

THE PALLIATIVE CARE HANDBOOK

A Good Practice Guide

Wessex Palliative Physicians

Ninth edition

2019

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WHAT MATTERS?

**“Ask what matters.
Listen to what matters.
Do what matters.”**

Finding out what matters most to each individual enables us to give appropriate care that is centred around their goals of care.

Planning ahead

The aim of future or **advance care planning (ACP)** is to establish **what matters** most to the patient in order to plan and give the care that suits them best. This might range from rehoming a beloved pet to concern for their family, wishes for organ donation or a fear of dying in pain.

Research has shown that patients and their families welcome the chance to have these discussions. They should not cause distress but give reassurance that compassionate care is being tailored to the individual. Giving patients some control in the last weeks, months or years of their life enables them to focus on living as well as possible to the very end.

The timing of these discussions is important. It is often helpful to include those close to the patient and for the health care professional to have built up a relationship with the patient.

Conversations can take place over several different occasions, updating information as time passes. Patients often change their minds; e.g. about where they would prefer their care to be, because, as end of life approaches, their needs change.

It can be helpful to give the patient: *Planning for your Future Care - A Guide*. There are also some handheld documents available for the patient to record their wishes themselves or with support from family or carers. (*E.G My Wishes booklet*) Your palliative care service will be able to advise on documents available locally.

Some patients will want to make this a more formal process, e.g. creating an Advance Decision to Refuse Treatment (ADRT). This enables patients to refuse life prolonging treatment; it needs to be written, signed and witnessed and include the phrase ‘even if my life were at risk’ for each treatment refused for it be legally valid and applicable. Examples of treatments that may be refused would be artificial feeding, assisted ventilation, and IV antibiotics requiring hospital admission.

The conversation should be documented and shared (with consent) in an agreed place, so that all professionals involved in their care know what really matters and aim to provide the care that matters to each individual patient.

GOLDEN RULES

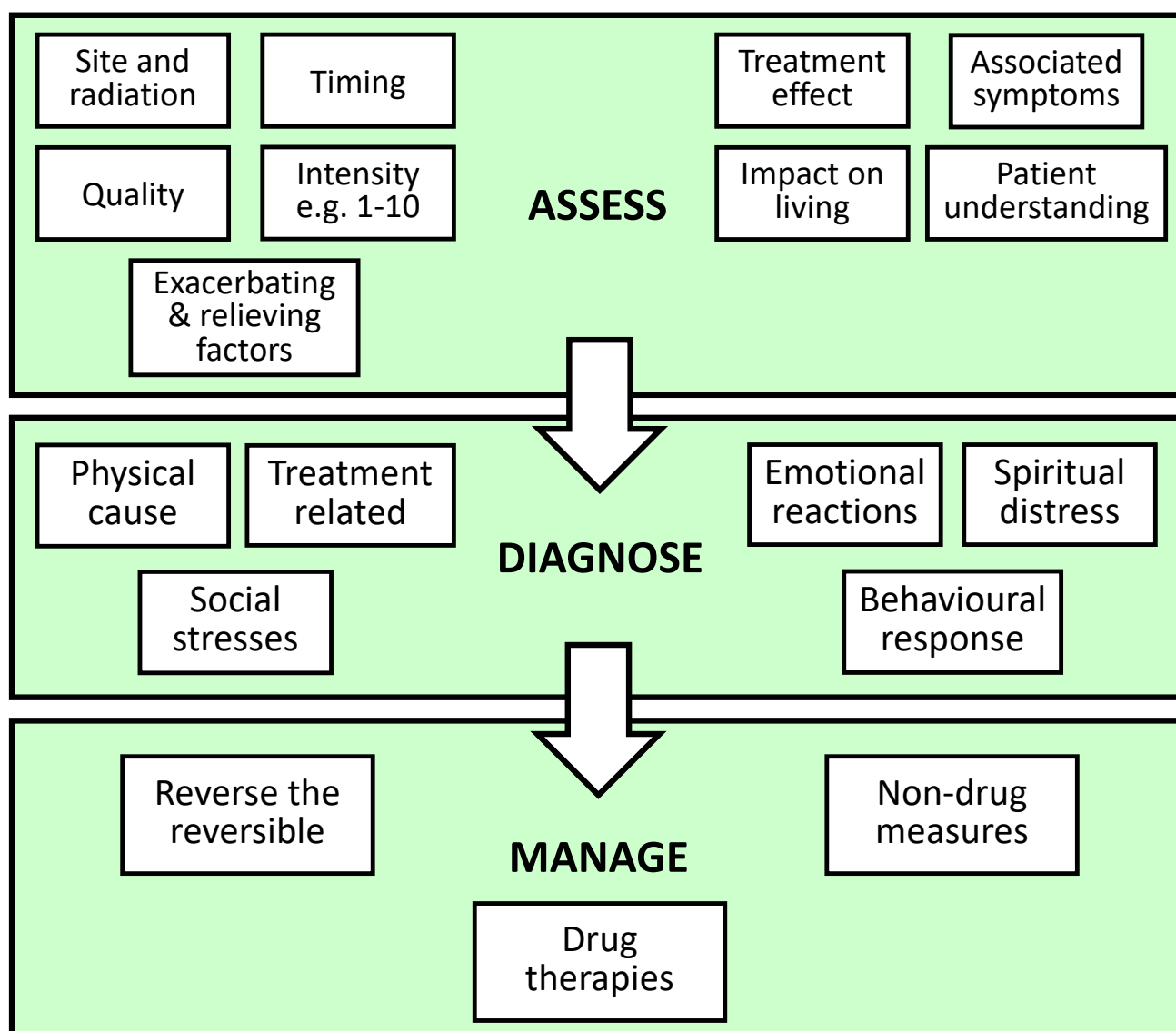
There are some key principles or '**Golden Rules**' which underpin symptom management. These include:

Assess and **diagnose** the cause of symptoms, before **planning** symptom **management**

Treat potentially **reversible** causes, where appropriate

Always consider **non-drug approaches** as they can be as important as the use of drugs

Management plan is influenced by prognosis and patient choice and depends on the **therapeutic goal**



Plan regular **REVIEW** and **reassessment** for all symptoms

Set **therapeutic goals** for drugs prescribed e.g. use opioids as analgesics, not for sedation

All drugs need a **review** date; the goal is to use the **minimum** effective dose

Adopt a **team** approach

Ask for **specialist advice** in difficult situations*

PAIN

All sections of this book focus on management of patients with advanced and progressive disease, including both malignant and non-malignant conditions. The advice is not meant to guide the management of chronic pain, which, though also multi-dimensional, requires long term management plans focusing more on psychological interventions and less on opioid use.

Pain is a complex symptom which is influenced by physical, psychological, social and spiritual factors (**total pain**). There are often components of pain which are not amenable to analgesia but which need to be assessed and treated alongside physical pain to achieve good symptom control. Be aware that the presence of non-physical aspects of pain may lower the physical pain threshold.

Multiple pains are common. In cancer patients with pain: one third will have one pain, one third will have two pains and one third will have three or more pains. Multiple pains are also common in non-malignant and co-morbid conditions. They may also occur as a result of age, debility and medical treatment.

Pain Assessment

Assessment and management of pain should follow relevant Golden Rules and the steps outlined for assessment of any symptom (*p4*). It is important to assess each pain separately to make a diagnosis and treat accordingly.

Pain assessment tools

Tools such as a numerical rating scale or a visual analogue scale may help the patient to describe the severity of the pain and the response to treatment. Tools are also available for assessment of pain in people with learning difficulties, dementia and other communication issues.

Pain management

Once a pain has been assessed and diagnosed, aim to treat any reversible cause and use non-drug measures. Alongside these, or if the cause is irreversible, the WHO Analgesic Ladder (*p6*) remains the basis for prescribing in all types of persistent pain.

NON-DRUG TREATMENTS

Include:

- Relaxation techniques
- Distraction
- Heat pad/ ice pack
- Physiotherapy and Occupational Therapy assessment and treatment to maximise function
- Psychological assessment and support
- Creative therapies
- Transcutaneous electrical nerve stimulation (TENS) and acupuncture

DRUG TREATMENTS

WHO Analgesic Ladder

- Introduced for the treatment of cancer pain
- The principles of the ladder are applicable to pain in those with progressive non-cancer conditions:
 - Use an analgesic appropriate to the severity of the pain
 - Analgesics should be given regularly
 - The oral route is preferred for all steps of the ladder
- Progress up the ladder until pain control is achieved, remembering co-analgesics
- The majority of patients taking opioids will also require laxatives

Co-analgesia (non-opioid medication) should be prioritised in non-malignant conditions and conditions with a longer prognosis.

| | | |
|--|---------------------------|----------------------|
| | | Severe Pain |
| | | Moderate Pain |
| Mild Pain | | |
| Paracetamol | Opioid +/- Paracetamol | |
| Co-analgesia NSAIDs, adjuvants | | |
| Disease directed therapies Radiotherapy, Chemotherapy, Immunotherapy, Surgery, Antibiotics | | |
| Physical therapies Nerve blocks, TENS, Acupuncture | | |
| Address psychological problems | | |

Paracetamol

- Helpful across the range of pain severity
- Can be given PO (tablet or liquid), via PEG, PR or IV
- Usual dose 0.5 -1g qds PO, maximum 4g in 24 hours
- Consider a fifth dose overnight if experiencing end of dose failure
- Risk of hepatotoxicity is increased in those who are malnourished or have abnormal liver function
- Reduce 24 hour dose in the frail elderly. 3g for those weighing 50kg, 2.4g for those weighing 40Kg
- Stop if clearly not effective

Opioids

The original WHO Analgesic Ladder categorized opioids as:

- **‘Weak’** (e.g. codeine, tramadol etc), for use in **moderate** pain, or
- **‘Strong’** (e.g. morphine, oxycodone, buprenorphine etc), for use in **severe** pain
- Lower doses of ‘strong’ opioids are preferred for moderate pain

NB. The long-term use of opioids for chronic, non-cancer, pain is not recommended due to the risk of dependency. Seek specialist advice*.

‘Weak’ Opioids

Codeine

- For moderate pain
- Codeine phosphate 30-60mg 4-hourly PO
- Codeine in combination with paracetamol e.g. Co-codamol 30/500, 2 tablets qds PO
- Codeine is metabolised to morphine to have its effect and there is a genetic influence over the speed and efficacy of this metabolism
 - 5-10% are slow metabolisers who may not respond to codeine - consider switching to morphine if there is no response to codeine after 5 days
 - 1-2% are fast metabolisers who may become toxic – a cautious conversion to morphine may still be appropriate
- Those with a sensitivity/allergy to morphine may also react to codeine
- Constipation is a common side effect

Tramadol (controlled drug)

- For moderate pain
- Dose 50-100mg qds PO (maximum 400mg/24 hours)
- Also available as a modified release (MR) preparation
- Has an opioid effect but also acts as a serotonin and noradrenaline reuptake inhibitor
- Nausea is a common side effect, as are low grade psychotic symptoms
- Risk of delirium in older patients. Use with caution
- Risk of serotonin syndrome (clonus, sweating, tremor, agitation, and in extreme cases, death) and seizures when given with other serotonergic drugs (e.g. antidepressants and antipsychotics)

Tapentadol*

- Please check your local guidelines as it is not recommended in all areas
- A ‘strong’ opioid with non-opioid properties
- Has an opioid effect but also acts as noradrenaline reuptake inhibitor
- Side effects as with other strong opioids
- It also carries the risk serotonin syndrome and seizures

‘Strong’ Opioids

- Morphine remains the gold standard, the preferred first choice opioid
- Oxycodone is used second line when an opioid switch is necessary (*p14*), or where morphine has not been effective in what is assessed as an opioid responsive pain
- Buprenorphine and fentanyl are used via the transdermal route for stable pain (*p9*)
- Alfentanil and fentanyl are used CSCI in severe renal failure (eGFR <30ml/min) (*p23*)*
- Diamorphine is reserved for those needing higher doses due to its greater solubility compared to morphine
- Methadone is reserved for specialist initiation*

Morphine

If patients do not achieve useful relief of pain from morphine or when rapid titration has not been effective or toxicity occurs, referral to a specialist in palliative or pain medicine is strongly recommended*. Additional adjuvants are likely to be needed.

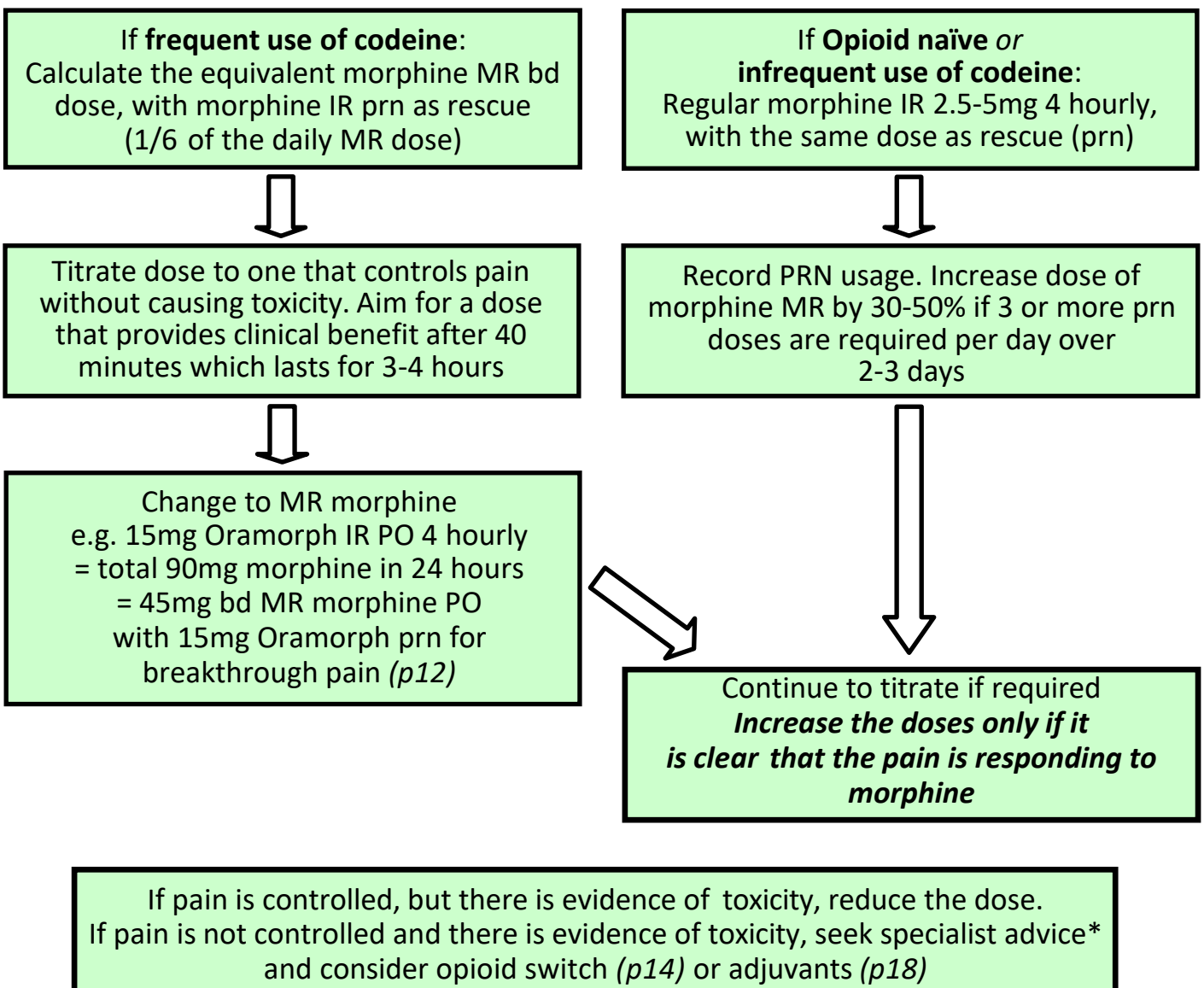
- Morphine remains the first-line opioid for severe pain (except in renal impairment),
- Oral is the preferred route
- Not all pains are opioid responsive, and some respond better to one opioid than another due to individual differences in drug pharmacokinetics
- Elderly and cachexic patients and those with renal impairment may need lower doses, reduced frequency or alternative opioids: see table on (p23)
- We recommend that all opioids are prescribed by drug name indicating whether it is immediate or modified release form, e.g. morphine IR, oxycodone MR etc

Commencing oral (PO) opioids

Calculate the morphine equivalent of any codeine or tramadol to guide starting dose (p11)
e.g. The codeine in Co-codamol 30/500 2 qds (total 240mg) = morphine 24mg/24hrs.

Start with either:

- Morphine sulfate IR (e.g. Oramorph) 2.5-5mg 4 hrly (15-30mg/day) *or*
- Morphine sulfate MR 10mg-15mg bd PO (20-30mg/day)



TRANSDERMAL OPIOIDS

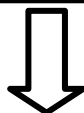
- Useful in stable pain or when oral route is difficult
- Contraindicated for acute pain and in severe uncontrolled pain requiring rapid dose titration, due to their long elimination half-life
- Use with caution in patients with cachexia as absorption may be unpredictable, so conversion charts may not apply
- Cutting matrix patches is not recommended. Reservoir patches should never be cut.

Suggested management (for stable pain)

Notes

Calculate current total 24 hr morphine PO equivalent dose (consider including prn doses) and use the conversion table as a guide to which TD drug and dose to commence.

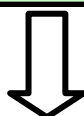
For opioid naïve patients, the lowest strength buprenorphine patch (BuTrans 5mcg/hr) may be appropriate.



Apply patch.
Continue current opioid regime for 12 hours before stopping.

TD medications take at least 12hours to reach effective plasma levels.

It can take up to 3 patch changes to reach steady-state plasma concentrations of TD drugs

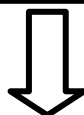


Options for rescue medications:

- PRN dose of IR morphine or oxycodone appropriate to the total daily morphine PO equianalgesic dose
- Morphine or oxycodone SC if unable to tolerate oral medication
- Consider other types of analgesia

Some patients experience a degree of withdrawal when switching from morphine or oxycodone to fentanyl which can be managed with small doses of regular IR PO morphine or oxycodone for the first few days.

Fentanyl is not as constipating as other opioids so laxatives may need to be reduced



When using a patch, wait at least 72 hours before titrating dose. Titrate by a maximum of 25-50% of dose.

Dose increases will take at least 12 hours to take effect

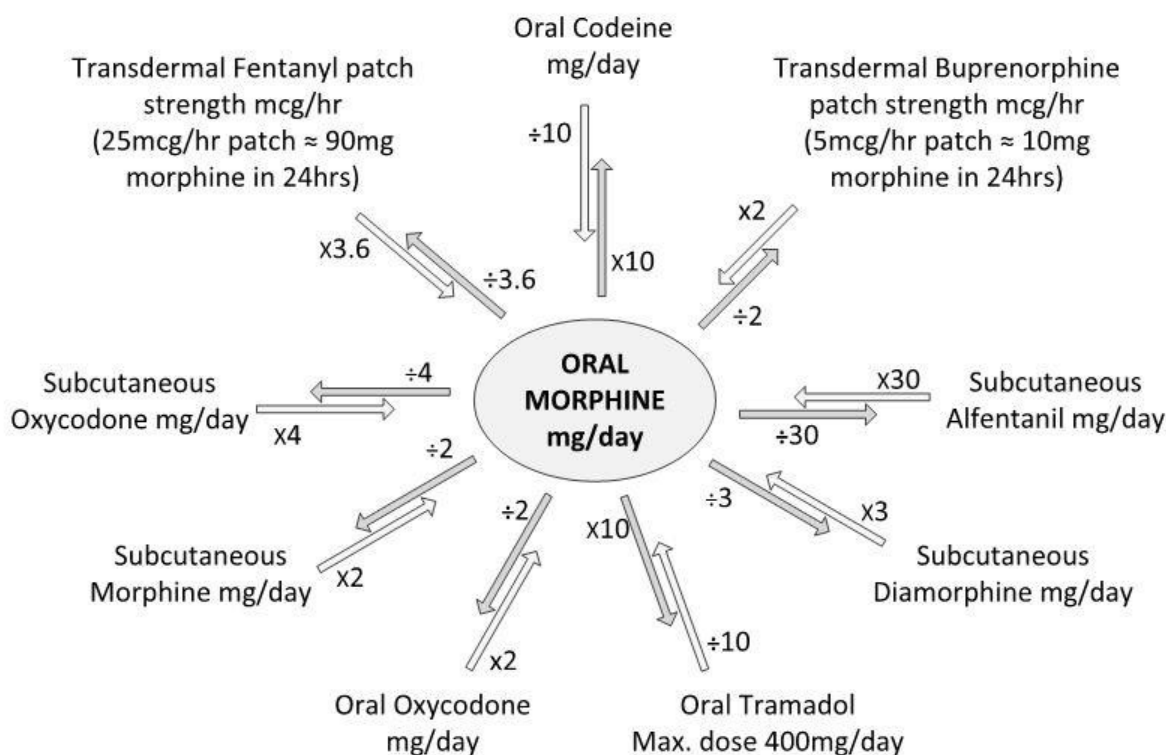
Plasma levels of TD drugs remain raised for at least 24 hours after removal of patch – remove patch for at least 12 hours prior to switching to alternative drug routes. Seek specialist advice*

In the last days of life patches should be continued. Unless transdermal absorption is in doubt there is no need to convert to CSCI syringe driver medication.*

OPIOID CONVERSIONS

- The conversions given are approximate (data mainly from single dose studies) and vary between individuals. The charts should be used only as a guide
- Always calculate doses using morphine as the standard and then adjust to suit the patient and the situation
- In the table doses have been rounded up or down to fit with the preparations available
- At higher doses consider a reduction in the dose when converting from one strong opioid to another as there is a risk of toxicity - it is safer to start lower and titrate up as needed (*p14*)
- Consider a 30-50% dose reduction when converting from a less sedating to a more sedating opioid eg fentanyl to morphine, oxycodone or diamorphine
- Caution should be used in renal (*p23*) and hepatic failure (*p22*)
- Seek specialist advice for conversions at higher doses*
- Remember to prescribe an appropriate dose of rescue (PRN) medication.
 - We recommend this to be a $\frac{1}{6}^{\text{th}}$ of the total daily dose
 - Some may recommend $\frac{1}{10}^{\text{th}}$ of the total daily dose
 - Prescribe maximum hourly so that patients do not have to wait for rescue analgesia.
 - In the case of fentanyl or buprenorphine, use the appropriate 4 hourly dose of morphine or oxycodone as the prn opioid (*NOT SL fentanyl or buprenorphine*)
- Avoid patch use in unstable pain.
- For parenteral use we recommend the subcutaneous route.
- The conversion to and from methadone* is variable and complex and should only be attempted in an inpatient specialist unit (high risk of accumulation and toxicity)

OPIOID CONVERSION DIAGRAM



Opioid Conversion Chart

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| 'Strong' opioids | | | | | | | | | | | | | | Patches | | 'Weak opioids' | |
|------------------|-----------------|------------------|-------------------|------------------|----------------|-----------------|------------------|--------------------------------|------------------|-------------------|------------------|--------------------------------|------------------|---|---|------------------|-------------------|
| Morphine | | | | | Oxycodone | | | | | Diamorphine | | Alfentanil | | Fentanyl | Buprenorphine | Tramadol | Codeine Phosphate |
| Oral (mg) | | | Subcutaneous (mg) | | Oral (mg) | | | Subcutaneous ¹ (mg) | | Subcutaneous (mg) | | Subcutaneous ² (mg) | | Transdermal Patch (mcg/hr) <i>Stable pain only</i> | Transdermal patch (mcg/hr) <i>Stable pain only</i> | Oral (mg) | Oral (mg) |
| 4 hr dose (IR) | 12 hr dose (MR) | 24 hr total dose | 4 hr dose | 24 hr total dose | 4 hr Dose (IR) | 12 hr Dose (MR) | 24 hr total dose | 4 hr dose | 24 hr total dose | 4 hr dose | 24 hr total dose | 4 hr dose | 24 hr total dose | Change every 72 hours | Change at intervals indicated | 24 hr total dose | 24 hr total dose |
| 1.25 | | 10 | | | | | | | | | | | | | 5 7 days | 100 | 120 |
| 2.5 | 10 | 20 | 1.25 | 10 | 1.25 | 5 | 10 | 1.25 | 5 | 1.25 | 5 | 0.125 | 0.5 | | 10 7 days | 200 | 240 |
| 5 | 15 | 30 | 2.5 | 15 | 2.5 | 10 | 20 | 1.25 | 10 | 1.25 | 10 | 0.125 | 1 | 6-12 | 15 7 days | 300 | |
| 7.5 | 20 | 40 | 5 | 20 | 5 | 10 | 20 | 2.5 | 10 | 2.5 | 15 | 0.25 | 1.5 | 12 | 20 7 days | 400 | |
| 10 | 30 | 60 | 5 | 30 | 5 | 15 | 30 | 2.5 | 15 | 2.5 | 20 | 0.25 | 2 | 12-25 | 35 72 hrs | | |
| 15 | 45 | 90 | 7.5 | 45 | 7.5 | 25 | 45 | 3.75 | 25 | 5 | 30 | 0.5 | 3 | 25-37 | 52.5 72 hrs | | |
| 20 | 60 | 120 | 10 | 60 | 10 | 30 | 60 | 5 | 30 | 7.5 | 40 | 0.75 | 4 | 37-50 | 70 72 hrs | | |
| 30 | 90 | 180 | 15 | 90 | 15 | 45 | 90 | 7.5 | 45 | 10 | 60 | 1 | 6 | 50-75 | | | |

¹Some units recommend a 1:1 conversion from CSCI morphine to CSCI oxycodone* rather than the 2:1 conversion in the table above.

²Some units recommend an 18:1 conversion from PO morphine to CSCI alfentanil* rather than the 30:1 conversion in the table above.

*Seek specialist advice when doses are greater than the equivalent of 180mg PO morphine in 24 hours

Consider reducing the equianalgesic dose by 25-33% if converting from a less sedating opioid, e.g. fentanyl to morphine, oxycodone or diamorphine, as sedative actions may be greater for an equianalgesic dose.

BREAKTHROUGH PAIN

Breakthrough pain is a transient exacerbation of pain occurring despite adequate background analgesia – exclude poorly controlled background pain and pain occurring shortly before the next dose of regular opioid (end-of-dose failure) which are managed by titrating up the regular opioid.

- May be associated with an exacerbating factor (incident pain) or be spontaneous
- Encouraging patients, or carers, to maintain a record of use of breakthrough doses will be helpful to guide when an increase in background pain relief may be needed
- The dose of breakthrough medication is usually $\frac{1}{6}$ th of the total daily opioid dose (*p10*) e.g. A patient on morphine MR 120mg bd PO (=240 mg morphine PO per day) should have morphine IR (Oramorph or Sevredol) 40mg prn PO ($240 \times \frac{1}{6}$)
- Some will need individual titration to establish the breakthrough dose*

| Problem | Features | Suggested management |
|--------------------------------------|---|---|
| Incident pain | Pain associated with an incident e.g. movement, swallowing, defaecating, coughing, dressing changes, weight-bearing | <ul style="list-style-type: none">• Manage precipitating factors• Rescue medication of IR opioid at least 30 minutes prior to incident• Consider NSAIDs/ adjuvants• Consider SL / buccal / nasal fentanyl preparations |
| Spontaneous breakthrough pain | Pain occurs without an obvious trigger, e.g. colic, neuropathic pain | <ul style="list-style-type: none">• Rescue medication of IR opioid• Consider adjuvants• Consider titrating background analgesia |

NB:

Some patients appear to gain psychological as well as pain benefit from use of PRN short acting opioids, possibly by allowing the patient to have control over their pain management.

Increasing their background pain relief may lead to drowsiness or opioid toxicity without any reduction in the frequency of PRN use. Accepting PRN use >3 times per day and keeping background pain relief relatively low may work best in these patients.

Sublingual / Buccal / Nasal fentanyl*: for Incident Pain

- Patient **must** be taking a minimum of 60mg morphine/24 hours PO (or equivalent) for at least one week
- Expensive compared with oramorph and oxynorm
- Licensed for use in breakthrough cancer pain as they are eliminated more quickly (also slightly faster acting) compared with traditional IR opioids
- Give at least 15 minutes prior to an incident likely to cause pain
- Dose **is not related to background** opioid dose
- Drugs are not interchangeable
- Start at lowest dose and titrate up to effective level

OPIOID SIDE EFFECTS AND TOXICITY (shaded boxes indicate immediate action is required)

| Side effect | Notes | Suggested management |
|--|--|---|
| Constipation (p40) | Virtually inevitable | <ul style="list-style-type: none"> • Proactive prescribing of softening & stimulant laxatives • Methylnaltrexone* or naloxegol* rarely needed |
| Nausea (p30) | Usually settles after a few days Less likely with slow titration | Consider <ul style="list-style-type: none"> • Haloperidol 0.5-1.5mg nocte PO or • Domperidone 10mg tds PO or • Metoclopramide 10mg tds PO |
| Dry mouth (p36), Hiccup (p51), sweating (p57) | | <ul style="list-style-type: none"> • Manage symptomatically • Consider opioid switch if severe |
| Toxicity myoclonus, hallucinations, delirium, sedation | May be precipitated by rapid dose escalation, accumulation (particularly methadone, and fentanyl patches), renal or hepatic impairment, dehydration or infection | Seek specialist advice* <ul style="list-style-type: none"> • Reduce dose • Monitor respiratory rate • Correct renal impairment if appropriate • Consider opioid switch and adjuvants • Consider admission |
| Respiratory depression Respiratory Rate (RR) <8bpm | Sign of severe toxicity Consider the cause e.g. change in renal function Consider urgent bloods and give IV or SC fluids if dehydrated to aid opioid clearance | Seek specialist advice* <ul style="list-style-type: none"> • Stop regular opioid (remember to remove patches) and use PRN opioids at half dose until improvement in RR and conscious level • Use naloxone (20-100mcg IV and repeat every 2 minutes depending on respiratory rate) only if severe as will cause reversal of analgesia with sudden severe pain When stable: <ul style="list-style-type: none"> • Restart opioid at half dose or consider a switch to short acting opioid. |
| Opioid-induced hyperalgesia (OIH) Widespread and worsening pain, hyperalgesia, allodynia, myoclonus, delirium, sedation +/- fits | Pain can be increased paradoxically as a result of taking an opioid. It can occur at any dose and with any opioid. It should be considered if: <ul style="list-style-type: none"> • Tolerance to opioids develops rapidly • dose increases result in worsening pain or have short-lived benefit • the pattern of pain changes (distribution beyond the original site) | Seek specialist advice* <ul style="list-style-type: none"> • Reduce dose by 30-50% • Consider opioid switch, NSAID and/or adjuvants Failure to recognise OIH can result in an escalating dose of opioid and a risk of increasing toxicity. |

OPIOID SWITCHING

If pain is opioid responsive but the patient is experiencing adverse effects/ side effects from the opioid being taken, consider switching to an alternative strong opioid.

The table below considers options for switching from morphine.

| Issue with oral morphine | Suggested switch | Notes |
|---|---|---|
| Unable to achieve good pain control without causing toxicity | Oxycodone PO | <ul style="list-style-type: none"> Many people who do not tolerate morphine will tolerate another opioid (provided pain is opioid responsive) |
| Dysphagia, Poor oral concordance, Uncertain absorption, Intractable constipation, Questionable compliance | Buprenorphine or fentanyl TD | <ul style="list-style-type: none"> Only for stable and well-controlled pain as titration is difficult buprenorphine and fentanyl are less constipating than other opioids |
| Nausea or vomiting, Inability to tolerate oral medication in the terminal phase | Continuous subcutaneous infusion (CSCI) via syringe driver | <ul style="list-style-type: none"> Convert to same opioid SC that has been given orally Prescribe SC prn doses |
| Renal impairment* (eGFR<30) (p23) | Buprenorphine or fentanyl TD Alfentanil or fentanyl CSCI For PRN use: Low dose and infrequent oxycodone IR PO or SC or fentanyl buccal/SL/SC | <ul style="list-style-type: none"> The majority of opioids accumulate in renal impairment Buprenorphine, alfentanil and fentanyl are safer There is little evidence for oxycodone but accumulation is less likely than with morphine |

Other options (for specialist initiation only*) include:

- Tapentadol* (p7) – A strong opioid with non-opioid properties. At maximum doses it is much stronger than tramadol.
- Methadone* - difficult titration and can accumulate, however may be useful in complex and neuropathic pain and in chronic kidney disease.

INSTRUCTIONS TO THE PATIENT AND CARER ABOUT OPIOID USE

- Emphasise the need for regular administration
- Explain about rescue (PRN) medication for breakthrough pain (p12)
- Warn about possible side effects
- Explain need for regular and ongoing laxatives (p40)
- Nausea can be a problem initially – take antiemetic regularly for the first few days and PRN after that (p30)
- Reassure that when used for pain relief, problems with tolerance and psychological dependence are very rare
- Advise not to stop abruptly due to potential withdrawal effects

OPIOIDS AND TRAVEL

Opioids and driving

In 2015 the law on driving after taking certain drugs, including some medicines, was introduced in England and Wales was changed. There are now legal limits for blood levels of cannabis and cocaine (which can be checked at the roadside) and medicines including opioids and benzodiazepines.

Stable doses of appropriately titrated opioids do not preclude driving, however patients taking such medication should be advised about the law. The majority of patients that are fit to drive and are taking stable doses of opioid medicines as directed are unlikely to be above the specified limit and therefore would not be committing an offence.

Patients may continue to drive if:

- The medication(s) has/have been prescribed and the patient has taken it/them in accordance with the advice they have been given
- The medication(s) has/have not caused the patient to be unfit to drive

Advise patients they should:

- Not drive until they know how the opioid affects them. This may be several days after starting the drug, changing the dose (up or down), or following an opioid switch.
- Not drive for 3 hours after taking a rescue dose of medication (PRN)
- Not drive if they have combined their usual opioid with another sedating medication or with alcohol
- Not drive if they feel drowsy, dizzy, unable to concentrate or make decisions, or have blurred or double vision
- Drive only if feeling alert and entirely safe to do so
- Start with a short and familiar drive with a companion
- Carry proof of the opioid medication prescribed e.g. repeat prescriptions
- Inform the DVLA and their insurance company

N.B. It will remain an offence to drive while one's ability is impaired and, if in doubt, do not drive.

Opioids and travel abroad

Patients should be advised to carry all their medication in their hand luggage in its original packaging together with a covering letter from a doctor.

They should check with The Home Office and the Consulates of the countries they will be travelling to, or through, for more details

| Duration of travel | Requirements |
|--------------------|--|
| Less than 3 months | <ul style="list-style-type: none">• Medical letter stating demographics, place and dates of travel and full details of drugs.• Import and export requirements for all countries to be entered should be fulfilled |
| More than 3 months | <ul style="list-style-type: none">• Everything as above plus export license (available from the Home Office website). <i>(Unless arrangements can be made for a prescription to be completed in the destination country)</i> |

PAIN ASSOCIATED WITH CANCER

Cancer pain can be due to:

- The **direct effect** of the tumour (e.g. infiltration, pressure)
- **Treatments** associated with the cancer (e.g. surgery, radiotherapy, immunotherapy) or their side effects (e.g. constipation, mucositis)
- **Procedures** (e.g. dressing changes, pressure sores, movement, muscle stiffness)
- **Unrelated pathology**. In 15 – 20% of patients with cancer and pain, the pain is not caused by the cancer itself (e.g. osteoarthritis)

All types of pain can show some response to opioids. The cause of the pain always needs to be established as these additional management approaches will vary according to pain type and cause.

| Bone Pain: Dull, aching, exacerbated by movement, tender over bone | |
|--|--|
| Possible Cause | Management options |
| Bone metastases, arthritis (consider hypercalcaemia) | NSAIDs (p18) Bisphosphonates (if radiotherapy and analgesics are insufficient) <ul style="list-style-type: none"> • Can reduce pain of bone metastases, particularly in those associated with myeloma, breast and prostate cancer • Use pamidronate 90mg IV over 4 hours every 4 weeks, or zoledronate 4mg IV over 15 minutes every 6 weeks • Side effects include osteonecrosis of the jaw and hypocalcaemia • Require caution when used in those with eGFR <30ml/min Oncology/orthopaedic referral for consideration of: <ul style="list-style-type: none"> • Radiotherapy (<i>first line for bone metastases</i>) • Radioactive isotope treatment (in patients with multiple sclerotic metastases) • Denosumab (Monoclonal antibody) • Internal fixation of long bones following or at risk of fracture • Vertebroplasty in isolated vertebral collapse |
| Liver Capsule pain: Sharp, stabbing, right upper quadrant or right shoulder tip | |
| Possible causes | Management options |
| Liver metastases, immunotherapy, other liver disease | <ul style="list-style-type: none"> • NSAIDs (p18) • Dexamethasone 8mg od PO/SC for 5 days then assess benefit and stop if no improvement (p69) • Some may be considered for surgical resection |
| Raised Intracranial Pressure (ICP): Headache worse in the morning, associated with vomiting | |
| Possible causes | Management options |
| Brain tumour, brain metastases | <ul style="list-style-type: none"> • Dexamethasone 8 – 16mg PO/SC daily (p69) • Consider neurosurgical referral for consideration of tumour debulking, resection if isolated metastasis, shunt insertion |
| Pancreatic Pain: Central abdominal pain, radiating through to the back | |
| Possible causes | Management options |
| Pancreatic tumour, pancreatitis | <ul style="list-style-type: none"> • Often multifactorial and may need combination of opioid, NSAID (p18) and neuropathic agents (p19) • Interventional pain referral for coeliac plexus block (p20) |

| Smooth Muscle Spasm: Crampy, colicky, intermittent pains | |
|--|--|
| Possible causes | Management options |
| Bowel/Bladder/Biliary: Constipation, bowel obstruction, ureteric obstruction, bladder spasm, immunotherapy | <ul style="list-style-type: none"> • Treat constipation if present (<i>p40</i>) • Review medication as prokinetic drugs (metoclopramide, domperidone) may be the cause of the smooth muscle spasm • Use an anticholinergic for relief of pain although this may worsen constipation; other side effects including dry mouth. (avoid using with a prokinetic as they have opposing actions on the bowel) <ul style="list-style-type: none"> ◦ Hyoscine Butylbromide: oral absorption is poor: give 20mg PRN SC or 60- 120mg/24hr CSCI ◦ For intestinal colic consider mebeverine or alverine citrate. ◦ For bladder spasm, exclude UTI: consider, oxybutynin SR, tolterodine, amitriptyline, trospium* |
| Oesophageal Pain: Intermittent chest pain, related to swallowing | |
| Possible causes | Management options |
| Oesophageal tumour, candida infection | <ul style="list-style-type: none"> • Treat oesophageal candidiasis <ul style="list-style-type: none"> ◦ Nystatin oral suspension 3-5ml qds PO for at least 7 days ◦ Fluconazole 50-100mg od PO for 14-30 days • Use drugs for relief of smooth muscle spasm: <ul style="list-style-type: none"> ◦ Nifedipine MR 20mg bd PO ◦ GTN - try SL, if effective consider TD patch ◦ Benzodiazepines |
| Rectal and Pelvic Pain: Tenesmus, pain exacerbated by bowel action, deep seated pelvic pain | |
| Possible causes | Management options |
| Pelvic and Rectal tumours, constipation | <p>If constipation is excluded:</p> <ul style="list-style-type: none"> • NSAIDs (<i>p18</i>) • Neuropathic agents (<i>p19</i>) • Drugs for relief of smooth muscle spasm: <ul style="list-style-type: none"> ◦ Nifedipine MR 20mg bd PO (beware of hypotension) ◦ GTN - try SL, if effective consider TD patch ◦ Benzodiazepines (e.g. diazepam) • Local (PR) steroid (Colifoam, Predsol) • Oncological referral for local radiotherapy • Interventional pain referral for sacral plexus nerve block* |
| Skeletal Muscle Pain: Ache, stiffness, worse in the morning, spasms | |
| Possible causes | Management options |
| Debility, Immunotherapy, Motor Neurone Disease, Parkinson's Disease May be difficult to identify if overlying long bone or spinal metastases. | <p>For spasticity from neurogenerative disorders</p> <ul style="list-style-type: none"> • Baclofen, starting dose 5mg tds PO • Diazepam, starting dose 2mg nocte PO • Clonazepam, starting dose 0.25-0.5mg nocte PO <p>For painful muscle spasm from surrounding tissue injury</p> <ul style="list-style-type: none"> • Diazepam as above • NSAID (<i>p18</i>) |

ADJUVANT ANALGESIA FOR SPECIFIC PAINS

- Medication which helps the management of specific and mixed pains
- May have opioid sparing effects
- Down titration of opioids may be required if the adjuvant is effective
- Always consider whether side effects are a result of the adjuvant or of opioids and which needs to be reduced

NON-STEROIDAL DRUGS (NSAIDs)

NSAIDs are particularly useful for pain caused by inflammation or exacerbated by movement, however the risk/benefit balance must always be considered.

Serious gastrointestinal events

- 1 in 500 with 2 months of treatment,
 - likely increased in debilitated patients at end of life
 - likely decreased by gastro-protection.
- Depends on the drug, dose and duration, concurrent medications and age
 - risk higher in >65 yrs.
 - Risk higher in combination with corticosteroids (e.g. dexamethasone or prednisolone)
- Celecoxib has the lowest risk
- Ibuprofen is relatively lower risk
- Diclofenac and Naproxen are moderate risk
- Ketorolac* is high risk

Serious thrombotic events (stroke and myocardial infarction)

- The absolute risk remains small for serious thrombotic events (stroke, myocardial infarction)
- Celecoxib, Ibuprofen and naproxen have been found to be the least likely to increase risk

Other serious side effects

- Exacerbation of cardiac failure (*p76*)
- Exacerbation of renal failure (*p78*)
- Risk of bronchospasm is very low. (5% of asthmatics react to aspirin)

Prescription of NSAIDs

- Take into account an individual's risk factors and use the lowest dose possible to achieve pain control
- Always consider a proton pump inhibitor (PPI) e.g. omeprazole 20-40mg od PO alongside the NSAID
 - **First line:** celecoxib 100-200mg bd PO
 - **Second line:** ibuprofen 400mg tds PO or naproxen 500mg bd PO
 - **Third line:** diclofenac SR 75mg bd PO or 100mg od PR or IM
 - **CSCI*:** diclofenac (75mg/ 24hrs) and ketorolac may be given CSCI under specialist supervision*

NEUROPATHIC PAIN

Pains in patients with cancer often have a neuropathic element due to infiltration of nerve(s) by tumour. The nature of the pain is often described as sharp, shooting, stabbing, and there is often an associated area of altered sensation (hypersensitivity, hot, cold, numb) or function (flushing, weakness, tone). Nerve plexus pain may present as a deep ache without areas of abnormal sensation.

- Opioids (*p6-14*) can be of benefit however it is often limited
- Prescribing an adjuvant/co-analgesic provides additional benefit and an opioid dose sparing effect
- Tricyclic or mixed action antidepressants and/or antiepileptics are commonly used to manage this pain. These medications have similar efficacies with NNT ranging from 3-5. It will take 5-14 days once titrated to a therapeutic level to assess efficacy
 - **First line adjuvant treatment is either an antidepressant or gabapentin/ pregabalin: the choice can be determined by side effect profile and any other beneficial effects**
 - **If 1st line treatment has limited efficacy – add in drug from an alternative group**
 - **If 1st line treatment has no effect – change to drug from an alternative group**

Your Specialist Palliative Care Team or Acute/Chronic Pain Team will be happy to provide advice. If pain is localised it may respond to specific nerve blocks or other interventions (*p20*). Referral is suggested if not responding to standard treatment.

Anticonvulsants

Gabapentin

- Start with 300mg nocte PO
- Increase dose in increments of 300mg every 2-3 days to a maximum of 1200mg tds
- Reduce starting and increment dose to 100mg in the elderly and those with an impaired eGFR (*p23*)
- Side effects include sedation, which often improves after the first few days
- The capsules can be opened and their contents sprinkled on food if the patient is finding them difficult to swallow

Pregabalin

- Start 50-75mg bd PO
- Increase dose every 3 days in increments of 50mg bd, to a maximum dose of 600mg daily in bd or tds doses
- Reduce starting and increment dose in the elderly and those with impaired eGFR (*p23*)
- Side effects include sedation, which often improves after the first few days

NB From April 2019 Gabapentin and Pregabalin are classified as Class C controlled drugs.

Other anti-epileptics such as carbamazepine may help – seek specialist advice*.

Antidepressants

Amitriptyline

- Start with low dose 10mg nocte PO
- Increase after 3 days to 25mg nocte PO
- If required, increase weekly by 25mg to a maximum of 150mg od PO
- Side effects include sedation, dry mouth (*p36*), constipation (*p40*), postural hypotension, and urinary retention
- Avoid use with tramadol (risk of serotonin toxicity) or if the patient is at risk of cardiac arrhythmias
- Lofepamine, nortriptyline and dosulepin are alternatives

Duloxetine

- Start with 30mg od PO, increase to a maximum of 60mg bd if tolerated

Corticosteroids (p69)

Dexamethasone

- Useful for short term relief of pressure, particularly in
 - spinal cord compression (16mg od PO/SC)
 - nerve root compression (8mg od PO/SC)
- Give in the morning so as not to affect sleep
- Give for 5-7 days and assess response
 - stop if no beneficial effect
 - If benefit, slowly reduce dose to lowest effective dose, stopping if possible
- Prescribe a Proton Pump Inhibitor e.g. omeprazole 20-40mg od PO
- Side effects include insomnia, agitation, hyperglycaemia (check blood sugar one week after starting or if symptomatic)

Other options (for initiation by a specialist*) might include:

Benzodiazepines

Clonazepam

- Start at 0.5mg nocte PO
- Use 0.25mg in the frail/ elderly
- Side effects include daytime somnolence, cognitive impairment
- Sedation may limit dose increases

Diazepam

- 2mg – 10mg od nocte PO may help, especially if there is an element of muscle spasm in addition

Others*

capsaicin cream, NSAID gels, methadone, ketamine (NMDA antagonist), lidocaine patch, acupuncture, and interventional procedures may be considered by specialists.

PAINS AMENABLE TO INTERVENTIONAL PROCEDURES*

Many pains are amenable to intervention by a pain management specialist anaesthetist. Neural blockade can be temporary or semi-permanent. Injected steroids are particularly useful when pain is due to compression of the nerve.

- Consider a referral to Pain Clinic if the patient has a pain in a specific area, (chest wall, spine, hip, perineum, distribution of coeliac or brachial plexus), particularly if there is a suspected neuropathic element
- Neural blockade may be temporary (injection of steroid or local anaesthetic), or semi-permanent (neurolytic techniques)
- Intrathecal or epidural infusions may help in difficult pains, where usual routes of administration are not effective or tolerated
- In unilateral pain, particularly the chest pain associated with mesothelioma, early referral for percutaneous cervical cordotomy is recommended (limited number of centres e.g Portsmouth Hospitals Trust - for referral details see Mesothelioma UK website)

PAIN ASSOCIATED WITH NEUROLOGICAL DISEASE

The most common neurological condition seen by palliative medicine teams is Motor Neurone Disease (MND) and 70% of patients report pain as being a major symptom. It is often an issue in other neurological disease, for example Parkinson's Disease (PD), Progressive Supranuclear Palsy, Multiple Systems Atrophy, Multiple Sclerosis, and Huntington's Disease.

In all cases, treat reversible causes and where appropriate, try non-pharmacological management approaches first. Where pain persists follow the WHO analgesic ladder and consider:

| Likely cause | Management |
|--|--|
| Joint stiffness | <ul style="list-style-type: none">• Repositioning• Physiotherapy• Heat pad• Optimise management with dopamine agonists in Parkinson's Disease• NSAIDs (<i>p18</i>)• Intra-articular joint injection |
| Pressure areas | <ul style="list-style-type: none">• Regular turning• Pressure relieving mattress/cushion• Optimise nutrition |
| Spasticity (Specialist MDT management*) | <ul style="list-style-type: none">• Physical & positional goal orientated therapies• Botulinum toxin• Baclofen – high side effect burden for both drugs• Gabapentin, clonazepam/diazepam |
| Muscle cramps | <ul style="list-style-type: none">• Quinine sulfate (night cramps), clonazepam, diazepam |
| Altered sensation | <ul style="list-style-type: none">• Neuropathic agents (<i>p19</i>) |

PAIN ASSOCIATED WITH RESPIRATORY AND CARDIAC DISEASE

Common causes of pain:

- Chest wall/ back pain from muscle strain and cachexia
- Pleuritic pain
- Bone pain from osteoporosis following long term steroid use.

Follow the WHO analgesic ladder (*p6*), bearing in mind that:

- NSAIDs may worsen fluid retention in patients with cardiac failure (*p76*) and so should be avoided
- NSAIDs may cause a deterioration in respiratory function in patients with asthma
- Opioids commenced at low doses and titrated safely will REDUCE the sensation of breathlessness
- In patient at risk of CO₂ retention slow titration of opioids over weeks will minimise the risk of respiratory depression

PAIN ASSOCIATED WITH LIVER DISEASE

Pain in end-stage liver disease may result from:

- Pressure sores/general discomfort secondary to weight loss/cachexia
- Abdominal distension secondary to ascites
- Subcostal discomfort if liver enlargement or scarring

Be aware that cognitive impairment secondary to encephalopathy may result in difficulties reporting pain.

Prescribing in hepatic impairment

Drug metabolism is usually only affected when hepatic impairment is severe, as evidenced by encephalopathy, varices, ascites or evidence of impaired synthetic function (raised prothrombin time/INR, hypoalbuminaemia) and deranged liver function tests (particularly bilirubin >100mcg/l).

Drugs tend to have an increased half-life and be more sedating in hepatic impairment.

| Drug | Change in severe hepatic impairment* | Comments |
|--------------------------------------|--------------------------------------|--|
| Normal dosing | | |
| Fentanyl | Usual dose | Monitor as may still accumulate |
| Reduce dose | | |
| Paracetamol | ↓ dose | Hepato-toxic drug |
| Amitriptyline | ↓ dose | Titrate slowly |
| Gabapentin/Pregabalin | ↓ dose | Titrate slowly |
| Same dose but Increase dose interval | | |
| Morphine | Same dose, ↑interval | Use immediate release |
| Diamorphine | Same dose, ↑interval | Accumulates |
| Benzodiazepines | Same dose, ↑interval | Use short-acting e.g. lorazepam and midazolam |
| Use with caution | | |
| Ibuprofen | Usual dose | If benefit outweighs increased risk of bleeding from impaired platelet aggregation |
| Diclofenac | Usual dose | |
| Avoid | | |
| Celecoxib | Avoid | Accumulates |
| Codeine | Avoid | Prodrug - Reduced metabolism to morphine |
| Tramadol | Avoid | Accumulates |
| Oxycodone | Avoid | Accumulates |
| Buprenorphine | Avoid | Accumulates |
| Alfentanil | Avoid | Unpredictable accumulation |

PAIN ASSOCIATED WITH RENAL DISEASE

- Avoid NSAIDs. In the terminal phase, once the risks/ benefits have been carefully assessed, short term use may be appropriate.
- Dialysis will affect the clearance of many drugs – seek renal team specialist help

| Likely cause | Management |
|--|-------------------------------------|
| Muscle spasm/ cramps | • Muscle relaxants/ quinine |
| Neuropathic pain secondary to peripheral neuropathy | • Neuropathic agents (<i>p19</i>) |
| Restless legs syndrome | • Clonazepam / gabapentin |
| Bone pain from osteoporosis, renal osteodystrophy | • Consider orthopaedic intervention |
| Complex ischaemic pain from vasculitis, peripheral vascular disease, calciphylaxis | • Consider ketamine* |
| Osteomyelitis | • Treat infection |

Prescribing in renal impairment

| Drug | Renal Impairment – eGFR (ml/min) | | | Comments |
|--|--|---|---|---|
| | 60-90 | 30-60 | <30 | |
| NSAIDS | Half normal starting dose | Avoid | Avoid | Nephrotoxic |
| Midazolam | ↓dose | ↓dose, ↑interval | ↓↓dose, ↑interval | Renally excreted. Protein binding reduced. Increased end-organ sensitivity. |
| Diazepam | Usual dose | ↓dose | ↓dose Avoid <15ml/min | |
| Clonazepam | 0.5mg nocte PO | 0.25mg nocte PO | Start lower | |
| Amitriptyline | Usual dose PO | 10mg nocte PO | 10mg nocte PO | |
| Gabapentin | Starting dose 100-300mg od PO Max 600mg tds | Starting dose 100-300mg on PO Max 300mg tds | Starting dose 100mg alt. days PO Max 300mg bd | May accumulate. If eGFR < 15 Max 300mg nocte PO |
| Pregabalin | Starting dose 75mg bd PO Max 300mg bd | Starting dose 50mg bd PO Max 150mg bd | Starting dose 25-50mg od PO Max 150mg od | If eGFR < 15 Max dose 75mg od PO |
| Baclofen | 5mg tds PO | 5mg bd PO | 5mg od PO | Avoid <15ml/min |
| Codeine | Usual dose | ↓dose, ↑interval | Avoid | Renal excreted drugs and active metabolites. Will accumulate and cause toxicity |
| Tramadol | Usual dose | ↓dose | ↓dose, ↑interval | |
| Morphine | ↓dose | ↓dose, ↑interval | Avoid | |
| Diamorphine | Usual dose | ↓dose, ↑interval | Avoid | |
| Oxycodone | Usual dose | Usual dose | ↓dose | Metabolites are less toxic than those of morphine |
| Fentanyl Alfentanil Buprenorphine Methadone* Hyoscine butylbromide | Usual dose – relatively safe in renal impairment | | | |

BREATHLESSNESS

- Common in palliative care (40-80%)
- Often multi-factorial
- There is frequently a psychological component – being breathless is usually frightening and patients often have unspoken fears about how they will die
- Assess triggers - both physical (e.g. movement, cough, talking, chest pain, eating, defaecation) and emotional
- Investigations e.g. chest x-rays, scans and blood tests may be needed to exclude reversible causes but are often of limited value; oxygen saturation will guide the use of oxygen
- A therapeutic trial of treatments, either singly or in combination, is often necessary to find out what works for an individual patient

Management

- **Consider reversible causes of breathlessness and treat where appropriate** (*see table on page 26*)
- **Consider the role for further oncological interventions e.g. chemotherapy, radiotherapy or immunotherapy.**

Symptomatic treatments

These are appropriate in most breathless patients, alongside management of potentially reversible causes, if appropriate. Management should be individualised to the patient. Trials of different interventions, both drug and non-drug, should be considered.

Non-Drug measures

Episodes of breathlessness are distressing, but often short-lived; highlighting the value of non-drug measures. This should include:

Communication

- Explore the patient's fears about breathlessness
- General and specific reassurance (e.g. that the patient will not suffocate)
- Explanation of the mechanisms of breathlessness

Strategies

- Provide a strategy to regain control of their breathing during an acute episode of breathlessness
- Crisis management plan developed with the patient and family – '*what to do*' if suffering from acute episodes of breathlessness

Patient-led

- A fan (hand held or fixed) or cool air across the face
- 'Calming hand' or 'rectangular/square' breathing (*See diagrams p25*)
- Visualisation e.g. looking at well-loved pictures can help someone to relax
- Positioning for easier breathing (sitting up / leaning forward), individualised to the patient

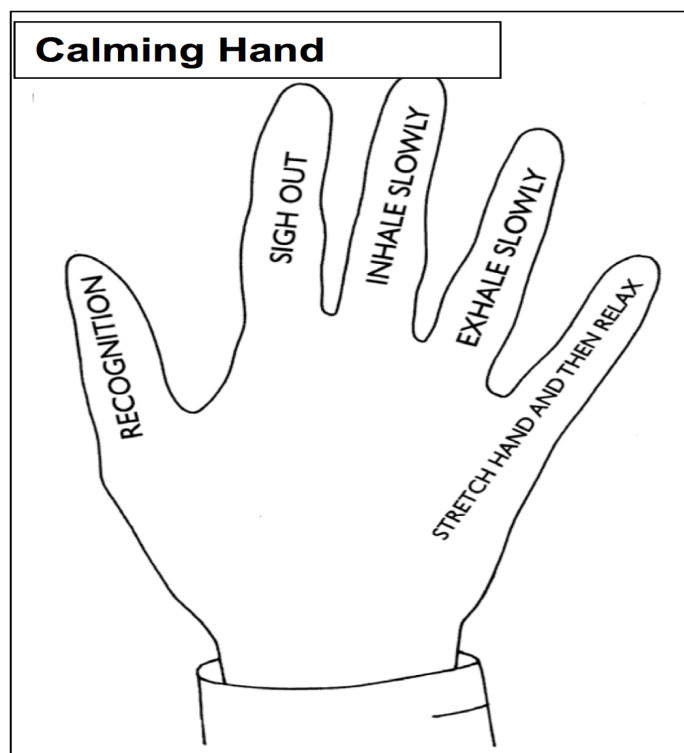
Complementary Therapy

- Acupuncture, aromatherapy, reflexology

Pulmonary Rehabilitation

- Consider referral to a physiotherapist and/or specialist nurse- led rehabilitation service
- Counselling and re-adaptation

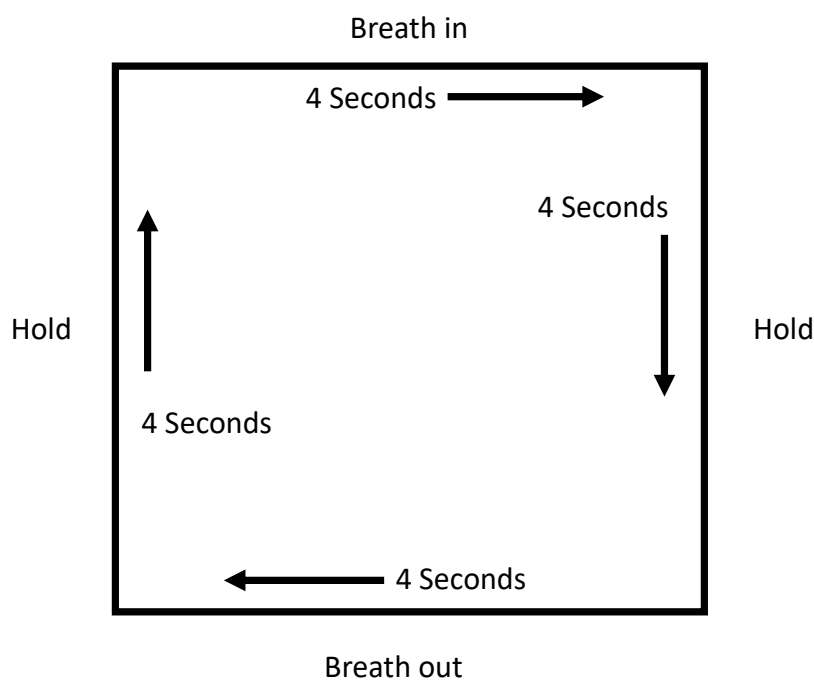
Calming hand exercise



- **Recognition** - Recognise signs of panic early and hold your thumb firmly
- **Sigh out** - Sigh out and remember to relax shoulders and chest (“flop and drop”)
- **Inhale and exhale slowly** - Slow breathing helps to reduce the sensation of breathlessness
- **Stretch and relax your hand** Continue to repeat the above steps until feeling calmer

Diagram adapted from Phyllis Tuckwell Hospice ‘Calming Hand’ leaflet

Square/rectangular breathing



- Breath out
- Hold for a count of 4
- Breath in
- Hold for a count of 4
- Repeat the process

| Treatments for specific causes of breathlessness | |
|--|---|
| Cause | Management |
| Lung tumour (primary or metastases) | <ul style="list-style-type: none"> Radiotherapy Chemotherapy Dexamethasone 4-8mg daily (<i>p69</i>) |
| Lymphangitis carcinomatosa | <ul style="list-style-type: none"> Dexamethasone 8-16mg daily (<i>p69</i>) |
| Large airway narrowing | <ul style="list-style-type: none"> Dexamethasone 8-16mg daily (<i>p69</i>) Radiotherapy (liaise with oncology team) Stenting (liaise with oncology/respiratory/thoracic surgeons)* |
| Bronchospasm | <ul style="list-style-type: none"> Inhaled/nebulised bronchodilators Inhaled/nebulised steroids |
| Effusions | <ul style="list-style-type: none"> Pleural effusion: drainage, pleurodesis Pericardial effusion: drainage, formation of pericardial “window” Ascites: drainage (<i>p44</i>) |
| Laryngeal obstruction | <ul style="list-style-type: none"> Urgent ENT opinion Dexamethasone 8-16mg daily (<i>p69</i>) Tracheostomy may be required |
| Superior vena cava obstruction | <ul style="list-style-type: none"> Urgent oncology opinion Dexamethasone 16mg daily (<i>p69</i>) |
| Infection | <ul style="list-style-type: none"> Antibiotics if appropriate |
| Respiratory secretions; Not imminently dying | <ul style="list-style-type: none"> Nebulised saline Mucolytics (carbocysteine) Physiotherapy |
| Imminently dying | <ul style="list-style-type: none"> Positioning Antisecretories (<i>p86 & 90</i>) |
| Pulmonary emboli | <ul style="list-style-type: none"> Anticoagulation if appropriate (<i>p65</i>) |
| Pulmonary oedema | <ul style="list-style-type: none"> Diuretics Consider ACE inhibitor |
| Arrhythmias | <ul style="list-style-type: none"> Dependent on arrhythmia Seek advice from cardiologist |
| Chest wall/pleuritic pain | <ul style="list-style-type: none"> See Pain section (<i>p6-20</i>) Seek advice from specialist palliative care team and/or local pain clinic |
| Deconditioning | <ul style="list-style-type: none"> Gentle exercise to optimise cardiovascular and muscle function and fitness Review corticosteroids (which cause proximal myopathy) (<i>p69</i>) |
| Motor Neurone Disease, other neuromuscular conditions | <ul style="list-style-type: none"> Consider nasal or mask Non-Invasive Ventilation (NIV) Seek respiratory advice early* |
| Anaemia (<i>p62</i>) | <ul style="list-style-type: none"> Correction of iron/B12/folate deficiency, Iron infusion therapy IV Transfusion if appropriate (Hb<70g/L) |

Drug therapies

- **Nebulised saline** may help where there are tenacious secretions
- **Opioids** (*p6-14*) often help reduce the subjective sensation of breathlessness, particularly when there is breathlessness at rest; there is no evidence that they shorten life or cause significant respiratory depression when used appropriately
 - If opioid naïve, start on 1-2mg of immediate release morphine 4 hourly prn PO or 5-10mg Morphine Sulfate MR bd PO and titrate upwards to a maximum of 30mg in 24 hours. In some non-malignant conditions, and in the presence of renal impairment, lower doses and less frequent administration may be sufficient
 - If already on morphine for pain, the dose may need to be increased and specialist palliative care advice should be sought*
 - If the patient is unable to take oral medication, opioids can be given via syringe driver (CSCI)
 - Nebulised opioids are no longer advised
- **Anxiolytics** (*p92*) may be used alone or in combination with opioids, if there are secondary anxiety symptoms. Benzodiazepines are not recommended as first line unless panic/anxiety is prominent or the patient is in the last weeks of life. In such circumstances consider prescribing:
 - Diazepam 2-10mg PO daily for background control
 - Lorazepam 0.5 -1mg SL (quick-acting) for acute crises and panic attacks
 - Midazolam 2.5-10mg SC stat or 5-20mg per 24 hours by CSCI if patient is not able to take oral medication. (Higher doses only in certain circumstances)
 - Levomepromazine 6.25mg nocte/BD PO or 6.25-12.5mg/24 hours CSCI can also be considered

The route of administration will depend on the severity of the patient's condition. For general information on the place of anxiolytic antidepressants refer to section on anxiety (*p92*)

- **Oxygen (Refer to local guidelines)**
 - Has variable effects
 - Patients with oxygen saturations <90% or those who experience desaturations may benefit from oxygen
 - Difficult to predict who will benefit other than by individual therapeutic trial.
 - In those with chronic hypoxia aim for oxygen saturations between 88-92%
 - Nasal cannula often preferred to a mask
 - For some patients the burden of continuous attachment/dependence on oxygen may outweigh its benefit
- **Steroids** e.g. Dexamethasone (*p69*) can be helpful for alleviating breathlessness in some circumstances

Refractory/severe breathlessness

- Refractory/severe breathlessness in the dying patient is distressing and frightening for patients and their families
- After discussion with the patient and family, a syringe driver with opioid +/- anxiolytic may be needed*
- The aim is to achieve the required balance between sedative side effects and the control of breathlessness and anxiety; according to patient's wishes

Decisions about ventilation

- When a patient may be at risk of respiratory failure, the risks/benefits of mechanical ventilation (invasive or non-invasive) should be considered and, where appropriate, discussed with the patient in order to avoid crisis decisions about ventilation
- It may be helpful at this stage to discuss 'stopping rules'
- Careful documentation of the decision is necessary
- For patients with progressive neuromuscular conditions, early discussion with the respiratory team/specialist palliative care is advised*

Sudden major airway obstruction in the palliative care setting

- This is a palliative care emergency. It is likely to require urgent sedation, e.g. midazolam 10mg IV or SC
- The cause should then be treated where possible if appropriate

HOARSE VOICE

Hoarseness is relatively common either as a presenting symptom (e.g. laryngeal cancer) or a complication (e.g. vocal cord paralysis caused by recurrent laryngeal nerve palsy associated with mediastinal lymphadenopathy). Patients may withdraw from social interaction as they find speaking an effort and they are concerned people cannot understand them.

Causes/Risk factors

- Recurrent laryngeal nerve palsy secondary to mediastinal lymphadenopathy
- Lung cancer
- Laryngeal cancer
- Laryngitis
- Acid reflux
- Smoking
- Post-nasal drip
- Allergies
- Hypothyroidism
- Overuse of voice
- Injury

Management

A Consider reversible causes where possible.

B Non-drug measures

- Allow the patient time to communicate
- Reassure the patient that they can be understood, even if their voice is a whisper
- Consider referral to ENT for vocal cord injection (e.g. Teflon or gel) to bulk the paralysed vocal cord and enable the normal vocal cord to close against it
- Referral to Speech and Language Therapist

COUGH

Cough is a physiological mechanism to protect the airways. When perceived as excessive it should be considered a symptom.

- Prolonged bouts of coughing are exhausting and frightening
- Take a comprehensive history paying attention to time course, exacerbating factors (e.g. position, swallowing, exercise), associated symptoms (e.g. breathlessness, wheeze), sputum (colour, quantity, consistency) and haemoptysis
- Examine the patient fully and consider further investigations such as Peak Expiratory Flow Rate and chest X-ray if it will help guide the management plan

Management

A Consider reversible causes where possible, *refer to specific treatment table*

Management depends on the cause and the therapeutic goal

B Non-drug measures

- Positioning
- Chest physiotherapy and optimise cough technique

C Drug therapies

Consider the type of cough:

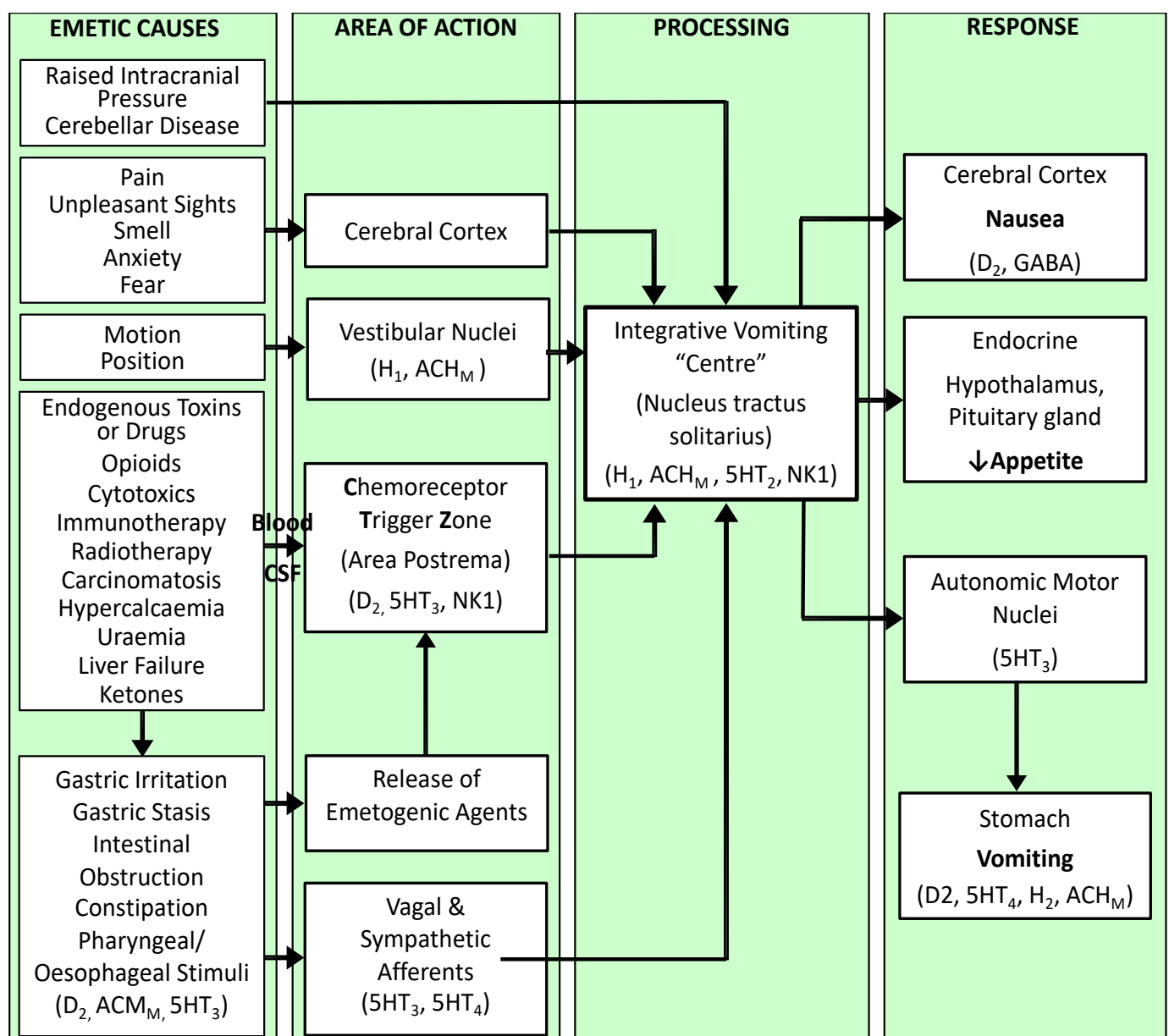
- wet / dry cough
- patient able to cough effectively /unable to cough effectively
 - Mucolytics – if wet and patient able to cough effectively
 - Nebulised saline 2.5-5mls prn to qds
 - Carbocisteine 1.5-2.25g PO daily in divided doses
 - Cough suppressants (anti-tussives) – if dry cough, or if patient unable to cough effectively
 - Simple linctus
 - Opioids - Codeine linctus 5-10mls qds PO *or*
 - IR morphine 1-2.5mg 4 hourly PO and titrate according to effect.
 - Methadone can also be used in low dose*

| Treatments strategies for specific causes of cough | |
|--|--|
| Asthma/COPD | • Optimise therapy with bronchodilators, steroids etc. |
| Cardiac failure (p76) | • Optimise therapy |
| Gastro-oesophageal reflux | • Proton pump inhibitors, ranitidine, antacids, prokinetics • Review GI feeding if in place |
| Lung/mediastinal tumour | • Dexamethasone 4-8mg daily (p69) • Radiotherapy/chemotherapy if appropriate |
| Infection | • Antibiotics if appropriate |
| Lymphangitis carcinomatosa | • Dexamethasone 8-16mg daily (p69) |
| Drugs e.g. ACE inhibitors, Immunotherapy | • Stop/review need for drug and consider switching to alternative treatment |
| Post-nasal drip | • Antibiotics • Steroid nasal spray |

NAUSEA AND VOMITING

- **Nausea** describes the unpleasant feeling of needing to vomit
- **Vomiting** is the forceful expulsion of gastric contents through the mouth.
- **Retching** describes rhythmic, laboured, spasmodic movements of the diaphragm and abdominal muscles usually occurring in the presence of nausea and often resulting in vomiting.
- **Regurgitation** is the passive expulsion of material from the pharynx or oesophagus through the mouth.
- **Reflux** is the passive expulsion of material from the stomach. It can lead to burning/painful/nausea sensations

Physiology



Receptor type **antagonists**: ACH_M=muscarinic cholinergic: D₂=dopamine type 2: NK₁= neurokinin 1: 5HT₂, 5HT₃=5-hydroxytryptamine type 2 & type 3.

Receptor type **agonists**: 5HT₄=5-Hydroxytryptamine type 4: GABA=gamma-aminobutyric acid

Causes/Risk factors

There are many causes of nausea and vomiting and often more than one cause is present. Nausea and vomiting can be complex to manage and it is important to recognise the contribution of psychological, social and spiritual factors as well as the purely physical.

| Cause | Clinical features | Drug therapy (p32 & 33) |
|--|---|--|
| Raised intracranial pressure (p46) | Worse in morning, may be associated with headache and drowsiness | <ul style="list-style-type: none"> • Dexamethasone • Cyclizine • Levomepromazine |
| Cerebellar disease | Ataxia, past-pointing, dysarthria | <ul style="list-style-type: none"> • Dexamethasone • Cyclizine • Levomepromazine |
| Anxiety (p92) (Anticipatory) | Anxiety or apprehension e.g. pre-chemotherapy | <ul style="list-style-type: none"> • Levomepromazine • Benzodiazepines |
| Motion, positional | Worse on movement or travelling | <ul style="list-style-type: none"> • Cyclizine • Prochlorperazine • Hyoscine hydrobromide |
| Drugs, endogenous toxins | May be apparent from drug history (coincides with starting drug); renal failure, hypercalcaemia (p67) | <ul style="list-style-type: none"> • Metoclopramide • Haloperidol • Levomepromazine |
| Chemotherapy, radiotherapy, Immunotherapy | Symptoms worse at time of treatment or in subsequent days or weeks | <ul style="list-style-type: none"> • Consult oncology colleagues • Early N/V: <ul style="list-style-type: none"> ◦ 5HT₃ antagonists ◦ Domperidone • Delayed N/V: <ul style="list-style-type: none"> ◦ Dexamethasone ◦ Levomepromazine ◦ Prokinetics |
| Gastric stasis | Early satiety (fullness after small meal) | <ul style="list-style-type: none"> • Metoclopramide • Domperidone • Erythromycin* |
| Gastric irritation | May be associated with epigastric discomfort, acid indigestion | <ul style="list-style-type: none"> • Review medication • Antacids • H₂ antagonists • Proton pump inhibitors |
| Intestinal stasis | Constipation, abdominal fullness, reduced bowel sounds | <ul style="list-style-type: none"> • Metoclopramide |
| Intestinal obstruction (p34) | Dependent on level of blockage. Little bowel movement or flatus PR; vomiting brings relief from nausea, or may be little nausea; may be faeculant material in vomit; colic; abdominal distension, scanty or tinkling bowel sounds, empty rectum | <ul style="list-style-type: none"> • See p34 |
| Constipation (p40) | Reduced frequency of passing hard stool; may have stool in rectum | <ul style="list-style-type: none"> • See p40 |
| Indeterminate | No discerning features | <ul style="list-style-type: none"> • Metoclopramide • Levomepromazine • Cyclizine • Trial of other |

Management

A Consider reversible causes

- If drug induced consider stopping, reducing or changing drug
- Treat cause, if appropriate e.g. hypercalcaemia (p67)

B Non-drug measures

- These include relaxation and psychotherapeutic techniques, acupuncture, ginger and Seabands (acupressure at Nei-Kuan P6 acupressure point in the distal forearm)
- Diet should also be assessed

C Drug therapies

- When nausea and vomiting are multifactorial, a broad-spectrum antiemetic (e.g. levomepromazine) may be most appropriate
- In established nausea and vomiting, use antiemetics via non-oral routes for initial control e.g. CSCI via syringe driver
- Some patients require more than one antiemetic*

Antiemetic drug profiles

† avoid in Parkinsonism and dystonia

| Drug | Usual starting dose | Maximum daily dose | Comment |
|------------------------------|--|---|---|
| Cyclizine | 25-50mg tds PO 50-100mg/24hr CSCI 25-50mg prn PO/SC | 150mg PO/24hrs 75-150 CSCI/24hr | <ul style="list-style-type: none"> • H₁ antihistamine with anticholinergic action (ACH_M) • Avoid in heart failure. • Skin irritation if SC (avoid if possible) |
| Dexamethasone | 4mg-8 od PO 3.3-6.6mg od SC (dose depends on cause) | 8-16 mg daily PO 6.6-13.2mg daily SC | <ul style="list-style-type: none"> • Reduces intracerebral swelling, other modes of action uncertain. • Risk of side effects. • 5-7 day trial • Set review date. |
| Domperidone | 10mg bd PO | 20mg tds-qds PO | <ul style="list-style-type: none"> • Dopamine D₂ antagonist and prokinetic. • Unlikely to cause sedation / extrapyramidal effects |
| Haloperidol † | 0.5-1.5mg nocte PO 2.5mg SC/ CSCI/24hr 0.5-1.5 mg prn PO/SC | 5-10mg PO/SC/ CSCI/24hr | <ul style="list-style-type: none"> • Dopamine D₂ antagonist, not prokinetic. • Often used for opioid induced nausea. • May cause extrapyramidal effects |
| Hyoscine hydrobromide | 300mcg SL (Kwells) 1mg/72hr by transdermal patch 800mcg /24h CSCI 200mcg prn SC | 600mcg up to qds SL 2.4mg /24h CSCI (unusual to use this dose for control of N/V) | <ul style="list-style-type: none"> • Antimuscarinic anticholinergic (ACH_M) • Sedating |

| Drug | Usual starting dose | Maximum daily dose | Comment |
|---|--|--|---|
| Levomepromazine † | 6.25mg nocte od PO/SC 6.25mg/24h CSCI | 25mg nocte od PO/SC 25mg/24h CSCI | <ul style="list-style-type: none"> • Antagonist at multiple sites (5HT₂, D₂, ACh_M/H₁). • Can cause hypotension in susceptible patients, drowsiness, dry mouth and other anticholinergic effects. • Use lowest effective dose. • Sedative at higher doses. • Might lower the seizure threshold. |
| Metoclopramide † | 10mg tds PO 30mg/24h CSCI 10mg prn PO/SC | 20mg tds-qds PO 60mg/24h CSCI <i>(note MHRA suggest restrict to 30mg/24h to reduce risk of side effects)</i> | <ul style="list-style-type: none"> • Dopamine D₂ antagonist • 5HT₄ agonist (bowel prokinetic). • 5HT₃ antagonist at higher doses (100mg daily). • May cause extrapyramidal effects (monitor for tremor, restlessness) |
| Prochlorperazine † | 5mg tds PO 3mg bd buccal | 10mg tds PO 6mg bd buccal | <ul style="list-style-type: none"> • Predominantly D₂ antagonist • Weak ACh_M/H₁ antagonist • Can give IM • Avoid SC as is irritant |
| Olanzapine † | 2.5-5mg OD PO | 5-10mg PO | <ul style="list-style-type: none"> • Dopamine D₂ antagonist • Moderate ACh_M/5HT₂ antagonist • Helpful in cases refractory to other antiemetics |
| 5HT₃ antagonists Ondansetron | 4mg bd-tds PO/SC | 8mg bd-tds PO 24mg/24h CSCI | <ul style="list-style-type: none"> • Potent 5HT₃ antagonists. • Used to control early vomiting after chemotherapy and radiotherapy. • Avoid prolonged use - cause constipation |
| Granisetron | 1mg od PO/SC | 2mg od PO/SC | |
| Neurokinin 1 antagonists* (NK1) e.g Aprepitant | | | <ul style="list-style-type: none"> • Used as an adjunct with emetogenic chemotherapy |

† avoid in Parkinsonism and dystonia

INTESTINAL OBSTRUCTION

- Intestinal obstruction in association with advanced cancer is often complex and difficult to control
- Early discussion with specialist palliative care team is recommended*
- There are often both mechanical (intestinal narrowing) and functional (poor motility) elements

Diagnosis

The range of symptoms depends on level of blockage, but these include:

- Vomiting often with little preceding nausea
- Constipation, although some flatus and/or stool may still be passed
- Abdominal distension and generalised discomfort
- Colic may or may not be a feature
- Bowel sounds may be hyperactive or scanty
- Review previous operation notes
- Abdominal CT scan or x-ray may be helpful
- Exclude simple constipation by history, abdominal and rectal examination

Causes/Risk factors

- Most common with primary tumours of ovary and colon, but may occur with almost any metastatic cancer, including breast and lung
- Tumour mass within lumen
- Tumour on peritoneal surface causing oedema or adhesions
- Infiltration within bowel wall preventing normal peristalsis
- Damage to autonomic nerve plexuses by tumour infiltration of mesentery
- Pancreatic carcinoma may cause gastric stasis by unknown mechanism
- Adhesions, radiation fibrosis, metabolic disturbance, constipation, sepsis

Management

This will depend on the site of obstruction; whether complete or incomplete; whether a single site or multiple sites; degree of bowel motility – the presence or absence of colic; the patient's general condition; and the patient's wishes.

A Consider Reversible causes

Consider surgery or stenting (large bowel) if there are clinical features to suggest a single site of obstruction, especially where colic is a prominent symptom, or where distension is such as to require venting.

B Non-Drug measures:

If inoperable, aim to control symptoms without the need for continuous 'drip and suck'. However:

- Nasogastric intubation or percutaneous venting gastrostomy may be preferred by patients with gastroduodenal obstruction where drug treatment has been unsuccessful
- Hydration with 1+ litres per day SC or IV may relieve thirst (not dry mouth), but may increase vomit volume

C. Drug therapies

Constant abdominal pain (usually tumour related)

- Opioids (*p6-14*) e.g. morphine, oxycodone by CSCI

Colic

- Avoid/stop
 - Stimulant (e.g. senna) and bulking (e.g. Ispaghula husk) laxatives
 - Avoid prokinetic antiemetics (metoclopramide, domperidone)
- Use anticholinergic/antispasmodics
 - Hyoscine butylbromide 40 - 120mg daily CSCI
 - Mebeverine and alverine PO may help if intermittent partial obstruction

Nausea and vomiting (*p30-33*)

Aim to abolish nausea and to reduce vomiting to a minimum.

- **If no colic**
 - start metoclopramide, dose range 30-60mg/24hrs CSCI
- **If colic**, or metoclopramide ineffective,
 - start hyoscine butylbromide, dose range, 60-120mg/24hrs CSCI to reduce intestinal secretions
 - +/- levomepromazine 6.25-25mg/24hrs CSCI
- **If vomiting persists**, review oral intake.
Consider:
 - Ranitidine 150-200mg/24hrs CSCI to reduce gastric secretions
 - Octreotide* 250-500micrograms/24hrs CSCI (maximum effective dose likely to be 1200micrograms/24hrs) to reduce intestinal secretions
 - 5HT₃ antagonist (e.g. ondansetron 16mg/24hrs or granisetron 1-2mg/24hrs CSCI)
 - Nasogastric tube insertion
 - Venting gastrostomy

Laxatives (*p40*)

- Check that lower rectum is empty
- Do not use if there is complete obstruction
- If there is partial or intermittent obstruction, use faecal softeners with caution:
 - Docusate sodium up to 200mg tds PO
 - Magnesium hydroxide mixture 20 - 30 ml od or bd PO
 - Macrogols (e.g. movicol) 1 sachet up to tds PO

Shrinkage of tumour masses

- Hormone/cytotoxic therapy is occasionally indicated, especially in primary tumours of ovary, colon or breast, if the patient's overall condition is good
- Radiotherapy is occasionally appropriate for low large bowel tumours
- Dexamethasone 6.6-13.2mg SC or IV daily (equivalent to 8- 16mg PO) may help to relieve peri-tumour oedema and so relieve obstruction (*p69*)

General measures

- Treat dry mouth (*p36*)
- Treat symptomatic gastro-oesophageal reflux

MOUTH PROBLEMS

Good mouth care is essential to the wellbeing of debilitated patients. Although mouth problems are very common (up to 90% of patients in some surveys), it is often a neglected area of care.

Diagnosis

- **Thorough inspection of the oral cavity is required – use a torch.**
 - Note the state of the lips, teeth/dentures (remove the dentures for examination), mucous membranes and tongue
 - Note the type and volume of saliva
- Assess nutritional status
 - Consider the quality of diet and adequacy of fluid intake
- Assess mental state
 - This will determine the patient's ability and willingness to participate in their care

Causes/Risk factors

- Dry mouth (xerostomia)
 - Especially from drugs (opioids, tricyclic antidepressants, antimuscarinics), dehydration (reduced intake or diuretics)
 - local radiotherapy
- Poor oral and dental hygiene
- Poor oral intake leading to decreased mastication
- Poor nutritional state, especially if leading to vitamin deficiencies
- Infections: viral, bacterial and fungal
- Anti-cancer therapies
 - Some cytotoxics can cause mucositis and acute ulceration;
 - Radiotherapy can cause mucositis
 - Immunotherapy can cause mucosal sores
- Bisphosphonates and Denosumab* can cause osteonecrosis of the jaw, particularly when dentition is poor.
- Corticosteroids and diabetes predispose to oral candidiasis
- Oral tumours

Management

A Consider Reversible causes

- Treat oral infections *e.g.*
 - Metronidazole for fungating tumours in the mouth,
 - Aciclovir for herpes orolingivitis (can be extremely painful)
- Attend to oral intake, diet and consider vitamin deficiencies

B Non-Drug measures

- Maintain frequent attention to good oral hygiene
- Alcohol-free chlorhexidine mouthwash may be used in debilitated patients - inhibits plaque formation and is antiseptic
- Maintain good denture care by cleaning and rinsing thoroughly; Patients may benefit from general advice on denture care

C Drug therapies

- Review medications causing dry mouth, *e.g.* drugs with anticholinergic effects

Specific mouth problems

| Symptom | Non-Drug measures | Drug therapies |
|--|---|--|
| Lack of good quality saliva | Salivary stimulants: Sugar free chewing gum | <ul style="list-style-type: none"> • Pilocarpine 5 - 10mg tds PO (or 4% 1 - 2 drops flavoured to taste) • bethanecol 10mg tds PO |
| | Saliva substitutes: Sips of water or ice cubes may give short term relief | <ul style="list-style-type: none"> • Spray e.g. Xerotin • (non-acidic, no animal products) • Gels e.g. Biotene oral balance |
| Oral candidiasis 'thrush' | Increase the flow of saliva (see above) Ensure that dentures are thoroughly cleaned and disinfected | <ul style="list-style-type: none"> • Nystatin oral suspension 3 - 5ml qds buccal then swallowed. Treat for at least 7 days <i>(NB. Higher than doses recommended in the BNF)</i> • Miconazole oral gel 5-10ml qds for 5-7 days • Fluconazole 50mg od PO for 7 days. Less effective in xerostomia. <i>NB. that there is increasing resistance to triazole antifungals</i> |
| Painful mouth | | <ul style="list-style-type: none"> • Benzydamine hydrochloride mouthwash or spray • Soluble aspirin gargle • Flurbiprofen lozenges • systemic NSAIDs • Oramorph liquid held in the mouth • local anaesthetic (lidocaine) spray (may cause initial stinging) |
| Aphthous ulcers | | <ul style="list-style-type: none"> • May respond to local steroid e.g. hydrocortisone 1 qds |
| Angular cheilitis | | <ul style="list-style-type: none"> • Miconazole gel if secondary to oral candidiasis |
| Chemotherapy induced mucositis | | <ul style="list-style-type: none"> • Mugard • Sucralfate suspension • Gelclair |
| Excessive salivation or drooling with swallowing problems | Botulinum toxin* injection to the salivary glands to reduce salivation (<i>refer to Head and Neck Team</i>) In severe cases, radiotherapy* to the salivary glands may be considered, but can cause excessive dryness | <p>May be helped by:</p> <ul style="list-style-type: none"> • Amitriptyline 10-25mg PO or PEG od • Hyoscine hydrobromide patch 1mg/72hrs TD changed every 3 days • Atropine eye drops 1% SL or PEG qds • Hyoscine butylbromide CSCI (<i>p86 & 90</i>) • Glycopyrronium PO or CSCI <p><i>May make the saliva unacceptably sticky, in which case consider propranolol</i></p> |

ANOREXIA

Loss of appetite is common in advanced illness. It may or may not be distressing for the patient themselves but is often a source of concern for family members:

"If only he would eat..."

Clinical features

- A reduced interest in food which at its most severe may manifest as nausea
- Often associated with taste changes
- May increase (appetite diminishes) as the day goes on
- Distinguish from mouth problems, difficulties with swallowing, and early satiety due to gastric stasis

Causes/Risk factors

- Extensive malignancy (can be a presenting symptom)
- Uncontrolled symptoms
- Psychological, emotional and spiritual distress e.g. anxiety and depression
- Drugs, e.g. chemotherapy, immunotherapy, digoxin

Management

A Consider reversible causes:

- Review drugs
- Treat nausea (*p30*), pain (*p6-23*) and other symptoms
- Treat depression (*p91*): mirtazapine rather than SSRIs which can increase anorexia

B Non-drug measures

- Aim to provide frequent, small, attractive portions within pleasant and social surroundings
- Reduce psychological distress with support and counselling

C Drug therapies

If drugs are needed and there are no contra-indications:

- Alcohol before meals
- Dexamethasone 2 - 4mg or prednisolone 10 - 30mg od PO (but note risk of side effects especially if continued for more than a few weeks (*p69*))
- Megestrol acetate 160 - 320mg daily PO
 - may take 2 - 3 weeks to respond
 - increased risk of thrombosis

ANOREXIA CACHEXIA (FATIGUE) SYNDROME

Diagnosis

- A syndrome of loss of appetite, fatigue, and profound weight and muscle loss.
- A rise in acute-phase proteins, e.g. CRP, and platelets maybe indicators

Causes/Risk factors

- Usually associated with cancer but may occur with heart failure and chronic infection or inflammation
- Cytokine release leading to proteolysis, lipolysis, increased resting energy expenditure, and hypothalamic disturbances including anorexia

Management

A Consider reversible causes

Correct associated problems (see above)

B Non-drug measures

Fatigue management programme - gentle but regular exercise programme to reduce muscle loss and promote adaptive behaviour

C Drug therapies (*rarely indicated*)

Consider:

- Dexamethasone 2 - 4mg mane PO as a short course for one week then review (*p69*),
or
- NSAIDs to reduce inflammatory process (*p18*)

Evidence is unclear on the place of:

- Fish oils sources of eicosapentaenoic acid (EPA), e.g. Maxepa
- Nutritional supplements (e.g. Prosure)
- Anabolic steroids
- Methylphenidate*

CONSTIPATION

Constipation is common in patients with advanced disease. It can cause abdominal pain and urinary retention. Even if not eating, patients can become constipated due to accumulation of faecal matter formed from gut secretions, cells and bacteria. It is far better to anticipate and prevent constipation than to wait until treatment is urgent.

Diagnosis

Constipation should be considered if there is a history of passing harder and/or less frequent stools than normal. Faecal impaction may present with overflow ('spurious diarrhoea'). The rectum can be empty or impacted, collapsed or cavernous. Assess anal sensation and tone if concerns about spinal cord or sacral nerve root lesion/s. Exclude intestinal obstruction. Abdominal CT scan if examination unclear.

Causes/Risk factors

- Drugs, especially opioids, anticholinergics (e.g. antidepressants, antispasmodics), ondansetron
- Inactivity, immobility, weakness
- Dehydration due to poor fluid intake, vomiting, polyuria, fever
- Poor nutrition, reduced fibre intake
- Hypercalcaemia
- Spinal cord compression or sacral nerve root lesion
- Concurrent disease including painful anal conditions, neurological disorders
- Lack of privacy

Management

A Consider reversible causes

Reduce or eradicate underlying cause(s) as far as possible

B Non-drug measures

If general condition allows, mobilise and encourage fluids; facilitate privacy

C Drug therapies

- Use softeners if stool is hard, stimulants if soft stool is not expelled
- Patients taking regular opioids will usually require either a laxative combination or an adequate dose of macrogols. Macrogols alone are often sufficient
- An opioid switch to a transdermal opioid might help
- Opioid antagonists are reserved for resistant cases*

| Drug action | Specific oral treatment |
|------------------|---|
| Stimulant | <ul style="list-style-type: none">• Senna 7.5-30mg as tablets or liquid nocte or bd PO• Bisacodyl tablets 5 - 20mg nocte or bd PO |
| Softening | <ul style="list-style-type: none">• Docusate sodium capsules 200mg nocte or bd PO• Macrogols (e.g. Movicol) 1 sachet od or bd PO |
| Osmotic | <ul style="list-style-type: none">• Magnesium hydroxide 20 - 30ml od or bd PO (Lactulose not advised as it causes excess wind and will increase abdominal distention) |

For resistant constipation

- Macrogols can be used to treat faecal impaction: e.g. movicol up to 8 sachets/day for up to 3 days
- Sodium picosulphate* solution 5 - 10ml od or bd PO is rarely used

Rectal measures

- Suppositories or enemas PR may be needed in established constipation and in the context of spinal cord compression
- If there are faeces in the rectum, suppositories of glycerol or bisacodyl are usually given
- If the rectum is empty but the colon is loaded with hard stool, use an arachis oil retention enema overnight followed by phosphate enema. (NB arachis oil is peanut oil so check for allergy)
- Manual dis-impaction should be a last resort, and consent obtained after full explanation. Sedation may be required as the therapy may cause pain and distress

Opioid antagonists*

Opioid antagonists eg methylnaltrexone SC and naloxegol PO for opioid induced constipation should be used under specialist direction*

DIARRHOEA

Diarrhoea is an increase in the fluid content of stools (either through increased secretion or reduced absorption) with increase in stool frequency. It is often multifactorial.

Diagnosis

The patient who speaks of 'diarrhoea' may be referring either to the frequency or to the looseness of bowel motions. An accurate history and examination are crucial: assess for watery/liquid stools usually with an increased stool frequency.

Causes/Risk Factors

- Impacted faeces with overflow (spurious diarrhoea)
- Infections, including *C. difficile*, upper GI bacterial overgrowth, Giardia lamblia
- Side effects of some drugs, e.g. chemotherapy, immunotherapy, antibiotics, PPIs, NSAIDs
- Previous treatment: pelvic radiotherapy, extensive bowel resection
- Excess laxative use
- Partial intestinal obstruction (*p34*)
- On initiation of enteral feeding
- Pancreatic insufficiency, characterized by bulky, offensive stools which float (steatorrhoea)
- Effects of some tumours, e.g. carcinoid, mucus secretion in rectal cancer
- Other - e.g. inflammatory bowel disease, bile salt malabsorption, secondary lactose intolerance, autonomic neuropathy (diabetes, paraneoplastic)

Management

A Consider reversible causes

Screen for infections and prescribe antibiotics as appropriate

B Non-drug measures

Address dehydration if appropriate

C Drug therapies

Review all drugs, including laxatives and non-prescription drugs. Stop causal drugs.

Symptomatic treatments

- Loperamide 2 - 4mg every 6 hours PO; binds to opioid receptors in gut
- Codeine phosphate 30 - 60mg tds – qds PO
- Co-phenotrope (Lomotil) 2 tablets up to qds PO

Specific treatments

| Cause | Specific treatment |
|--|---|
| Radiotherapy induced | • Local / systemic steroids (<i>p69</i>) |
| Pancreatic insufficiency Steatorrhoea | • Pancreatic enzymes (Creon capsules; 3 strengths) |
| Bacterial overgrowth / Blind loop | • Metronidazole |
| Faecal fistula | • Octreotide |
| Carcinoid | • Octreotide |
| Bile salt malabsorption | • Colestyramine <ul style="list-style-type: none">◦ Poorly tolerated.◦ Ineffective in complete biliary obstruction |

FISTULAE

- A fistula is an abnormal connection between two hollow organs (e.g. bladder and bowel, or trachea and oesophagus)
- Management is often complex and will depend on the site and size of fistula, the complications, the patient's general condition and their wishes
- Consider early referral to your specialist palliative care team*

Causes/Risk factors

- Locally advanced cancer eroding through one organ to the next
- Radiotherapy
- Surgery

| Fistula site | Clinical features |
|---------------------|---|
| Tracheo-oesophageal | <ul style="list-style-type: none">• Difficulty swallowing• Recurrent aspiration pneumonia |
| Rectovesical | <ul style="list-style-type: none">• Faecal matter in urine• Gas in urine• Recurrent UTI• Leakage of urine rectally |
| Rectovaginal | <ul style="list-style-type: none">• Faeculent matter passed per vagina |
| Vesicovaginal | <ul style="list-style-type: none">• Leakage of urine vaginally |
| Enterocolic | <ul style="list-style-type: none">• Diarrhoea |
| Enterocutaneous | <ul style="list-style-type: none">• Localised discharge of copious fluid• Can lead to dehydration, electrolyte depletion and skin irritation |

Management

A Consider reversible causes

Consider surgical intervention if appropriate (e.g. defunctioning colostomy, tracheal stent)

B Non-drug measures

- Maintain good skin care
- Prevent excoriation with a barrier product
- Collect effluent in a closed stoma bag. Ensure a good seal to minimise leakage and odour
- If necessary seek advice from stoma care nurses

C Drug therapies

- Metronidazole may be helpful if there is blind loop or overgrowth of anaerobes.
- Octreotide* by CSCI may be helpful in reducing effluent (p90)

ASCITES

The diagnosis is made from clinical assessment:

- Symptoms of progressive abdominal distension which may be accompanied by:
 - Breathlessness
 - Early satiety
 - Vomiting
 - Constipation
 - Lower limb oedema
 - Shifting dullness and a fluid thrill on examination.
- Abdominal ultrasound is used to confirm if appropriate.
- Exclude tumour masses, organomegaly, distended bladder, intestinal obstruction.

Causes/Risk factors

- Peritoneal metastases - may be associated with extra-abdominal primary sites
- Tumour obstructing retroperitoneal and/or diaphragmatic lymph system
- Hypoalbuminaemia, usually associated with extensive liver metastases
- Secondary sodium retention
- Venous compression or thrombosis of inferior vena cava or hepatic vein
- Other concurrent disease, e.g. heart failure, cirrhosis

Management

A Consider reversible causes

For example: anticoagulation for thrombosis

B Non-drug measures

If symptoms are minor, explanation and reassurance may be sufficient.

Paracentesis

- May be appropriate for patients with a tense, uncomfortable, distended abdomen, especially if associated with breathlessness
- Ultrasound recommended to identify suitable location for drain insertion
- Drain up to a maximum 5 litres of fluid per 24 hours
- Sudden release of abdominal tension may lead to venous decompression, hypotension and collapse. This risk can be reduced for patients with portal hypertension by using IV albumin
- Remove drain once drainage slows or stops. There is no advantage in draining to dryness. If leakage continues after drain is removed, place stoma bag over puncture site
- Indwelling drainage systems (eg Rocket or PleurX) for selected patients requiring repeated paracentesis

c Drug therapies

| Drug group | Drug | Comment |
|--|--|--|
| Analgesia (p6-23) | <ul style="list-style-type: none"> Range from paracetamol to strong opioids | For abdominal pain or discomfort of distension |
| Antiemetics (p30) | <ul style="list-style-type: none"> Metoclopramide or domperidone | For gastric stasis |
| Diuretics | <ul style="list-style-type: none"> Spironolactone (especially if low albumin) 50 - 200mg od PO Furosemide (especially if dependent oedema) 40 - 80mg od PO | Diuretics should be considered particularly when hepatic metastases &/or cirrhosis. Monitor electrolytes, renal function and blood pressure. |
| Corticosteroids (p69) | <ul style="list-style-type: none"> Dexamethasone 4-8mg od PO (3.3-6.6mg od SC) – monitor for response | May reduce lymph blockage |
| Laxatives | <ul style="list-style-type: none"> (p40) | Relieving constipation may lessen distension |
| Cytotoxic chemotherapy (local/systemic) | <ul style="list-style-type: none"> Seek oncological advice | May be appropriate, especially for primary carcinomas ovary, breast or colon. |

RAISED INTRACRANIAL PRESSURE

Clinical features include:

- Severe headache which may be worse when lying down or straining
- Vomiting, seizures, diplopia, cognitive changes, and restlessness may occur
- Papilloedema may be present
- A CT/MRI scan may be appropriate

Causes/Risk Factors

- Cerebral metastases (common with some primaries, e.g. lung, breast, melanoma and rare with others, e.g. prostate)
- Primary cerebral tumour
- Leptomenigeal disease
- Other causes – abscess, cerebro-vascular event, sagittal sinus thrombosis, secondary hydrocephalus following surgery

Management

A Consider reversible causes

Discuss with oncology or neurosurgical colleagues if/as appropriate

B Non-drug measures

- Raise the head of the bed
- Consider cranial irradiation or neurosurgery (removal of tumour or shunt) for malignancy dependent on prognosis/status

C Drug therapies

- **Dexamethasone** (*p69*)
 - 4-8mg PO or 3.3-6.6mg SC /24hrs can give temporary relief from mild symptoms.
 - Higher doses (16mg/24hrs) can be used if symptoms severe or risk of herniation
 - With time, symptom relief decreases and side effects increase so ideally reduce the dose after 1 week and discontinue after 2-4 weeks
 - In the absence of other treatment (e.g. radiotherapy), symptoms may recur during dose reduction in which case reduce the dose more gradually
 - Some patients may need long-term “maintenance” therapy

NB Metabolism of corticosteroids is increased by carbamazepine, enzalutamide, phenobarbital and phenytoin. E.g. phenytoin may reduce bio-availability of dexamethasone to 25-50%. Dexamethasone can cause both increased and decreased phenytoin levels.

Specific treatments

| Symptom | Drug Group | Drug options |
|-----------|----------------|---|
| Headaches | Analgesics | <ul style="list-style-type: none"> • Paracetamol/Opioids (<i>p6-14</i>) • NSAIDs (<i>p18</i>) |
| Vomiting | Antiemetics | <ul style="list-style-type: none"> • E.g. cyclizine (<i>p30</i>) |
| Fits | Antiepileptics | <ul style="list-style-type: none"> • (<i>p47</i>) |

- **Antiepileptics** should not be used for primary prophylaxis in the presence of cerebral metastases (outside of the peri-surgical setting). They should be reserved for those who have had at least one seizure

FITS (Seizures)

- Approximately 20% of patients with cerebral tumours will have seizures
- The majority of seizures secondary to cerebral primary or secondary tumours have a focal onset
- This may not always be obvious as they can rapidly progress to secondary generalized seizures
- Consider a diagnosis of subclinical 'silent' seizures as a possible cause of unexplained intermittent confusion or drowsiness
- Exclude syncopal attacks, cardiac arrhythmias, TIAs etc

Causes/Risk Factors

- Previous epilepsy, brain trauma or surgery, brain tumour (primary or secondary)
- Drugs which lower seizure threshold: e.g. phenothiazines, tricyclics, tramadol
- Drug interactions:
 - Anticonvulsants have many variable and unpredictable interactions
 - significantly carbamazepine and phenytoin can reduce the effect of steroids
- Drug withdrawal, e.g. steroids, alcohol
- Metabolic disturbance, e.g. hypoxia, hyponatraemia, hypoglycaemia

Management

A Consider reversible causes

e.g. drugs, metabolic causes

B Non-drug measures

Clear explanation and support for patient and family regarding management

C Drug therapies

Secondary Prevention of further fits

- Review dexamethasone dose if appropriate (*p69*)

i. Oral route available

| Drug | Starting Dose | Dose range | Comments |
|--|-----------------|---|--|
| First line: Levetiracetam | 250-500mg bd PO | <ul style="list-style-type: none">• Most need at least 500mg.• increase by 250-500mg bd every 2 weeks.• Maximum dose 1.5g bd. | Decrease dose in renal impairment |
| Second line: Sodium Valproate | 150-200mg bd PO | <ul style="list-style-type: none">• Increase by 150-200mg bd every 3 days• 90% require <1.5g/24hrs• Maximum 2.5g in 24hrs | Teratogenicity unlikely to be relevant in this setting |
| Third line: Oxcarbazepine | 75-150mg bd PO | <ul style="list-style-type: none">• Increase by 75-150mg weekly• Maximum dose 2.4g daily | |

- NB** • Phenytoin is best avoided because of difficulties with drug interactions and pharmacokinetics. If patient is already on it, check and optimise dose levels and albumin. Hypoalbuminaemia will make phenytoin level appear falsely low.
- Avoid combination therapy (increased risk of drug reactions and of toxicity; limited evidence of benefit vs monotherapy). If needed, discuss with neurologist*.

ii. Oral route not available

| Drug | Dose | Comments |
|-------------------|--|---|
| Levetiracetam * | (p47) | <ul style="list-style-type: none"> Can be given via CSCI Dose is equivalent to oral |
| Midazolam | 20-60mg/24hrs via CSCI (p90) | <ul style="list-style-type: none"> Generally used first line in the last days of life because of familiarity, benefit for other symptoms, and compatibility with other drugs |
| Sodium Valproate* | (p47) | <ul style="list-style-type: none"> Useful if wanting to avoid sedation Can be given via CSCI Dose is equivalent to oral NB <i>cannot be mixed with other drugs, so needs separate syringe driver</i> |
| Phenobarbital* | Start with 100mg/24 hours via CSCI. If seizures occur, titrate to a maximum of 400mg/24hrs (see below for doses in status epilepticus) | <ul style="list-style-type: none"> Used as 2nd line alternative to above drugs Stat SC boluses reported to cause local skin irritation (it is very alkaline), so should only be given IM when undiluted May be given via CSCI, or IV if diluted x 10 with water for injection. NB <i>Never mix with another drug, so needs separate syringe driver</i> |
| Carbamazepine | 250-500mg bd PR | |

Immediate management of the fitting patient

- First aid precautions
- Explanation and reassurance
- Protect airway
- Oxygen if cyanosed
- Check blood sugar

If:

- No prior history of seizures; *or*
- Previously did not resolve spontaneously; *and /or*
- Caused distress:
 - Give midazolam immediately - 10mg buccal, SC or IV
 - Otherwise only give midazolam if seizure does not spontaneously resolve after 5 minutes or a second seizure occurs within an hour of the first
 - Lorazepam 4mg is an alternative given IV slowly, 2mg/ min

If seizures persist (*Status Epilepticus*):

- Repeat midazolam once after 20 mins if SC or buccal, 10 mins if IV
- If seizures have not ceased unlikely to respond to further midazolam
- ***At this point decision required regarding the most appropriate place of care: possible hospital transfer, for consideration of intubation/ventilation, or if this is a terminal event for hospice admission or ongoing support in place of choice.***

If hospital transfer not appropriate use:

- Levetiracetam* 1000-2000mg CSCI in 24 hours
- Phenobarbital* 10-15mg/kg bolus up to a maximum of 1g IM (split larger doses between different sites), or diluted IV bolus at a maximum rate of 100mg/min

MALIGNANT SPINAL CORD COMPRESSION (MSCC)

- **This is an oncological emergency. Early diagnosis and urgent treatment** within hours **are vital** to improved outcome, mobility and continence
- Occurs in 5-10% of patients with advanced cancer. (most commonly breast, lung, prostate, lymphoma and myeloma)
- Thoracic spine is commonest site (70%), Lumbar spine (20%), cervical spine (10%)
- Once paralysis is established only 5% walk again, but some survive more than one year

Causes/Risk factors

- Epidural invasion from vertebral body metastasis is the commonest aetiology others include:
- Bony deformity from vertebral body collapse
- Paravertebral node invasion
- Blood borne epidural/intradural metastases
- Primary spinal cord tumour
- All patients at risk of MSCC should be provided with information on symptoms and what to do if they develop.

Presentation

- It is essential to be alert for early signs, which can be subtle
- Do not wait for signs to become unequivocal
- Often history is of back pain with or without radiation in the territory of a nerve root, followed by sensory changes, bladder or bowel disturbance, and leg weakness, but can be any combination of these
- If at thoracic level there is likely to be a sensory level with brisk reflexes;
- If cauda equina compression (below L2), reflexes may be diminished

Management *(Please refer to local guidelines)*

A Immediate

This depends on many factors: previous functional ability/performance status, prognosis, if well enough for investigation and treatment, whether already paraplegic, and patient preference

All acute hospitals treating patients with MSCC should have an MSCC coordinator with 24-hour availability. They should provide first point of contact, give immediate advice and perform initial telephone triage. OOH, referral may be to the acute medical service.

NICE advises

- Contact MSCC coordinator **within 24 hours** if diagnosis is cancer and there are any of the following symptoms:
 - Pain in thoracic or cervical spine
 - Progressive lumbar spinal pain or severe unremitting lower spinal pain
 - Spinal pain aggravated by straining (coughing, sneezing, straining at stool)
 - Nocturnal spinal pain preventing sleep.
 - Localised spinal tenderness
- Contact MSCC coordinator **immediately** (oncological emergency) if any of the following:
 - Neurological signs of spinal cord/cauda equina compression
 - Includes radicular pain, limb weakness, difficulty walking, sensory loss, bladder or bowel dysfunction
- Commence dexamethasone 8-16mg PO or SC unless contraindicated (p69)

B Further management

- If MSCC considered likely and pending assessment and treatment, nurse flat with spine neutrally aligned (including log rolling) as there may be spinal instability
- The MSCC co-ordinator will advise and co-ordinate management as appropriate. They will consider urgent liaison/referral to clinical oncologist/acute oncology service/neurosurgical team for:
 - Organization of urgent **MRI** scan or CT scan if MRI unavailable/not possible
 - Urgent **radiotherapy** is the definitive treatment for all unless:
 - Suitable for spinal surgery *or*
 - Complete tetraplegia/paraplegia for >24 hours AND pain well controlled *or*
 - Overall prognosis is very poor *or*
 - Patient declines
 - **Surgery**: NICE recommends consideration of surgery where prognosis > 3 months, patient is fit enough for surgery, AND at least one of the following applies:
 - Paraplegia not present for > 48 hours
 - An unstable spine
 - Deterioration in neurological function
 - Pain despite previous radiotherapy

C Non-drug measures

- Specialist palliative care assessment for management and/or rehabilitation of patients with established paraplegia is recommended and may include:
 - Pain relief
 - Pressure area care
 - Urinary catheter
 - Bowel regulation – allow some constipation and use regular enemas or suppositories
 - Maintaining circulatory and respiratory functioning
 - Physiotherapy and occupational therapy assessments: wheelchair, home modifications
 - Psychological readjustment.

D Drug therapies

- Dexamethasone (*p69*): Inhibits inflammation, stabilizes vascular membranes and reduces spinal cord oedema. Can lead to great reduction in pain and early improvement in function
 - Give stat dose of dexamethasone 16mg PO (13.2mg SC/IV if PO not possible)
 - Continue 16mg daily PO or 13.2mg SC with gastric protection (eg PPI)
 - After completion of radiotherapy/surgery the dose should be reduced every 5-7 days and stopped
 - If, during tapering, neurological function deteriorates, the dose should be increased again temporarily
 - Monitor blood glucose levels in all patients receiving corticosteroids
- Analgesia (*p6-24*)
- Consider prophylaxis against venous thromboembolism (*p65*)

HICCUP

A pathological respiratory reflex characterised by diaphragmatic spasm and abrupt closure of the glottis.

Causes/Risk factors

- Peripheral (diaphragmatic or phrenic nerve irritation)
 - Gastric distension or irritation
 - Liver enlargement/involvement
 - Intrathoracic lymphadenopathy and/or tumour
 - Tumour irritation/involvement of diaphragm
- Central (medullary stimulation)
 - Raised intracranial pressure
 - Brain stem CVA or tumour
 - Metabolic (uraemia, hypokalaemia, hypocalcaemia, hyperglycaemia, hypocapnia)

Management

A Consider reversible causes

Consider underlying cause, see risk factors

B Non-drug measures

Symptomatic treatments

- Pharyngeal stimulation
'Grandmother's remedies' e.g. sipping cold water, crushed ice, spoonful of granulated sugar. These mostly cause pharyngeal stimulation and are often effective, at least temporarily
- Elevation of pCO₂ inhibits hiccup reflex in brainstem:
 - Breath holding
 - Re-breathing into a paper bag

C Drug therapies

| Cause | Specific treatment |
|---|---|
| Reduce gastric distension/irritation: | <ul style="list-style-type: none">• Prokinetics e.g. metoclopramide 10-20mg tds/qds PO,• Proton pump inhibitors, ranitidine, antacids,• Defoaming agents e.g. simeticone, antiflatulants e.g. peppermint water |
| Muscle relaxants | All have central suppressant effects <ul style="list-style-type: none">• Baclofen 5-20mg tds PO (NB sedation)• Nifedipine 10-20mg tds PO (NB lowers blood pressure)• Midazolam 10-60mg/24hrs via CSCI if patient in the last days of life |
| Central suppression of the hiccup reflex | <ul style="list-style-type: none">• Haloperidol 1.5-3mg nocte PO• Gabapentin: For acute relief, "burst gabapentin" can be used: 400mg tds PO for 3 days, then 400mg od for 3 days, then stop. Can be repeated if necessary. (Reduce dose in renal impairment or if frail)• Levomepromazine 6.25 – 12.5mg daily PO or CSCI |
| In intractable hiccup | <ul style="list-style-type: none">• Phrenic nerve block |

RESTLESSNESS

This may be akin to delirium in someone very close to death, or may occasionally reflect unresolved psychological distress, especially if this has previously been a problem.

Causes/Risk factors

- Physical discomfort – unrelieved pain, distended bladder or rectum, inability to move, insomnia, uncomfortable bed, breathlessness
- Drugs – opioid toxicity (especially in renal, liver impairment) hyoscine hydrobromide (paradoxical agitation), dopamine antagonists (akathisia), steroids
- Infection
- Raised intracranial pressure
- Biochemical abnormalities – hypercalcaemia, uraemia, hypoxia
- Psychological/spiritual distress – anger, fear guilt. Consider especially if patient has been unwilling to discuss illness

Management

A Consider reversible causes

- Accurately assess the patient
- Ameliorate all physical elements if possible, e.g. analgesia, catheterisation

B Non-drug measures

- Must be multi-professional approach involving family or main carers.
- Listen to the patient and address anger, fear and guilt if possible
- May be very distressing for the family who will need much support. Their presence may help or worsen the patient's agitation

C Drug therapies

- If there are hallucinations or frank delirium
 - Haloperidol, olanzapine, risperidone and quetiapine (*p54*)
 - Levomepromazine 6.25-25mg PO/SC or 6.25-50mg via CSCI over 24 hours*
 - If symptoms are intractable, may need to add:
 - Diazepam 2mg bd or 5mg nocte PO
 - Midazolam 2.5-5mg prn SC or 10-60*mg CSCI over 24 hours
- Under specialist supervision* the following may be required
- Clonazepam* 0.5-2mg via CSCI over 24 hours
 - Phenobarbital* IM or CSCI

DELIRIUM

Delirium is typified by acute confusion, often with visual illusions or hallucinations, together with increased or decreased psychomotor activity and fluctuating level of consciousness or attention. It must be distinguished from **dementia**, which is associated with gradual onset poor short-term memory and no impairment of consciousness, and which will not be considered here. However, acute delirium may develop in an individual with pre-existing cognitive impairment

Diagnosis

- Common, often reversible however often diagnosed late
- Use Confusion Assessment Method (CAM) can help to diagnose delirium:
Three of the following four possible features:
 - **acute onset and fluctuating *and***
 - **inattention****plus either**
 - **disorganised thinking *or***
 - **altered level of consciousness**
- Evidence from the history, examination, or investigations that there may be a physical cause (collateral history is very important)
- Delirium can be hyperactive, hypoactive or mixed
- Hypoactive delirium is far more common, and easily missed or diagnosed as depression

Causes/Risk factors

- Age and pre-existing cognitive deficit
- Drugs – e.g. opioids, tricyclic antidepressants, antimuscarinics, any sedative drug, baclofen; corticosteroids may cause hypomania
- Opioid toxicity exacerbated by uraemia*, dehydration or infection is an important cause of confusion and hallucinations. Look for constricted pupils, myoclonic jerks, skin hyperaesthesia and reduced respiratory rate. (p13)
- Infection, especially within respiratory and urinary tracts
- Biochemical abnormalities – see list under drowsiness (p56)
- Intracerebral causes – space occupying lesions, infections, stroke
- Environmental changes – interruption from staff, excessive unfamiliar stimuli, inpatient admission
- Social isolation
- Poor symptom control – pain, constipation, urinary retention, anxiety, depression
- Alcohol or drug withdrawal, including nicotine

Management

A Consider reversible causes

- Treat or minimise any possible causes, including drugs, metabolic abnormalities
- Treat infections if appropriate
- Oxygen if cyanosed/hypoxic and oxygen saturations are <90%
- Dexamethasone up to 16mg per day if cerebral tumour or raised ICP (p69)

B Non-drug measures

- Minimise stimuli: nurse in room with diffused lighting, little extraneous noise, and few staff changes
- Attempt to keep patient in touch with reality and environment
- Allay fear and suspicion – explain all procedures, don't change position of patient's bed, if possible have a friend or relative of patient present
- Stress that patient is not going mad and that there may well be lucid intervals.

C Drug therapies

If paranoid, deluded, agitated or hallucinating **AND** distressed

(may also be needed for hypoactive delirium if patient is distressed):

Lower doses are recommended, use higher doses only following specialist advice*

NB. Review early, as symptoms may be exacerbated by sedative effects of medication.

| Drug | Dose range | Dose | CSCI in 24hr | Comment |
|------------------|---|------|--------------|--|
| Antipsychotics | | | | |
| Haloperidol† | 0.5-3mg od PO/SC Repeat after 2hr if necessary | | 2-10mg* | All four are equally effective <ul style="list-style-type: none">• Effectiveness may be limited. Review if symptoms not improving• Haloperidol often used first line• † Avoid in Parkinson's Disease and in Lewy Body Dementia (D₂ antagonists) |
| Olanzapine† | 2.5-5mg nocte PO up to 10mg/24hr | | | |
| Risperidone† | 0.25mg-1mg nocte PO up to 2mg/24hr | | | |
| Quetiapine† | 25-300mg PO/24hr | | | |
| Levomepromazine† | 6.25-25mg nocte or bd PO/SC | | 25-50mg* | <ul style="list-style-type: none">• More sedative• Higher doses may be used by specialists* |
| Benzodiazepines | | | | |
| Lorazepam | 0.5-1mg prn SL Up to 4mg/24hr | | | <ul style="list-style-type: none">• May worsen delirium• Preferred choice in:<ul style="list-style-type: none">◦ Alcohol and drug withdrawal◦ Parkinson's disease◦ Lewy body dementia• Add to antipsychotics for acute distress and to control dangerous behaviour• Higher doses of midazolam may be used by specialists* |
| Diazepam | 5mg 8-12hr PO/PR up to 10mg PO/PR 6-8hr | | | |
| Midazolam | 2.5-5mg prn SC 1-2hr | | 5-30mg* | |

INSOMNIA

Insomnia is a subjective complaint of poor sleep. This can mean insufficient, interrupted or non-restorative sleep or sleep at the wrong time. It is important to clarify whether the issue is an inability to get to sleep due to anxiety, confusion; a tendency to wake repeatedly due to urinary problems, pain or anxiety; or early morning waking due to depression.

Causes/Risk factors

- Anxiety or depression
- Poor symptom control
- Nocturia
- Environmental changes – inpatient admission – interruptions by staff
- Fear – e.g. of going to sleep or of nightmares
- Beware of well-intentioned reassurance that “you will die in your sleep”
- Ensure delirium is not missed
- Drugs – stimulants (caffeine etc.), steroids (worse if given later than 2pm), diuretics, opioids (vivid dreams, hallucinations), fluoxetine, propranolol (nightmares)
- Drug withdrawal – alcohol, benzodiazepines, barbiturates

Management

A Consider reversible Causes - Minimise the causes

- Control symptoms as far as possible
- Keep interruptions to a minimum
- Reduce drug therapy or give stimulants early in the day
- Counsel about fear and anxieties

B Non-drug measures

- Establish good sleep hygiene (e.g. a consistent bed time ritual)
- Encourage relaxation techniques

C Drug therapies

- Zopiclone 3.75-7.5mg PO, zolpidem 5-10mg PO or zaleplon 5-10mg PO have fewer residual effects than benzodiazepines
- Benzodiazepines e.g. temazepam 10-20mg PO are rarely first line
Benzodiazepines and zopiclone may help patients get off to sleep but do not ensure a good night's sleep – patients may wake repeatedly
- A tricyclic antidepressant e.g. amitriptyline may help to ensure a better night's sleep
- Antidepressant for depression
- Melatonin 2mg 1-2hr before bedtime PO starting dose with maximum dose of 10mg daily

Note –

- All drugs used as a single dose at night
- Short term use advised
- Hypnotics may increase risk of falls and nocturnal confusion, especially in the elderly
- Use low dose Haloperidol evening or at bedtime if any evidence of delirium (p53)

DROWSINESS

Causes/Risk factors

Organic

- Disease progression and likely impending death
- Infection, especially within respiratory and urinary tracts
- Raised intracranial pressure
- Post-ictal

Biochemical

Metabolic abnormalities:

- uraemia, especially if on opioids
- hyper/hypoglycaemia
- hypercalcaemia
- hyponatraemia
- hepatic failure
- respiratory failure (blood gas analysis likely to be inappropriate)

Drugs

- Opioids, tricyclic antidepressants, benzodiazepines, antimuscarinics, antihistamines
- Even drugs that have previously been well tolerated may cause problems if renal impairment or new drug interactions

Other

- Fatigue
- Insomnia
- Psychological withdrawal

Management

A Consider reversible causes

- Correct physical causes listed above if indicated
- Assess accurately; if the patient is near to death due to advanced disease, further interventions are unlikely to be appropriate

B Non-drug measures

Give explanation and reassurance to patient and family, this symptom commonly causes high levels of distress

C Drug therapies

Review dose of opioids and other sedative drugs

- Specific:
 - Dexamethasone up to 16mg PO or 13.2mg SC daily for raised intracranial pressure (p69)
 - Antidepressants for retarded depression (p91)
- General:
 - Dexamethasone 2-4mg daily PO may act as stimulant
 - Methylphenidate* initially may act as stimulant

SWEATING/HYPERHIDROSIS

Sweating can have many causes and if due to fever from infection may be reversible. It can be endocrine related (menopause, diabetes, hyperthyroidism, carcinoid) or due to a neoplastic fever from extensive malignancy or lymphoma.

It is a side effect of many drugs (e.g. opioids, antidepressants, steroids, alcohol, tamoxifen, goserelin, ciprofloxacin, esomeprazole) and can also be a sign of intense pain or overwhelming anxiety/fear (then mainly confined to axillae, palms, and soles).

A Consider reversible causes

- Address underlying cause if identifiable and possible such as infection or treatment of underlying malignancy (e.g. hormone therapy or immunotherapy)

B Non-drug measures

- Environment – fans, adjust ambient temperature,
- Avoid heavy bedclothes, wear cotton clothes or wicking material rather than synthetic or mixed fibres, use moisture absorbing mattress covers
- Frequent baths or sponging
- Consider Acupuncture
- Some people benefit from preparations of sage

C Drug therapies

| Order | Treatment |
|--|--|
| 1st Line: | |
| Endocrine Cause specific (e.g. breast or prostate cancer) | <ul style="list-style-type: none"> • Sertraline 25-50mg mane PO • If symptoms persist, switch to <ul style="list-style-type: none"> ◦ Venlafaxine. Start at 37.5mg mane PO, Increasing to bd after 1 week if necessary <i>or</i> ◦ Gabapentin dose as for neuropathic pain (<i>p19</i>) |
| Opioid-induced | <ul style="list-style-type: none"> • Opioid switch (e.g. from morphine to oxycodone) • If symptoms persist, <i>add</i> propantheline 15mg tds PO |
| Paraneoplastic | <ul style="list-style-type: none"> • Paracetamol <i>and/or</i> ibuprofen PO • If symptoms persist, <i>switch</i> to dexamethasone 4mg od mane PO <i>plus</i> omeprazole 20mg mane PO. Reduce to the minimum effective dose (<i>p69</i>) |
| 2nd line | <ul style="list-style-type: none"> • Ranitidine 150mg bd PO |
| 3rd line | <ul style="list-style-type: none"> • Gabapentin – doses as for neuropathic pain (<i>p19</i>) • Antimuscarinic (e.g. propantheline 15mg tds PO) |
| 4th line | <ul style="list-style-type: none"> • Specialist referral*: options include clonidine* |

ITCH

Itch can have a profound impact on quality of life with symptoms including disturbed sleep. The cause can be **histamine mediated** (allergies, acute urticaria, insect bites) but is commonly **histamine unrelated**. Risk factors include:

- Hepatic disease e.g. biliary obstruction
- Chronic renal failure
- Systemic opioid therapy
- Lymphoma
- Paraneoplastic phenomenon
- Immunotherapy
- Parasites, e.g. scabies, fleas
- Iron deficiency
- Skin diseases, e.g. eczema, psoriasis
- Graft versus host disease after allogenic bone marrow transplant

A Consider reversible causes

- For example: active treatment of underlying cancer/ lymphoma with chemotherapy, steroids and radiotherapy will alleviate paraneoplastic itch
- Avoid provocative influences e.g. rough clothing, vasodilators, overheating
- Some emollients contain lanolin which may in itself worsen itching

B Non-drug measures

- Try to break the itch/scratch cycle – clip nails, cotton gloves, paste bandages
- Use distraction measures
- Avoid washing with soap/bubble bath; use a pH balanced soap substitute or emollient bath additives
- Apply emollients topically to combat dryness (**NB**. *Risk of fire if smoking when using paraffin based emollient as it can be absorbed into dressings and clothing*)
- Aqueous cream +/- menthol
- Consider early advice from dermatologist or palliative medicine physician*

C Drug therapies: Direct at the underlying cause where possible

NB: Regular emollients are an important part of treatment regardless of the cause

| Cause | 1 st line options | 2 nd line options | 3 rd line options (specialist use)* |
|---------------------------------|---|--|---|
| Cholestasis ¹ | Alleviate biliary obstruction if possible (eg biliary stent or dexamethasone 8mg od PO) | Sertraline 25mg mane PO increasing to 50mg mane after 7 days if necessary | Rifampicin* Danazol* Opioid antagonists* ² |
| Uraemia | Gabapentin (dose adjusted to degree of renal failure) | Sertraline 25mg mane PO increasing to 50mg mane after 7 days if necessary | Opioid antagonists* ² |
| Opioids | Antihistamine (eg loratadine 10mg mane) | Opioid switch (eg morphine to oxycodone) | Opioid switch to buprenorphine* |
| Advanced Heart Failure | Sertraline 25mg mane PO increasing to 50mg mane after 7 days if necessary | | Gabapentin* Mirtazepine* |
| Other | Check LFTs and U&E Look for scabies Antihistamine if skin rash | Sertraline 25mg mane PO Increasing to 50mg mane after 7 days if necessary | Mirtazepine* |

¹ Colestyramine requires intact enterohepatic circulation to work so is ineffective in complete biliary obstruction

² Use if not taking opioid. Opioid antagonists will reverse opioid pain control

MALIGNANT ULCERS/FUNGATING WOUNDS

These occur when there is tumour infiltration of epithelium and its surrounding blood and lymphatic vessels, which then appear as crater-like wounds or nodular lesions. A central necrotic area may develop which may become infected. Seek specialist advice if problems associated with the ulcer persist or psychological distress is high.

A Consider reversible causes

- Unless treatment of the underlying cause is possible, a fungating wound is not reversible
- Treat secondary infection as this will exacerbate symptoms (pain, bleeding, and malodour)

Assessment is helpful:

- Prioritise the problem which the patient considers to be most important
- Explore meaning of ulcer to individual, impact on relationships, body image, and identity
- Identify location, size, nature of ulcer - these affect choice of dressing and fixation
- Check amount of devitalised tissue in ulcer - affects need for cleansing and debridement
- Condition of surrounding skin - if skin is macerated, protective barrier or film may be needed
- Consider potential for serious complications, haemorrhage, vessel/airway obstruction and plan accordingly

B Non-drug measures

- Utilise the patient's prioritised concerns to determine the goals of care Patients should be enabled to manage dressing changes if this is their wish
- Cleanse the wound only if it is producing excess exudate or has loose necrotic tissue Consider early discussion with Tissue Viability Nurse

C Drug therapies

| | |
|------------------|--|
| Dressings | <ul style="list-style-type: none">• Type of dressing and frequency of change should be determined by agreed goals• Refer to BNF Wound Management Products Appendix 5, local wound care formulary/guidance and Tissue Viability Nurse• If wound visible consider skin coloured dressing |
| Pain | For the wound itself: <ul style="list-style-type: none">• Consider topical morphine or diamorphine 10mg mixed with hydrogel*• Systemic analgesics including neuropathic agents may be required (p6-23)• Consider breakthrough analgesia for dressing changes, (p12) |
| Bleeding | <ul style="list-style-type: none">• Consider alginate dressing• Other options: tranexamic acid (oral, IV or topical), adrenaline 1:1000 topically to wound or in dressing, cautery, radiotherapy, sucralfate paste and embolization |
| Malodour | <ul style="list-style-type: none">• Activated charcoal dressing• Consider topical or systemic metronidazole |
| Itch | <ul style="list-style-type: none">• (p58)• Consider Transcutaneous Nerve Stimulation (TENS) |

LYMPHOEDEMA

The diagnosis needs to be made accurately from the history and examination; and lymphoedema differentiated from other causes of limb swelling such as heart failure, immobility, venous insufficiency and obstruction, limb dependency hypoalbuminaemia, and chronic renal failure,

Causes include:

- Primary congenital or familial lymphoedema
- Secondary obstruction from tumour spread, surgery, or radiotherapy or recurrent streptococcal infections

A Consider reversible causes

Treatment is aimed at improvement and control, as cure is not possible

B Non-drug measures

Management is based on:

- Skin care
- Manual lymphatic drainage (specialist massage)
- Compression
- Exercise

Treatment should be undertaken by a trained practitioner and early referral to the local lymphoedema service will give the best chance of maximum improvement. Clear explanation of the lymphatic system, reasons for the condition and the means of treatment will encourage compliance. Monitor progress by regular measurement and assessing skin condition.

Effective skin care

- Regular emollients and careful attention to hygiene
- Optimise skin condition
- Minimise the risk of infection.
- Follow the local emollient formulary

Manual Lymphatic drainage

- Regular simple light superficial massage may help; should be taught by a trained practitioner

Compression (Should only be applied by trained practitioner)

- Compression bandaging is generally used for a limited period to reduce limb volume, particularly if the limb is misshapen, or fibrosis or lymphorrhoea are present
- Hosiery is then worn to maintain the reduction in volume. It is removed at night and during acute cellulitis. It is only initiated by trained practitioners: ill fitting hosiery can be painful and/or cause ischaemic damage

Exercises

- Breathing
- Movement around affected limb
- Promotes muscle pump

C Drug therapies

- Corticosteroids may help to reduce lymphadenopathy but may increase fluid retention. Give dexamethasone 8mg od PO with omeprazole 20mg od PO for one week. If effective reduce in 2mg increments per week to the minimum effective dose. If ineffective taper to zero (*p69*)
- “Pure” lymphoedema does not respond to diuretics however furosemide may help if there is concurrent fluid retention) e.g. heart failure or hypoalbuminaemia. If using, stop after one week if no improvement
- Consider spironolactone instead if hyperaldosteronism is suspected (e.g. liver cirrhosis or hepatic metastases)

Management of lymphoedema-associated of cellulitis

- Lymphoedema hampers leukocyte surveillance resulting in localized immunocompromise
- Use antibiotics as per local cellulitis guidelines but treat for longer (e.g. 14 days from the time of clinical response)
- If systemically unwell, consider the need for admission
- If first line antibiotics ineffective at 48 hours, substitute second line oral treatment
- Avoid compression garments and advise bed rest and limb elevation during the acute attack
- Provide adequate analgesia
- Some areas prescribe prophylactic or “in case” antibiotics for re current cellulitis. Seek microbiological advice or follow local antibiotic guidance

MISCELLANEOUS

ANEMIA/BLEEDING/THROMBOEMBOLISM/HYPERCALCAEMIA/ STEROID USE/DIABETES MANAGEMENT/END STAGE LONG-TERM CONDITIONS

ANAEMIA

Diagnosis is based on symptoms e.g. tiredness, weakness, breathlessness on exertion. Alongside blood counts – haemoglobin, RBC indices, platelets and WBC; consider iron studies, B12 and folate. Ferritin is unreliable in advanced malignant disease.

Causes/Risk factors

Increased rate of RBC loss:

- Bleeding
 - acute (anaemia may not be revealed immediately)
 - chronic (microcytic, reticulocytes, thrombocytosis)
- Haemolysis
 - primary, secondary e.g. autoimmune process, drugs, infection (macrocytosis, reticulocytes, raised bilirubin)

Reduced RBC production:

- Chronic disease and renal disease (normochromic, normocytic or microcytic)
- Bone marrow infiltration – leukaemia, lymphoma, carcinoma (especially carcinomas of prostate or breast)
- Aplastic anaemia – especially drugs (including NSAIDs, antibiotics, antiepileptics, antipsychotics, hypoglycaemics, but many drugs have been implicated)
- Sideroblastic secondary to malignancy
- Infection, debility
- Deficiency of iron (microcytic), B12 or folate (macrocytic), or mixed deficiency
- Often mixed picture e.g. anaemia of chronic disease and iron deficiency (no reliable blood tests)

Management

A Consider reversible causes

Where possible and review medication e.g. anticoagulants, NSAIDs

B Non-drug measures

Manage symptoms and explain to the patient the cause of their symptoms

C Drug therapies (Refer to local guidelines)

- Consider iron (consider IV replacement), B12 or folate if deficient
- Consider blood transfusion
 - Do not transfuse unless a specific symptom benefit is anticipated
 - If the anaemia is chronic, patients may adapt even if Hb <70g/l
 - Consider transfusion if Hb < 70g/l. (<79 if anaemia causing symptomatic heart failure)
 - Use 1 - 2 units maximum per day
 - Transfuse to a target of 70-90g/l
 - Transfusion can cause heart failure in debilitated or elderly patients
 - Reassess one week after transfusion for any symptomatic relief
 - If little relief then transfusion need not be repeated if the haemoglobin falls again
 - Consider other causes and treatments for symptoms

BLEEDING (HAEMORRHAGE)

Causes/Risk Factors

- Direct tumour invasion
- Platelet or coagulation disorders, including disseminated intravascular coagulation, heparin-induced thrombocytopenia
- Infection, which may cause haemoptysis, haematuria, vaginal bleed, fungating wounds
Drugs – anticoagulants, antiplatelet drugs, NSAIDs, SSRI antidepressants
- Peptic ulceration

Management

A Consider reversible causes

- Stop anticoagulants and review medication; consider reversing anticoagulants and discussing with haematology
- Treat any infection which may be exacerbating bleeding

B Non-drug measures

- Consider radiotherapy when bleeding is due to malignancy, especially haemoptysis, haematuria or cutaneous bleeding
- Consider palliative surgical techniques including endoscopic laser or cautery, or radiological embolisation for tumour where feasible and appropriate

C Drug therapies

- Consider replacement of blood, platelets, clotting factors, fluids
- Consider chemotherapy, if appropriate
- Tranexamic acid 500mg -1.5g bd - qds PO (slows clot breakdown); take caution in haematuria as may lead to clot retention
- Etamsylate 500mg qds PO (*if available*). (Enhances platelet adhesion within capillaries; of limited value in thrombocytopaenia)
- Tranexamic acid and etamsylate can be used in combination

Specific treatments

| Site of bleeding | Management options |
|------------------|---|
| Nasal | <ul style="list-style-type: none">• Packing and cautery |
| Oral | <ul style="list-style-type: none">• Tranexamic acid mouthwash 10ml of 5% solution• Sucralfate suspension 2g in 10ml bd PO if available |
| Haemoptysis | <ul style="list-style-type: none">• Tranexamic acid PO, see above• Radiotherapy is often helpful in lung tumours |
| Liver | <ul style="list-style-type: none">• Consider embolization |
| Upper GI | <ul style="list-style-type: none">• Stop NSAIDs• Proton pump inhibitors (e.g. omeprazole 20-40mg daily)• Consider embolization• Consider octreotide* |
| Lower GI | <ul style="list-style-type: none">• Tranexamic acid PO or 100mls of 5% solution as enema od or bd |
| Skin | <ul style="list-style-type: none">• Kaltostat dressing• Topical adrenaline 1 in 1000 to soak dressing• Topical tranexamic acid 500mg in 5ml water applied on gauze dressings. Apply pressure for 10 mins then leave in situ covered with a dressing• Sucralfate suspension 2g in 10ml bd PO (if available) |
| Haematuria | <ul style="list-style-type: none">• Consider tranexamic acid PO or etamsylate (if available), see above |

Severe terminal haemorrhage

Severe, catastrophic haemorrhage is a rare event in cancer illness. It is extremely distressing for patients, their families, and health professionals when it occurs

Those at risk include:

- Tumour eroding through an artery e.g. head and neck, lung, upper gastrointestinal and pelvis
- Where the disease presented with bleeding eg. haemoptysis in lung cancer
- Smaller warning bleeds. These may or may not herald a larger bleed
- Co-existing disease increasing risk eg. gastrointestinal bleeding, oesophageal varices liver failure
- Severe thrombocytopaenia in haematological malignancy
- The presence of clotting abnormalities e.g in liver failure
- Local infection at the tumour site
- On potentiating drugs eg. heparin, enoxaparin

Management

In advance:

- There is a dilemma between informing patients and relatives and risking anxiety and not informing them and leaving them unprepared
- Dark towels or sheets will help mask the blood. (It looks less dramatic against dark colours such as green or navy blue). Advise that they are readily at hand
- Give carers a supply of buccal midazolam 10mg as part of an advance care plan and instruct them in its use. This will allow them to help patient distress should death not be immediate
- Ensure anticipatory 'just in case' medication is in place (*p86*)
- Ensure a decision not to resuscitate is in place

When it happens:

- Stay with the patient
- Remain focused on the support of the patient
- Verbal reassurance and physical touch help
- Administer midazolam 5-10mg IV or IM for the relief of psychological distress
- If needed administer an opioid (morphine sulfate, oxycodone or diamorphine) IV or IM for pain (*p6-14*)
- If the haemorrhage is slow and not immediately terminal use suction as appropriate
- If the haemorrhage is rapid and catastrophic there may not be time to administer medication
- Relatives and staff who witness the event will need support

VENOUS THROMBOEMBOLISM

- Some degree of venous thromboembolic disease (VTE) is extremely common in patients with cancer and to a lesser extent with other advanced disease. (Occurs in 20% of patients with cancer through their lifetime)
- Suspect pulmonary emboli in patients with episodic and otherwise unexplained breathlessness or confusion. Measurement of oxygen saturation with a finger probe may be helpful
- Serological tests such as D-Dimers are unhelpful in advanced cancer
- Doppler scans will reveal deep vein thrombosis (DVT) in large veins
- CT pulmonary angiography can detect even small pulmonary emboli. (Some of which may be incidental and do not need treatment)

Causes/Risk factors

- Malignant disease
- Pelvic disease
- Recent chemotherapy or surgery
- Immobility from hip fracture/spinal cord compression
- Cardiac failure
- Respiratory failure
- Central venous catheter
- Thrombophilia
- Age >65yrs
- Drugs e.g. megestrol acetate, Hormone Replacement Therapy

Management

Thromboprophylaxis

- **Refer to local protocols.**
- Assess whether patient is at risk of VTE
- Take into account any risk of bleeding and expected prognosis
- Discuss with the patient whether they wish to have active prophylaxis with anti-embolism stockings and low molecular weight heparin (LMWH) as appropriate, balancing risks and benefits to optimise quality of life
- The best evidence in favour of thromboprophylaxis is in potentially reversible co-existing acute conditions e.g. patient admitted to hospital for intravenous antibiotics for community acquired pneumonia
- If the patient is in the last few weeks of life then thromboprophylaxis is often not appropriate and is not routine. In the last few days of life it is not appropriate

Treatment of DVT and /or PE

- **Refer to local guidelines.**
- If there is symptomatic or objective evidence of VTE, treatment dose LMWH is more effective in VTE associated with malignancy and less likely to cause less bleeding than warfarin and DOACs but requires daily injections
- LMWH followed by warfarin is cheaper but requires more frequent blood tests. INR may be very difficult to keep stable in those with advanced disease and variable nutritional intake

Direct acting oral anticoagulants (DOACs – eg Rivaroxaban, apixaban, dabigatran)

- Have fewer side effects, reduced bleeding risk compared to warfarin and have no need for INR measurement. Not yet clear whether they are as effective at treating cancer related DVT/PE as LWMH. They are unsuitable in renal failure
- Regularly re-assess the patient to ensure that the current management strategy is appropriate to the stage of their illness and their wishes

HYPERCALCAEMIA OF MALIGNANCY (HCM)

- HCM is the commonest paraneoplastic syndrome
- Most commonly due to ectopic production of parathyroid hormone related peptides [PTHrP] and can occur in the absence of bone metastases
- It occurs in 10% of solid cancers (e.g. breast, lung, kidney, bladder, head and neck etc) and 30% of those with myeloma
- It is a poor prognostic sign (median survival 3-4 months)
- There is a high risk of recurrence following treatment (2-4 weeks) and its level requires monitoring
- Resistant hypercalcaemia is usually an indication of entering the terminal phase and the aims of treatment should be reviewed

Diagnosis

- Corrected serum calcium > 2.7 mmol/l
- Symptoms usually only become troublesome above 2.9 mmol/l
- Those with rapid rates of rise in levels are generally more symptomatic
- Those with slow rates of rise in levels may tolerate higher levels with fewer symptoms
- Levels > 4 mmol/l may be fatal
- Any combination of the following symptoms can occur: nausea, loss of appetite, thirst, polyuria, confusion, fatigue, emotional disturbances, constipation and abdominal pain

Causes/Risk factors

- PTHrP secreting tumours, e.g. carcinoma of lung
- Bone metastases
- Dehydration
- Renal impairment
- Tamoxifen flare

Management

The decision whether to treat HCM, or not, should be guided by their current clinical state, their performance status before the episode, the extent of disease and their prognosis, and the prospect for disease directed therapies.

A Consider reversible causes

- E.g. stop thiazide diuretics, vitamin D/calcium supplements

B Non-drug measures

- Explanation and psychological support for patient and family

C Drug therapies

- Relieve associated symptoms
 - Nausea and vomiting with haloperidol or levomepromazine (*p30*)
 - Relieve thirst
 - Manage constipation (*p40*)
- Decide whether **specific treatment** is appropriate
 - If calcium <3.0mmol/l correct dehydration using saline IV may be appropriate. Remember in malignancy the cause of the hypercalcaemia is not treated so the benefit may be temporary.
 - If serum calcium >3.0mmol/l, or >2.8mmol/l and still symptomatic after IV rehydration, use IV bisphosphonates.

Drugs for the acute management of HCM

| Drug | Dose | Onset and Duration of action | Comment |
|---|--|--|--|
| Zoledronic acid | 4mg in 100ml saline Over 15 mins IV | Onset 24-48 hours Duration 30 days | More potent/effective than pamidronate Adjust dose in renal impairment |
| Pamidronate | 90mg in 500ml saline Over 2 - 4 hours IV | Onset 24 hours Duration 7-14 days | More effective than BNF recommended doses Adjust dose in renal impairment |
| Ibandronate* | only bisphosphonate licensed for use if eGFR is <30ml/min Please use under specialist direction | | |
| Denosumab* <i>A monoclonal antibody and not a bisphosphonate</i> | | Onset 9 days (median) Duration 100 days | An option for refractory HCM (unlicensed indication) |

o Notes

- Bisphosphonates can take 72hrs to take effect so avoid rechecking calcium before day 4
- If return to normocalcaemia, plan to recheck three weeks after treatment
- If serum calcium still raised after 7 days, IV bisphosphonate can be repeated
- If serum calcium still raised after second dose of bisphosphonate consider denosumab*
- Hypocalcaemia may occur in some treated with either bisphosphonates or denosumab and can require calcium replacement therapy

D. Further management

- Unless disease directed therapies are available which reduce the drive for HCM it will recur
- Explore patient wishes regarding future treatment, consider ceilings of treatment and document advance care plans (*e.g. Future Planning Template*) as a further episode within weeks is to be expected unless disease directed therapies can reduce the drive for hypercalcaemia
- Bisphosphonates and denosumab and will fail to sustain a response at some point.

NB Oral bisphosphonates have no place in the acute treatment of HCM. They may be used to maintain normocalcaemia and as prophylaxis in myeloma and breast carcinoma.

Denosumab* is used by oncologists to reduce skeletal related events (e.g. fracture and spinal cord compression), and treatment related osteoporosis, and can be used to maintain normocalcaemia in breast and prostate cancer and some solid tumours. It can be used in resistant or recurrent HCM where repeated treatment with bisphosphonates fails to normalise the serum calcium. It may be useful in patients with renal impairment not able to be treated with bisphosphonates.

STEROID USE

Corticosteroids are frequently prescribed in palliative care with good effect but there is a lack of evidence to support their effectiveness and to guide dosage. It is important to document the starting date and dose clearly with the indication for use, then review regularly.

General points

- Dexamethasone is the preferred drug
- Discuss potential benefits and side effects with patient
- Prescribe as a single, or two, morning doses to avoid sleep disturbance
- Give a 5 - 7 day trial as assess effect
 - if there is no benefit - stop
 - If benefit achieved - reduce to lowest effective dose and then review regularly
- Stop if ineffective or when benefit lost (see below)
- Check blood sugars weekly if on 8mg dexamethasone or more
- Avoid co-administration with a NSAID, if feasible: increased risk of GI side effects
- There is an increased risk of bleeding with concurrent use of SSRI and NSAID - so patients should be prescribed PPI for gastric protection (eg omeprazole 20mg od PO)
- Dose needs increasing (up to double) when used together with hepatic enzyme inducers e.g. phenytoin or carbamazepine which reduce its effectiveness through more rapid metabolism

Indications

- Always consider alternatives to steroids
- The initial dose of dexamethasone varies for different indications:
 - Anorexia/cachexia (p38 & 39)
 - Intestinal Obstruction (p34)
 - Symptomatic brain metastases
 - Malignant spinal cord compression (p49)

Stopping steroids

- Can withdraw immediately if less than 3 weeks treatment and less than 4 mg/day dexamethasone or 30mg/day prednisolone
- Otherwise tail off by 2mg every 5-7 days until 2mg od, then by 0.5mg every 5-7 days (betamethasone 0.5mg tabs are a more cost-effective alternative)
- After cranial irradiation start reducing 2 weeks after completion of treatment e.g. Dexamethasone 16 - 12 - 8 - 6 - 4 - 2mg at intervals of 3 days; if symptoms recur, return to previous effective dose

Common problems

- Usually related to higher or longer-term doses but some patients can be particularly sensitive and develop problems within weeks/at lower doses)
- Early: oral thrush, hyperglycaemia, heartburn, sleep disturbance, mania
- Late: proximal myopathy, skin atrophy, bruising, depression, face & body shape changes
- Change in mood is common, in addition to depression; mania, delirium and psychosis can occur

Steroid equivalents (approximate)

| | | | |
|----------------------|----------------------|----------------------|------------------------|
| Dexamethasone 2mg | Betamethasone 2mg | Prednisolone 15mg | Hydrocortisone 50mg |
|----------------------|----------------------|----------------------|------------------------|

DIABETES MELLITUS

Aims (in last months of life)

- To be **Asymptomatic**, preferably with blood sugars (BS) between **6-15 mmol/l**
- Avoid diabetes related emergencies:
 - Hypoglycaemia
 - Symptomatic hyperglycaemia
 - Diabetic ketoacidosis
 - Hyperosmolar hyperglycaemic state (HHS)
- Reduce burdens of blood glucose monitoring; simplify therapy; relax dietary restrictions
- Avoid foot complications, pressure damage, poor wound healing, sepsis and symptomatic dehydration in frail immobile patients
- Respect for patient and carer preferences and awareness of potential anxieties for those who have been self-managing their diabetes for many years and who are used to trying to control their blood sugars tightly
- Discuss changes in goals and therapy openly
- Simplify insulin regimen e.g. moving to once daily insulin such as Glargine (Lantus)

Management (in the last weeks of life,)

Refer to End of Life Diabetes Care Clinical Care Recommendations 2018, Diabetes UK (free, online).

Refer also to your local guidelines

| Diabetes | Management |
|--|---|
| Type 1 with stable control | <ul style="list-style-type: none"> • Continue usual insulin regimen with BS monitoring. • Counsel about less strict BS targets, awareness of the effect of reduced oral intake, and hypos |
| Type 2 Diet controlled | <ul style="list-style-type: none"> • Monitor daily pre-supper |
| Type 2 Tablet controlled | <ul style="list-style-type: none"> • Stop oral therapy and monitor capillary glucose twice daily for 24 hours. • BS raised manage as follows: |
| Step 1. Recurrent daily BS >15 2. Recurrent daily BS remains >15 3a Recurrent daily BS remains >15 3b Recurrent daily BS fall to <6 | <ul style="list-style-type: none"> ◦ Consider oral non-insulin therapy (see notes below) ◦ Stop oral therapy ◦ Start Insulin Lantus 8-12 units mane SC and monitor pre-supper ◦ Titrate insulin Lantus by 4 units each day ◦ Halve the insulin Lantus dose |

| Diabetes | Management |
|-------------------------------------|---|
| If on, or starting, steroids | <ul style="list-style-type: none"> • Give once daily dose in the morning • Test BS 18:00 (pre-meal) |
| If BS > 15 | Start gliclazide 40mg od and titrate in 40mg increments up to 240mg od. |
| If BS still >15 | <p>On maximum dose of gliclazide with no day or night hypoglycaemic symptoms:</p> <ul style="list-style-type: none"> • add in evening dose gliclazide (40mg and increase up to 80mg) <i>or</i> • start morning intermediate acting insulin instead (e.g. Insulatard, Humulin I or Insuman Basal 10 units at 08.00) <p>Titrate dose to achieve BS 6-15 before evening meal</p> |
| If BS still >15 | Increase insulin by 4 units increments and review daily until stable |

Notes

- BS is measurement of choice if appropriate as urine dip is:
 - Unreliable and only useful if negative
 - Ketones induced by starvation/weight loss
 - Positive likely for capillary glucose >14 mmol/l, possibly lower in sepsis/illness
- Consider the potential for:
 - Deterioration of renal and liver function. Check if drug doses need to be reduced e.g. metformin, gliclazide, some DPP4 inhibitors ('gliptins) and some SGLT-2 inhibitors, and gliclazide
 - Reduced oral intake as appetite reduces
 - Sepsis
 - Weight loss due to cachexia improving insulin resistance
 - Medication side effects contributing to symptoms (e.g. abdominal pain with GLP-1 analogues)
 - Stopping pioglitazone, Gliptin inhibitors, GLP-1 agonists and SGLT-2 inhibitors in last weeks to months of life
- Avoid
 - bd insulin mixtures (risk of hypoglycaemia)
 - qds regimens (multiple tests and injections)
 - bd steroids (prolonged hyperglycaemia)
 - Bolus/prn Actrapid (poor control)
 - Metformin (GI side effects, large pill, works by reducing energy absorption)
 - Sulphonylureas (risk of hypoglycaemia, and long duration of action in organ failure)
 - Glitazones

Withdrawal of treatment In the last days of life

Type 1 diabetes mellitus

- In the last few days of life, can allow BS >15 if asymptomatic
- Presumption in favour of continuing some background insulin (long acting preferred; stop short acting, especially if not eating)
- The decision to stop insulin completely should generally be taken only after discussion with the patient (if they still have capacity) and family
- It is appropriate to stop insulin injections completely when the patient is unconscious as part of the dying process and when all other life-prolonging treatments have been stopped
- If it is decided that insulin should be continued, a simple regimen can be used, e.g. once daily morning insulin Glargine (Lantus) at reduced dose (75% of usual dose) with the minimum of routine monitoring, e.g. once daily at 18.00. Reduce further if BS <8mmols/l, increase if BS > 20mmols/l

Type 2 diabetes mellitus

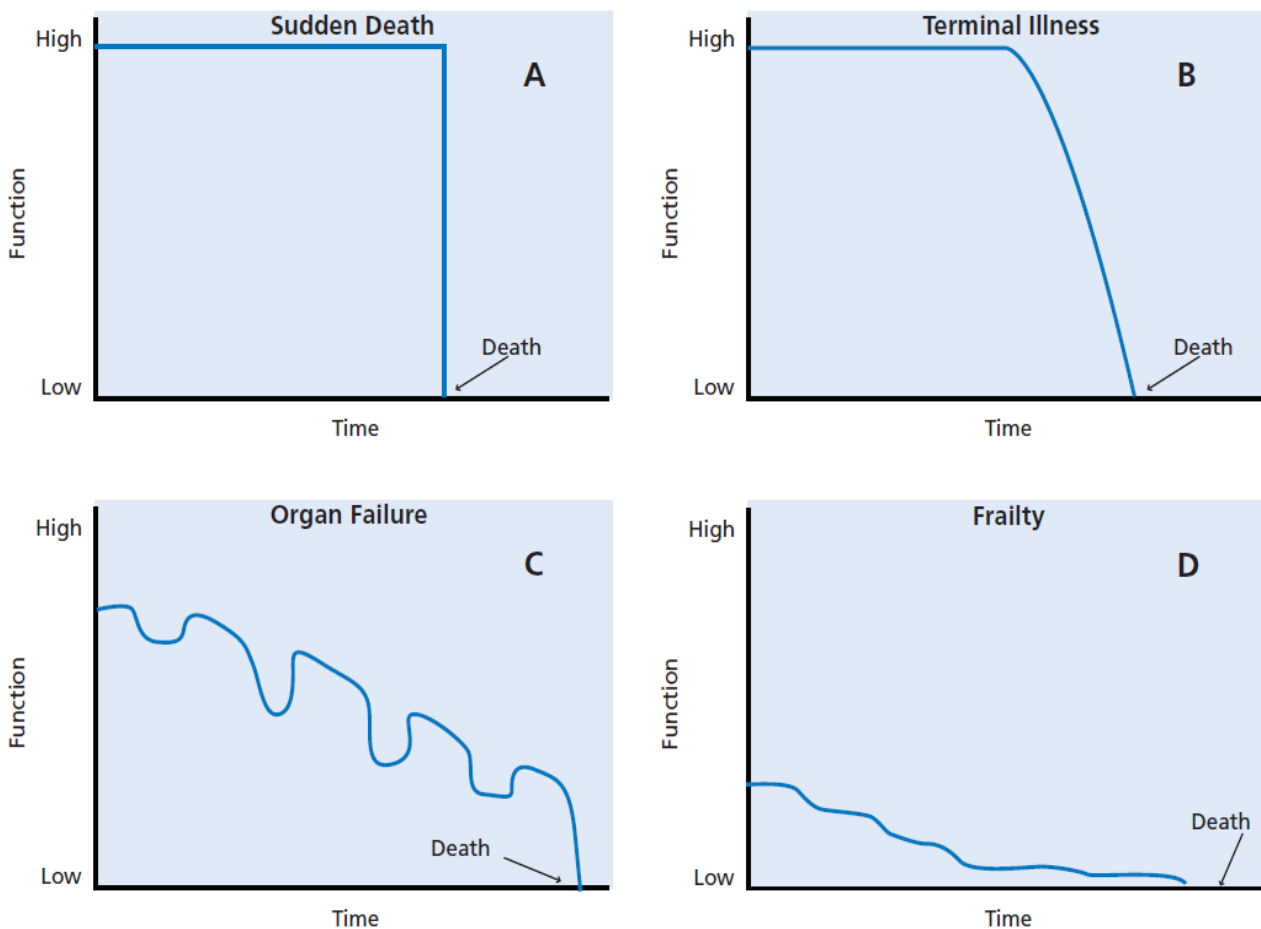
- Stop oral hypoglycaemics, glucagon-like peptide-1 (GLP-1) receptor agonist injections, and BS monitoring when the patient becomes unable to swallow
- Consider stopping low-dose insulin (e.g. insulin <15units total daily dose).
- If the patient requires a total daily dose of >15 units of insulin, or a decision is made to continue insulin therapy, manage as for type 1 diabetes (see above)

Hypoglycaemia (BM <4)

- Consider as a cause of any clinical deterioration
- Treat with sugar PO or PEG, e.g. 200ml fruit juice, 5 . glucotabs etc
- Consider glucose IV or glucagon IM if unconscious (glucagon may not be effective in liver disease)
- Recheck BS after 15 mins to ensure improving.
- Once BS >4 and patient can swallow give a starchy snack e.g. a banana
- Review usual diabetes treatment plan.

END STAGE IN LONG-TERM CONDITIONS

General principles – four broad illness trajectories



1. **Prognostication** in trajectories C & D above is particularly challenging; palliative care interventions may need to be stepped up and down. Patients value clear decision-making and sensitive communication. Patients with a probable prognosis of <12 months in an acute hospital admission should be offered a sensitive conversation about their prognosis, initiated by the health professional, and a ceiling of treatment documented. Not all patients will want to know, but most do.

Other prompts to initiate a conversation include:

- diagnosis of a life-limiting condition
- following acute exacerbations
- hospital at home interventions
- rehab interventions, regular care plan reviews,
- deterioration despite optimal treatment
- patient request
- life changing events e.g. bereavement

Indicators of end stage disease may be general (see Looking ahead below), others will be more specific to the condition (see the specific clinical indications for each condition in the following pages).

2. Looking ahead (see also Advance Care Planning (p81))

- Triggers: –
 - “Would you be surprised if this patient was to die in the next year?”
 - Repeated hospital admissions
 - Increasing dependency for activities of daily living
 - Weight loss >10% in 6 months
 - Low/Falling albumin
 - Low/Falling eGFR
 - Multiple comorbidities
 - Advanced age
- Patients (and carers) are often used to living with their long-term condition, and do not perceive themselves as dying from it
 - The illness may have become indistinguishable from their life story.
 - Phased introduction of supportive care or ‘dip in, dip out’ interventions may feel more natural to patients and clinicians
- Discussion with patient (and carers as appropriate)
 - About their understanding of severity of disease and likely prognosis,
 - Preferences for future care and treatment
 - What to do or where to go in a crisis (written care plans for this are helpful)

3. Symptom control, for restoration or maintenance of dignity and quality of life:

- Optimisation of medical management of condition, treatable causes of deterioration, and iatrogenic problems
- Palliation of disease-specific symptoms

4. Holistic assessment of patient’s and carers’ needs for physical, psychological, emotional, social, financial and spiritual support

5. Information exchange facilitates care coordination

- Ensure that the information/choices above are communicated to the relevant hospital team, GP, community team and support services and others, as appropriate

6. Rationalization/deprescribing of medication

- Reduce or stop medication where continuing benefit is doubtful

7. Reduction of healthcare bureaucracy

- Reducing hospital attendances for multiple clinic appointments and tests when multiple specialties involved

8. Triggers for Specialist referral:

- Poorly controlled symptoms or high symptom distress
- Complex needs or problems that require additional help
- Complex Advance Care Planning (p81)
- Care in dying (days) and hospice inpatient care is thought to be appropriate given the patient’s circumstances

NB. Patients with increasing frailty are often more appropriately managed by a specialist frailty team rather than a specialist palliative care team

END STAGE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Specific clinical prognostic indicators:

- On long term oxygen therapy
- Hypoxia whilst on supplemental oxygen
- Episodes of respiratory failure or and on Non-Invasive Ventilation (NIV)
- Multiple hospital admissions
- Right heart failure
- Pericardial effusion
- Cachexia and loss of muscle mass
- FEV1 < 30% predicted
- Dyspnoea MRC grade 4
- Smoking

Specific treatments

| Symptoms | Management |
|--------------------------------|---|
| Breathlessness (p24) | <ul style="list-style-type: none">• Pulmonary rehabilitation programme• Breathing exercises (e.g calming hand, square breathing)• Hand held fan• Low dose opioid e.g. morphine 1-2mg prn PO (Max 30mg morphine PO or equivalent in 24hr)• Benzodiazepines (e.g. SL lorazepam) can be helpful for associated anxiety/panic but their safety profile and efficacy is less certain than low dose opioids for breathlessness• Home nebulisers• Assess for supplementary oxygen• Occupational therapy support |
| Pain (p6-23) | <ul style="list-style-type: none">• Often due to steroid side effects (e.g. osteoporotic fractures)• Risk of bronchoconstriction with NSAIDs in aspirin sensitive asthma patients (20%) |
| Low mood and Anxiety | <ul style="list-style-type: none">• Psychological, social and Occupational Therapy support• Antidepressants if prognosis allows• Lorazepam 0-5-5mg SL for panic |
| Nausea (p30) | <ul style="list-style-type: none">• Standard measures |
| Constipation (p40) | <ul style="list-style-type: none">• Standard measures |
| Muscle deconditioning | <ul style="list-style-type: none">• Physiotherapy and Occupational Therapy assessment and treatment |

END STAGE HEART FAILURE

Specific clinical prognostic indicators:

- Heart failure NYHA Stage III or IV
- Ejection fraction $\leq 20\%$
- Albumin $<25\text{g/L}$
- Failure to respond to diuretics
- Increasing frequency of hospital admissions
- Worsening co-morbidities
- Lack of further treatment options
- Syncope
- Sustained hypotension

Specific treatments

- ***Optimal medical management doubles prognosis***

| Symptom | Management |
|--------------------------------|---|
| Breathlessness (p24) | <ul style="list-style-type: none">• Optimisation of medical treatment, especially diuretics• Low dose opioid (e.g. morphine 1-2mg PO) (p24)• Benzodiazepine with slow titration limited to those with a lot of anxiety. Beware much higher risk of delirium and assume renal impairment in older adults, even if blood tests• Good evidence for survival AND quality of life benefit in HFREF (heart failure with reduced ejection fraction) for ACEi, ARB2i, valsartan, ivabradine (stop in AF, or HR >70), digoxin, and spironolactone so higher threshold for discontinuation.• Beta agonist bronchodilators not advisable in angina or aortic stenosis• Consider palliative short-burst oxygen to aid recovery from exertion• Profiling bed for paroxysmal nocturnal dyspnoea• Have a plan in place for crisis and for admission avoidance |
| Oedema | <ul style="list-style-type: none">• Balance dose of diuretics against symptomatic hypotension and dehydration• Furosemide SC may be appropriate in some<ul style="list-style-type: none">◦ Furosemide 40mg PO is equivalent to bumetanide 1mg PO◦ Usually only one loop diuretic is titrated to effect◦ Useful synergistic effect from adding in metolazone 2.5mg twice weekly PO or, bendroflumethiazide 5-10mg od PO if loop diuretic resistant• High threshold for discontinuation of diuretics• Good skin care, cautious hosiery compression of legs, scrotal support |
| Ascites (p44) | <ul style="list-style-type: none">• Treat symptoms not blood tests• Renal function not as useful as how patient feels in guiding diuretic dose; most useful measure for monitoring is weight or circumference of most oedematous area e.g. leg/abdomen• Consider paracentesis for symptoms• Spironolactone titration likely to be more helpful than loop diuretic in hepatic congestion |
| Nausea (p30) | <ul style="list-style-type: none">• Avoid cyclizine as may exacerbate heart failure |

| Symptom | Management |
|---|---|
| Poor appetite (p38) | <ul style="list-style-type: none"> • May be exacerbated by gastrointestinal oedema • Avoid dexamethasone as appetite stimulant, as may worsen fluid retention • Relax low salt and low fat dietary restrictions |
| Dry Mouth (p36) | <ul style="list-style-type: none"> • Assess total body fluid – may be caused by excessive diuresis • Treat oral candidiasis (thrush) • Humidify oxygen if using • Ice chips • Artificial saliva • Chewing gum |
| Constipation (p40) | <ul style="list-style-type: none"> • Magnesium hydroxide and lactulose have reduced effectiveness • Avoid macrogols and bulking agents due to risk of fluid overload |
| Fatigue (p39) | <ul style="list-style-type: none"> • Deconditioning may compound fatigue caused by heart failure • Consider dose reductions of cardiac medicines, e.g. beta blockers • Consider treatment of anaemia with iron infusion • Consider risk of fluid overload with blood transfusion • Exclude hypothyroidism, diabetes mellitus, hyponatraemia • Optimise pacemaker settings |
| Low mood and depression (p91) | <ul style="list-style-type: none"> • Psychological, social and occupational therapy support • Fatigue management interventions • Reduce social isolation • Cognitive change may be subtle – sequencing, planning, attention, working memory, and learning memory impaired early. Language and other memory preserved • Avoid methylphenidate and caution with tricyclic antidepressants as arrhythmogenic • Timing of diuresis to avoid sleep disturbance; consider urinary catheter; night sedation |
| Pain (p6-23) | <ul style="list-style-type: none"> • Avoid NSAIDs and steroids because of fluid retention • Consider frequency of angina before stopping beta blocker or long acting nitrates • Avoid nitrates in aortic stenosis • Low dose tricyclic antidepressant for neuropathic pain • Avoid gout altering medication or diuretics during an acute attack: Consider colchicine or prednisolone for shortest possible course and monitor for fluid retention • If TENS is applied do not site electrodes directly over pacemaker/ICD |
| Care of the dying (p81) | <ul style="list-style-type: none"> • Review oral medication. • Consider use of furosemide CSCI for symptom control although the evidence for this is limited • Hyoscine butylbromide or glycopyrronium CSCI can be used to dry secretions • Contact cardiology department or refer to local policy to arrange switching off implantable cardiac defibrillator (ICD) after discussion with patient or family as appropriate. • Place a strong magnet over the ICD to deactivate immediately if needed |

END STAGE KIDNEY FAILURE

Specific clinical prognostic indicators:

- eGFR <15
- Decision not to commence dialysis
- Difficult physical and psychological symptoms despite optimal tolerated replacement therapy (e.g nausea and vomiting, anorexia, pruritis, intractable fluid overload)
- Contemplating withdrawal from dialysis (e.g due to reduced functional status)
- Deterioration from concurrent illness e.g cancer

Specific treatments

† *need dose reduction (p23)*

| Symptom | Management |
|-------------------------------------|---|
| Pain (often bone) (p6-23) | <ul style="list-style-type: none"> • Paracetamol • Avoid NSAIDs unless last days of life and assessed risk/ benefit • Consider strong opioids <ul style="list-style-type: none"> ◦ e.g. prn oxycodone 2.5mg SC or alfentanil 100mcg SC (very short half-life) ◦ Regular background analgesia: fentanyl / buprenorphine TD patch or fentanyl* or alfentanil* CSCI (will mix with most drugs) |
| Neuropathic pain (p19) | <ul style="list-style-type: none"> • Amitriptyline • Gabapentin† • Pregabalin† |
| Nausea (p30) | <ul style="list-style-type: none"> • Metoclopramide • Haloperidol • Levomepromazine† |
| Hiccups (p51) | <ul style="list-style-type: none"> • Metoclopramide |
| Itch (p58) | <ul style="list-style-type: none"> • Gabapentin† • Sertraline • Opioid antagonists |
| Restless legs | <ul style="list-style-type: none"> • Gabapentin† • Clonazepam 0.5mg od PO • Pramipexole |
| Care of the Dying (p81) | <ul style="list-style-type: none"> • Caution with opioids such as morphine, oxycodone and diamorphine which will accumulate and may cause toxicity • Alfentanil or fentanyl safer than morphine (p23) • Be prepared for significant restlessness (p49) |

Little difference between dialysed and non-dialysed patients in dosing, although gabapentin often given only on dialysis day.

END STAGE PROGRESSIVE NEUROLOGICAL DISEASE

Includes conditions such as Motor Neurone Disease, Parkinson's Disease, Progressive Supranuclear Palsy, Multiple System Atrophy, Multiple Sclerosis, and others. Many of the factors are applicable to decline from Dementia and frailty

Specific clinical prognostic indicators:

General across the conditions

- Marked decline in physical state and performance status (e.g. Barthel/ ECOG/ Karnofsky)
- Increasing frailty with increasing dependence: Includes reducing mobility, falls, incontinence, increasing risk of pressure damage
- Failing nutritional status despite optimal appropriate support which may include PEG or parenteral feeding
- Increasingly complex symptoms and medical complications
- Increasing cognitive Impairment
- Progressive dysphagia with risk of aspiration pneumonia
- Increasing breathlessness or respiratory failure
- Increasing difficulty in communication: speech or otherwise despite optimal support

Plus

- **Motor Neurone Disease**
 - Respiratory deterioration despite maximal appropriate respiratory support: including withdrawal of such support*
- **Parkinson's Disease**
 - Symptoms less well controlled with increasing 'off' periods
 - Drug treatment less effective and/or increasingly complex
 - Psychiatric signs e.g. depression, anxiety, hallucinations, psychosis

Specific treatments

| Symptoms | Management |
|---|---|
| Breathlessness (p24) | <ul style="list-style-type: none">• Assess for supplementary oxygen• Cough assist and non-invasive ventilation (particularly in MND)• Physiotherapy and Occupational Therapy support |
| Salivary drooling (p37) | <ul style="list-style-type: none">• Amitriptyline• 1% Atropine eye drops• Hyoscine butylbromide, glycopyrronium, Hyoscine hydrobromide• Botox injections of salivary glands*• Radiotherapy* |
| Pain | <ul style="list-style-type: none">• See p21 |
| Low mood and Anxiety | <ul style="list-style-type: none">• Psychological, social and Occupational Therapy support• Antidepressants if prognosis allows• Lorazepam 0-5-1mg SL for panic |
| Constipation | <ul style="list-style-type: none">• See p40 |
| Nausea | <ul style="list-style-type: none">• See p30-33 |
| Muscle deconditioning and weakness | <ul style="list-style-type: none">• Physiotherapy and Occupational Therapy assessment and treatment |

END STAGE LIVER FAILURE

Specific clinical prognostic indicators:

- Advanced cirrhosis
- Hepatocellular carcinoma
- Rapidly reaccumulating or intractable (diuretic resistant) ascites
- Hepatorenal failure
- Severe portal hypertension, particularly recurrent variceal bleeding
- Presence of hepatic encephalopathy
- Bacterial peritonitis
- Severely reduced hepatic synthetic function: hypoalbuminaemia (<25g/L), prolonged INR and APPT
- Cachexia and loss of muscle mass
- Hyponatraemia

Specific treatments

| Symptoms | Management |
|---|--|
| Pain (p22) | <ul style="list-style-type: none"> • Paracetamol limited to 2-3g in 24hr • Opioids with caution • Avoid NSAIDs: risk of fluid retention, GI erosions and bleeding, renal injury |
| Fatigue/ Muscle deconditioning | <ul style="list-style-type: none"> • Physiotherapy and Occupation Therapy assessment and treatment |
| Ascites (p44) | <ul style="list-style-type: none"> • Dietary sodium restriction • Spironolactone up to 400mg daily • Furosemide up to 160mg daily • Therapeutic paracentesis if well enough to tolerate it |
| Nausea (p30) | <ul style="list-style-type: none"> • Drugs acting on CTZ e.g. haloperidol |
| Peripheral oedema | <ul style="list-style-type: none"> • Treatment of ascites |
| Itch (p58) | <ul style="list-style-type: none"> • Non-drug measures • Topical emollients • Sertraline, ondansetron and opioid antagonists |
| Muscle cramps | <ul style="list-style-type: none"> • Correct biochemical abnormalities and renal injury • Quinine sulfate |
| Hepatic encephalopathy | <ul style="list-style-type: none"> • Avoid dehydration, constipation (p40) and electrolyte abnormalities • Beware sedatives or other drugs as a cause • Treat sepsis if appropriate • Appropriate nutritional support • Lactulose: Start with 30-50mls tds and aim for 2-3 soft bowel movements daily |
| Low mood and Anxiety | <ul style="list-style-type: none"> • Psychological, social and Occupational Therapy support |
| Variceal haemorrhage (p64) | <ul style="list-style-type: none"> • May be a terminal event • Recommend dark linen and protective equipment • benzodiazepines IM/SC/PR and opioids IM/SC can help manage distress |

END OF LIFE:

ADVANCE CARE PLANNING/DNACPR/LAST DAYS

FUTURE AND ADVANCE CARE PLANNING

Future care planning is the process of timely, voluntary discussions between an individual and their healthcare professionals to establish future preferences for care. Such proactive discussions can help the patient and family prepare for death and may involve **Advance Care Planning (ACP)** in case the patient should later lose capacity to make such decisions. This allows the patient to maintain some influence or control over their future care.

Discussion about the future preferably takes place before a deterioration in the patient's condition, while they are well enough to take part in the discussion and express their preferences.

Triggers or prompts for ACP include:

- The Surprise Question:
'Would you be surprised if this patient was to die in the next year?'
- AMBER care bundle criteria. *'Is the patient:*
 - *Clinically unstable or deteriorating with little reversibility? and*
 - *At risk of dying in the next one to two months?'*
- Clinical prompts e.g. repeated hospital admissions, shift in treatment focus, loss of function
- Community care needs assessment
- Care home admission
- Enquiry by the patient

Before initiating an ACP discussion, the healthcare professional must consider whether ACP is likely to provide overall benefit to the individual at that time. The healthcare professional should have knowledge of likely disease events, treatment options and local services available. It is usually helpful to include family/carers in these discussions (with the patient's permission)

Discussions could include:

- Exploring the patient's and family's insight into the disease
- Future expectations
- Treatment choices
- Organ donation
- Patient's preferences and priorities for care at the end of life (e.g. being pain free, avoiding being a burden): "what is important to you?"
- Patient's preferred place(s) of care when their condition deteriorates – it is often helpful to explore a range of alternatives
- Patient's beliefs and values
- Anything the patient feels is important to them

The healthcare professional needs to exercise skill and sensitivity to:

- Know when and how to instigate ACP
- Avoid pressurising the patient to take part
- Recognise when to stop discussion

Discussion(s) can be aided by introducing the leaflet: *Planning for your Future Care – A Guide* which also covers organ donation, wills and funeral planning.

Advance Care Planning spans a spectrum from open conversations to formal, legally binding documents.

Outcomes include:

- No wish to discuss further at this time
- The patient identifying one or more persons to speak on their behalf to help healthcare professionals make a best interest decision (this is not the same as legally appointing a Lasting Power of Attorney)
- A Statement of Wishes and Preferences (eg using the My Wishes booklet)
- A treatment escalation plan (p83)
- DNACPR decision (p83)
- The patient making an Advance Decision to Refuse Treatment (ADRT)
- The patient appointing a Lasting Power of Attorney (for health and welfare and/or property and financial affairs)

(Information and forms available from The Office of the Public Guardian www.gov.uk)

With the patient's consent, these preferences should be:

- Communicated to all professionals involved in their care
- Documented appropriately e.g. on the electronic database systems (e.g. Future Planning Template), or local alerting systems

All Advance Care Plans should be reviewed every so often to check that they still accord with the patient's preferences, as wishes can change as illness progresses.

TREATMENT ESCALATION PLANS (INCLUDING DNACPR DECISIONS)

A DNACPR (Do Not Attempt Cardiopulmonary Resuscitation) or 'Allow a Natural Death' decision can be part of an advance decision made by the patient.

It is more commonly made:

- When the patient is becoming more unwell, e.g. when setting ceilings of treatment
- As part of the AMBER Care Bundle in hospital patients
- On completion of the ReSPECT form (where it is in use)
- For patients with ICDs, when deactivation is discussed

CPR is very unlikely to be successful in patients in the terminal phase of a life-limiting illness. However, if the patient is not in a terminal phase and there is a realistic chance that CPR will restore cardiac output and breathing, then the possible benefits and potential adverse outcomes should be discussed with the patient and the decision made in partnership with them.

Making a DNACPR decision can:

- Help to promote dignity in the dying phase
- Facilitate a patient staying at home when they are dying
- Allow a family and staff to concentrate on interventions which support the patient's comfort

Decision-making can sometimes be hard because:

- Policy documents do not distinguish between an expected death and unheralded cardio-pulmonary arrest
- The general public have unrealistic expectations of the success rates of CPR attempts
- There is a lack of understanding about how CPR can lead to adverse outcomes, even where the restoration of cardiac output is successful

The following framework is suggested to facilitate decision-making:

- Recognise that open discussion with patients and their family is best practice
- Explanation that the illness is progressing and death will naturally happen; rather than focus discussion on CPR alone

Communication with patients and their families should include:

- Informing them of the reason for the DNACPR decision
- A discussion about what care **will** be given, rather than what will not be done
- Emphasis that a DNACPR decision only relates to CPR and does not involve withholding other treatments
- Emphasis that any decision is based on clinical judgement, not on age or 'worth' of the patient's life
- Explanation that an anticipated death can be dignified and peaceful

When appropriate, negotiate the resuscitative interventions which may be carried out in the event of sudden collapse

Best practice is based on the principles of shared decision making. Deciding not to include the patient is only justified if the degree of distress is expected to be harmful. Information should not be withheld just because it is difficult to convey and/or is upsetting to the patient and family.

NB. Refer to local DNACPR policy/guidelines

Further information is available at www.resus.org.uk

THE LAST FEW DAYS OF LIFE

Principles and key elements

Five national **priorities** have been recognised as essential for the dying patient.

1 Recognise the possibility the person is likely to be dying

It is important to recognise when a patient is dying. As this is not always easy, the patient should be reviewed by a senior clinician in hospital, or GP in the community.

When a patient has an advanced and progressive life-limiting illness and is deteriorating with no (appropriately) reversible cause, dying might be recognised if they are:

- Becoming progressively weak and bedbound
- Drowsy for much of the day
- Having difficulty swallowing tablets
- Losing interest in food and drink
- Losing their attention span or becoming confused

2 Communicate with the person and those important to them

- Explain that predicting dying can be difficult
- Explain that the patient appears to be dying
- Discuss reasons for reviewing clinical interventions, drugs and other treatments including nutrition/hydration with the patient and family/friends
- Ensure effective communication amongst all involved
- Inter-professional communication should be explicit: that the patient is believed to be dying, that death can be expected. This may include permission for qualified nurses to verify death

3 Involve them in decision making about treatment and care

- All decision-making should be carried out in partnership with the patient and their family/friends.
- If available, use a Personalised Care Plan (eg for the last days of life) to guide care and decision-making, as all these decisions should be recorded so that everyone involved knows the focus of care.

NB. One should be familiar with the Personalised Care Plan operating in your area/service

- Remember a person can change their mind.

4 Support the needs of both the patient and those important to them

- Ensure practical and emotional support offered to family and carers
- Support both before and after death
- Check religious, spiritual and cultural needs and meet them where possible

5 'Plan, and Do' with an individual plan of care

Practical Care

- While the patient is able to take sips, offer drinks frequently. A narrow straw will be easier to use than a broad one when the patient is very weak
- Mouth care is essential e.g. clean mouth and tongue with soft brush or sponge, use saliva replacement if patient is conscious and has dry mouth
- Continence management - consider how bowel and bladder care will be managed and whether a urinary catheter is appropriate. Monitor for development of urinary retention
- Skin care – ensure appropriate care of pressure areas and wounds is offered

Maintain Comfort to achieve a pain free and comfortable death

- Adopt a problem-solving approach to symptom control (*p4*)
- Review all drugs and keep only the essentials to maintain comfort. Stop any remaining long-term prophylactic medications e.g. anti-hypertensives, warfarin, statins
- Anticipatory prescribing: Analgesic, Antiemetics, Anxiolytics, Antisecretory
- Assess and review clinical interventions e.g. blood tests, diagnostic imaging and medical treatments e.g. clinically assisted hydration and nutrition
- Anticipate and plan for possible complications e.g. haemorrhage
- Regularly reassess the patient

Identify a person to coordinate and organise care and support and provide information as to whom to contact for information and support, day or night.

Make every possible effort to enable the patient to receive the end of life care they want, including being in the place of their choice, which may have changed over time.

Planning for Death

- To avoid inappropriate resuscitation attempts particularly at home, check that the patient's DNACPR status is known and recorded for all visiting health professionals (*p83*)
- If the diagnosis is mesothelioma, asbestosis or other industrial disease, remember to warn the family that the Coroner's team will be notified after death and it is very likely that a post mortem will be necessary. Other notifiable causes of death are listed on the back of the Medical Certificate of Death
- If a non-medical practitioner is qualified to verify death make this explicit in the community notes indicating that this is an "expected death" and that coroner involvement is not indicated
- Check whether cultural or religious rituals are expected to be adhered to after death
- Provide information and/or contact numbers about procedures immediately after death

ANTICIPATORY PRESCRIBING: GUIDANCE ON MEDICATION FOR SYMPTOM CONTROL

When a patient is dying, swallowing often becomes difficult.

Prescribe medicines essential to maintain comfort by non-oral routes (usually SC):

- 'As needed' or prn
- Regularly if the patient has an ongoing symptom or was taking the drug regularly when they could swallow – using a syringe driver for continuous subcutaneous infusion (CSCI) (p87-91)
- Choice of drug will be guided by the patient's current symptoms and previous drug requirements
- **Please be sure to refer to local guidelines**

Symptoms which commonly develop in the last hours or days of life include:

- Pain
- Agitation
- Respiratory Tract Secretions
- Nausea and Vomiting
- Dyspnoea

It is good practice to prescribe **anticipatory drugs ('just in case')** to help with these symptoms:

- prn on the hospital drug chart *or*
- prn on the community drug chart *and*
- to ensure medication is available in the patient's home

Drugs commonly required: dose recommendations prn and SC

| Symptom | Medication prn SC | Notes |
|--|---|--|
| Pain (p6-23) | Morphine sulfate 1-5mg if opioid naïve Higher dose as appropriate to previous dosing | <ul style="list-style-type: none">• If previously taking oxycodone use that• The dose may need to be adjusted• Caution in renal failure (p23) |
| Restlessness Agitation (p52) | Midazolam 2.5-5mg | <ul style="list-style-type: none">• If frank delirium use an antipsychotic rather than midazolam alone |
| Respiratory tract secretions (p90) | Hyoscine butylbromide 20 mg (max 120mg in 24 hrs) or Glycopyrronium 200-400 mcg (max 1.2mg in 24hr) | <ul style="list-style-type: none">• Another alternative is Hyoscine Hydrobromide 400-600mcg (max 2.4mg/24hrs) although this may cause sedation and confusion |
| Nausea and vomiting (p30) | Haloperidol 0.5-3mg (max 10mg in 24hr) or Levomepromazine 6.25-12.5mg (max 25mg in 24hr) or Cyclizine 25-50mg (max 150mg in 24hr) | <ul style="list-style-type: none">• Continue the patient's regular antiemetic if symptoms are well controlled• Higher doses of haloperidol and levomepromazine may be used as an antipsychotic.• Site irritation and limited compatibility with other drugs may limit use of cyclizine |
| Breathlessness (p24) | Morphine sulfate 1-2.5mg prn | <ul style="list-style-type: none">• Increase as appropriate |

SYRINGE DRIVERS

A syringe driver is a small, portable battery-powered pump. It administers drugs subcutaneously by continuous infusion. It offers an alternative route of drug administration with little impact on patient mobility or independence. By maintaining steady drug plasma levels, a syringe driver may improve symptom control.

Indications

For administering drugs when the oral route is difficult or inappropriate. It is **not** only for patients who are in the final stages of their illness. If the problem resolves, it may be possible to return to the oral route.

Consider setting up a syringe driver if:

- Severe nausea and/or vomiting
- Severe oral tumours, sores or infections
- Dysphagia
- Intestinal obstruction
- Poor absorption of oral drugs (rare)
- Weak, unconscious or sedated patient
- Patient preference

Before setting up the syringe driver, explain to patient and family the reason for using it, how it works and the possibility of infusion site reactions. Provide a patient information leaflet where available.

Setting up the Syringe Driver

NB Also refer to local syringe driver policy and procedure

- Syringe drivers are set up by clinicians with appropriate training in the use of the specific delivery device (e.g. a McKinley T34 device)
- Ensure the battery is good
(*MHRA recommends Duracell MN 1604 for the McKinley T34 device*)
- Use a Luerlock syringe
- Prime the line
- Label the syringe with the patient's name, drug(s) and dose(s), diluent and date and time started
- Site syringe driver in anterior chest wall or upper arm (anterolaterally), back (away from spine and scapulae), anterior abdominal wall, anterior thigh. Do not site near a joint or bony prominences and avoid skin folds, broken, oedematous, infected or recently irradiated skin. Do not site in abdomen if patient has ascites
- Check syringe driver and infusion site one hour after setting it up, then every four hours (in hospital), and daily in community settings, and document

Practical Points

- Use as few drugs in the syringe driver as possible (usual maximum 4)
- Medicines administered via a syringe driver may take some time to achieve steady state
 - When continuing drug and switching from oral to CSCI at equi-effective doses a steady state may already exist
 - It takes 5 half-lives for a drug to reach a steady state when first commenced
 - A loading dose will reduce the time to a steady state
 - Use prn medications to relieve symptoms if necessary during this period
- Infusion site reactions may occur as a result of irritant solutions or metal allergy. Consider:
 - Changing the diluent to 0.9% saline, where compatible with other drugs
 - Change to less irritant drug, e.g. change cyclizine to another anti-emetic
 - If the reaction occurs shortly after commencing a combination of drugs, consider removing the last drug added: site reactions may indicate precipitation even if the syringe contents appear clear.
 - Diluting the solution as much as possible, e.g. dilute to 23ml in a 30ml syringe in a McKinley T34 syringe driver
 - Using a plastic cannula instead of a butterfly needle (and always in patients allergic to metal)
 - Change the insertion site every 2-3 days
 - Add dexamethasone 0.66mg (0.2ml of a 3.3mg/1ml ampoule) to solution (if compatible); check local guidelines
 - Apply hydrocortisone 1% cream to insertion site and cover with occlusive dressing
- Certain drug combinations may precipitate within the syringe. If this occurs, stop the syringe pump and:
 - Check drugs are compatible
 - Switch to 0.9% saline as diluent (where compatible)
 - Dilute the solution as much as possible, e.g. using a 30ml syringe in a McKinley T34 syringe pump
 - Separate drugs into two syringe drivers
 - Draw up dexamethasone and ranitidine last when used in combination
 - Avoid exposure of solution to sunlight and heat (e.g. electric blankets)
 - Seek specialist advice on alternative drug combinations*

Drugs used in the syringe driver (p87-90)

- All doses are prescribed per 24 hours SC
- When deciding drug doses, titrate according to the total of regular and prn drug requirements in last previous 24 hours
- Always start at the lower end of the dose range

Diluent (*Check local guidelines*)

- Water for injection is the commonest recommended diluent, *however*
 - Some units prefer 0.9% saline
 - 0.9% saline must be used for several drugs e.g. levomepromazine, dexamethasone, octreotide* and ketorolac*
 - 0.9% saline is incompatible with cyclizine

SYRINGE DRIVER CSCI DRUGS

Prescriptions may include: (all doses are CSCI over 24 hours)

NB. Not all drug combinations are compatible: check with your local Specialist Palliative Care Service, pharmacy, or The Palliative Care Formulary's latest edition

| Use | Medication | Dose ranges in CSCI over 24hr | | Comments |
|-------------------------------|-------------------------|---|--|--|
| | | Usual starting dose | Typical maximum ^{a*} | |
| ANALGESIC (p6-23) | Morphine sulfate | 5-15mg if opioid naïve (or a dose based on prior oral opioid dose) | Seek advice for rapid titration or doses higher than 60mg* | |
| | Oxycodone | 5-10mg if opioid naïve (or a dose based on prior oral opioid) | Seek advice before exceeding 40mg or if previous increases/ PRNs are ineffective | Alternative to morphine and diamorphine. Relatively expensive |
| | Diamorphine | 5-10mg if opioid naïve (or a dose based on prior oral opioid; | Seek advice before exceeding 40mg or if previous increases/prns are ineffective | More expensive than morphine; useful if volume of morphine too great to fit into syringe |
| | Alfentanil | 0.5-1mg if opioid naïve (or a dose based on prior oral opioid (p10) | Seek advice before exceeding 4mg or if previous increases/prns are ineffective | Used in severe renal failure (p23) Or where accumulation of the drugs above |
| ANTIEMETIC (p30-33) | Metoclopramide | 30mg | 80mg | Extrapyramidal effects occur, particularly at higher doses. Avoid in Parkinson's disease |
| | Haloperidol | 1.5-3mg | 10mg | |
| | Levomepromazine | 6.25mg | 25mg | |
| | Cyclizine | 75-100mg | 150mg | Often causes site irritation. Limited compatibility |
| ANXIOLYTIC | Midazolam | 5-10mg | 30-60mg (60mg in the imminently dying) | Seek specialist advice if uncertain about the appropriateness of higher doses |

| Use | Medication | Dose ranges in CSCI over 24hr | | Comments |
|--|-----------------------|--|------------------------------------|---|
| | | Usual starting dose | Typical maximum dose ^{a*} | |
| ANTI-SECRETORY | Hyoscine Butylbromide | 60mg | 120mg | Respiratory secretions |
| | | 60mg | 240mg* | Higher dose range for intestinal obstruction or to relieve intestinal colic. |
| | Glycopyrronium | 600mcg | 1.2mg | |
| | Hyoscine Hydrobromide | 400mcg | 2.4mg | Sedating; may cause agitation Rarely used |
| DELIRIUM or TERMINAL AGITATION (p52 & 53) | Haloperidol | 0.5-3mg | 5-10mg | Seek specialist advice if uncertain about the appropriateness of higher doses. Generally avoided in Parkinson's disease |
| | Levomepromazine | 12.5mg-25mg (25-75mg for severe agitation) | 100-200mg | |
| | Midazolam | 5-10mg | 60mg | |
| OTHER | Dexamethasone (p69) | Dose depends on indication (see individual symptom sections) 3.3mg SC \equiv 4mg PO | | Alternatively, give as a separate morning SC bolus May precipitate when higher doses used with other drugs. |
| | Diclofenac* (p18) | 75mg | 75mg | Needs a separate pump; cannot be mixed with other drugs |
| | Levetiracetam (p47) | 500-1000mg (or 1:1 conversion from PO dose) | 3g | For seizures. Allows continuation of previous oral medication |
| | Octreotide* (p34) | 300-600mcg | 1.2mg | Used for intestinal obstruction (p34) and fistulae (p40) |
| Occasionally used on specialist advice | | Fentanyl*, furosemide*, ketorolac*, ondansetron*, phenobarbital*, ranitidine* | | |

^a Seek specialist advice before exceeding

DEPRESSION

It is important to consider the differential diagnoses: adjustment reaction, depression, hypoactive delirium and dementia. Be aware that many of the usual somatic symptoms of depression such as anorexia, weight loss and sleep disturbance may already be present in patients with advanced progressive disease, including cancer. Depression may be hidden behind a brave but hollow smile or even overt joking. A therapeutic trial of antidepressants may be appropriate.

Diagnosis

Biological symptoms

- Diurnal variation in mood; may be agitation
- Sleep disturbance especially with frequent or early morning waking

Psychological symptoms

- Persistent, pervasive low mood with loss of pleasure and enjoyment
- Withdrawal from relationships and activities
- Morbid guilt, feelings of helplessness and worthlessness/low self-esteem
- Persistent negative thinking style regarding all aspects of life, past, present and future
- Excessive rumination
- Suicidal ideas and intentions

Causes/Risk factors

- Past history of depression
- Need to adjust to many life changes over a short period of time
- Loss of previous roles, loss of planned future
- Poor symptom control
- Immobility and isolation with poor quality of life and lack of support
- Uncertainty about illness or prognosis
- Early dementia
- **Drugs** – corticosteroids (long term use, or on withdrawal), benzodiazepines, some cytotoxics, antihypertensives and narcoleptics

Management

A Consider reversible causes

Minimise the causes: see above

B Non-drug measures

Provide psychological support or therapies

C Drug therapies are recommended in moderate or severe depression.

NICE guidance is that first line of treatment should be with an SSRI (e.g. Sertraline Citalopram). If there is a lack of response or unacceptable side effects, consider a switch to another SSRI or to Mirtazapine. Mirtazapine is an alternative anxiolytic antidepressant with a side effect profile of increased appetite, weight gain and improved sleep, which may be useful in some patients. A tricyclic antidepressant may be helpful if pain or poor sleep are prominent features. Consider specialist referral for depression in the last few weeks of life: options include multi professional support and use of methylphenidate.

ANXIETY

Common features include:

- Feeling of being on edge, restless or agitated, apprehension
- Inability to concentrate
- Physical effects such as sweating, tachycardia, staring eyes with dilated pupils
- Anxiety may be a presenting feature of an underlying depression

Causes/Risk factors

- Past history of anxiety
- Poor symptom control
- Inadequate/inaccurate/conflicting information
- Unfamiliar surroundings
- Uncertainty about the future, concern for family/finances etc.
- Fears about pain, suffering, and loss of dignity at the end of life
- Fear that new symptoms indicate disease progression and the approach of end of life
- Early dementia
- Depression
- **Drugs** – e.g. caffeine, steroid treatment, salbutamol therapy, methylphenidate,
 - SSRIs – both starting and withdrawing treatment may be associated with anxiety
 - Withdrawal of drugs e.g. opioids/benzodiazepines/alcohol/nicotine
- Akathisia – inner restlessness caused by antipsychotics eg. haloperidol, metoclopramide

Management

A Consider reversible causes

e.g. drugs, unexpressed fears

B Non-drug measures

- Appropriate information, discussion and support for patient/family
- Relaxation techniques, Mindfulness and complementary therapies
- Crisis management plan
- Provide psychological support or therapies for persistent anxiety

C Drug therapies

- Treatment of depression if present using anxiolytic antidepressant e.g. citalopram, tricyclic antidepressant or mirtazapine
- Treat if confusion /delirium is exacerbating anxiety

Specific drug treatments

| Drug and dosing | |
|--|--|
| Immediate (Acute relief of panic) | <ul style="list-style-type: none">• Lorazepam 0.5-1mg SL |
| Short term | <ul style="list-style-type: none">• Diazepam 2mg bd and/or 5mg at night PO• Haloperidol 0.5-3mg nocte PO• Olanzapine 2.5mg nocte up to 5mg bd PO |
| Longer term | <ul style="list-style-type: none">• Anxiolytic antidepressant• Haloperidol or olanzapine as for short term• If unable to swallow or has syringe driver for other reasons, consider midazolam 10-20mg, haloperidol 1.5-3mg or levomepromazine 6.25-12.5mg per 24 hours via CSCI |

BREAKING BAD NEWS

Bad news is any information which alters a patient's view of their future for the worse. The bigger the gap between expectation and reality the worse the news. Giving bad news means entering a therapeutic dialogue: listening and responding; which will affect how patients and families will cope. The aim is to:

- Maintain trust between patient, family/carer and health professionals
- Enable appropriate adjustment for the reality of the situation
- Encourage informed choice of management options
- Reduce uncertainty about the future or at least acknowledge it
- Enable patients to regain a feeling of some control over their situation

The following framework describes one approach to breaking bad news:

1. Preparation

- Know the facts and potential management plan
- Arrange for privacy, sufficient seating and avoidance of interruptions
- Whenever possible offer the patient the chance to have a close family member or friend present

2. Assess the existing level of understanding (may need repeating as further information given)

- *"What do you understand about your illness/what is happening?"*
- *"What did the doctor tell you?"*

3. Check if more information wanted and at what level

- *"Do you want to go on or is that enough for now?"*
- Again, this may need to be repeated as you give further information

4. Allow denial

- Allow the patient to control the pace of information flow, and to whom the information should be given

5. Sharing the information

- Start from where the patient is. Give warning shots and further information in small chunks. Know when to stop
- Be clear and simple, avoiding jargon, and above all be gentle
- Avoid assumptions about understanding i.e. check that they have heard what you believe you have said

6. Elicit concerns

- What is worrying the patient most?

7. Respond to the patient's feelings

- Identify the patient's feelings and acknowledge them
- Give an empathic response such as *"this sounds really hard for you"*
- Listen for and observe the emotional content and behaviour
- Allow them time to think through the situation and ask questions.
"Is there anything else you'd like to say or ask me?"

8. Summary and plan

- Summarise what has been said, emphasising the positive
- Outline future treatment if appropriate, using written or printed material if possible. Foster realistic hope, e.g. *"We may not be able to cure you but there are things we can do to make you feel better and help you cope with your illness"*
- Recheck their understanding. Ask who may be told of the diagnosis/information

9. Make arrangements for further contact

- Offer early review
- Ask who may be told of the diagnosis/information

10. Ensure others are informed of what was said

- Tell the General Practitioner and other staff on duty as soon as possible
- Record as exactly as possible what was said, so that it can be repeated later and to avoid any misunderstanding
- Giving the patient a recording of the interview is popular and effective

Remember

- Make sure the patient feels the focus of attention
- Much of what you communicate is by non-verbal means and behaviour
- Move at the patient's pace, giving information that is appropriate for the time
- If using euphemisms, try to find out what they understand by these words
- Express your humanity and warmth, and interest in their care
- Breaking bad news does not have to be done at one session, it is often best done in stages
- Ensure that you are answering the questions that you are being asked
- Avoid jargon
- Do not tell lies
- Do not be afraid of them expressing negative feelings or crying
- Be prepared for an initial stunned silence or anger
- Some direct questions are best answered initially by asking *"What makes you ask that?"*
This may enable them to explain the worry behind the question

It is a breach of confidentiality to tell relatives without a patient's consent, where the patient has the capacity to agree to or refuse disclosure

(Breaking Bad News: A Ten Step Approach: Kaye.P)

DEALING WITH DENIAL AND COLLUSION

DENIAL

Denial is a basic coping mechanism that allows us to continue to function when faced with difficult information or events. It may be practised by the patient, family or professionals. Denial is not necessarily unhealthy and can be normal, as in the first stage of accepting bad news. It may be appropriate to explore the denial where it has created situations that are harmful such as preventing appropriate treatment, adequate symptom control, or future planning for dependents.

Assessment

- Is it healthy or unhealthy? That is, is it reducing or increasing distress?
- Is there an appropriate reason for challenging denial?
- Is it really denial? Many people have a good understanding of the situation but do not wish to talk about it
- Is other health professionals' denial contributing?

Management

- Gently explore what the person understands of what they have been told
- Using the framework outlined in *Breaking Bad News (p93)*, gently move the person towards a better understanding of reality, particularly with regard for the particular need identified for challenging the denial. It is often helpful to use such phrases as *"What if?"* or *"Let's look at the worst scenario even if it may not happen"*
- Be prepared to modify denial in stages; as far as possible at the patient's pace; and accept that it is unrealistic to expect all patients to come to terms with their mortality
- Ensure that extra support is available following the challenging of denial. Support family or carers who may be finding the patient's denial stressful
- Alert other health professionals involved of any changes in the patient's understanding
- It is possible to remain alongside a person in denial without challenging or colluding with their denial

COLLUSION

Collusion usually occurs when the family members conspire among themselves or with professionals to withhold information from or lie to the patient. It is often well intentioned, acting in what is believed to be the best interests of the patient. However, this inevitably creates tension because, ethically and legally, the patient has the right to information and to authorize disclosure of information to family.

Management

1. Explore the family's understanding and reasoning

- Establish whether they are trying to protect themselves or the patient
- Recognise that they may have valid concerns about the patient's capabilities and past behaviour patterns
- Show understanding of their situation

2. Reassurance and explanation.

- Reassure that you will not walk in and impose information
- Explain that:
 - The patient has a right to information
 - Honesty is an important part of maintaining trust in a doctor-patient relationship
 - The patient may be aware that truth is being held from them, however they may not feel able to challenge this
 - There are usually stressful consequences of living out an ever-increasing lie
 - If the patient asks direct questions, their understanding and wishes will be explored before answering the question appropriately and sensitively
- Offer to facilitate a joint conversation between the family and patient if they are finding it too difficult

3. Gently explore the patient's understanding

- Assess their desire for further information
- Pass this on to the family, with the patient's consent, to enable more communication

4. Respect and accept complex family dynamics

- Do not presume to know what is best for families.

Occasionally patients collude with professionals to withhold information from their family. This is more difficult as the patient has to give permission for disclosure of information, however the principles are the same as above - exploration of reasoning; explanation of consequences; reassurance of sensitive handling and offer facilitation.

PSYCHO-SOCIAL AND SPIRITUAL CARE

Palliative care extends far beyond pain relief and the alleviation of symptoms. Psychological, emotional, spiritual and social needs of both patient and their family/carers should be addressed.

This holistic assessment is important in ensuring that the patient and family have optimal support in any care setting. It also ensures that discharge planning is effective (hospital/hospice staff should check that these plans are acceptable to the patient, family, carers and Primary Health Care Team).

The framework for needs assessment should include:

- Psychological needs
- Spiritual issues
- Social needs
- Information needs
- Carers' needs

Many factors influence the way in which patients and families cope with their illness and the following need to be considered during an assessment:

- The history of the illness and their understanding of what is happening, including their emotional and psychological response
- How the illness is affecting the person's ability to carry out their role, for example as parent, partner, lover, breadwinner
- Family history – who is around, where are they, how important are they, how supportive are they?
- Constructing a family tree (genogram) is often helpful both for establishing relationships and for use as a therapeutic tool in helping people talk about their issues
- Life stresses – for example what is happening with regard to money, jobs, housing, children, sources of support; and how the person has previously coped with stressful situations in life
- Hopes and fears – what is the worst thing that can happen, what are the plans for the future, what losses and disappointments have occurred, what unfinished business is there, and what do they still wish to accomplish?

During assessment it should become apparent whether further expert professional help is required for psychological, spiritual and social care. Those available will include specialist palliative care staff, clinical psychologists, counsellors, chaplain/spiritual advisors and adult and children's social workers.

SPIRITUAL CARE

Spiritual care is one of the central aspects of palliative care. It is difficult to define spirituality as it is a construct dependent on each individual's belief system. It requires providing a person with the space to talk about and explore their belief system. Facilitating these conversations allows for the clinician or chaplain to address distress arising from any crisis in their belief system that has been caused by their experience of having a life-shortening illness. Often conversations concerning spirituality relate to themes such as a belief (or lack of belief) in God, the afterlife, or the soul, or they may focus on the person's sense of the meaning (or lack thereof) of their life.

- Any problem, conversation or contact may involve spiritual as well as physical, psychological or social issues
- Spirituality is to do with how we live, what we treasure and value, and peace of mind.
- Spirituality is relational in its expression, i.e. feeling the need to connect with someone or something
- The term spiritual may therefore include anything that affects a person's sense of wellbeing or wholeness. A useful question to open a conversation could be *'Do you feel at peace?'*
- All patients have spiritual needs while only some will have religious needs

The primary task when faced with spiritual questions is to help the person towards some relief of distress. This does not necessarily require specialist help – all health professionals should be prepared to make initial assessments and identify these issues.

Spiritual distress

When a person experiences a life crisis they will look to their spiritual values, beliefs, attitudes and religious practices to make sense of it. If these do not enable them to cope with the crisis, then they may experience spiritual distress.

Expressions of spiritual distress include:

- **fear** about the future, about dying and what happens after death
- **loss** of identity or roles (such as parenthood, work)
- **helplessness** and loss of control over what is happening
- **anxiety** about relationships, body image or sexuality
- **suffering** excessively from physical symptoms, especially pain
- **anger**
- **guilt** or shame
- **hopelessness**, despair, feeling alone or unloved
- **exploration** of meaning and purpose of their life
- **breaking** with religious or cultural ties
- desire to **reconnect** with past religious or cultural support

Dealing with spiritual distress

- Accept that there is unlikely to be a specific answer – it's OK not to know
- Listen attentively and be prepared to face uncertainties – just by “being there” you can help the patient to make connections and embark on their own search for meaning
- Do not be afraid to ask simple questions about their fears, losses and feelings, “the future”, sense of control, past regrets, values, beliefs and religious needs. Offer the support of a chaplain or other spiritual leader particularly if you feel out of your depth or there is a requirement for religious input

Basic principle

1. Provide a safe caring environment.

- Good symptom control
- Show willingness to listen
- Value their role and appearance, and belief systems

2. Attend to:

- Signs of their wishing to explore spiritual issues
- Ask yourself “*Why am I being told this? And why now?*”
- Your own verbal and non-verbal behaviour and reactions (patients can be reluctant to embarrass professionals if they sense that they are causing discomfort)

3. Listen to:

- Questions
- Expressions of fear, anger, loss
- Their story

4. Assess in terms of:

- Past, present and future. Ask simple questions as outlined above
- What help is needed?

5. Reassure and help with:

- Good physical care in illness and dying
- Respect for their integrity, worth and values
- Information as requested
- “Unfinished business”
- Personal support – “being alongside”
- Care for family and carers
- Reviewing of life
- Arranging provision of spiritual counselling if needed e.g. to help face mortality
- Arranging provision of religious and sacramental care, according to faith

Above all – be there

6. Attend to yourself:

Facing intense feelings or distress can leave us feeling uncomfortable, inadequate, helpless or vulnerable. The task is to live with our own uncertainties. It is therefore important to explore difficult issues or share concerns with colleagues, e.g. through individual or group supervision.

CULTURE

In our society there is a wide variety of people of different faiths, ethnic backgrounds and countries of origin. Within these groups, each individual will express their cultural attitudes uniquely, as they are influenced by upbringing, background, environment, beliefs and life experience.

Cultural attitudes can particularly influence:

- Language and use of colloquialisms
- The roles of the family
- How symptoms or illness are described and understood
- Attitudes towards expressing emotion and discussing private issues with those outside the family
- Ethical issues, including autonomy and confidentiality
- Attitudes towards conventional Western therapies, complementary or alternative therapies, food and diet
- Attitudes towards pain relief
- Attitudes towards death and dying
- Rituals surrounding death (see below)
- Preferred place of care – home, care home, hospital or hospice
- Acceptance of help and support

Health professionals should show their awareness by:

- Ensuring appropriate language interpretation services are used
- Demonstrating willingness to listen and a wish to understand cultural differences and implications
- Meeting specific requirements (such as food, privacy, opportunity to practice religious observances etc.) wherever possible
- Being prepared to negotiate boundaries and details of care
- Ensuring that there is access to an appropriate religious advisor

Do not make assumptions - ASK.

Remember that each person is unique, regardless of cultural background and professed faith

BEREAVEMENT

Grief is a natural process experienced by anyone who has to adjust to a significant loss. An appreciation of what is 'normal' is required in order to recognise when and what type of intervention is needed. Bereavement has been described in terms of **tasks of grief**:

Initial shock, numbness and disbelief before emotional reality of the loss is felt. Seeing the body after death, attending the funeral or visiting the grave are often important in facilitating acceptance of the reality of the death.

The pain of separation which affects behaviour and emotions. The bereaved usually suffer overwhelming periods of sadness as they are faced with the day-to-day reality of their loss. They may try to reduce this by avoiding reminders of the deceased. They may also find themselves 'searching' for the bereaved, dreaming about them or actually seeing or hearing them. Visual or auditory hallucinations at this time are normal. Agitation, restlessness and an inability to concentrate can result from the conflict between this searching and avoiding behavior.

A range of emotions other than sadness may be experienced. Anxiety may be due to loss of the familiar routine and feelings of insecurity. Anger may be directed towards the deceased for abandoning them, towards God, or (justly or unjustly) towards professionals. It may simply manifest as general irritability. Feelings of guilt may occur when anger is directed internally.

It is common for physical symptoms related to over-activity of the autonomic nervous system to be experienced, e.g. palpitations, insomnia, diarrhoea and fatigue. A transient hypochondriasis can occur, but it is abnormal if it persists.

Despair or depression. As the pangs of grief and anxiety reduce in frequency and severity the bereaved may lose interest and purpose in life. They feel hopeless and become withdrawn. This may last for months.

Eventually the loss is **accepted** and life without the deceased is adjusted to.

The task of **resolution and reorganisation** is entered when emotional energy is reinvested in new relationships and activities, although anniversaries often trigger renewed grief.

For some, part of the work of grieving may be undergone before the death (**anticipatory grieving**).

A key characteristic of the experience of grief is a pattern of oscillating between periods of intense grief ('waves of grief'/feeling overwhelmed by the loss) and periods of greater stability in which the bereaved person is able to feel a respite from intense feelings as well as being more engaged in life and optimistic (more controlled/ functioning). When feelings and functioning are balanced, there is resilience; when not vulnerability will result. The pattern of oscillating from one state to another will continue for some time and is entirely normal. It can be helpful to explain that this is normal to people so that do not feel that they are constantly 'going back to square one' every time that the grief intensifies again.

Recognising this pattern is key for clinicians when assessing whether a person may require additional support. When assessing a grieving person's coping, gently explore for evidence of both aspects of the dual process (i.e. good days/moments and difficult/grief filled days/moments).

For most people, no formal psychotherapeutic intervention is needed as their personality, previous life experiences, social network and loving relationship with the deceased enable them to come to terms with their loss, and often to grow personally through it. Often all that is required is a watchful eye to check that their grief is continuing normally. Written information explaining what may be experienced and giving useful contact numbers is often appreciated.

Those requiring a greater degree of support may benefit from meeting with a volunteer with training in listening skills and with knowledge of the bereavement theory described here. Many people take comfort from being reassured that their experiences are 'normal' by an informed person/clinician. A chaplain may also be helpful to those who wish to explore changes in their faith in the light of their bereavement.

Some find meeting with a group of individuals who have undergone a similar experience can be supportive. These groups may or may not have a trained facilitator. Many areas have their own voluntary bereavement and counselling groups including branches of CRUSE.

The needs of children and adolescents are specific to their stage of development and can be quite complex: they may also benefit from specialist support.

There is no clear boundary between what is 'normal' and what is 'complicated' grief, and it is often a question of unusual intensity of reaction or of timing (duration).

Recognition of those likely to develop a **complicated grief** reaction can also allow early supportive intervention and prevent its development.

Risk factors include:

- Unexpected/untimely death
- A death experienced as traumatic or unpleasant
- Ambivalent relationship
- Excessively dependent relationship
- Child/adolescent (may be protected/excluded)
- Social isolation
- Excessive use of denial, preventing anticipatory grieving
- Unresolved anger
- Previously unresolved losses
- Previous psychiatric illness
- History of alcoholism/drug abuse
- Other concurrent stressful life events

Some of these complicated grief reactions can be dealt with by the primary health care teams, social workers, psychotherapists or trained counsellors. Some people require specialist help from clinical psychologists or psychiatrists. It is important for all professionals to realise the limitations of their own skills and to identify when to refer to their local specialist bereavement service.

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| <i>Co-phenotrope</i> | 42 | <i>Ketorolac</i> | 18, 87, 90 |
| <i>Creon</i> | 42 | <i>Lactulose</i> | 40, 77, 80 |
| <i>Cyclizine</i> | 31, 32, 46, 76, 86, 88 89 | <i>Levomepromazine</i> | 27, 31, 33, 35, 51, 52, 54, 78, 86, 89, 90, 92 |
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| <i>Diazepam</i> | 17, 20, 21, 23, 27, 52, 54, 92 | <i>Loratidine</i> | 58 |
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| <i>Difflam</i> | 37 | <i>Macrogol</i> | 35, 40, 41 |
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| | | <i>Methylnaltrexone</i> | 13, 41 |

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ABBREVIATIONS used in drug dosing

| | | | |
|------|--|-------|-------------------------|
| IR | <i>immediate release</i> | MR | <i>modified release</i> |
| SL | <i>sublingual</i> | TD | <i>transdermal</i> |
| PO | <i>by mouth</i> | SC | <i>subcutaneous</i> |
| PR | <i>per rectum</i> | IM | <i>intramuscular</i> |
| PEG | <i>via gastrostomy</i> | IV | <i>Intravenous</i> |
| CSCI | <i>continuous subcutaneous infusion (via a syringe driver)</i> | | |
| od | <i>once a day</i> | mane | <i>in the morning</i> |
| bd | <i>twice a day</i> | nocte | <i>at night</i> |
| tds | <i>three times a day</i> | prn | <i>as needed</i> |
| qds | <i>four times a day</i> | | |

Always refer to local Specialist Palliative Care guidelines for advice on management in palliative care.

USEFUL READING LIST

- Palliative Care Formulary 6th edition (2018) for advice on drugs in palliative care www.palliativedrugs.com
- Scottish Palliative Care Guidelines: www.palliativecareguidelines.scot.nhs.uk
- E-Learning for Health www.e-lfh.org.uk/programmes/end-of-life-care/
- Palliative Care Adult Network Guidelines <http://book.pallcare.info>
- Planning for your Future Care – A Guide www.ncpc.org.uk/publications/planning-your-future-care
- www.dyingmatters.org

CREDITS

The Palliative Care Handbook, commonly known as **‘The Green Book’**, has been written to provide advice on clinical management in palliative care. It is a consensus guide for all staff working with patients with palliative care needs.

The First edition was produced in 1993 by The Dorothy House Foundation, Bath. The book was adopted by all the Specialist Palliative Care units in Wessex in 1997 with the production of the fifth edition. This edition, the ninth, has been reviewed and revised by clinicians working in the multi-professional specialist palliative care services in the areas listed below under the direction of The Wessex Palliative Physicians. Credit is due to all who have contributed to the production of this new edition.

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