostic Index (PPI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PPS</strong> (see table above)</td>
<td><strong>PPS</strong> (see table above)</td>
</tr>
<tr>
<td>100</td>
<td>If 10-20 → Score 4</td>
</tr>
<tr>
<td>90</td>
<td>If 30-50 → Score 2.5</td>
</tr>
<tr>
<td>80</td>
<td>If &gt; 50 → Score 0</td>
</tr>
<tr>
<td>70</td>
<td><strong>Oral Intake</strong></td>
</tr>
<tr>
<td></td>
<td>If severely down →</td>
</tr>
<tr>
<td></td>
<td>Score 2.5</td>
</tr>
<tr>
<td></td>
<td>If moderately down →</td>
</tr>
<tr>
<td></td>
<td>Score 1</td>
</tr>
<tr>
<td>60</td>
<td>If normal → Score 0</td>
</tr>
<tr>
<td>50</td>
<td><strong>Oedema</strong></td>
</tr>
<tr>
<td></td>
<td>If present → Score 1</td>
</tr>
<tr>
<td></td>
<td>If absent → Score 0</td>
</tr>
<tr>
<td>40</td>
<td><strong>Dyspnoea at rest</strong></td>
</tr>
<tr>
<td></td>
<td>If present → Score 3.5</td>
</tr>
<tr>
<td></td>
<td>If absent → Score 0</td>
</tr>
<tr>
<td>30</td>
<td><strong>Delirium</strong></td>
</tr>
<tr>
<td></td>
<td>If present → Score 4</td>
</tr>
<tr>
<td></td>
<td>If absent → Score 0</td>
</tr>
<tr>
<td>20</td>
<td>* Add the scores together to</td>
</tr>
<tr>
<td></td>
<td>determine the total</td>
</tr>
<tr>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Return to contents page  † = off-label route or use  †† = unlicensed ‘special’  # = specialist-initiated
Prognostication in end-stage organ failure

The course and natural history of end-stage organ failure (e.g. liver failure due to cirrhosis) is very variable and it is harder to be reasonably sure about the prognosis when compared to advanced metastatic cancer. Acute deteriorations are more often reversible and so knowing when to withdraw (or not offer) treatment can be quite difficult.

The following categories and classification systems should be used as a very broad and general guide only.

**Cirrhosis:** The Child-Pugh scoring system is helpful in determining prognosis:
- Child’s A (Score < 7) cirrhosis → 80% 1-year survival
- Child’s B (Score 7-9) cirrhosis → 60% 1-year survival
- Child’s C (Score > 9) cirrhosis → 40% 1 year survival

<table>
<thead>
<tr>
<th>Score for:</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild</td>
<td>Severe</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Mild</td>
<td>Severe</td>
</tr>
<tr>
<td>Bilirubin (µmol/l)</td>
<td>&lt; 34</td>
<td>35-49</td>
<td>&gt; 50</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>&gt; 35</td>
<td>29-34</td>
<td>&lt; 28</td>
</tr>
<tr>
<td>INR</td>
<td>&lt; 1.7</td>
<td>1.8-2.3</td>
<td>&gt; 2.4</td>
</tr>
</tbody>
</table>

Special cases:
- Hepatorenal syndrome is associated with a particularly poor prognosis with a 50% death rate within 1-month. There are treatments available so seek specialist advice regarding this.

**Chronic Kidney Disease:** The GFR is helpful in determining prognosis:
- Stage 5 → 70% 1-year survival for patients who elect to not have dialysis

<table>
<thead>
<tr>
<th>Stage</th>
<th>eGFR</th>
<th>Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt; 90</td>
<td>Normal function</td>
</tr>
<tr>
<td>2</td>
<td>60-90</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>30-60</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>15-30</td>
<td>Severe</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15</td>
<td>End-stage</td>
</tr>
</tbody>
</table>

Special cases:
- Anuria is associated with a particularly poor prognosis (when compared to oliguria)
- Severe hyperkalaemia may cause fatal cardiac arrhythmias and sudden death

**Congestive Cardiac Failure:** The New York Heart Association Classification is helpful in determining prognosis:
- NYHA Class 4 with a hospital admission due to cardiac failure within the last 6-months → 50% 1-year survival

<table>
<thead>
<tr>
<th>Class</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Mild dyspnoea on ordinary activities</td>
</tr>
<tr>
<td>3</td>
<td>Marked limitation in activity</td>
</tr>
<tr>
<td>4</td>
<td>Almost bed-bound due to symptoms</td>
</tr>
</tbody>
</table>

Special cases:
- Hypotension and a raised creatinine is associated with a particularly poor prognosis

**Chronic Obstructive Pulmonary Disease:** Frequent admissions for acute exacerbations is helpful in determining prognosis:
- Patients admitted at least twice for exacerbations of COPD in the last 12 months → 80% 1-year survival

<table>
<thead>
<tr>
<th>Negative prognostic factors for COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 &lt; 35% predicted</td>
</tr>
<tr>
<td>Frequent admissions for exacerbations</td>
</tr>
<tr>
<td>Hypercapnia</td>
</tr>
<tr>
<td>Home oxygen</td>
</tr>
<tr>
<td>Cor pulmonale</td>
</tr>
<tr>
<td>Multiple medical comorbidities</td>
</tr>
</tbody>
</table>

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Opioids – Starting, Titrating and Troubleshooting

Before starting opioids

- Is there a treatment (e.g. radiotherapy) to target the cause specifically?
- Should a non-opioid be tried first?
  - Is the patient’s prognosis many months or years? If so, exhaust non-opioid options first (long-term opioids have endocrine and immune adverse effects)
  - Is the pain unlikely to respond fully to an opioid? (See table below)

### Type of pain

<table>
<thead>
<tr>
<th>Type of pain</th>
<th>Helpful adjuvant agents include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathic</td>
<td>Gabapentin or amitriptyline†</td>
</tr>
<tr>
<td>Muscular spasms</td>
<td>Baclofen</td>
</tr>
<tr>
<td>Colicky abdominal pain</td>
<td>Hyoscine butylpromide (Buscopan)</td>
</tr>
<tr>
<td>Bone pain</td>
<td>Non-steroid anti-inflammatory drugs Bisphosphonates</td>
</tr>
</tbody>
</table>

### Renal impairment

<table>
<thead>
<tr>
<th>Type</th>
<th>Opioid choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Morphine</td>
</tr>
<tr>
<td>Mild</td>
<td>*Fentanyl or oxycodone</td>
</tr>
<tr>
<td>Severe</td>
<td>*Fentanyl</td>
</tr>
</tbody>
</table>

* = Less likely to accumulate

Starting opioids

- All opioids have similar efficacy and side-effects
- Morphine is a good first choice except in renal failure or if a patch is preferable
- Start with low doses and titrate up as needed using both a regular long acting opioid and a PRN immediate release formulation (see below). Initial doses are based on age and frailty

<table>
<thead>
<tr>
<th>Type of pain</th>
<th>Helpful adjuvant agents include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathic</td>
<td>Gabapentin or amitriptyline†</td>
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<tr>
<td>Muscular spasms</td>
<td>Baclofen</td>
</tr>
<tr>
<td>Colicky abdominal pain</td>
<td>Hyoscine butylpromide (Buscopan)</td>
</tr>
<tr>
<td>Bone pain</td>
<td>Non-steroid anti-inflammatory drugs Bisphosphonates</td>
</tr>
</tbody>
</table>

For young adults

Oramorph (morphine immediate release) 5-10mg 2-hourly PRN +/- Zomorph (morphine slow release) 10mg twice daily

For elderly, frail adults

Oramorph (morphine immediate release) 2.5-5mg 2-hourly PRN +/- MST Continus (Morphine slow release) 5mg twice daily

- Always follow-up patients closely to avoid toxicity when starting and changing doses. Advise patients to seek medical advice if they are requiring ≥ 3 break-through (PRN) doses of opioid a day.
- Prophylactic laxatives are almost always indicated (e.g. bisacodyl)

Side-effects

- If problematic side effects develop, consider these two options:
  - Is a non-opioid more appropriate (e.g. neuropathic)? → Reduce opioid dose + add a non-opioid agent
  - Is it worth trying a different opioid? → Opioid switch (e.g. from morphine to oxycodone)
- Helpful treatments for adverse effects include:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>PRN anti-emetics, e.g. metoclopramide</td>
</tr>
<tr>
<td>Constipation</td>
<td>Increase or combine laxatives (e.g. add a softener if colicky pain)</td>
</tr>
<tr>
<td>Confusion</td>
<td>Reduce opioid dose. If significant agitation, †haloperidol may be necessary.</td>
</tr>
</tbody>
</table>

- Drowsiness and respiratory depression are very serious and are dose-related
Long-acting opioids (e.g. modified release morphine and oxycodone, transdermal fentanyl)

- Are given to provide continuous background pain relief
- Can be given orally (via slow released tablets), topically (via patches) or subcutaneously (via continuous infusions) (or via any combination of these)

Short-acting opioids (e.g. oral solutions of morphine or oxycodone)

- Are given to provide analgesia for breakthrough pain
- For patients on long-acting opioids, a dose of one-sixth to one-tenth of the total daily dose of opioid is usually required as the PRN dose (e.g. a person taking twice daily 60 mg of slow-release oral morphine will probably require breakthrough doses of 20 mg immediate-release oral morphine 2-hourly PRN)

Approximate Equianalgesic Doses

<table>
<thead>
<tr>
<th>Morphine (milligrams)</th>
<th>Oxycodone (milligrams)</th>
<th>Fentanyl (micrograms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>SC</td>
<td>Oral</td>
</tr>
<tr>
<td>5</td>
<td>2.5</td>
<td>≈5</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>≈10</td>
</tr>
<tr>
<td>15</td>
<td>7.5</td>
<td>10</td>
</tr>
<tr>
<td>30</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>60</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>90</td>
<td>45</td>
<td>60</td>
</tr>
<tr>
<td>120</td>
<td>60</td>
<td>80</td>
</tr>
</tbody>
</table>

Consider seeking specialist advise if titrating above 120mg of morphine daily or equivalent, particularly if anticipating longer term (≥months) use: alternatives could limit longer term adverse effects

<table>
<thead>
<tr>
<th>Approximates at a glance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For Morphine</strong></td>
</tr>
<tr>
<td>1mg SC morphine</td>
</tr>
<tr>
<td>≈ 2mg oral morphine</td>
</tr>
<tr>
<td>≈ 0.66mg SC oxycodone</td>
</tr>
<tr>
<td>≈ 1.33mg oral oxycodone</td>
</tr>
<tr>
<td>≈ 15microgram SC fentanyl</td>
</tr>
<tr>
<td>1mg oral morphine</td>
</tr>
<tr>
<td>≈ 0.5mg SC morphine</td>
</tr>
<tr>
<td>≈ 0.33mg SC oxycodone</td>
</tr>
<tr>
<td>≈ 0.66mg oral oxycodone</td>
</tr>
<tr>
<td>≈7.5microgram SC fentanyl</td>
</tr>
<tr>
<td><strong>For Oxycodone</strong></td>
</tr>
<tr>
<td>1mg SC oxycodone</td>
</tr>
<tr>
<td>≈ 1.5mg SC morphine</td>
</tr>
<tr>
<td>≈ 3mg oral morphine</td>
</tr>
<tr>
<td>≈ 2mg oral oxycodone</td>
</tr>
<tr>
<td>≈22microgram SC fentanyl</td>
</tr>
<tr>
<td>1mg oral oxycodone</td>
</tr>
<tr>
<td>≈ 0.75mg SC morphine</td>
</tr>
<tr>
<td>≈ 1.5mg oral morphine</td>
</tr>
<tr>
<td>≈ 0.5mg SC oxycodone</td>
</tr>
<tr>
<td>≈11microgram SC fentanyl</td>
</tr>
<tr>
<td><strong>For Fentanyl</strong></td>
</tr>
<tr>
<td>1microgram SC fentanyl</td>
</tr>
<tr>
<td>≈ 0.067mg SC morphine</td>
</tr>
<tr>
<td>≈ 0.13mg oral morphine</td>
</tr>
<tr>
<td>≈ 0.05mg SC oxycodone</td>
</tr>
<tr>
<td>≈ 0.1mg oral oxycodone</td>
</tr>
</tbody>
</table>

* A 25 microgram/hour patch of fentanyl = a daily dose of 24x25 = 600 microgram of fentanyl

Use the tabled information to determine the approximate dose when converting one opioid to another. Choosing a dose a little lower than the converted dose is generally the safest option. For example, a patient receiving doses of 10mg of oral oxycodone could change to 5-7.5mg of SC morphine.

Titrating Doses

If pain is poorly controlled but the opioids are having some benefit, the long-acting background opioid dose can be gradually increased taking the previous 24-hour breakthrough requirements into account. In general it is safest to increase the background dose of opioid by no more than 33% in one go. If increasing doses of opioids are not helping, think about other analgesic options.

For example, if a patient on 100mg of daily long-acting oral morphine has 3 breakthroughs of 10mg oral morphine in 24-hours, the oral long-acting dose could be increased to 130mg daily.

Return to contents page † = off-label route or use †† = unlicensed ‘special’ # = specialist-initiated
Starting and titrating a continuous subcutaneous infusion (CSCI)

In patients who are unable to swallow (e.g. near the end of life) or who are not absorbing oral medications (e.g. vomiting), it is often helpful to give medications via a continuous subcutaneous infusion.

In an opioid-tolerant patient who can no longer take oral opioids:

Convert the total daily oral dose of opioid to its subcutaneous equivalent and reduce the dose by a small amount (e.g. 25%) for safety.

Do the same for any other medications required for symptom control.

Write up the infusion.

Ensure any PRN medications are also written up SC.

**Worked Example:**

A patient on 30mg oral twice daily MR oxycodone
= 60mg total daily dose of oral oxycodone
= 30mg total daily dose of SC oxycodone
→ Reduce to 20mg daily SC oxycodone

The patient is also on 10mg oral three times a day metoclopramide
= 30mg total daily dose of oral metoclopramide
= 30mg total daily dose of SC metoclopramide

Write up the infusion as:
Oxycodone 20mg via CSCI over 24 hours and 
Metoclopramide 30mg via CSCI over 24 hours [using water as diluent - see page 6]

Write up any PRN analgesia:
Oxycodone 5mg SC 2-hourly PRN

In an opioid-naïve patient for whom opioids via CSCI are appropriate:

Start the infusion at a low dose (e.g. 10mg of daily SC morphine).

Determine if any other medications are needed via CSCI.

Write up the infusion.

Ensure any PRN medications are also written up.

**Worked Example:**

In an opioid-naïve elderly patient entering the terminal phase of an illness who has agitation and grimacing, write up the infusion as:
Morphine 10mg via CSCI over 24 hours
Midazolam 10mg via CSCI over 24 hours
[using water as diluent - see page 6]

Write up appropriate PRN medications:
Morphine 2.5mg 1-hourly SC PRN for pain
Midazolam 2.5mg 1-hourly SC PRN for agitation

Titrating up the dose of opioid in a CSCI in a patient with poorly controlled pain:

Ensure the PRN doses of opioid are having some effect (if not, this may be an opioid-resistant pain), then determine the total dose of PRN opioid over the last 24 hours.

Increase the dose of the CSCI by a maximum of either the total dose of PRN opioid over the last 24 hours OR 33% of the total daily CSCI dose (whichever is lower)

Ensure the new PRN opioid dose remains between about one-sixth to one-tenth of the 24-hour CSCI dose of opioid.

**Worked example:**

A patient is on 100mg of morphine via CSCI over 24 hours. He used 3 x PRN doses of 10mg of SC morphine yesterday
= 30mg of PRN morphine in 24 hours

Rewrite the new morphine infusion
Morphine 130mg over 24 hours via CSCI

Rewrite the new PRN morphine dose
Morphine 15-20mg hourly SC PRN for pain
Difficult Pains – Incident, Neuropathic, Bony and Muscular

**Incident Pain**

This is pain that occurs predictably on specific activities (e.g. pain that occurs when standing up and walking).

Aim to reduce underlying causes and triggers if possible, e.g.
- Bony instability (e.g. splints, orthopaedic surgery)
- Painful ulcers (e.g. treat infection)
- Movement induced pain (e.g. an OT and physiotherapy review to assess suitability for equipment)

Optimise regular analgesia for background pain, remembering that neuropathic pain and muscular spasms are common.

Treatment with a short acting (immediate release) opioid 15 to 30 minutes prior to any activity that causes pain can be particularly helpful.

**Neuropathic Pain**

This is pain that occurs due to direct damage to the peripheral or central nervous system (e.g. due to a tumour invading the nerve). Common characteristics include shooting, stabbing or burning style pain. Allodynia (pain on light touch) is sometimes also present.

If neuropathic-sounding pain is not responding to simple analgesia, consider adding an adjuvant agent:

*Common first-line agent:* Amitriptyline or gabapentin

*Common second-line approach:* If partial response to first-line, combine both amitriptyline and gabapentin together. If first line brought no benefit, switch to the other agent.

Typical third-line approach: add an alternative anti-epileptic drug (e.g. valproate, carbamazepine) and withdraw the gabapentin.

If pain control remains poor, refer to the palliative care team. Specialist options include:
- Methadone via CSCI or orally (page 26)
- Lidocaine via CSCI (page 27)
- Ketamine via CSCI or orally (page 28)

---

**Example treatment for incident pain:**

Oramorph PRN dose 30 minutes prior to getting out of bed for a shower in the morning

**If pain persists, specialist-initiated options include**

- rapid onset opioids; topical opioids; interventional anaesthesia; identifying additional targets for non-opioid adjuvants

**Amitriptyline†**

*Starting dose:* 10mg at night
*Titrate if necessary:* up to 50mg at night over 2 weeks. Only increase further if partial benefit already seen

**Gabapentin**

*Starting dose:* 300mg at night (or 100mg at night if frail)
*Titrate if necessary:* up to a maximum of 900mg three times daily over 3 weeks (or lower if frail or renal impairment)

**Valproate†**

*Starting dose:* 200mg MR at night
*Titrate in 200mg steps if necessary:* up to a maximum of 800mg MR at night over 2 weeks

---

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Painful Bony Metastases

Bony metastases often respond well to anti-inflammatory medications such as NSAIDs and steroids (e.g. dexamethasone 4mg orally each morning with a proton pump inhibitor).

Both NSAIDs and steroids have their difficulties in terms of side effects, so consider these carefully prior to initiating. Consider using a proton pump inhibitor when commencing an NSAID or steroid.

For incident pain (e.g. pain on walking) → consider a PRN quick-acting opioid prior to exertion (see pages 10 and 11).

For pain unresponsive to medications → consider referring for radiotherapy (speak to the patient’s own oncologist if possible; otherwise, discuss with the on-call clinical oncologist at Southampton Hospital on 023 8077 7222 bleep 1414).

Think about the fracture risk:
- Helpful guides for fracture risk:
  - Limbs: Mirel’s score ≥ 9 associated with ≈ 33% fracture risk
  - Spine: SINS ≥ 7 is considered to define high fracture risk
- In cases of high fracture risk → consider referral to an orthopaedic surgeon for prophylactic pinning (for non-spinal surgery ask for the on-call orthopaedic surgeon via St Mary’s Hospital switchboard – 524 081; for spinal surgery, ask for the on-call spinal surgeon via Southampton Hospital switchboard – 023 8077 7222).

If there is worsening back pain or reduced mobility → think about the possibility of spinal cord compression.

<table>
<thead>
<tr>
<th>Mirel’s Scoring System (for upper and lower limbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spine Instability Neoplastic Score (SINS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine location</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Pain with movement / loading</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Bone lesion type</td>
</tr>
<tr>
<td>Lytic</td>
</tr>
<tr>
<td>Mixed</td>
</tr>
<tr>
<td>Blastic</td>
</tr>
<tr>
<td>Radiographic spinal alignment</td>
</tr>
<tr>
<td>Subluxation</td>
</tr>
<tr>
<td>De novo deformity</td>
</tr>
<tr>
<td>Normal alignment</td>
</tr>
<tr>
<td>Vertebral body collapse</td>
</tr>
<tr>
<td>&gt; 50% collapse</td>
</tr>
<tr>
<td>&lt; 50% collapse</td>
</tr>
<tr>
<td>&gt; 50% of body involved (but no collapse)</td>
</tr>
<tr>
<td>None of the above</td>
</tr>
<tr>
<td>Posterolateral involvement</td>
</tr>
<tr>
<td>Bilateral</td>
</tr>
<tr>
<td>Unilateral</td>
</tr>
<tr>
<td>None</td>
</tr>
</tbody>
</table>
Muscular spasms

Are relatively common in advanced neurological conditions (such as motor neuron disease) as well as in patients with recent soft tissue injury.

Consider trialling regular baclofen (which is a muscle relaxant)
- Initial dose of baclofen is 5mg orally, three times a day
- Titrate up if necessary by 5mg orally three times a day every 3 days to 20mg orally three times a day
- When stopping baclofen, do so slowly over 2 weeks to avoid withdrawal symptoms
- Baclofen is renally cleared and dose reduction is required in renal failure

In muscular spasms associated with soft tissue injury, NSAIDs are a good first choice

Consider referring for a palliative care opinion in difficult cases of pain. Options that may be considered include neuropathic medications (e.g. †gabapentin) and acupuncture.

Colicky abdominal pain

Consider trialling hyoscine butylbromide (Buscopan)
- 20mg four times daily orally or SC, regularly or PRN
- Can be given by CSCI (60mg over 24 hours via CSCI; titrate to 120mg over 24 hours if necessary)
- Avoid using with prokinetic agents such as metoclopramide as they have opposing actions

If constipation is contributing → reduce stimulant laxatives and increase softener laxatives

If bowel obstruction might be contributing → investigate and treat this as appropriate (page 24)

Rectal pain

Refer early as this is often difficult to treat. Options include:

First-line:
- Opioids (page 9-10)
- Steroids or NSAIDs

If pain persists, consider:
- Neuropathic agents (e.g. gabapentin)
- GTN (try sublingually initially, or topically if sphincter spasm suspected)
- Topical anaesthetics
- Specialist referral (options include †nifedipine, #methadone or #ketamine)

Refractory pain

Pain that remains severe despite simple analgesia, opioids and adjuvant agents may require specialist medications or procedural interventions. Seek specialist advice in these instances, but options may include:
- Psychological support and counselling
- Specialist medications (e.g. methadone or lidocaine)
- Procedural interventions (e.g. coeliac plexus block or intra-thecal analgesia)
Systemic Symptoms

Fatigue
Is often a sign of progressive disease. Causes are usually multiple. Consider reversible causes and treat these if they appear to be playing a significant role in fatigue.

Non-pharmacological management may include:
- Mild exercise programs and routines
- Education and counselling
  - Accepting fatigue as part of the illness
  - Modifying activities and goals appropriately

Pharmacological management:
- Steroids improve energy and appetite in some patients
  - Trial dexamethasone† for 1 week at 4mg orally daily
  - If no improvement, cease dexamethasone
  - If significant improvement, continue dexamethasone. Consider use in short courses (e.g. 2-4 weeks) and/or reducing dose to 2mg daily to reduce risk of side effects. Consider a proton pump inhibitor.
- Consider referral. Specialist options include psychostimulants#

Anorexia (poor appetite)
Is a sign of advanced disease that is often more distressing to relatives than it is to patients. Before treating with medications, try exploring the patient’s and family’s concerns.

If depression is playing a role, consider an antidepressant (NB mirtazepine has appetite-stimulant effects)

A trial of steroids† as described above in the “Fatigue” section may be worthwhile where appetite rather than weight loss is the primary concern (steroids do not improve muscle mass or strength).

Peripheral oedema and lymphoedema
Swollen lower limbs often reflect multiple underlying aetiologies.

In patients with acutely worsened oedema (especially if unilateral) ➔
- Consider a DVT (even when bilateral) and investigate with ultrasound if appropriate. The presence of a PICC line in a swollen upper limb should raise the suspicion of an upper limb DVT
- Consider cellulitis and treat with antibiotics (for a 14-day course if associated with lymphoedema)

In patients where peripheral oedema may be connected to right heart failure or hypoalbuminaemia (usually bilateral) ➔ Consider a trial of diuretics (e.g. furosemide 40 mg orally in the morning).

Refer patients early if thought to have lymphoedema due to lymphatics obstruction (often unilateral) ➔ In addition to hosiery, manual lymphatic drainage and compression bandaging, patient education is important (EMH lymphoedema team: 529 511, ext: 127)

Anaemia and transfusions
For people in the community with palliative care needs, transfusions can be arranged via EMH (533 331).

Be clear about the intended aim of blood transfusions. If symptoms don’t improve as hoped, it may be that anaemia is not the main cause of the dyspnoea or fatigue. Future transfusions are thus unlikely to help.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Potential treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia of chronic disease</td>
<td>Transfusion</td>
</tr>
<tr>
<td>Hypercalcaemia of malignancy</td>
<td>Zolendronic acid</td>
</tr>
<tr>
<td></td>
<td>Parenteral fluids</td>
</tr>
<tr>
<td>Steroid-induced diabetes mellitus</td>
<td>Reduce steroid dose</td>
</tr>
<tr>
<td></td>
<td>Insulin</td>
</tr>
<tr>
<td>Infection</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Mood and adjustment disorders</td>
<td>Counselling Supportive care (e.g. JCC day services)</td>
</tr>
<tr>
<td></td>
<td>Antidepressants</td>
</tr>
</tbody>
</table>

† = off-label route or use
†† = unlicensed ‘special’
# = specialist-initiated
## Skin Symptoms

### Itch (pruritus)

Pruritus has many causes and in a palliative care patient experiencing an itch, there may be no connection between the itch and the palliative illness. Thinking carefully about the cause often helps guide treatment.

Before trying oral medications, try emollients and other measures

- If the itch might be histamine-related → try a non-sedating anti-histamine, e.g.
  - Cetirizine 10mg daily regularly or PRN
- If the itch is related to opioid use → consider one or more of the following options
  - Converting to a different opioid
  - An anti-histamine, e.g. cetirizine 10mg daily
  - An SSRI, e.g. † sertraline 25mg in the morning, increasing to 50mg after 1 week if necessary
- If itch is thought due to cholestatic jaundice → one of the following agents may be tried:
  - Cholestyramine 4g orally three times daily
  - † Sertraline 25mg in the morning, increasing to 50mg after 1 week if necessary
  - Specialist options include † rifampicin 150mg twice daily and † naltrexone
- If itch is associated with dialysis or renal failure despite optimising electrolyte balance → one of the following agents may be tried:
  - † Sertraline 25mg in the morning, increasing to 50mg after 1 week if necessary
  - A sedating anti-histamine, e.g. chlorphenamine (especially if disturbing sleep)
  - Consider referral. Specialist options include ‡ gabapentin, ‡ capsaicin cream

### Wounds

If a wound related to cancer (e.g. from local invasion of the skin) develops, consider doing both of the following:

1. Discuss with a radiation oncologist to see if radiotherapy may be appropriate
2. Refer to a tissue viability nurse for follow-up and appropriate dressings

### General measures

| T | Treat the underlying cause if possible and appropriate |
| T | Remove precipitants (e.g. medications) |
| T | Stop using soap |
| T | Try moisturizer / emollient creams |

### Referring for specialist help in difficult cases:

- If a primary skin problem is suspected and a rash is present, refer to dermatology
- If a systemic problem is suspected, refer to palliative care

### If pain is an issue

- Treat secondary infection
- Systemic analgesia is appropriate
- Pre-emptive analgesia 30 minutes prior to dressing change may help
- For difficult cases, consider specialist referral. Options include topical opioids# or topical lidocaine#

### If bleeding is an issue

- Consider referral for radiotherapy opinion as this may control bleeding
- Dress with gauze soaked in
  - 1:1000† adrenaline (avoid using at extremities: risk of ischaemic damage) or
  - † tranexamic acid (use contents of an ampoule)
- Tranexamic acid 500mg orally three times a day can reduce bleeding (maximum dose 1.5g three times a day)
- If a massive, terminal bleed anticipated, ensure midazolam is available

### If malodour is an issue

- Metronidazole gel often reduces smell (e.g. Anabact)
- If topical therapy ineffective, try metronidazole 400mg orally twice daily
Gastrointestinal Symptoms

Nausea and Vomiting

Treat, if possible, underlying contributing factors (e.g. hypercalcaemia [page 23], constipation [page 18], bowel obstruction [page 24]).

Parenteral treatment (e.g. via CSCI) is typically required in patients who are vomiting. Converting to oral anti-emetics is often then appropriate after the patient has been stable for a few days. Sometimes nausea improves only slightly with mono-therapy and, in these cases, combination therapy with multiple drugs of different classes acting on different receptors is usually effective.

If metabolic or toxic causes are suspected (e.g. uraemia, medication-induced) → †haloperidol is a good first option, e.g.
  o Haloperidol 1mg twice daily orally (or 2mg via CSCI daily)
  AND/OR
  Haloperidol 1mg 4-hourly PRN orally or subcutaneously

If vestibular pathology is the main mechanism (e.g. movement induced or vertigo) → antihistamine-antiemetics are good first options, e.g.
  o Cyclizine 50mg three times a day orally or subcutaneously either regularly or PRN (or 150mg via CSCI daily)

If gastric stasis or distension is probably the main mechanism (or the main mechanism is unclear) → metoclopramide is a good first option (or domperidone if at risk of extrapyramidal symptoms), e.g.
  o Metoclopramide 10mg three times daily pre-meals orally (or 30mg/24hrs via CSCI)
  AND/OR
  Metoclopramide 10mg three times daily PRN orally or subcutaneously

If nausea persists → consider changing to a drug that acts on multiple receptors, e.g. levomepromazine (NB prescribe a tablet cutter if quartering a 25mg size tablet)
  o Levomepromazine †6.25mg orally or SC nocte PLUS
  o Levomepromazine †6.25mg orally or SC three times a day PRN

If nausea still persists → add a third-line agent, e.g. 5-HT3 antagonist
  o Ondansetron 8mg orally or 4mg †subcutaneously twice daily (or 8-16mg via CSCI daily)
  5-HT3 antagonists are also first-line for chemotherapy or radiotherapy induced nausea

Further options for nausea include →
- Steroids, e.g. dexamethasone 8mg orally (especially if nausea related to raised intra-cranial pressure) with a proton pump inhibitor
- Benzodiazepines, e.g. †lorazepam 0.5mg 6-hourly sublingually PRN (especially if anxiety is contributing)

Hiccups

If appropriate, treat the underlying cause if it is known (e.g. dexamethasone for cerebral metastases).

For difficult cases, specialist options include †nifedipine, ††benzodiazepines and †valproate.

First-line:
If caused by gastric distension → try metoclopramide
If cause is neurogenic → try ††gabapentin (same dose as neuropathic pain)

Second-line:
Haloperidol 1.5mg twice daily orally or SC

Third-line:
†Baclofen 5mg twice daily (maximum 10mg three times)

Return to contents page  † = off-label route or use  †† = unlicensed ‘special’  # = specialist-initiated
**Constipation**

Anticipate constipation, especially in patients prescribed opioids, and start prophylactic laxatives where appropriate. If appropriate encourage increased fluids and fruit intake and encourage mobilization if appropriate. Avoid ispaghula (e.g. Fybogel) as it worsens constipation if fluid intake is inadequate.

*Initial therapy →* oral therapy with a softener and/or stimulant is appropriate
- Macrogol 1 sachet twice daily regularly (or PRN) (a softener for hard stools)
  AND/OR
  Bisacodyl 5-10mg orally at night regularly (or PRN) (a stimulant)
  (Doses can be titrated up or down based on level of constipation. Titrate up the softener if stool hard and/or colic present; titrate stimulants up if patient struggling to expel soft stool)

*If constipation continues →* consider rectal treatments, e.g.
- Bisacodyl 1 suppository daily PRN (if stools soft)
- Glycerine 1 suppository or Micolette 1 enema daily PRN (if stool hard)

*For severe, refractory constipation →* options include
- High dose softener (Macrogol 8 sachets over a day)
- High bowel intervention, e.g. Phosphate enema (if stool soft); Arachis oil enema (if stool hard; cannot be given if peanut allergy present)
- Methylenealtrexone if opioid-induced
- Manual evacuation (ensure PRN analgesia / sedation available)
- If obstruction suspected, see page 24

*In constipation associated with spinal cord compression →*
- Oral laxatives
  PLUS
  Bisacodyl suppository each morning (or every second morning)

<table>
<thead>
<tr>
<th>Methylenealtrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripherally acting opioid antagonist</td>
</tr>
<tr>
<td>Used for opioid-induced constipation refractory to appropriately titrated laxatives and enemas</td>
</tr>
<tr>
<td>Dose:</td>
</tr>
<tr>
<td>- 12mg SC (if &gt; 62 kg)</td>
</tr>
<tr>
<td>- 8mg SC (if &lt;62kg and &gt; 38kg)</td>
</tr>
<tr>
<td>Repeat on day 2 if required</td>
</tr>
<tr>
<td>Can result in a massive bowel action within an hour. Is a commode required?</td>
</tr>
<tr>
<td>Can cause severe abdominal cramps.</td>
</tr>
<tr>
<td>Ensure SC hyoscyamine butylbromide (Buscopan) +/- opioids available</td>
</tr>
<tr>
<td>Contraindicated in bowel obstruction</td>
</tr>
<tr>
<td>Dose reduction required in renal</td>
</tr>
</tbody>
</table>

**Diarrhoea**

*If constipation with overflow could be the cause →* treat the constipation

*Is there a treatable cause →*
- Medication side-effect (e.g. due to antibiotic) require modification of medications
- Infections (e.g. *Clostridium difficile*) may require antibiotics
- Pancreatic insufficiency as suggested by steatorrhoea (e.g. due to pancreas cancer) requires Creon

*For diarrhoea requiring symptomatic treatment →*
- *First-line:* loperamide 2-4mg PRN initially (consider a regular dose based on PRN requirements)
- *Second-line:* hyoscine butylbromide (Buscopan) 60-120mg via CSCI over 24 hours

For refractory diarrhoea, refer. Specialist options include octreotide.

For faecal incontinence → in the home, seek advice from a district nurse in the first instance. To speak to a continence nurse specialist, phone 552 457.
Respiratory Symptoms

Dyspnoea

Consider the aetiologies of dyspnoea and treat these as appropriate, taking the patient’s overall state and prognosis into consideration. Thinking about the diagnosis is especially important when there is dyspnoea that acutely worsens or progresses without good explanation. Of particular relevance in the palliative care patient population are questions to do with reversible causes of dyspnoea →

- **Pulmonary emboli** (think of this especially if dyspnoea out of proportion to extent of disease)
- Pleural effusion (or a pericardial effusion or massive ascites)
- Acute respiratory infection
- **Superior vena caval obstruction** (look for oedema and distended veins in the head and upper limbs)

All of these conditions can be diagnosed with appropriate imaging and have specific treatments that can bring significant symptomatic relief and prolong a person’s life. See “Treating Significant Complications” section (pages 23 to 25).

Also think about the particular symptomatic treatments for specific conditions

Finally consider symptomatic treatments regardless of cause →

Movement of air (e.g. via a fan) usually helps.

**If there is dyspnoea at rest** → low doses of opioids may help, e.g. for opioid-naïve patients
- †MST (Morphine SR) 5 mg orally twice daily
- ††Oramorph 2.5 mg orally 2-hourly PRN
  (See the pages 9-10 for information on dosing and opioid choice)

**If there is significant anxiety and fear associated with dyspnoea** → anxiolytics may help; choice partially depends on life expectancy
- Months → Citalopram 10mg orally daily
- Weeks → Lorazepam 0.5-1mg sublingually up to four times daily PRN

**If there is evidence of hypoxia (e.g. SaO2 < 92%)** → oxygen may help, e.g.
- Oxygen continuously for dyspnoea at rest (titrate to symptoms)
  OR
  Oxygen 2-4 litres on exertion and PRN for exertional dyspnoea
  (Use oxygen cautiously in patients who are at risk of CO2 retention, e.g. those with COPD)

**Options for pulmonary oedema:**
- Increase diuretic therapy. Furosemide can be given via CSCI (see page 5). Higher doses are needed in severe renal failure
- Control rapid atrial fibrillation (e.g. with digoxin)
- Long-acting nitrates, especially at night (e.g. transdermal GTN patch) if blood pressure permits

**Options for exacerbation of COPD:**
- Short burst of increased dose of steroids, e.g. prednisolone 30mg daily for 1-2 weeks
- Antibiotics
- Optimise bronchodilator therapy (e.g. review inhaler technique; salbutamol more frequently)

**Options for motor neuron disease:**
- Non-invasive ventilation (NIV). Assessment accessed by referral to St Mary’s respiratory team. Deciding to have or not have NIV is a huge decision and involves delicate discussions. NIV may be appropriate if any of these present:
  o Abnormal nocturnal oximetry OR
  o FVC < 50% predicted OR
  o Orthopnoea

**Options for anaemia:**
- Transfusion (e.g. if Hb < 85) – see page 15

**Options for multiple pulmonary metastases or lymphangitis carcinomatosis:**
- Dexamethasone 8mg orally daily plus a proton pump inhibitor

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<th>Condition specific symptomatic treatments to consider</th>
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<tr>
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</tr>
<tr>
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</tr>
</tbody>
</table>
Cough

In a patient with cough, think about the cause and treat any reversible causes (e.g. proton pump inhibition if gastro-oesophageal reflux playing a significant role)

For ongoing troubling productive coughs — aim to aid expectoration by
- Chest physiotherapy
- †Nebulized sodium chloride 0.9% 5ml four times daily
- Carbocisteine 750mg three times daily
- If too weak to expectorate (e.g. in a dying person) dry secretions with †hyoscine butylbromide and suppress cough with †opiods

For ongoing troubling dry coughs — consider cough suppression with low-dose opioids, e.g. for opioid-naive patients
- †Oramorph 2.5mg 2-hourly PRN
  (See pages 9-10 for details on opioid dosing and choice)
- If due to large airway irritation (e.g. hilar lymphadenopathy), consider dexamethasone 8mg orally daily with a proton pump inhibitor
- If cough persists, refer: specialist options include #sodium cromoglycate, #SSRIs and #gabapentin.

Haemoptysis

If appropriate, refer for a radiation oncology opinion (if due to malignancy) and/or investigate for other causes (e.g. pulmonary emboli)

If haemoptysis is bothersome, consider:
- †Tranexamic acid 500mg orally three times a day (maximum dose 1.5g three times a day)
  (This increases risk of DVT and stroke. Use with caution in renal failure)

In an acute, massive bleed, immediate treatment directed at comfort is usually appropriate (see “Massive, terminal haemorrhage” box below)

In an acute massive bleed where procedural intervention is appropriate, however, consider:
- Referral to a respiratory physician for an opinion regarding bronchoscopic treatment of bleeding source
  OR
  Referral to an interventional radiologist for angiogram and bronchial artery embolization
- WHILST
  Giving supportive care (e.g. oxygen, blood replacement and correcting any clotting defects)

### Massive, terminal haemorrhage (e.g. massive haemoptysis with respiratory distress)

| Be present with the patient and family |
| Use dark coloured towels and sheets (as these make blood less visible) |
| If time permits and patient distress is great then give parenteral (IV if easily accessible; otherwise SC): |
  - High dose benzodiazepines, e.g. midazolam 10mg immediately, repeated every 10 minutes until comfortable
  - Opioids, e.g. morphine sulphate 10mg, repeated after 10 minute if needed |

### Acute airways obstruction (e.g. due to rapid tumour growth)

If life-saving acute treatment is appropriate
- Get immediate help to maintain the airway from a paramedic, anaesthetist or ENT specialist
- For malignant causes, give high dose steroids (dexamethasone 13.2mg SC or IM [i.e. four 3.3mg ampoules] plus a proton pump inhibitor) and get urgent advice from an oncologist

If terminal care is appropriate
Treat with high doses of opioids and benzodiazepines (similar to the treatment for massive, terminal haemorrhages)
Neurological Symptoms

Agitated delirium

Agitated delirium is common in advanced illnesses. It is a bad prognostic marker in patients with advanced cancer and, if not caused by an easily reversible aetiology, it may indicate that the patient is entering the last few weeks of life.

Consider the underlying causes and treat these if appropriate and possible.

Non-pharmacological measures such as reassurance, orientation and lighting, close contact by loved ones and a quiet environment are very important.

Short-term low-dose antipsychotics reduce distressing symptoms and may improve outcomes (e.g. the likelihood of returning to live independently). Haloperidol is often a good first-line option:

- Haloperidol 0.5mg at night orally or SC
  AND
  Haloperidol 0.5mg PRN three times daily orally

If sleep disturbance is a prominent problem, quetiapine may be preferred to haloperidol

- Quetiapine 12.5mg twice daily orally
  AND
  Quetiapine 12.5mg PRN twice daily orally

If anxiety is playing a large role, adding a benzodiazepine may be appropriate (but be aware that benzodiazepines alone can sometimes exacerbate delirium).

Terminal restlessness

Is the term used to describe agitation and delirium in an imminently dying patient. Use of continuous subcutaneous infusions (with additional PRN subcutaneous benzodiazepines and anti-psychotics) is often required. Start with low doses initially and titrate up as needed. A typical starting CSCI order may look like this:

- †Haloperidol 2.5mg via CSCI over 24 hours
  AND
  †Midazolam 10mg via CSCI over 24 hours
- PLUS PRN medications:
  †Midazolam 2.5-5mg hourly PRN for distress or agitation
  AND
  †Haloperidol 0.5 to 2.5mg SC hourly PRN for hallucinations or agitation

For terminal restlessness that is refractory to treatment with high doses of midazolam and haloperidol (e.g. >30mg/day and >10mg/day respectively), consider switching haloperidol to †levomepromazine 12.5 to 25mg SC hourly (seek advice if 2 or more doses ineffective or if benefit lasts less than an hour) or seeking advice (specialist options include ‡phenobarbital - see page 30).

<table>
<thead>
<tr>
<th>Cause</th>
<th>Possible treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalcaemia</td>
<td>‡Zolendronic acid IV or ‡SC fluids</td>
</tr>
<tr>
<td>Hyponatraemia (due to SIADH)</td>
<td>Fluid restriction Oral sodium ‡Demeclocycline</td>
</tr>
<tr>
<td>Cerebral primary or metastases</td>
<td>Increase dexamethasone dose</td>
</tr>
<tr>
<td>Medications (e.g. dexamethasone, morphine)</td>
<td>Reduce dose or change to an alternative</td>
</tr>
<tr>
<td>Sepsis (e.g. UTI)</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>Lactulose</td>
</tr>
</tbody>
</table>
Seizures

Focal seizures with secondary generalization are a scary complication of brain tumours, both primary and secondary. Primary prophylaxis with anti-epileptics does not reduce the risk so is not recommended in patients with cerebral tumours. However, preventative anti-epileptic medications are usually appropriate after a first seizure because further seizures are likely.

Seizures may also occur because of metabolic disturbances (e.g. hyponatraemia) or as part of a pre-existing epilepsy. As with all problems in palliative care, the management needs to be tailored to the individual patient based on the stage of illness and patient’s function and previously expressed wishes.

Treating a seizure – the acute setting

A quick-acting benzodiazepines is usually the best initial treatment.

If outside of hospital →
- Midazolam 5-10mg buccally or †subcutaneously
- Exclude hypoglycaemia
- Repeat the dose of midazolam 15 minutes later if the seizure is ongoing
- If the cause is known and the seizure has stopped, hospital admission may not be required. The community palliative care team can assist in altering anti-epileptic medicines in the home. If the cause is unknown, hospital admission is appropriate – it may be appropriate to call an ambulance, especially if the seizure is still happening.

If in a hospital setting →
- Lorazepam 4 mg slowly IV until seizure stops.
  - Watch SaO2 and support the airway
  - Exclude hypoglycaemia.
  - If lorazepam is not available, midazolam 5-10mg IV, subcutaneously or buccally is an alternative
- Get help / discuss with an experienced doctor
- If seizure has not settled within 15 minutes →
  - Repeat the benzodiazepine dose
- If the seizure continues, further benzodiazepines are unlikely to be effective. Seek urgent advice from a senior doctor regarding the appropriateness of referral to ITU
  - If ITU is appropriate, call ITU whilst giving IV phenytoin
  - If ITU is inappropriate and the patient is thought to be imminently dying, seek advice from the hospital palliative care team. Prepare the family that death may be near. #Phenobarbital can be used for seizures refractory to midazolam (see page 30)

Preventing further seizures

Treat any underlying precipitants. If already on anti-epileptics, modify dose if appropriate.

For seizures due to cerebral tumours, levetiracetam or sodium valproate are good first-line options:
- Levetiracetam 500mg orally twice daily (maximum dose: 1,500 mg twice daily)
  OR
- Sodium valproate MR 200mg twice daily (typical maximum 800mg twice daily)

Remember to advise a patient against driving following a seizure.

For seizures in a patient entering the last days of life, replace oral anti-epileptics with:
- †Midazolam 20mg over 24 hours via CSCI + Midazolam 5-10mg SC PRN for any further seizures

Return to contents page † = off-label route or use †† = unlicensed ‘special’ # = specialist-initiated
Treating Complications of Advanced Cancer

Hypercalcaemia

Hypercalcaemia can worsen energy levels, pain, confusion and constipation. Corrected levels > 3.0 mmol/L almost always cause symptoms. Corrected levels > 2.75 mmol/L may contribute to symptoms. The Community Palliative Care Team can treat hypercalcaemia in the home or outpatient setting (phone: 533 331).

Give:

- † Haloperidol 1.5mg SC if nausea or agitated delirium present
- IV or SC fluids if dehydrated (and review need for nephrotoxic medications, e.g. NSAIDs)
- Zolendronic acid 4mg IV over 15 minutes (dose reduce in renal failure; avoid if eGFR < 30)

Recheck calcium 3-5 days later. Repeat doses of zolendronic acid can be given every one to two weeks, but if this is required it suggests the patient is nearing the very end of life and continued attempted treatment may be inappropriate.

Spinal Cord Compression

Suspect this in any patient with advanced malignancy who develops weakness or problems with mobility acutely. Usually also associated with new or worsening back pain.

Investigation of choice is an urgent MRI (that day). Image the entire spine +/- brain. If meningeal metastases are suspected (e.g. multiple unrelated nerve roots affected), image with gadolinium contrast.

Usual treatment:
- Dexamethasone 16mg orally daily (or in divided doses) (also give a proton pump inhibitor)
- Urgent referral for consideration of emergency spinal surgery or radiotherapy (for most cancers, speak to Clinical Oncology at Southampton Hospital – 023 8077 7222, bleep 1414)

Do not delay investigating and treating possible spinal cord compression unless active treatment is inappropriate because early treatment may save a patient from paraplegia or quadriplegia.

Cerebral metastases

Present in a legion of ways (e.g. confusion, drowsiness, headache, vomiting, hiccups, seizures). If symptoms are problematic, give dexamethasone 8-16mg orally daily (plus a proton pump inhibitor). Arrange contrast-enhanced CT or an MRI in patients where treatment would be considered.

Treatment options may include radiotherapy or, for solitary lesions, neurosurgery. Discuss with the patient’s own oncologist if possible in the first instance. Otherwise, speak to the on-call clinical oncologist at Southampton Hospital on 023 8077 7222, bleep 1414. Radiotherapy can improve symptoms and prolong life by a number of months. Wean dexamethasone post-radiotherapy over 4 weeks unless symptoms flare-up. Complications of cerebral irradiation include memory loss and a change in personality.
Malignant Bowel Obstruction

Bowel obstruction in malignancy is complex in aetiology. The underlying pathology may cause a physical, mechanical obstruction. Alternatively there may be pathology causing a predominantly ileus type scenario. This booklet distinguishes between an ileus-type picture (referred to as “pre-bowel obstruction” here) and a mechanical, physical obstructive picture (referred to as “malignant (mechanical) bowel obstruction” here). In practice both mechanisms may be occurring together and the disease varies along a spectrum.

Bowel obstruction is common in pelvic (e.g. ovarian cancer) malignancies with peritoneal spread. It also occurs in gastrointestinal malignancies such as colorectal cancer and pancreas cancer.

“Pre-Bowel Obstruction”

Suspect this in at risk patients with vomiting, abdominal distension, reducing frequency of bowel movement and an absence of colicky abdominal pain.

First-line treatment includes:
- Metoclopramide 30mg CSCI over 24 hours (if colicky pains occurs, stop metoclopramide as this worsens colic and manage as a mechanical bowel obstruction)
- Sodium docusate 200mg twice daily orally

If no improvement after 2-3 days add dexamethasone 6.6mg SC daily and increase metoclopramide to 60mg/24hrs (monitor for evidence of extrapyramidal effects).

If still no improvement after 3-5 days, consider speaking to a palliative care physician

Malignant (Mechanical) Bowel Obstruction

A pre-bowel obstructive picture may progress to a full blown obstruction with colicky abdominal pain, worsened vomiting and distension, and absolute constipation; or this may occur de novo. This often heralds the last few weeks of a person’s life. Consider gaining a surgical opinion if the patient has minimal disease with a good performance status and an otherwise relatively long life-expectancy.

Treat vomiting and distension with anti-secretory agents:
- Hyoscine butylbromide 120mg via CSCI over 24 hours and Ranitidine 150mg via CSCI over 24 hours

Additional symptomatic relief is important, including:
- Haloperidol for any ongoing nausea (e.g. 1mg 2-hourly PRN)
- An opioid for analgesia
- Minimal oral intake: give parenteral fluids (e.g. sodium chloride 0.9% SC 1 litre/day) if maintaining hydration is appropriate

If the aim is to try and restore bowel movements, consider:
- Dexamethasone 6.6mg SC daily may reduce peri-tumour oedema
- Sodium docusate orally and softeners per rectum in case constipation / hard stools are playing a role
- SC fentanyl rather than morphine (less impact on peristalsis)

If vomiting persists:
- If minimal oral intake, add octreotide 600mcg via CSCI over 24 hours (an anti-secretory agent)
- Anti-secretory drugs will be less effective if eating and drinking – consider an NG tube or venting PEG

If nausea persists, switch haloperidol to levomepromazine 6.25mg via CSCI over 24 hours.

To also consider:
Consider investigating with a CT abdomen to (a) confirm the diagnosis (and to distinguish from an ileus) and (b) determine if obstruction is unifocal or multifocal

If unifocal obstruction on CT scan, consider asking for advice if the lesion may be amenable to endoscopic stenting (speak to the colorectal surgeons at St Mary’s; 552 042)

In intractable nausea and vomiting, consider a venting gastrostomy (speak to the gastroenterology physicians at St Mary’s, 534 228)

For oesophageal or pyloric stents, speak to the upper GI CNS; 534915

Return to contents page  † = off-label route or use  †† = unlicensed ‘special’  # = specialist-initiated
Ascites

Common in both cancer and cirrhosis. Treatment varies depending on the stage and cause of a patient’s illness and may include:

1. Simple measures (e.g. “no added” dietary salt in patients with cirrhosis)
2. Medications (e.g. diuretics)
3. Procedures (e.g. paracentesis — page 29)

Recurrent ascites can be treated with repeat taps or an indwelling drain (e.g. a PleurX catheter – speak to interventional radiology at Southampton Hospital – 023 8120 4331). See page 29 for guidance on ascitic taps.

Pulmonary embolism

When suspected, CT-PA is the investigation of choice. If contraindicated (e.g. raised creatinine or contrast allergy) then a VQ scan +/- US leg of veins is an alternative.

First-line treatment is long-term enoxaparin 1.5mg/kg SC daily. Dose reduction required in renal failure or for thrombocytopaenia. If very high bleeding risk, IVC filter insertion can be used instead of anti-coagulation (speak to interventional radiology at Southampton Hospital – 023 8120 4331)

Superior Vena Cava Obstruction

When suspected, a CT venogram of the chest is warranted if investigating and treating is appropriate.

Dexamethasone 13.2mg SC [i.e. four 3.3mg ampoules] daily plus a proton pump inhibitor and urgent referral to an interventional radiologist for stenting (speak to interventional radiology at Southampton Hospital – 023 8120 4331) and/or a radiation oncologist (speak to Clinical Oncology at Southampton Hospital – 023 8077 7222, bleep 1414) for radiotherapy is the active treatment of choice.

Miscellaneous Problems

<table>
<thead>
<tr>
<th>Problem</th>
<th>Potential intervention</th>
<th>Who to call for advice on interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive uropathy</td>
<td>Ureteric stenting</td>
<td>Urology secretary at St Mary’s Hospital – 552 024</td>
</tr>
<tr>
<td>Obstructive jaundice</td>
<td>ERCP + stent</td>
<td>Gastroenterologists at St Mary’s Hospital – 534 228</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>Drainage</td>
<td>Cardiology at St Mary’s Hospital - 552 445 or 534 114</td>
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Diuretics for ascites in portal hypertension:

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone</td>
<td>First-line agent</td>
<td>Initial dose: 100 mg daily</td>
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<td></td>
<td></td>
<td>Maximum dose: 400 mg daily</td>
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<tr>
<td>Furosemide</td>
<td>Second-line agent</td>
<td>Initial dose: 40 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum dose: 160 mg</td>
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Ensure appropriateness of diuretics by first checking creatinine and electrolytes.
Reduce dose or stop diuretic therapy if creatinine rises > 150 or sodium < 125 or significant potassium abnormalities develop whilst on therapy.
Methadone Guidelines (Specialist-initiated)

Methadone often provides good analgesia in patients with terminal illnesses. It has unusual pharmacokinetics with a very long half-life of days and toxicity can occur unexpectedly after a week or more of an apparently well tolerated dose regimen. Thus it is only initiated and titrated by palliative care or pain specialists.

Indication: Pain refractory to other treatment, especially pain associated with a neuropathic component, opioid-tolerance or central sensitisation

Some advantages of methadone
Unaffected by renal failure.
Often brings significant benefits at low doses allowing for major reduction in the dose other opioids. It may also be beneficial in opioid-induced hyperalgesia.

Commencing methadone
Guidelines for using methadone in the palliative context vary widely. This guideline suggests a conservative approach where low-dose methadone is added on top the patient's current analgesia.

Before starting exclude a prolonged QTc by performing an ECG.
Start at 5mg orally at night. Continue any pre-existing regular and PRN analgesia.

Increasing the dose
If inadequate analgesia is achieved within 3-5 days, increase the dose to 5mg twice daily. Monitor for adverse effects.
Continue increasing the dose every 5-7 days by 5mg a day if tolerated. Do not exceed 15mg twice daily without seeking advice from a senior palliative care physician.
Recheck the ECG after 2-4 weeks to ensure that the QTc interval remains < 0.5.
Consider gradually reducing the dose of other background opioids such as a fentanyl patch whilst titrating up the methadone, especially if adverse effects or a poor response to these opioids (or opioid-induced hyperalgesia) is suspected.

Long-term dosing and stopping methadone
If significant side effects occur (e.g. sedation and reduced respiratory rate) then stop the methadone and reduce other opioids. In serious cases naloxone may be needed.
If there is no apparent improvement with methadone cease it.
If there is good analgesia, consider reducing the dose of other long-acting opioids and continuing the methadone longer term.
**Subcutaneous Lidocaine Infusion Guidelines (Specialist-initiated)**

A subcutaneous infusion of lidocaine is a useful treatment option in patients with a terminal illness who have severe pain refractory to other treatments. It requires careful assessment, consent and monitoring by a clinician familiar with its place, use and evidence-base relative to alternatives. Thus it is only initiated and titrated by palliative care or pain specialists.

**Indication:** Pain (especially neuropathic pain) refractory to other analgesia.

**Before starting**

Exclude contraindications by performing an ECG. Do not use in patients who are on anti-arrhythmics without first discussing with a cardiologist. Exhaust all other available treatment options before using in patients in the “precautions” group.

Check the blood pressure and heart rate.

Communicate and gain consent.

**Commencing an infusion**

Start at a dose of 500mg via CSCI over 24 hours (500mg = 25ml of lidocaine 2%; no diluent is needed). Consider beginning at 250 mg over 24 hours in those with altered pharmacokinetics (e.g. frailty; renal or hepatic impairment).

Recheck the blood pressure and pulse after 0.5, 1, 1.5, 2, 4 and 8-hours post commencing the infusion and (b) the following day. Discuss with medical team if:

- pulse drops below 60bpm or more than 20bpm below the pre-dose baseline
- systolic blood pressure drops below 100mmHg or more than 20mmHg below the pre-dose baseline

Recheck the ECG after 4 hours and the following day.

**Increasing the dose**

If inadequate analgesia is achieved, consider increasing the infusion rate by 250-500mg every 24-48 hours to a maximum dose of 2,000mg per day. With each increase in dose, repeat the same blood pressure, pulse and ECG monitoring as when first commenced.

**Stopping an infusion**

If bradycardia, hypotension, a cardiac arrhythmia or any other significant adverse effects occur, cease the infusion.

If, 24-hours after reaching the maximum dose, there has been no improvement in pain, cease the infusion.

If good analgesia occurs, consider gradually tapering the infusion by reducing in 250-500 mg increments every 24-48 hours. Consider complementing the reduction in lidocaine with a corresponding increase in other analgesic agents, e.g. methadone.

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**Absolute Contraindications**

- AV block
- Stokes-Adams attacks
- Wolf-Parkinson-White syndrome
- Previous sensitivity

**Precautions**

- Arrhythmias
- Cardiac failure
- Seizures
- Liver failure
- Renal failure

**Adverse Effects**

- Most are dose-related and are unlikely with doses under 2mg/kg/hour.
- Cardiovascular – hypotension, bradycardia
- Neuromuscular – light-headedness, tingling, muscle spasm, dysphasia, seizures, drowsiness
- Respiratory arrest
Ketamine for refractory pain (Specialist-initiated)

*Ketamine is a useful treatment option in patients with a terminal illness who have severe pain refractory to other treatments. Trials are conflicting, titration requires particular expertise and serious adverse effects can occur. Thus it is only initiated and titrated by palliative care or pain specialists.

**Indication:** Pain (especially neuropathic pain) refractory to other analgesia.

**Before starting**

Check blood pressure, heart rate, respiratory rate and conscious level. Exclude contraindications. If longer term use (>weeks) is anticipated, ensure hepatotoxicity and urotoxicity are considered when obtaining consent and arranging monitoring.

Prescribe PRN haloperidol for hallucinations and PRN midazolam for anxiety.

Continue to check blood pressure, heart and respiratory rate and conscious level three times daily until a stable effective dose is reached.

**Subcutaneous administration regimen**

Commence 100mg via continuous SC infusion over 24 hours. Consider beginning at 50 mg over 24 hours in those with altered pharmacokinetics (e.g. frailty; renal or hepatic impairment).

PRN ketamine 25mg 4-hourly can be prescribed in addition to PRN opioids.

If inadequate analgesia is achieved, consider increasing the infusion rate by 100mg every 24-48 hours to a maximum dose of 500mg per day. Continue to monitor blood pressure, heart rate, respiratory rate and conscious level until a stable effective dose is reached.

**Oral administration regimen**

Commence 10mg orally three times daily and 10mg PRN 4 hourly.

If inadequate analgesia is achieved, consider increasing in 10mg steps three times daily every 24-48 hours to a maximum dose of 100mg three times daily. Continue to monitor blood pressure, heart rate, respiratory rate and conscious level until a stable effective dose is reached.

**Stopping ketamine**

If significant side effects occur (especially sedation and reduced respiratory rate) then stop the ketamine.

If, 24 hours after reaching the maximum dose, there has been no improvement in pain, stop the ketamine (tapering is not required).

If good analgesia occurs, consider gradually tapering the dose by similar increments and rate as the above titration. If pain recurs, consider either an oral or SC maintenance dose (discuss monitoring arrangements for hepatotoxicity and urotoxicity with a consultant) or another analgesic agent, e.g. methadone.

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**Absolute Contraindications**

- Previous serious reaction
- Recent or poorly controlled seizures
- Raised intracranial pressure
- Uncontrolled hypertension

**Precautions**

- Brain metastases
- Psychosis or delirium
- Previous strokes
- Severe cardiac failure
- Tachyarrhythmias
- History of glaucoma

**Adverse Effects**

- Improved efficacy of other opioids resulting in opioid toxicity
- Sympathomimetic effects - raised blood pressure, tachycardia
- Psychomimetic effects – vivid dreams, agitation, hallucinations, sedation
- Urotoxicity – recurrent UTI-like symptoms
- Hepatotoxicity

**SC Ketamine**

<table>
<thead>
<tr>
<th>5mg oral</th>
<th>5mg SC</th>
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Compatible with: (use NaCl 0.9% unless otherwise stated):

<table>
<thead>
<tr>
<th>Haloperidol</th>
<th>Methadone (WFI)</th>
<th>Midazolam</th>
<th>Morphine</th>
<th>Haloperidol + midazolam (WFI)</th>
<th>Morphine + haloperidol</th>
<th>Morphine + midazolam</th>
<th>Oxycodone (WFI)</th>
<th>Oxycodone + haloperidol</th>
<th>Oxycodone + midazolam</th>
</tr>
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</table>
Ultrasound-guided Abdominal Paracentesis (Hospice Protocol)

**Indication:** To relieve abdominal discomfort (and dyspnoea) due to significant amounts of ascites.

**Technique**
- Exclude contra-indications. Gain consent
- Lie the patient supine with the abdomen exposed
- Select a site where there is shifting dullness. Confirm the presence of a deep pocket of ascites here with an ultrasound. Mark the skin clearly with a pen
- Wash your hands and put on sterile gloves
- Clean the skin with anti-septic solution
- Draw up lidocaine. Using a small-gauge needle, insert the needle at a right-angle to the skin, drawing back as you proceed until you get a flash-back of ascites. If you do not get a flash-back then abandon the procedure (and organize via radiology), otherwise slowly inject the anaesthetic whilst withdrawing the needle. Wait a few minutes.
- Insert the drainage catheter at a right-angle to the skin. On getting flash-back, insert the needle another centimetre and then withdraw the needle whilst inserting the plastic tube fully.
- Ascitic fluid should now be draining. Attach a drainage bag. Ensure the catheter and bag tubing is attached firmly to the abdominal wall (e.g. with sticky-tape).
- Allow drainage to occur. You may need to empty the bag a number of times. Drainage may take several hours. For ascites due to portal hypertension, albumin replacement is recommended if draining more than 5 litres
- Once the drainage stops or slows significantly, remove the catheter and cover the wound site with a dressing. If leakage of ascites occurs in the hours and days following the procedure, a colostomy bag can be used to prevent soaking of shirt and sheets.
- Monitor blood pressure and pulse hourly for 4-hours post procedure and review the patient if these become abnormal.

**Equipment Required**

<table>
<thead>
<tr>
<th>Equipment</th>
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<tbody>
<tr>
<td>Sterile gloves</td>
</tr>
<tr>
<td>Basic dressing pack</td>
</tr>
<tr>
<td>Anti-septic skin preparation</td>
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<tr>
<td>Small gauge needle (e.g. 23 gauge)</td>
</tr>
<tr>
<td>Small syringe (e.g. 5 or 10 ml)</td>
</tr>
<tr>
<td>Local anaesthetic (e.g. 1% lidocaine)</td>
</tr>
<tr>
<td>Large gauge long IV line or equivalent (e.g. 14 gauge AngioCath)</td>
</tr>
<tr>
<td>Drainage bag (e.g. 2 litre drain bag with male connection)</td>
</tr>
<tr>
<td>Surgical-tape (e.g. Micropore)</td>
</tr>
<tr>
<td>Dressing (e.g. Tegaderm)</td>
</tr>
<tr>
<td>Sharps container</td>
</tr>
<tr>
<td>PLUS</td>
</tr>
<tr>
<td>Hand-held or portable ultrasound</td>
</tr>
</tbody>
</table>

**Potential complications include:**

- Infection (e.g. cellulitis)
- Bleeding
- Bowel perforation or organ damage
- Hypotension
- Leakage of ascites

The first 4 complications are rare and risk can be minimized by:

1. Using a sterile technique
2. Checking for bleeding risks and INR and platelets prior to procedure
3. Using an ultrasound to confirm a deep pocket of ascites
4. Albumin replacement (for large taps of ascites due to portal hypertension)

**Albumin Replacement Formula:**

Give 100ml of 20% albumin for every 2.5 litres drained

**Be cautious if:**

- INR > 1.5  Platelets < 100
- **Correct as appropriate if:**
  - INR > 2  Platelets < 50
Subcutaneous Phenobarbital Infusion (Specialist-initiated)

Indications:

- Terminal agitation refractory to other treatments (e.g. midazolam > 60mg/day and either haloperidol > 10mg/day or levomepromazine > 100mg/day)
- Status epilepticus or recurrent seizures in an imminently dying patient that has been refractory to benzodiazepine therapy

For Refractory Terminal Restlessness: (see also page 21)

**Initial dose:**

Give "phenobarbital 200mg IM

If agitation continues, give up to 2 further doses IM, 30 minutes apart

**Starting a continuous subcutaneous infusion:**

Commence an infusion at a dose of between 800mg and 1,200mg over 24 hours via CSCI (diluent is water). Use the higher dose for large patients or those who required a larger loading dose. Use the lower dose for other patients.

**Additional medications:**

Prescribe phenobarbital 200mg IM 2-hourly PRN for ongoing agitation

Continue antipsychotics and midazolam initially – these can be discontinued once agitation is well controlled.

Do not stop opioids (phenobarbital is not an analgesic).

For Refractory Seizures: (see also page 22)

**Initial dose:**

Give phenobarbital 100mg IM (undiluted) or IV (over 2 minutes, diluted in 5ml of water for injection)

**Starting a continuous subcutaneous infusion:**

Commence an infusion at a dose of 100mg over 24 hours via CSCI.

**For additional seizures:**

Give phenobarbital 100mg IM / IV.

Titrate the infusion up a further 100mg.
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