



LANARKSHIRE PALLIATIVE CARE

Guidelines



Introduction: Palliative Care Guidelines Third Edition

Palliative care

- aims to improve the quality of life of patients and their families facing the problems associated with any life limiting illness.
- provides relief from pain and other distressing symptoms.
- integrates the psychological and spiritual aspects of patient care.
- offers a support system to help patients live as actively as possible until death.
- offers a support system to help the family cope during the patient's illness and in their own bereavement.
- uses a team approach to address the needs of patients and their families.
- affirms life and regards dying as a normal process.
- intends neither to hasten or postpone death.
- is relevant in combination with many other treatments directed at the underlying illness.

Palliative care is part of the care delivered by a wide range of health and social care professionals working in the community, in care homes and in hospitals. Some patients with more complex problems will benefit from advice, assessment or care from a palliative care specialist. Details of how to access local specialist services are included in the Guidelines and are available online.

These Guidelines reflect a consensus of opinion about good practice in the management of adults with a life limiting illness. They have been developed by a multidisciplinary group of professionals working in the community, hospitals and specialist palliative care services and approved by local Formulary and Clinical Policy Committees. There is a separate section on the website covering paediatric palliative care.

Every effort has been made to ensure the accuracy of the text and that evidence informed information has been included. Adherence to guideline recommendations will not ensure a successful outcome in every case. It is the responsibility of all professionals to exercise clinical judgement in the management of individual patients. Palliative care specialists occasionally use or recommend other drugs, doses or drug combinations than those given here.

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Palliative Care Guidelines: websites

The printed Palliative Care Guidelines, additional guidelines, more information about specialist services, information for patients and further professional resources are available online.

NHS Lothian intranet: http://intranet.lothian.scot.nhs.uk/nhslothian/healthcare/a_z/p/palliative_care.aspx

NHS Lothian website: <http://www.nhslothian.scot.nhs.uk/ourservices/palliative/>

SHOW website: <http://www.palliativecareguidelines.scot.nhs.uk>

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Specialist Palliative Care Services in NHS Lanarkshire

Services

- Inpatient
- Outpatient
- Day care, home assessment, home care and telephone advice.

Referral

A referral form is required for inpatient care for patients with life limiting illness and uncontrolled symptoms or complex physical, psychological, spiritual or family needs.

A referral form can be downloaded from www.st-andrews-hospice.com

Hospice Inpatient Units

St Andrew's Hospice, Airdrie

Henderson Street, ML6 6DJ

Tel: 01236 766951

Fax: 01236 748786

<http://st-andrews-hospice.com>

Strathcarron Hospice, Denny (Cumbernauld/ Kilsyth area)

Randolph Hill, FK6 5HJ

Tel: 01324 826222

Fax 01324 824576

<http://strathcarronhospice.org>

Hospital Palliative Care Teams

Macmillan Palliative Care CNS

Hairmyres Hospital

Direct line 01355 584656

Monklands District General Hospital

Direct line: 01236 712156

Wishaw General Hospital

Direct line: 01698 366053

Palliative Care Pharmacist

Macmillan Area Lead Pharmacist- Palliative Care

St Andrew's Hospice

Tel: 01236 772021

Senior Clinical Pharmacist- Palliative Care

Hairmyres Hospital

Tel: 01355 584887

Community Palliative Care Services

Available Monday to Friday, 9am-4:30pm

Macmillan Community Nursing Team

Calder Unit, Udston Hospital

North Team

Tel: 01698 723278

Fax: 01698 723282

South Team

Tel: 01698 723297

Fax: 01698 723282

Clydesdale Palliative Care Service

Roadmeetings Hospital

Tel: 07880 787213

Palliative Care Day Services

St Andrew's Hospice Day Unit

Tel: 01236 766951

Fax: 01236 748786

Dalziel Centre Day Unit

Tel: 01698 245026

Fax: 01698 245044

Kilbryde Day Hospice- Day Unit

Tel: 01355 593484

Fax: 01355 593496

Palliative Care Out of Hours

Contact St Andrew's Hospice for medical/ nursing advice on complex patients. Community pharmacy palliative care network stocks essential medications.

Alfentanil in Palliative Care

Description

Potent, short-acting opioid analgesic; used 3rd line so seek specialist advice.

Preparations

Injection 500 micrograms/ml	2ml, 10ml ampoules	Used as a subcutaneous infusion or sublingually/ subcutaneously. A higher concentration preparation can be ordered, but is only for named patient use with specialist supervision.
Sublingual/ buccal spray 5mg/5ml (1 metered dose = 140 micrograms)	5ml spray	Pharmacist can order spray on a named patient basis if advised by a palliative care specialist.

Indications

- **Third line** injectable opioid for moderate to severe opioid responsive pain in patients unable to tolerate morphine, diamorphine or oxycodone due to persistent side effects (eg. sedation, confusion, hallucinations, itch).
(See: Pain management, Choosing & Changing opioids)
- Injectable analgesic for moderate to severe, opioid responsive pain in patients with Stage 4-5 chronic kidney disease (eGFR <30ml/min), or severe acute renal impairment.
- Episodic/ incident pain
 - o Pain often related to a particular event (eg. movement, dressing changes); sudden in onset, can be severe, but may not last long.
 - o Different from breakthrough pain occurring when the dose of regular analgesic has worn off. Assessed and treated independently of the regimen used to manage any continuous/ background pain.

Cautions

- **Liver impairment:** reduced clearance
Dose reduction of 30-50% may be necessary.
- **Renal impairment:**
No dose reduction needed. Not removed by dialysis.

Drug interactions

- Diltiazem, fluconazole, clarithromycin, erythromycin slow clearance of alfentanil.
Anticonvulsants may reduce its effect. See BNF.

Side effects

Drowsiness, skin rash.

Dose & Administration

- Alfentanil for moderate to severe opioid responsive pain
 - o Continuous subcutaneous infusion in a syringe driver/ pump over 24 hours.
 - o Stability and compatibility – see: Subcutaneous medication chart.
 - o Titrate larger doses in multiples of 250 micrograms.
 - o Prescribe doses of over 1000 micrograms in milligrams (mg).
 - o Prescribe about 1/6th of the 24hour dose **hourly** for breakthrough pain as alfentanil has a very short duration of action. The same dose can be given subcutaneously or sublingually.

Dose & Administration

Alfentanil for episodic/ incident pain

- Starting dose: 100-250 micrograms.
- Give a dose five minutes before an event likely to cause pain; repeat if needed
- Increase dose up to 500 micrograms according to response.
- Give by subcutaneous injection or sublingually. The dose is the same.
- Consider an alfentanil spray if the patient is being discharged home.

Dose Conversions

- Alfentanil is approximately thirty times more potent than oral morphine

Oral morphine 30mg	≈ subcutaneous alfentanil 1mg (1000 micrograms)
Subcutaneous morphine 15mg	≈ subcutaneous alfentanil 1mg (1000 micrograms)
Subcutaneous diamorphine 10mg	≈ subcutaneous alfentanil 1mg (1000 micrograms)
Oral oxycodone 15mg	≈ subcutaneous alfentanil 1mg (1000 micrograms)
Subcutaneous oxycodone 7.5mg	≈ subcutaneous alfentanil 1mg (1000 micrograms)

- Alfentanil is approximately four times less potent than fentanyl.

A patient whose pain is controlled on a subcutaneous alfentanil infusion can be converted to a fentanyl patch. Apply the patch and stop the infusion 12 hours later.

Alfentanil SC 24 hour infusion dose	Alfentanil SC hourly as required dose	Fentanyl patch dose given over 72 hours
500 micrograms	100-200 micrograms	Do not use a patch
1 mg (1000 micrograms)	200-250 micrograms	12 micrograms / hour
2mg- 3 mg	300-500 micrograms	25 micrograms / hour
3mg- 4mg	500 micrograms	37 micrograms / hour
4mg- 5mg	Seek advice	50 micrograms / hour
6mg- 7mg	Seek advice	62 micrograms / hour
8mg	Seek advice	75 micrograms / hour

- As with all opioid conversions, these are approximate doses.
- Dose conversions should be conservative and doses rounded down.
- Monitor the patient carefully so that the dose can be adjusted if necessary.
- If the patient has opioid toxicity, reduce dose by 1/3rd when changing opioid.
(See: Choosing & Changing opioids)

Resources

Professional

Palliative Care Drug Information online: <http://www.palliativedrugs.com>

Patient

Patient leaflet on website: Alfentanil

Discharge planning/ Community use:

- The community pharmacist, GP, and community nurse should be informed.
- The unscheduled care service should be informed that the patient is receiving this third line opioid.
- The Community Pharmacy Palliative Care Network stocks a limited supply of alfentanil injection for emergency use.
- Alfentanil can be prescribed by the patient's GP for the indications listed in liaison with local palliative care specialists.

Key references

1. Dean M. Opioids in renal failure and dialysis patients. *J Pain Symptom Management* 2004;25(5): 497-504
2. Urch CE, Carr S, Minton O. A retrospective review of the use of alfentanil in a hospital palliative care setting. *Palliative Medicine* 2004; 18:516-9

Anorexia / Cachexia in Palliative Care

Introduction

Anorexia / cachexia syndrome is a complex metabolic process found in many end-stage illnesses. Characterised by loss of appetite, weight loss and tissue wasting, it impacts significantly on quality of life. It causes anxiety and distress for patients and, perhaps even more, for carers.

Assessment

- Look for any reversible problems that may exacerbate anorexia including:
 - pain
 - nausea
 - heartburn
 - dyspnoea
 - vomiting
 - gastritis
 - depression
 - constipation
 - anxiety
 - dysphagia
 - medication
- oral problems: dry mouth, ill fitting dentures, ulcers, candidiasis etc.
- odours – fungating lesion, fistulae, cooking smells, and incontinence can contribute to anorexia.
- delayed gastric emptying (eg. due to local disease, autonomic neuropathy) causing early satiety, and vomiting of undigested foods that relieves nausea
- Find out about patient and carer perspectives on weight, body image, nutrition, dietary intake. Psychosocial aspects are very important.
- Fatigue is commonly associated with anorexia/ cachexia. (see: Fatigue)

Management

General

- Prevention or early identification and treatment of contributory symptoms.
- Acknowledge the psychological impact on the patient and carer; ongoing discussion and support are needed.

Medication

Limited benefit, but worth considering, as may improve quality of life.

Corticosteroids

- Established role in short-term improvement of appetite.
- Rapid effect, but tends to decrease after 3-4 weeks.
- May also reduce nausea, and improve energy/ general feeling of well being.
- No significant effect on nutritional status.
- Starting dose: oral dexamethasone 4mg or prednisolone 30mg in the morning. Consider need for a proton pump inhibitor.
- Side-effects: fluid retention, candidiasis, myopathy, insomnia, gastritis.
- Prescribe for 1 week, if no benefit, stop. If helpful, reduce to lowest effective dose; review regularly and withdraw if no longer improving symptoms.

Progestogens

- Improve appetite and increase weight in patients with cancer.
- Take a few weeks to take effect but benefit more prolonged than steroids.
- More appropriate for patients with a longer prognosis.
- Megestrol acetate - starting dose 160mg orally daily for one month, then review. Dose range (160-800mg). No evidence for optimal dose.
- Side effects: nausea, fluid retention, increased risk of thromboembolism.
- Reduce dose gradually if used for more than 3 weeks (adrenal suppression).

Prokinetics

- Used for early satiety, delayed gastric emptying, gastroparesis or nausea.
- Metoclopramide 10mg or domperidone 10-20mg (less long term side-effects) given three times a day half an hour before meals.

Non-drug

- Address concerns about the importance to the patient and carer of giving nourishment, refusing food, and eating as a social activity.
- Explain that a gradual reduction in oral intake is natural as part of the illness.
- Offer information and practical advice about nutrition in advanced illness, diet and management of anorexia.

Practice Points

- Supplementary drinks are expensive but can help selected patients after careful assessment of nutritional status, prognosis, and alternative options.
- See local Formulary for recommended preparations and advice.

Patient / carer advice points

- Gently encourage the patient to take what he or she can manage.
- Offer soft, easy to swallow foods; soup, pudding, nutritious drinks/ snacks.
- Small portions, attractively presented, offered more often through the day.
- Try not to talk about food all the time but keep the person involved in the social aspects of meals.

Resources

Professional

Macmillan Cancer Support (including Cancerbacup resources) <http://www.macmillan.org.uk>

Patient

Patient leaflet on website: Managing a poor appetite

Key references

1. Templeton A. Treating cancer patients with anorexia-cachexia syndrome. *European J Palliative Care* 2007; 14(5): 186-190
2. Shragge J E. The management of anorexia by patients with advanced cancer: a critical review of the literature. *Palliative Medicine* 2006; 20: 623-629
3. Poole K. Loss of weight & loss of appetite in advanced cancer: a problem for the patient, the carer or the health professional? *Palliative Medicine* 2002; 16: 499-506
4. Fainsinger R. Clinical assessment & decision making in cachexia and anorexia. In *Oxford Textbook of Palliative Medicine* 3rd Edition 2004, p533-546
5. Bruera E. Pharmacological interventions in cachexia and anorexia. In *Oxford Textbook of Palliative Medicine*, 3rd Edition 2004, p552-560
6. Strasser F. Pathophysiology of the anorexia/cachexia syndrome. In *Oxford Textbook of Palliative Medicine*, 3rd Edition 2004, p520-533
7. Davis MP. Appetite and cancer associated anorexia: a review. *Journal of Clinical Oncology* 2004; 22 (8): 1510-1517

Bowel Obstruction in Palliative Care

Introduction

Is due to mechanical obstruction (partial or complete) of the bowel lumen and/or peristaltic failure. Can be complex to manage and require specialist advice.

Assessment

- Exclude faecal impaction from history, rectal examination, abdominal X-ray. Can complicate or mimic any type of bowel obstruction.
- Some patients with a localised obstruction can benefit from surgery.
- Assess each patient on the basis of their clinical condition, likely benefits/ risks and patient preferences.

Contraindications to surgery

- Diffuse intra-abdominal cancer seen at previous surgery, or shown radiologically.
- Diffuse, palpable intra-abdominal masses.
- Massive ascites which recurs rapidly after drainage.
- High obstruction involving the proximal stomach.

Relative contraindications to surgery

- Non-symptomatic but extensive metastatic disease outside the abdomen.
- Frail or elderly patient with poor performance status or nutritional status.
- Previous radiotherapy to the abdomen or pelvis.
- Small bowel obstruction at multiple sites.

Clinical picture

Depends on the level, type and duration of bowel obstruction but may include:

- Constipation.
- Intermittent nausea, often relieved by vomiting undigested food.
- Worsening nausea and/ or faeculent vomiting (as obstruction progresses and small bowel contents are colonised by colonic bacteria).
- Continuous abdominal pain due to tumour and/ or nerve infiltration (eg. coeliac plexus involvement).
- Colic (in mechanical obstruction); altered bowel sounds.
- Abdominal distension (may be absent in gastro-duodenal obstruction or patients with extensive peritoneal spread).
- Faecal incontinence.

Management

General

- Frequent mouth care is essential (see: Mouth Care).
- Offer ice to suck, small amounts of food and drinks as wanted. Low fibre diet.
- If the patient is dehydrated and not dying, IV rehydration may be appropriate initially.
- SC fluids may be required for longer-term management of symptomatic dehydration or for a patient not wanting hospital admission. Hydration of 1-1.5 litres/ 24hours may reduce nausea but more fluid than this can result in increased bowel secretions and worsen vomiting. (see: Subcutaneous fluids).
- Laxatives +/- rectal treatment for constipation. (see: Constipation).

Interventional treatment

- Stenting (gastric outlet, proximal small bowel, colon) or laser treatment can palliate localised obstruction.
- NG tube may be appropriate to control vomiting initially; try to avoid long-term use.
- Venting gastrostomy in a fit patient with gastroduodenal or jejunal obstruction and persistent vomiting may relieve symptoms.
- TPN is only appropriate for a very small group of patients with a longer prognosis.

Medication

Peristaltic failure

May be due to autonomic neuropathy or intra-abdominal carcinomatosis.

Partial obstruction, reduced bowel sounds, **no colic**.

- Stop medication reducing peristalsis. (cyclizine, hyoscine, 5HT₃ antagonists, amitriptyline).
- Use a prokinetic antiemetic (SC metoclopramide (30-120mg /24hrs); stop if colic develops).
- Laxatives are often needed. (see: Constipation).
- Fentanyl patch for controlling stable, moderate to severe pain in patients with/ or at risk of peristaltic failure is less constipating than morphine or oxycodone (see: Fentanyl patches).

Mechanical obstruction

Target treatment at the predominant symptom(s).

- Laxatives (+/- rectal treatment) to treat/ prevent co-existent constipation.
Movicol (if volume of fluid is tolerated) is effective. Docusate sodium is an alternative.
Avoid stimulant laxatives (senna, bisacodyl, danthron) if patient has colic.
Stop all oral laxatives in complete obstruction.
- Dexamethasone (6-16mg) SC, IM or IV for 4-7 days may reverse partial obstruction.

Symptom	Drug	24 hour SC dose	Comments
Tumour pain/ colic	Morphine or diamorphine		Titrate dose.
Neuropathic pain	Fentanyl patch Adjuvant analgesic		See: Fentanyl patches Seek specialist advice.
Colic	Hyoscine butylbromide	40-120mg	Reduces peristalsis
Nausea	Cyclizine or hyoscine butylbromide	100-150mg 40-120mg	Anticholinergic antiemetic; reduces peristalsis.
	Add haloperidol	2.5-5mg	Add to the subcutaneous infusion or give as a single SC dose for persistent nausea.
	Change to levomepromazine	5-25mg	Use in a SC infusion or as a once or twice daily SC injection. Monitor for hypotension.
Vomiting (If nausea and pain are controlled, the patient may cope with occasional vomits)	Hyoscine butylbromide	40-120mg	Anti-secretory action.
	Octreotide	300-900 micrograms	Second line anti-secretory. More effective than hyoscine but expensive.

Practice points

- Most patients need a SC infusion of medication as oral absorption is unreliable.
 - Review treatment regularly; symptoms often change and can resolve spontaneously.
 - Do not combine anticholinergic antiemetics (cyclizine, hyoscine) with metoclopramide.
- See related guidelines; Subcutaneous medication, Nausea/ Vomiting, Levomepromazine.

Resources

Professional: Palliative Care Drug Information online: <http://www.palliativedrugs.com/>

Patient: Patient leaflet on website: Managing sickness and vomiting

Key References

1. Mercadante S. Medical treatment for inoperable malignant bowel obstruction: a qualitative systematic review. *J Pain Symptom Management* 2007; 33(2): 217-223
2. Ripamonti C. Pathophysiology and management of malignant bowel obstruction. In *Oxford Textbook of Palliative Medicine* 3rd Edition, 2004, p496-507

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Breathlessness in Palliative Care

Introduction

Breathlessness is a common and distressing symptom in advanced cancer, chronic obstructive pulmonary disease, lung fibrosis and heart failure.

Assessment

- Clarify pattern of breathlessness, precipitating / alleviating factors and associated symptoms.
- Is treatment of the underlying disease appropriate? Seek advice if in doubt.
- Look for any reversible causes of breathlessness: infection, pleural effusion, anaemia, arrhythmia, pulmonary embolism, or bronchospasm.
- Check oxygen saturation (if pulse oximeter available).
- Ask the patient to rate symptom severity and level of associated distress/ anxiety.
- Explore fears, impact on functional abilities, and quality of life.

Management

- Treat any reversible causes, if appropriate.
- If stridor or signs of superior vena cava obstruction - emergency referral to hospital.
- Give high dose steroids in divided doses: dexamethasone 16mg, or prednisolone 60mg.
- Oxygen: careful individual patient assessment. Important to avoid psychological dependence. A fan or air from a window may be just as effective.
If oxygen saturation is less than 90%, consider a trial of oxygen.
- Nebulised sodium chloride 0.9%, 5ml as required may help loosen secretions.

Medication

- **Bronchodilators:** by inhaler or spacer: Stop if no symptomatic benefit.
- **Steroids:** trial of dexamethasone oral 8-16mg daily for lymphangitis or airways obstruction that has responded to steroids before.
Unless starting emergency therapy, give steroids in the morning.
Stop if no effect after a week, or reduce gradually to lowest effective dose.
- **Opioids:** can reduce breathlessness, particularly at rest and in the terminal phase.
Give as a therapeutic trial; monitor patient response and side effects.
 - **No opioid before:**
 - o Immediate release morphine oral 2mg, 4-6 hourly or as required.
Increase slowly in steps of about 30%, if tolerated.
 - o If unable to take oral medication:
morphine SC 2mg, 4-6 hourly and/or 2 hourly as required.
or diamorphine SC 2.5mg, 4-6 hourly and/or 2 hourly as required.
 - **Elderly, frail patient or impaired renal function:**
 - o Morphine oral 1-2mg, 6-8 hourly as required; monitor closely for side effects.
 - **Opioid taken regularly for pain:**
 - o 25% of the 4 hourly breakthrough analgesic dose, given as required, may be adequate for breathlessness. Titrate according to response.
 - **Continuous breathlessness:**
 - o Consider using modified release (long acting) morphine.
 - o If the patient is dying, give morphine as a continuous SC infusion. Dose is based on previous regular dose and any as required doses.
Usually combined with midazolam SC in the infusion.
 - **Second line opioid:**
 - o Second line opioids can be used for breathlessness if the patient is unable to tolerate morphine due to side effects. (See: Choosing & Changing opioids)
 - **Anxiolytics: Start with a low dose and increase gradually as required and tolerated.**
 - o Lorazepam sublingually 0.5mg, as required for episodic anxiety, panic attacks.
 - o Diazepam oral 5mg, at night if more continuous anxiety.

Breathlessness in the last days of life (see: Last days of life)

- If unable to take an oral opioid, convert to the subcutaneous route. Prescribe the opioid SC, 2 hourly as required for respiratory distress. (see: Choosing & Changing opioids)
- Midazolam SC 2.5-5mg, hourly as required for anxiety/distress.
- Add midazolam SC 5-20mg over 24 hours to the subcutaneous infusion of opioid; titrate midazolam dose in 5-10mg steps according to the level of distress.
- Noisy breathing or respiratory secretions: hyoscine butylbromide SC 20mg, hourly as required (up to 120mg/ 24hours).

Non-drug management

- Holistic assessment and a multi-professional approach are essential.
- Enhance coping and functional ability using controlled breathing and anxiety management techniques, and by planning and pacing activities.
- Consider need for equipment/aids and a package of care.
- If prognosis is longer, a breathlessness support service, if available, may help.

Practice points

- Starting opioids at a low dose and titrating carefully is safe and does not cause respiratory depression in patients with cancer, airways obstruction or heart failure.
- Non-drug measures that maximise patient coping are essential. As the illness progresses, medication to relieve breathlessness becomes more necessary.
- Plan management of breathlessness in the last days of life with patient and family.
 - Discuss the option of sedation in the event of uncontrolled distress.
 - Anticipatory prescribing of as required medication for symptom control.
 - Complete a handover for the unscheduled care service or hospital at night team.

Patient/ carer advice points

- Keep the room well ventilated: open a window, use a fan, keep face cool.
- Anxiety /panic are distressing but do not cause harm or worsen the patient's condition.

Resources

Professional

Palliative Care Drug Information online <http://www.palliativedrugs.com/>

Patient

Patient leaflet on website: Managing breathlessness

Macmillan Cancer Support (including Cancerbackup resources) <http://www.macmillan.org.uk>

Roy Castle Lung Foundation <http://www.roycastle.org>

Cancer Research UK <http://www.cancerhelp.org>

Chest Heart and Stroke Scotland <http://www.chss.org.uk/>

British Lung Foundation Breathe Easy Support Network <http://www.lunguk.org/>

Key references

1. Chan K-S. Palliative medicine in malignant respiratory diseases. *Oxford Textbook of Palliative Medicine* 3rd Edition, 2004, page: 587-618
2. Jennings A. Opioids for the palliation of breathlessness in terminal illness. *Cochrane Database of Systematic Reviews* 2001, Issue 3 <http://www.cochrane.org/reviews/en/ab002066.html>

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Choosing and Changing Opioids in Palliative Care

Introduction

- Opioids are used for pain and breathlessness.
- Most palliative care patients respond well to titrated oral morphine.
- A small number of patients may need to be changed to another opioid:
 - Oral route is not available.
 - Pain is responding but patient has persistent, intolerable side effects. (Consider reducing the dose and titrating more slowly or adding an adjuvant analgesic before changing opioid)
 - Moderate to severe liver or renal impairment.
 - Poor compliance with oral medication.
 - Complex pain (consider adjuvant analgesics/ other pain treatments).

Choosing an opioid for moderate to severe pain

First line opioids: (see: Pain management)

Morphine

- Range of oral preparations; SC injection and in a syringe driver/ pump.
- Renally excreted, active metabolites – titrate morphine slowly and monitor carefully in chronic kidney disease.
- Consider other opioids in stage 4-5 chronic kidney disease, dialysis patients.
- Low doses and slow titration in liver impairment.

Diamorphine

- Highly soluble opioid used for SC injection and in a syringe driver/ pump.
- Use for high dose SC breakthrough injections (above 180mg SC morphine/ 24hrs). Powder preparation is diluted in a small volume of water for injections.
- As with morphine, cautious use in renal and liver impairment.

Second line opioids:

Oxycodone

- For moderate to severe pain if morphine/ diamorphine are not tolerated.
- Immediate and modified release oral preparations; SC injection; syringe driver/ pump.
- Low concentration of preparation limits dose for SC injection to 10mg (1ml).
- Avoid in moderate to severe liver impairment, clearance is much reduced.
- Mild to moderate renal impairment: reduced clearance so titrate slowly and monitor carefully. Avoid in stage 4-5 chronic kidney disease.

Fentanyl

- Topical patch lasting 72 hours; use if oral and SC routes unsuitable.
- For stable pain if morphine is not tolerated; dose cannot be changed quickly.
- No initial dose reduction in renal impairment but may accumulate over time.
- Liver impairment; dose reduction may be needed in severe liver disease.

Third line opioid: (seek specialist advice)

Alfentanil

- Short acting, injectable opioid for SC injection and in syringe driver/ pump.
- In episodic/ incident pain can be given sublingually or subcutaneously.
- Standard dose in renal disease including stage 4-5 chronic kidney disease.
- Clearance may be reduced in liver impairment; reduce dose and titrate.

Fourth line opioid: (specialist use only)

Methadone

- Oral methadone is used by specialists for complex pain; dosing is difficult due to the long half life; no renal excretion so standard dose in chronic kidney disease, half life prolonged in severe liver disease.

Opioid toxicity

- Wide variation in the dose of opioid that causes symptoms of toxicity.
- Prompt recognition and treatment are needed. Symptoms include:
 - Persistent sedation (exclude other causes)
 - Vivid dreams/ hallucinations; shadows at the edge of visual field
 - Delirium
 - Muscle twitching/ myoclonus/ jerking
 - Abnormal skin sensitivity to touch
- Reduce the opioid by a third. Ensure the patient is well hydrated. **Seek advice.**
- Consider adjuvant analgesics and/or alternative opioids if still in pain.
- Naloxone (in small titrated doses) is only needed for life-threatening respiratory depression. (see: Naloxone)

Changing opioid

- These doses / ratios are **approximate** (≈) and should be used as a **guide**.
- Dose conversions should be conservative and doses usually rounded down.
- Monitor closely; extra care if frail, elderly patient; renal or hepatic impairment.
- Always prescribe an appropriate drug and dose for breakthrough pain: 1/6th of the 24 hour regular opioid dose.

Equivalent doses of opioids recommended for use in palliative care

Immediate release morphine	Opioid dose	Oral morphine: opioid potency ratio
Oral morphine 5 mg	≈ Oral codeine 60mg or oral dihydrocodeine 60mg	1:10
Oral morphine 10mg	≈ SC morphine 5mg	2:1
Oral morphine 10mg	≈ SC diamorphine 3mg	3:1
Oral morphine 10mg	≈ Oral oxycodone 5mg	2:1
Oral morphine 10mg	≈ SC oxycodone 2-3mg	4:1
Oral morphine 60-90mg in 24hrs	≈ Fentanyl patch 25 micrograms/ hour	See: Fentanyl
Oral morphine 30mg	≈ SC alfentanil 1mg (1000 micrograms)	30:1 See: Alfentanil
Immediate release oxycodone		Oxycodone potency ratio
Oral oxycodone 5mg	≈ SC oxycodone 2-3mg	2:1 See: Oxycodone

Equivalent doses of opioids not generally recommended for palliative care

Opioid dose	Immediate release morphine	Morphine: opioid potency ratio
Oral tramadol 50mg	≈ Oral morphine 5-10mg	1:5 to 1:10
Oral nefopam 30mg	≈ Oral morphine 10mg	1:3
Buprenorphine patches 10 micrograms/ hour	≈ Oral morphine 10mg/ 24 hrs	
35 micrograms/ hour	≈ Oral morphine 30-60mg/ 24 hrs	
52.5 micrograms/ hour	≈ Oral morphine 60-90mg/ 24 hrs	
70 micrograms/ hour	≈ Oral morphine 90-120mg/ 24 hrs	
Oral hydromorphone 1.3mg	≈ Oral morphine 5-10mg	5:1 to 7.5:1

A guide to dose conversions FROM morphine TO second line opioid analgesics used for moderate to severe pain

- Use this chart as a **guide**. The doses are **approximate** and not exact equivalent doses.
 - Opioid bioavailability (particularly for oral morphine) and response are highly variable.
 - Always prescribe an appropriate drug and dose for breakthrough pain: 1/6th of the 24hour regular opioid dose.
 - **Reduce the dose by up to 30% when changing opioid if the patient is opioid toxic, frail or elderly and re-titrate.**
 - **Reduce the dose by up to 30% when converting from a second line opioid back to morphine and re-titrate.**
 - Check the information about individual drugs if the patient has renal or liver impairment.
 - Particular care is needed when changing between opioids at higher doses or when the dose of the first opioid has been rapidly increased as these patients are at greater risk of adverse effects.
- Morphine and oxycodone doses can be measured accurately in 1mg dose increments. Decimal places are not recommended.
 - Fentanyl: dose conversions from oral morphine are usually given as a range for each patch dose. The minimum dose of oral morphine when it would be safe to convert to fentanyl is shown in this table. Check fentanyl guideline.

Monitor the patient carefully

If in doubt – seek advice

A guide to dose conversions FROM morphine TO second line opioid analgesics used for moderate to severe pain →

Oral morphine			Subcutaneous morphine		Subcutaneous diamorphine		Oral oxycodone			Subcutaneous oxycodone		Fentanyl transdermal
4-hr dose	12-hr MR dose	24-hr total dose	4-hr dose	24-hr total dose	4-hr dose	24-hr total dose	4-hr dose	12-hr MR dose	24-hr total dose	4-hr dose	24-hr total dose	Patch strength (micrograms)
2 or 3mg	5mg	15mg	1mg	7 or 8mg	1mg	5mg	1 or 2mg	-	7 or 8mg	1mg	5mg	Do not use
5mg	15mg	30mg	2 or 3mg	15mg	2mg	10mg	2 or 3mg	5mg	15mg	1mg	7 or 8mg	12
10mg	30mg	60mg	5mg	30mg	2.5mg	20mg	5mg	15mg	30mg	2 or 3mg	15mg	25
15mg	45mg	90mg	7 or 8mg	45mg	5mg	30mg	7 or 8mg	20mg	45mg	3mg	20mg	37
20mg	60mg	120mg	10mg	60mg	7.5mg	40mg	10mg	30mg	60mg	5mg	30mg	50
30mg	90mg	180mg	15mg	90mg	10mg	60mg	15mg	45mg	90mg	7 or 8mg	45mg	62
40mg	120mg	240mg	20mg	120mg	10mg	80mg	20mg	60mg	120mg	10mg*	60mg	75
50mg	150mg	300mg	25mg	150mg	15mg	100mg	25mg	75mg	150mg	*	75mg	87
60mg	180mg	360mg	30mg*	180mg	20mg	120mg	30mg	90mg	180mg	*	90mg	100

MR = modified release (long acting)

* Morphine injection is available in a maximum concentration of 30mg/ml. Oxycodone injection is only available as 10mg/ml.

Another SC opioid will be needed for breakthrough pain if patient needs a dose that is in an injection volume above 1ml – **Seek advice**

Constipation in Palliative Care

Introduction

Constipation is the passage of small, hard faeces infrequently or with difficulty, and less often than is normal for that individual.

Assessment

- Normal and current bowel pattern (frequency, consistency, ease of passage, blood present, pain on passing stool).
- Current and previous laxatives taken regularly or as needed, and their effectiveness.
- Clinical features may mimic bowel obstruction or intra-abdominal disease.
 - Pain
 - Nausea/ vomiting, anorexia
 - Flatulence, bloating, malaise
 - Overflow diarrhoea
 - Urinary retention
- Cause of the constipation.
 - Medication: opioids, anticholinergics (hyoscine, cyclizine, tricyclic antidepressants), antacids, diuretics, iron, 5HT₃ antagonists.
 - Secondary effects of illness (dehydration, immobility, poor diet, anorexia).
 - Tumour in, or compressing, bowel wall.
 - Damage to lumbosacral spinal cord, cauda equina or pelvic nerves.
 - Hypercalcaemia.
 - Concurrent disease e.g. diabetes, hypothyroidism, diverticular disease, anal fissure, haemorrhoids, Parkinson's disease, hypokalaemia.
- Clarify cause before starting treatment of constipation.
 - Abdominal and rectal examination are essential.
 - To exclude bowel obstruction/ assess extent of faecal loading, an X-ray may be needed.

Management

General

- Encourage a good oral fluid intake (2 litres a day, if able); review diet.
- Ensure patient has privacy and access to toilet facilities.
- Address any reversible factors causing constipation.
- If current regimen satisfactory and well tolerated, continue it but review patient regularly and explain importance of preventing constipation.

Oral Medication

- Use oral laxatives if possible.
- Rectal treatment may be needed for faecal impaction, and for paraplegic or bedbound patients.
- If rectum is ballooned and empty, do not give rectal treatment.

Option A (combination of stimulant and softener)

Senna 2-4 tablets or bisacodyl 5-10mg, at bedtime in combination with docusate sodium 100mg capsule, twice daily

Option B (osmotic laxative)

Macrogol (Movicol®) 1-3 sachets daily

- Severe constipation; consider a higher dose for three days.

Option C (combined stimulant / softener, licensed for terminally ill patients)

Co-danthramer 1-2 capsules or co-danthramer suspension 5-10ml; at bedtime.

Co-danthramer strong 2 capsules or co-danthramer strong suspension 5ml; at bedtime.

Rectal Treatment

Soft loading: bisacodyl suppository, sodium citrate or phosphate enema.

Hard loading: glycerol suppository as lubricant/ stimulant; then treat as above.

Very hard loading: arachis oil enema overnight, followed by phosphate enema.

Paraplegic or bedbound patient

- Titrate laxatives or loperamide to keep stool firm, but not hard.
- Use rectal treatment every 1-3 days to avoid incontinence or an anal fissure.

Practice points

- Do not use an arachis oil enema if patient has nut allergy.
- Avoid co-danthramer if patient is incontinent as it may cause a local skin reaction.
- Frail or nauseated patients may not be able to tolerate the fluid volume needed with Movicol®.
- Bulk forming laxatives are not suitable if patient has a poor fluid intake and reduced bowel motility.
- Lactulose is not effective without a high fluid intake; causes flatulence and abdominal cramps in some patients.
- Almost all palliative care patients on opioids need a regular oral laxative.
- Review laxative regimen when opioid medication or dose is changed.
- If maximal laxative therapy fails, consider changing opioid to fentanyl.

Patient/ carer advice points

- Co-danthramer colours the urine red.

Resources

Professional

Palliative Care Drug Information online: <http://www.palliativedrugs.com/>

Patient

Patient leaflet on website: Managing constipation

Key references

1. Larkin PJ, Sykes NP, Centeno C. et al. The management of constipation in palliative care: clinical practice recommendations. *Palliative Medicine* 2008;22; 796-807.
2. Miles CL, Goodman ML, Wilkinson S. Laxatives for the management of constipation in palliative care patients (Systematic Review) 2006; Issue 4. The Cochrane Collaboration
3. Sykes N. Constipation. *Oxford Textbook of Palliative Medicine* 3rd Edition 2004: 483-493
4. Scottish Intercollegiate Guideline Network. *Control of pain in patients with cancer*. Edinburgh, 2008. SIGN Secretariat (SIGN 106)
5. Goodman S, Wilkinson S. Constipation management in palliative care. *Journal Pain Symptom Management* 2005; 29:238-44
6. Campbell T et al. The management of constipation in people with advanced cancer. *International Journal Advanced Nursing* 2001; 7(3): 110-119

Laxative drug information chart

Oral laxative	Starting dose	Time to act	Comments
Bisacodyl tablets 5mg	1-2 nocte	6-12 hours	<ul style="list-style-type: none"> Can cause abdominal cramps.
Senna tablets Senna liquid	2-4 nocte 10-20ml nocte	8-12 hours	<ul style="list-style-type: none"> Tablets may be difficult to swallow. Can cause abdominal cramps.
Codanthramer capsules Codanthramer suspension (1 capsule = 5ml) Codanthramer strong capsules Codanthramer strong suspension (2 capsules = 5ml)	1-2 nocte 5-10ml nocte 2 nocte 5ml nocte	6-12 hours	<ul style="list-style-type: none"> Combination laxative containing dantron and a softener. Colours the urine red. Licensed for use in terminally ill patients. Avoid if patient is incontinent as can cause a local skin reaction.
Docusate sodium capsules 100mg	1 twice daily	24-36 hours	<ul style="list-style-type: none"> Mainly a softener. Liquid preparation very unpalatable.
<i>Macrogol (Movicol®)</i>	1-3 sachets daily	1-3 days	<ul style="list-style-type: none"> Made up in 125ml of water per sachet. High dose (up to 8 sachets per day for 1-3 days in impaction). Available in half strength sachets.

Rectal preparations	Starting dose	Time to act	Comments
Bisacodyl suppository 10mg	10mg	15-60 minutes	<ul style="list-style-type: none"> Must be in contact with bowel wall to be effective.
Sodium citrate microenema	1-2	30-60 minutes	
Phosphate enema	1	15-30 minutes	<ul style="list-style-type: none"> Can cause local irritation. Warm to body temperature.
Glycerol suppository	1	15-30 minutes	<ul style="list-style-type: none"> Combined irritant and softener.
Arachis oil enema	1	15-60 minutes	<ul style="list-style-type: none"> Contains peanut oil; contraindicated in nut allergy. Warm to body temperature.

Cough in Palliative Care

Introduction

Cough has a useful protective function but symptomatic treatment may be indicated when it is distressing or affecting sleep/ activity.

Reversible causes should be identified and treated.

Management

- Ensure adequate analgesia – pain may be inhibiting effective coughing.
- Physiotherapy assessment if difficulty coughing retained secretions.

Management of common causes of cough in palliative care

Cancer related causes	Treatment
Stridor due to airway obstruction	Dexamethasone 16mg or prednisolone 60mg (if dexamethasone not available) orally. Seek oncology/ respiratory medicine advice.
Lymphangitis, disease progression	Seek oncology advice; consider a trial of steroids.
Tracheo-oesophageal fistula with aspiration (cough after swallowing)	Seek specialist advice – stenting may be possible.
Ineffective cough (eg due to recurrent laryngeal nerve palsy, weakness, pain)	Supportive care. Vocal cord injection may help a patient with laryngeal nerve palsy – refer to ENT.
Malignant pleural effusion	Consider pleural drainage +/- pleurodesis.
Pneumonitis	Seek oncology advice; corticosteroids.
Other causes	
Smoking	Smoking cessation advice if appropriate.
Aspiration	Antibiotics if infection, or an antisecretory such as hyoscine butylbromide (see: Last days of life).
Gastro-oesophageal reflux	Proton pump inhibitor Prokinetic eg. metoclopramide, domperidone.
Infection	Antibiotics – see local guidelines.
ACE inhibitor	Stop or switch to alternative medication.
Post-nasal drip	Nasal decongestant spray, nasal corticosteroid, antihistamine.
Cardiac failure, COPD, asthma	Optimise treatment.

Medication

- Simple linctus BP 5ml, 3 times daily.
- Nebulised 0.9% sodium chloride 2.5-5ml can help loosen secretions.
- Opioid: titrate according to response, monitor for side effects (eg constipation).
 - o Codeine linctus BP (15mg/ 5ml) 5-10ml, 6-8 hourly and/or at bedtime.
 - o Oral morphine liquid 2mg, 6-8hourly or at bedtime.
 - o Methadone linctus (2mg/5ml) 2.5ml at bedtime (specialist advice only).

Non-drug

- Posture - it is impossible to cough effectively when lying flat.

Key References

1. Morrice AH. British Thoracic Society recommendations for the management of cough in adults. *Thorax* 2006; 61:1-24
2. Leach M. Cough. *Oxford Textbook of Palliative Medicine*, 3rd Edition 2004, p 899-901

Delirium in Palliative Care

Definition

Disturbed consciousness and inattention with cognitive impairment; acute onset and fluctuating course as a physiological consequence of disease or treatment.
(Other terms: acute confusional state, agitation, terminal restlessness)

Assessment

- Common (30-85% of hospice inpatients), often reversible but diagnosed late.
- Three types:
 - Hyperactive – increased arousal and agitation.
 - Hypoactive – quiet, withdrawn and inactive: more common but often missed or misdiagnosed as depression.
 - Mixed pattern.
- Diagnosis depends mainly on careful clinical assessment; consider using Mini-Mental State Examination or Abbreviated Mental Test.
- Causes include:
 - Drugs (including: opioids, anticholinergics, steroids, benzodiazepines, antidepressants, sedatives).
 - Drug withdrawal (alcohol, sedatives, antidepressants, nicotine).
 - Dehydration, constipation, urinary retention, uncontrolled pain.
 - Liver or renal impairment, electrolyte disturbance (Na, Ca, glucose), infection, hypoxia, cerebral tumour or cerebrovascular disease.
 - Visual impairment and deafness are risk factors.

Differential diagnosis: depression, dementia (increased risk of developing delirium).

Management (treat underlying causes)

- If terminal delirium – see: Last days of life.
- Review all medication and stop any non-essential drugs.
- Maintain hydration, oral nutrition and mobility.
- Check for opioid toxicity (drowsiness, agitation, myoclonus, hypersensitivity to touch), reduce opioid dose by 1/3. Consider switching to another opioid if delirium persists.
See: Choosing & Changing opioids.
- Check for constipation, urinary retention or catheter problems.
- Check full blood count and biochemistry, including calcium.
- Check for infection (urine infection in the elderly).
- If nicotine dependent, consider using replacement patches.

Medication (if essential to control symptoms)

- Review regularly and withdraw medication as soon as the patient recovers.

First choice: haloperidol

- Dose: 0.5-3mg oral or subcutaneous (start with a low, oral dose).
- Repeat after 2 hours, if necessary.
- Maintenance treatment may be needed if cause cannot be reversed; use lowest effective dose: 0.5-3mg oral or 2.5mg SC, once daily.

Second choice: benzodiazepines

- Benzodiazepines do not improve cognition; may help anxiety.
- Used in alcohol withdrawal (often at higher doses), sedative and antidepressant withdrawal; preferred in Parkinson's disease.
- Lorazepam 0.5-1mg oral or sublingually.
- Midazolam SC 2.5-5mg, 1-2 hourly OR diazepam oral or PR 5mg, 8-12 hourly.

Medication (cont):

If more sedation is desirable and appropriate:

- Add or increase benzodiazepine (midazolam SC infusion 10-30mg/ 24hours in a syringe driver / pump or diazepam PR 5-10mg, 6-8 hourly).
- Change haloperidol to levomepromazine SC 12.5-25mg, once or twice daily by injection or as a subcutaneous infusion in a syringe driver/pump.

Non-drug

- Explain cause and likely course to patient, relatives and carers.
- Address anxiety; patients with delirium are often very frightened.
- Quiet area or side room; limit staff changes.
- Adequate lighting, minimise noise, provide a clock the patient can see.
- Gentle repeated reorientation and avoid confronting deficits.
- Try to maintain normal sleep-wake cycle.
- Patients who recover recall their experiences; explain the organic cause of their behaviour and symptoms.

Practice points

- Attention to the environment is essential.
- Opioid toxicity is a common cause of delirium, particularly in the elderly.
- Corticosteroids can cause florid delirium.
- Hypoactive delirium is frequently missed or misdiagnosed.
- Atypical antipsychotics offer no advantage over haloperidol.
- Adults with Incapacity Act covers the medical treatment of patients with cognitive impairment. See: Adults with Incapacity Act on website.
- In the acute situation, emergency treatment can be given without an Incapacity certificate if this is in the patient's best interest.

Patient / carer advice points

- Encourage the patient to keep taking oral fluids if able.
- The presence of a close relative or friend can help reassure the patient.

Resources

Professional

British Geriatrics Society Guidelines: <http://www.bgs.org.uk>

Patient

Mental Health Foundation: <http://www.mentalhealth.org.uk>

Key references

1. Young J, Inouye SK. Delirium in Older People. *BMJ* 2007; 334:842-6
2. Siddiqi N, House A. Delirium: an update on diagnosis, treatment and prevention. *Clinical Medicine* 2006; 6:540-543

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Depression in Palliative Care

Introduction

- All patients should be assessed for depression.
- Depression
 - is strongly and consistently associated with a poor quality of life.
 - causes more reduction in role and social functioning than would be due to the physical illness alone.
 - reduces physical functioning.
 - is often associated with symptoms that are difficult to control.
 - has a major impact on the patient's family.
- Treatment of depression can significantly improve quality of life and is as effective in palliative care as in other situations.

Assessment

- Physical symptoms commonly associated with depression may be due to physical illness or treatment so are less helpful in making a diagnosis.
 - Weight/appetite change
 - Insomnia
 - Loss of energy
 - Fatigue
 - Psychomotor slowing
 - Loss of libido
- Depressive symptoms in palliative care patients include:
 - Greater severity of dysphoric mood.
 - Excessive feelings of hopelessness, guilt, worthlessness.
 - Social withdrawal; loss of pleasure in daily activities.
 - A wish for earlier death (or suicidal thoughts).
 - A positive response to the question "Do you feel depressed?"
- Risk factors:
 - Personal or family history of depression.
 - Concurrent life stresses.
 - Absence of social support.
 - Oropharyngeal, pancreatic, breast and lung cancers (more common).
- Additional barriers to diagnosis:
 - Patient/family feeling that a "fighting spirit" is needed to maximise active treatment/ support from health professionals.
 - Difficulty deciding if depression is a primary problem or whether improving other symptoms would improve mood.
 - Concerns about polypharmacy and drug interactions.
 - Other physical/ psychological conditions mimicking depression.
 - Exclude hypoactive delirium (see: Delirium).
 - Review medication (haloperidol can cause motor retardation).
 - Complex care packages; many staff involved and lack of continuity.

Assessment tools:

- In primary care, the PHQ-9 is used as a screening tool.
- The Brief Edinburgh Depression Scale is suited to palliative care patients.
- The Hospital Anxiety and Depression questionnaire is widely available but relies on physical symptoms so may be less helpful.

Management

General

- In mild depression, psychological support can be as effective as medication.
- Adequate pain control may improve depressive symptoms significantly.
- Spiritual distress may be a component of depression, or distinct from it.
- Consider supportive psychotherapy or cognitive behavioural therapy.
- Patients with severe depression and/or suicidal ideation are uncommon but should be referred to psychological medicine / psychiatry for assessment.

Medication

- There is little difference in efficacy between antidepressants.
- Consider side effects and any co-morbid illnesses; check for drug interactions.
- A current or previously effective antidepressant should be used unless contraindicated.

Selective serotonin reuptake inhibitors (SSRI)

- o Sertraline:
 - 1st choice if recent cardiac event; normal dose in renal failure.
- o Citalopram: tablet and oral suspension
 - few drug interactions; useful for agitated depression/ anxiety; relatively safe if patient is at risk of seizures.
- o Fluoxetine:
 - long acting so low withdrawal risk; many drug interactions so may not be suitable in palliative care patients.

Side effects:

- nausea, vomiting, anorexia, dyspepsia, diarrhoea.
- risk of gastrointestinal bleeding – avoid or use with caution if history of GI bleeding, patient over 80 or taking NSAID/ aspirin.
- insomnia, sweating, impaired sexual function.
- vivid dreams, agitation, hyponatraemia.

Mirtazapine

- tablet and oro-dispersible tablet.
- sedative, particularly at lower doses; appetite stimulant.
- well tolerated in the elderly and patients with heart failure or diabetes.

Tricyclic antidepressants

- o Amitriptyline: also treats nerve pain.
- o Lofepramine: better tolerated than other tricyclics.

Side effects:

- avoid if cardiac disease or risk of seizures.
- dry mouth, hypotension and confusion limit dose.
- sedative/ anxiolytic action may be helpful.

Practice point

Antidepressants should be withdrawn gradually, if possible.

Resources

Professional

<http://www.depression-primarycare.org/clinicians/toolkits/materials/>

Patient

<http://www.patient.co.uk/>

Key reference

1. Lloyd-Williams M. Diagnosis and treatment of depression in palliative care. *European J Pall Care* 2002; 9(5): 186-8

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

What happens when someone is dying?

This leaflet aims to answer some of the questions you may have about the changes that happen when someone is close to death.

The process of dying is unique to each person. It can last a few hours or several days. Do ask your nurse or doctor if you need more help or information.

Everyone is different, but in most cases there are common signs and changes that show a person may be close to death.

1. Less need for food and drink

- As people get more unwell, it is normal for them not to feel like eating or drinking. When this happens it can be upsetting because we want to do everything to help the people we care for.
- Eating and drinking becomes more of an effort. The person needs help to take sips of fluid. A drinking beaker or straw can make sipping fluid easier. Moistening the person's lips and tongue with water or oral gel helps keep them comfortable.
- A drip is occasionally used to give people fluid into a vein or under the skin. As the process of dying continues the body does not need the same amount of fluid and cannot cope with it. Fluid from a drip can make breathlessness worse as it tends to build up in the lungs, and staff may advise that a drip is stopped.

2. Changes in breathing

- When someone is dying their need for oxygen may lessen and the way they breathe changes. People who have been breathless may feel less breathless at this time.
- As people get more unwell, their breathing may pause for a while and then start again. They use different muscles to breathe, which means their breathing will look different. Sometimes breathing can sound noisy or "rattling" because the person is no longer able to cough or clear their throat. This can sound distressing but is generally not upsetting for the person. Often changing the person's position can reduce the noise of breathing or an injection of medicine may be given.

3. Changes in how the person looks and behaves

- During the process of dying a person's skin may become pale and moist. Their hands and feet can feel very cold and sometimes look bluish in colour.
- Dying people often feel very tired and will sleep more. Even when they are awake, they may be drowsier than they have been. As people get more unwell they will be awake less and less. They will eventually not waken up at all. They may still be aware of the presence of family and friends so you can still talk to them.
- If you are worried about what is happening or have any questions, do ask.

Emergencies in Palliative Care

Introduction

- Patients receiving palliative care may deteriorate suddenly due to their illness or another acute medical or surgical problem.
- Management options depend on life expectancy, level of intervention needed, and an assessment of risks, benefits, side effects and likely outcome.
- Symptom control and supportive care may be the most appropriate management if the patient is dying. (see: Last days of life)
- Discuss treatment options with the patient and family. If possible discuss and document the patient's wishes in advance including those about resuscitation, hospital admission and transfer to an intensive care unit.
- Emergency treatment can be given but ongoing treatment in a patient lacking capacity to consent requires a Section 47 Certificate. (see: Adults with Incapacity Act on website)
- This guideline covers the following palliative care emergencies:
 - Bleeding events
 - Hypercalcaemia
 - Seizures
 - Spinal cord compression

Bleeding

- Acute haemorrhage can be very distressing for the patient and family.
- It is usually best to discuss the possibility with the patient and their family.
- An anticipatory care plan is helpful. This includes having sedative medication prescribed for use if needed.
- If the patient is at home, discuss options for sedation if family carers feel able to use these.
- Discuss resuscitation; document and communicate resuscitation status.
- Make sure all professionals / services involved are aware of the care plan, including out of hours services.

Management of severe, acute bleeding

Non-drug

- Call for help. Ensure carers at home have an emergency contact number.
- Put the patient in the recovery position.
- Apply direct pressure to any bleeding area; dark coloured towels are best.
- If resuscitation is appropriate, admit to hospital and manage according to local protocols for haemorrhage.
- If the patient has a massive haemorrhage and is clearly dying, support and non-drug interventions are more important until help arrives than trying to give sedative medication as the patient will usually lose consciousness rapidly.

Sedative medication

- If the patient is distressed, titrated doses of a rapidly acting benzodiazepine are indicated. The route of administration guides the choice of drug.
 - o IV access available: midazolam 5-20mg IV or diazepam (emulsion for IV injection) 5-20mg IV in small boluses until settled.
 - o IM injection: midazolam IM 5-10mg can be given into the deltoid muscle.
 - o Rectal route or via a stoma: diazepam rectal solution 5-10mg.
 - o Sublingual: midazolam 10mg can be given using the parenteral preparation or the buccal liquid (special order product).

Hypercalcaemia in Palliative Care

Introduction

- Hypercalcaemia is the commonest life-threatening metabolic disorder in cancer patients.
- Occurs most frequently in myeloma, and in breast, renal, lung and thyroid cancer.
- 20% of patients with hypercalcaemia do not have bone metastases.
- Common symptoms: malaise, thirst, nausea, constipation, polyuria, delirium.
- Treatment may not be appropriate in a dying patient at the end of life – seek advice.
- To reduce risk of renal toxicity from bisphosphonate treatment, consider withholding medication that affects renal function (eg. NSAIDs, diuretics, ACE inhibitors).

Patient presents with symptoms suggestive of hypercalcaemia.

Check calcium + urea & electrolytes, eGFR, albumin

Corrected calcium *
> 4.0mmol/L

Severe hypercalcaemia
can cause seizures
or arrhythmias - seek
consultant advice

Corrected calcium *
2.6 - 4.0mmol/L

Rehydrate with 1-3litres 0.9% NaCl IV
-check calcium, U & E next morning

Corrected calcium
normal *

Monitor calcium if
patient at risk of
hypercalcaemia.

Calcium is still raised – treat with pamidronate IV (reduce dose in renal impairment)♦

Corrected calcium (mmol/L)	Pamidronate dose	Diluent & maximum infusion rate
2.6 – 3.0	30mg	500mls NaCl 0.9% over > 60 minutes
3.0 – 3.5	60mg	500mls NaCl 0.9% over > 60 minutes
3.5 – 4.0	90mg	500mls NaCl 0.9% over > 90 minutes
> 4.0	90mg	500mls NaCl 0.9% over > 90 minutes

If calcium >3.0mmol/l, some units routinely give pamidronate 90mg as a higher dose may increase response and delay relapse.

Review treatment of
underlying cancer.

Continue IV fluids until patient able
to maintain oral hydration.

Calcium has
increased from
pre-treatment level
after rehydration
and pamidronate.

Seek advice; review
diagnosis and
treatment plan.

Monitor renal function.

Recheck calcium after 5 days.

Calcium has decreased from
pre-treatment level but is
still elevated.

Calcium normal

Maintain good hydration;
recheck calcium after 2-3
days. Do not repeat
pamidronate until 7 days
after first dose to avoid
causing hypocalcaemia.

♦ Pamidronate in renal impairment: seek advice

- GFR >20ml/min: give pamidronate over at least 90 minutes.
- GFR <20ml/min: consider risks & benefits of pamidronate. Maximum infusion rate 20mg/hr; consider dose reduction.

* Corrected calcium =
measured calcium +
(40 - serum albumin) X 0.02

Seizures in Palliative Care

Introduction

- Seizures (generalised or partial) occur in 10-15% of palliative care patients most often due to primary or secondary brain tumours, cerebrovascular disease, epilepsy, or biochemical abnormalities (eg. low sodium, hypercalcaemia, uraemia).
- An advance care plan is needed if the patient wishes to avoid hospital admission.

Assessment

- Exclude other causes of loss of consciousness or abnormal limb/ facial movement. (eg vasovagal episode (faint), postural hypotension, arrhythmia, hypoglycaemia, extrapyramidal side effects from dopamine antagonists, alcohol).
- Find out if the patient has had previous seizures or is at risk - history of epilepsy, previous secondary seizure, known cerebral disease.
- Is there a problem with usual antiepileptic drug therapy – unable to take oral medication, drug interactions – check BNF (eg.corticosteroids reduce the effect of carbamazepine, phenytoin).

Management

Acute seizure management

- Put the patient in the recovery position; move any objects that might cause injury.
- If seizure does not resolve quickly, anticonvulsant medication is needed.

Treatment options

- In hospital, diazepam (emulsion) IV in 2mg bolus doses up to 10mg or lorazepam 4mg by slow IV injection are used.
- Diazepam rectal solution 10-30mg given PR or via a stoma.
- Midazolam SC 5mg, repeated after 5 minutes.
- Buccal midazolam 10mg can be given using the parenteral preparation or the buccal liquid (special order product).

Persistent seizures

- IV phenytoin is used in hospital settings.
- Phenobarbital can be given as 100mg IM bolus dose followed, if needed, by a subcutaneous infusion of phenobarbital 200-400mg diluted in water for injection over 24 hrs. Seek advice from a palliative care specialist.

Chronic seizure control

- Most patients with a structural cause for seizures benefit from treatment.
- Follow SIGN guideline recommendations. Check BNF for drug interactions.
 - o Partial or secondary generalised seizures
 - sodium valproate, carbamazepine or lamotrigine.
 - o Primary generalised seizures – sodium valproate or lamotrigine.
- Dying patient unable to take oral medication - antiepileptics have a long half life so additional anticonvulsant treatment may not be needed.
 - o Midazolam SC 5mg or diazepam rectal solution PR 10mg, if required.
 - o Midazolam SC 20-30mg infusion over 24 hrs can be used as maintenance therapy.

Practice points

- Phenytoin is no longer a first line drug for chronic seizure control. It interacts with many drugs, and is prone to cause side effects including sedation in palliative care patients.

Professional resource

SIGN Guideline 70 (Epilepsy in Adults): <http://www.sign.ac.uk/>

Spinal Cord Compression

Definition

Malignant spinal cord compression occurs when the dural sac and its contents are compressed at the level of the cord or cauda equina.

- It affects about 5% of patients with cancer. Lung, breast, and prostate cancer are the commonest causes but it occurs in other cancers.
- Cord compression can be the initial presentation of cancer.
- Late diagnosis is common causing permanent loss of function and significant morbidity.

Assessment

- Consider cord compression in any patient with cancer.
- Thoracic cord compression is commonest but any part of the spine and multiple sites can be affected.
- Sites of pain and level of compression do not always correlate; X-rays and bone scans can be misleading.
- **Key signs and symptoms**
 - New, progressively severe back pain (particularly thoracic).
 - New spinal nerve root pain (burning, shooting, numbness) – may radiate down anterior or posterior thigh (like sciatica), or like a band around the chest or abdomen.
 - Coughing, straining or lying flat may aggravate pain.
 - New difficulty walking or climbing stairs; reduced power (motor weakness), sensory impairment or altered sensation in limbs.
 - Bowel or bladder disturbance - loss of sphincter control is a late sign with a poor prognosis.
- A full neurological examination should be done but may be normal initially.
- MRI is the correct investigation - images the whole spine.

Cauda equina syndrome

Compression of lumbosacral nerve roots below the level of the cord itself results in a different clinical picture.

- New, severe root pain affecting low back, buttocks, perineum, thighs, legs.
- Loss of sensation often with tingling or numbness in the saddle area.
- Leg weakness, often asymmetrical.
- Bladder, bowel and sexual dysfunction – occur earlier than in cord compression. Loss of anal reflex.

Management

- **Emergency referral is essential** – see local protocol for your NHS Board.
- High dose **dexamethasone**, unless contraindicated, should be started as soon as a diagnosis of cord compression is suspected: 16mg orally and then daily in the morning. Withdraw gradually after radiotherapy treatment.
- If clinical suspicion of spinal instability, transport as a spinal injury.
- Pain control – see Pain Management.
- If there is complete paraplegia and loss of sphincter control, radiotherapy may improve pain control but is unlikely to restore function.
- Patients with residual disability need a full multidisciplinary assessment and continuing supportive care including physiotherapy, occupational therapy, pressure area care, bladder and bowel care; social care, psychological and family support.

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Fatigue in Palliative Care

Introduction

A persistent, subjective feeling of tiredness, weakness or lack of energy (physical or mental) related to cancer or advanced chronic illness.

- Common (70-100% of patients receiving cancer treatment).
- Not related to level of activity. Not alleviated by rest or sleep.
- Affects physical function, cognitive ability, emotional and spiritual well-being.
- Multiple contributory causes but exact aetiology poorly understood.
- Fatigue is common in the last days of life and part of a normal dying process.

Assessment

Palliative care patients should be screened for fatigue and its impact.

- Symptom pattern, duration; associated or alleviating factors.
- Interference with function and quality of life.
- Severity: mild, moderate or severe, or rated on a 0-10 scale.

Disease status and treatment:

- Exclude cancer recurrence or progression.
- Hormone treatment often causes fatigue.
- Review medication - beta-blockers, sedative drugs, corticosteroids, opioids.

Contributing factors and associated symptoms: (see: relevant guidelines)

- pain
- anxiety, depression
- sleep disturbance
- anaemia
- poor nutrition or absorption
- fluid /electrolyte imbalance: check sodium, potassium, calcium, magnesium
- de-conditioning due to reduced activity level/ fitness or muscle wasting
- co-morbidities
 - o chronic infection
 - o cardiac or respiratory disease
 - o renal or hepatic impairment
 - o hypothyroidism, adrenal insufficiency, hypogonadism

Management

Combination of approaches tailored to the individual patient is likely to be required.

- Acknowledge the reality of the symptoms, and their effect on the patient /family.
- Explore understanding of the illness/treatment; explain possible causes of fatigue.
- An activity/ fatigue diary may help identify precipitants/ timing of symptoms.

Physical activity:

Graded exercise, both aerobic and strength training; consider physiotherapy referral.

Energy conservation: set priorities; pace; schedule activities at times of peak energy; eliminate non-essential activities; short daytime naps if sleep at night is not affected; attend to one activity at a time; conserve energy for valued activities.

Psychosocial interventions: stress management; relaxation therapy; sleep hygiene.

Medication:

- For cancer patients with anorexia/ cachexia related fatigue (see: Anorexia).
- Insufficient evidence to support the use of psychostimulants by non-specialists.

Resources

National Comprehensive Cancer Network Guideline: www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf
Patient leaflet on website: Managing fatigue

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Fentanyl Patches in Palliative Care

Description Potent opioid analgesic in a topical patch lasting 72 hours.

Preparations

Matrix patch	12, 25, 50, 75,100 micrograms/hour	Durogesic D-Trans® Matrifen®
Reservoir patch	25, 50, 75,100 micrograms/hour	Durogesic® Tilofyl®

Patients should stay on the same preparation and not switch formulation/ brand.

Indications

- **Second line** opioid for moderate to severe opioid responsive pain.
- Pain that is stable.
- Oral and subcutaneous routes are not suitable.
- Patient unable to tolerate morphine/ diamorphine due to persistent side effects.
- Compliance is poor, but supervised patch application is possible.

Cautions

- Fentanyl is a potent opioid analgesic; check the dose carefully. 25 microgram fentanyl patch is equivalent to about 60-90mg of oral morphine in 24 hours.
- Frail or elderly patients may need lower doses and slower titration.
- Heat increases the rate of fentanyl absorption. This can occur if patient is febrile or the skin under the patch is heated. Avoid direct heat sources, use anti-pyretic measures.
- **Liver impairment:** dose reduction may be needed in severe liver disease.
- **Renal impairment:** no initial dose reduction. May accumulate gradually over time. Monitor patient and reduce dose. Fentanyl is not usually removed by dialysis.
- If the patient has unstable pain or pain likely to change following treatment, do not start fentanyl. Seek advice and consider alternative opioids.

Side effects

- Similar to morphine but less constipation, nausea.
- If signs of opioid toxicity (eg sedation, delirium), remove the patch and seek advice. Fentanyl will be released from the site for up to 24 hours. Monitor the patient for 24-48 hours.
- Titrated naloxone is only needed for life-threatening, opioid induced respiratory depression (see: Naloxone).
 - o A low respiratory rate < 8 respirations/minute.
 - o Oxygen saturation <85%, patient cyanosed.
- An allergic reaction to the patch adhesive can occur – change opioid.

Dose & Administration

Starting a fentanyl patch

1. Choose a suitable patch - matrix patch allows titration in smaller increments.
2. Calculate the dose of fentanyl from the conversion chart given here or seek advice. Patch strengths can be combined to provide an appropriate dose.
3. The 12 microgram patch is licensed for dose titration, but may be used for patients needing a lower starting dose if recommended by a specialist.

Starting a fentanyl patch (continued)

4. Make sure the patient takes another regular opioid for the first 12 hours after the patch is first applied to allow the fentanyl to reach therapeutic levels:

Immediate release (quick acting) morphine or oxycodone	Apply patch; continue the immediate release opioid 4 hourly for the next 12 hours.
Modified release (long acting) 12 hourly morphine or oxycodone	Apply patch when the last dose of a 12 hourly, modified release opioid is given.
Subcutaneous infusion of morphine, diamorphine, oxycodone or alfentanil	Apply the patch and continue the infusion for the next 12 hours, then stop the infusion.

5. An immediate release opioid (e.g. oral morphine or morphine SC) must be available 1-2 hourly, as required, for breakthrough pain or to treat any opioid withdrawal symptoms (diarrhoea, abdominal pain, nausea, sweating). These can occur during the fentanyl initiation period due to the variable time to reach steady state. The correct 4 hourly equivalent dose should be used.
6. Change the patches every third day (72 hours) at about the same time.
7. Fentanyl is often less constipating than morphine; half dose of any laxative and titrate.

Adjusting the fentanyl patch dose

Review the fentanyl patch dose after 72 hours; drug levels will be at steady state.

- a) If the patient shows signs of opioid toxicity (drowsiness, confusion), reduce the dose and reassess the pain. Seek advice.
- b) If the patient still has pain which is opioid responsive, titrate the fentanyl dose in 12-25microgram/hour increments depending on the patch type in use. Remember to include the breakthrough doses used. It will take 12-24 hours for the new dose to take effect so give breakthrough analgesia at the correct dose, as required.

Changing fentanyl patches to another opioid

Fentanyl accumulates in the skin under the patch. It can persist for up to 24 hours after patch removal. Patients should be monitored carefully for signs of opioid toxicity for 24-48 hours if fentanyl is changed to another opioid.

1. Remove the fentanyl patch; prescribe an immediate release opioid, 1-2 hourly, as required, for the first 24 hours.
2. Calculate the opioid dose by converting from fentanyl to immediate release oral morphine using the conversion chart. Reduce the dose by 1/3rd.
3. To convert to any other immediate release opioid, refer to Choosing & changing opioids. Seek advice if in doubt.

Example of an initial dose calculation when discontinuing a fentanyl patch		
Fentanyl patch dose	Oral morphine dose	Subcutaneous morphine dose
50 micrograms/ hr x 72 hrs	20 mg, 1-2 hourly	10mg, 1-2 hourly

Remember that all opioid conversions are approximate; monitor the patient.

4. After 24 hours, review the doses used and prescribe a regular, 4 hourly dose of immediate release opioid in addition to the correct as required dose.
5. Titrate the patient's opioid requirements for at least 48 hours before converting to a modified release (long acting) opioid or a subcutaneous opioid infusion.

Fentanyl patches in the last days of life

1. If a patient is semi-conscious or close to death, continue the fentanyl patch, changing it every 72 hours.
2. If a new, opioid responsive pain develops, use subcutaneous morphine as required for breakthrough pain. Use the conversion chart to calculate the dose of morphine.
3. After 24 hours, the breakthrough doses of morphine given in that period can be totalled and this dose of morphine administered as a SC infusion in a syringe driver or pump over the next 24 hours in addition to the fentanyl patch.

Dose Conversions

- All opioid dose conversions are approximate.
- Round the dose down if the patient is pain free or frail; round up if the patient has pain and is less unwell or younger.
 - Reduce the dose by up to 30% when changing opioid if the patient is opioid toxic, frail or elderly and re-titrate.
 - Reduce the dose by up to 30% when converting from fentanyl back to morphine or another opioid and re-titrate.
- Patients should be monitored closely so that the dose can be adjusted if necessary.
- Manufacturers of the various formulations of fentanyl have issued different recommendations for dose conversion, as have drug regulatory bodies.
- Fentanyl is approximately 100-150 times more potent than oral morphine; this table provides a **guide** to dose conversions, but if in doubt seek advice.

Immediate release oral morphine ¹	Fentanyl patch dose (micrograms/hour)	24 hour oral morphine dose
5-10mg	12	30-60mg
10-15mg	25	60-90mg
15-20mg	37	90-120mg
20-30mg	50	120-180mg
30-40mg	62	180-240mg
40-50mg	75	240-300mg
50-60mg	87	300-360mg
60mg	100	360mg

¹ Assuming use of about 1/6th of the 24hour oral morphine dose.

- Converting from fentanyl given by IV infusion or via a PCA device.
 - Calculate the hourly dose of fentanyl (micrograms/ hour)
 - Prescribe the patch strength closest to this dose (micrograms/ hour)
 - Continue the IV fentanyl for the first 12 hours after the patch is applied.

Fentanyl patch care

- Apply to intact, non-hairy skin on the upper trunk or upper arm; avoid areas treated with radiotherapy, scar tissue or oedematous areas.
- Apply each new patch to a different skin site; clean the skin with water only as soap products can alter absorption. Make sure skin is dry.
- Fentanyl patches should not be cut.
- Record the date, time and site if the patch is changed by different people.
- Change the patch every 72 hours at about the same time of day.
- Check the patch daily to ensure it is still in place.
- If patch adherence is poor, use an adhesive dressing or tape; fentanyl is unsuitable for patients with marked sweating.
- Used patches still contain active drug. Fold the patch over so it sticks together. Dispose of it safely (sharps bin for inpatients, domestic waste in the community). Wash your hands after patch changes.

Heat / pyrexia increases the absorption of fentanyl and can cause toxicity.

- Avoid direct contact with heat (eg. hot water bottle, heat pad).
- Showering is possible as the patches are waterproof, but avoid soaking in a hot bath, saunas or sunbathing.
- If the patient has a persistent temperature of 39°, the patch dose may need reviewed.

Practice points

- Fentanyl patches are used for moderate to severe, **stable** pain.
- Do not change formulation/ brand.
- Do not change fentanyl patches to another opioid in a dying patient, continue the fentanyl patch and use an additional opioid as required.

Resources

Professional

Palliative Care Drug Information online: <http://www.palliativedrugs.com/>

Patient

Patient leaflet on website: Fentanyl patches

Discharge planning/ community use

- The same patch formulation should be prescribed and dispensed consistently for each patient.
- Ensure patients understand the safe use, storage and disposal of the patch, and the importance of not heating the skin under the patch.

Key references

1. Donner B. Long term treatment of cancer pain with transdermal fentanyl. *J Pain Symptom Management* 1998; 15:168-175.
2. Ahmedzai S. Transdermal fentanyl versus sustained release oral morphine in cancer pain: preference, efficacy and quality of life. *J Pain Symptom Management* 1997; 13:254-261.
3. Fine PG. Fentanyl in the treatment of cancer pain. *Seminars in Oncology* 1997; 24(5): 20-27.
4. Dean M. Opioids in renal failure and dialysis patients. *J Pain Symptom Management* 2004;25(5): 497-504.
5. Twycross R, Wilcock A. Eds. *Palliative Care Formulary* (3rd Edition) 2007, Palliativedrugs.com Ltd., Nottingham.

Fentanyl Patches

Other names: Durogesic D-trans®, Matrifen®, Durogesic®, Tilofyl®

You should stay on the same brand of fentanyl unless your doctor changes it. Check the name of the medicine on the box.

Q. What is fentanyl used for?

A. Fentanyl is used for moderate to severe pain that has not been well controlled on other regular pain killers. Fentanyl is used to control on-going pain. It is not used for pain that only lasts for a short time. You will be given a different, quick acting pain killer for breakthrough pain if you need it.

Q. How do I take fentanyl?

A. The fentanyl is inside a patch with a sticky back that is stuck on to the skin. The medicine passes from the patch through the skin into the body. Each patch is used once. The patches are waterproof so you can have a shower or go swimming. Check that the patch is still in place each day.

Q. How long does a fentanyl patch last?

A. Each patch lasts for three days. Change your patch (or all your patches) every third day, at about the same time of day. Use a calendar to record the day when you need to change your patch. You should not stop using fentanyl suddenly.

Q. How do I change my patch?

- A. (1) Wash your hands before and after changing your patch. Used patches still contain some of the medicine so need to be disposed of carefully. Take the old patch off, fold it in half so that it sticks together firmly and put it back in its original packet. The used patch can then be put in the bin with your household rubbish. Return any unused patches to your pharmacy.
- (2) Choose a place on the upper body or upper arm. The skin should not have any cuts, scars or spots and should not be too hairy. Clean the skin with water only – not soap. Make sure it is cool and completely dry.
- (3) Tear the packet with the new patch open. Peel off the plastic backing. Stick the patch on to the clean area of skin. Press it on firmly. Do not stick the patch on the same place twice in a row.
- (4) Keep patches, like all medicines, in a safe place and away from children.

Q. What do I do if a patch falls off or I forget to change it?

A. Stick a new one on as soon as you can. If you are very late changing your patch, you may need to take another pain killer until the fentanyl starts working again.

Q. What should I do if I still get pain while using fentanyl?

A. When you first start fentanyl or the dose is increased it takes time to work. Your doctor will give you extra pain killers to take if you need them until your patch is working. Some people find that doing certain things like having a bath or going for a walk brings on pain. Your doctor or nurse may suggest you take a quick acting pain killer before you start doing something that brings on pain.

If your pain is not well controlled and you need to take more than 2-3 doses of extra pain killer a day, tell your doctor or nurse.

Q. How will I know if fentanyl is not going to work for some of my pain?

A. Although fentanyl is a very good pain killer, it does not help all types of pain. You may still have pain despite using bigger doses of fentanyl and may feel unwell if the dose is too high. The answer below tells you what signs to look for.

Tell your doctor or nurse if this happens. Your doctor may need to reduce your dose of fentanyl and suggest other treatments to help the pain.

Q. Are there any side effects from using fentanyl?

A. Fentanyl is a safe and effective pain killer but can have side effects. It is important to know when the dose might be too high.

- **Too high a dose of fentanyl:**

Contact your doctor or nurse if you:

- are more sleepy than usual
- become muddled or confused
- have more difficulty walking or talking than usual

Contact a doctor urgently if the patient has:

- shallow breathing
- marked sleepiness
- a slow pulse or cold clammy skin

- **Heat effects:**

Heat speeds up the way the fentanyl is released from the patch.

- Avoid direct heat on the patch like a hot water bottle, electric blanket, heat pad, or heat lamp.
- Do not soak in a hot bath or sunbathe while using fentanyl patches
- If you develop a fever, try to keep your temperature down and contact your doctor if your temperature is 39° or higher.

- **Changing from another pain killer:**

A few people who change from another pain killer to fentanyl feel unwell in the first 24-48 hours with sickness, shivering, stomach pains or diarrhoea. Contact your doctor if this happens.

- **Constipation:**

Fentanyl tends to cause less constipation than some other strong pain killers but you may still need to take a laxative regularly.

- **Skin/rash irritation:**

If you develop itching or redness under the patch, tell your doctor or nurse.

- **Patch falls off frequently:**

Sweating or applying the patch to hairy skin may prevent it sticking well. Your nurse can give you some sticky tape or a dressing to keep the patch on.

Clipping or shaving excess hair may be needed in some people – do not use shaving foam, gel or soap as they affect the way the medicine goes into the skin.

Q. Can I drive?

A. You may be able to drive but you must discuss this with your doctor.
(Patient information leaflet: Strong pain killers and driving).

Q. Can I drink alcohol?

A. A small glass of wine, beer, sherry or whisky may help you feel better and improve your appetite. It is best to avoid taking more than this as you may become too drowsy.

(Discuss this leaflet with your doctor or nurse who will answer any questions you may have)

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Hiccup in Palliative Care

Introduction

Hiccups lasting more than 48 hours are not uncommon in patients with advanced cancer and can be very distressing.

Assessment

- Causes in patients with advanced cancer include:
 - Gastric stasis and distension (most common cause)
 - Gastro-oesophageal reflux
 - Metabolic disturbances (eg. uraemia, hypercalcaemia)
 - Infection
 - Irritation of diaphragm or phrenic nerve
 - Hepatic disease/ hepatomegaly
 - Cerebral causes (e.g. tumour, metastases)

Management

- Treat reversible factors.
- Hiccups often stop spontaneously. Treatment is only required if hiccups are persistent.
- Try simple physical manoeuvres initially and those that worked previously.

Medication

- Prokinetic: domperidone or metoclopramide oral 10-20mg, 8hourly.
- Treat any gastro-oesophageal reflux with a proton pump inhibitor.
- Dexamethasone oral 4-8mg in the morning may reduce compression/ irritation if the patient has a hepatic or cerebral tumour. Stop if no benefit after a week.
- Other options for intractable hiccups supported by limited evidence include:
 - haloperidol oral 0.5-1mg at bedtime for under 2 weeks to avoid side effects.
 - baclofen oral 5-20mg, 8 hourly (avoid abrupt withdrawal).
 - levomepromazine oral 3-6mg at bedtime (now used as an alternative to chlorpromazine; avoid if hypotensive).
 - nifedipine oral 5-20mg, 8 hourly (avoid if hypotensive).
- If other treatments are unsuccessful and the patient is very distressed, try midazolam SC 10-30mg / 24hours as an infusion via a syringe driver or pump, reducing the dose as the patient improves.

Non-drug

- Simple measures or 'home remedies' can be effective.
 - Sipping iced water or swallowing crushed ice.
 - Breathing into a paper bag particularly if the patient is hyperventilating.
 - Interrupting normal breathing e.g. holding breath.
 - Rubbing the soft palate with a swab to stimulate the nasopharynx.
- Acupuncture may be effective.

Resources

Professional

NHS National Library for Health: http://cks.library.nhs.uk/hiccups/quick_reference_guide

Patient

http://cks.library.nhs.uk/hiccups/patient_information

Key references

1. Regnard C. Hiccup. In *Oxford Textbook of Palliative Medicine*. 3rd Edition 2004, p477-9
2. Back I. *Palliative Medicine Handbook* <http://www.pallcare.info/>

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Hypercalcaemia in Palliative Care

Introduction

- Hypercalcaemia is the commonest life-threatening metabolic disorder in cancer patients.
- Occurs most frequently in myeloma, and in breast, renal, lung and thyroid cancer.
- 20% of patients with hypercalcaemia do not have bone metastases.
- Common symptoms: malaise, thirst, nausea, constipation, polyuria, delirium.
- Treatment may not be appropriate in a dying patient at the end of life – seek advice.
- To reduce risk of renal toxicity from bisphosphonate treatment, consider withholding medication that affects renal function (eg. NSAIDs, diuretics, ACE inhibitors).

Patient presents with symptoms suggestive of hypercalcaemia.

Check calcium + urea & electrolytes, eGFR, albumin

Corrected calcium *
> 4.0mmol/L

Severe hypercalcaemia
can cause seizures
or arrhythmias - seek
consultant advice

Corrected calcium *
2.6 - 4.0mmol/L

Rehydrate with 1-3litres 0.9% NaCl IV
-check calcium, U & E next morning

Corrected calcium
normal *

Monitor calcium if
patient at risk of
hypercalcaemia.

Calcium is still raised – treat with pamidronate IV (reduce dose in renal impairment)♦

Corrected calcium (mmol/L)	Pamidronate dose	Diluent & maximum infusion rate
2.6 – 3.0	30mg	500mls NaCl 0.9% over > 60 minutes
3.0 – 3.5	60mg	500mls NaCl 0.9% over > 60 minutes
3.5 – 4.0	90mg	500mls NaCl 0.9% over > 90 minutes
> 4.0	90mg	500mls NaCl 0.9% over > 90 minutes

If calcium >3.0mmol/l, some units routinely give pamidronate 90mg as a higher dose may increase response and delay relapse.

Review treatment of
underlying cancer.

Continue IV fluids until patient able
to maintain oral hydration.

Calcium has
increased from
pre-treatment level
after rehydration
and pamidronate.

Seek advice; review
diagnosis and
treatment plan.

Monitor renal function.

Recheck calcium after 5 days.

Calcium has decreased from
pre-treatment level but is
still elevated.

Calcium normal

Maintain good hydration;
recheck calcium after 2-3
days. Do not repeat
pamidronate until 7 days
after first dose to avoid
causing hypocalcaemia.

♦ Pamidronate in renal impairment: seek advice

- GFR >20ml/min: give pamidronate over at least 90 minutes.
- GFR <20ml/min: consider risks & benefits of pamidronate. Maximum infusion rate 20mg/hr; consider dose reduction.

* Corrected calcium =
measured calcium +
(40 - serum albumin) X 0.02

Itch in Palliative Care

Introduction

Itch may be localised or due to systemic disease. It can cause discomfort, frustration, poor sleep, anxiety and depression. Persistent scratching leads to skin damage – excoriation and thickening. Patients with itch usually have dry skin.

Assessment

- Examine the skin; look for local and systemic causes. May be multifactorial.
- Primary skin disease (eg. atopic dermatitis, contact dermatitis, psoriasis).
- Infection – candidiasis, lice, scabies, fungal infection.
- Medication – opioids (particularly morphine, diamorphine).
- Systemic diseases that can cause itch include:

Cholestatic jaundice	Chronic kidney disease	Iron deficiency +/- anaemia
Hepatitis		Lymphoma
Hepatoma	Thyroid disease	Leukaemia
Primary biliary cirrhosis	Diabetes	Multiple myeloma
		Polycythaemia
Paraneoplastic syndrome		Mycosis fungoides

Management

- Treat underlying cause(s). Review medication to exclude a drug reaction.
- Use an emollient or aqueous cream frequently as a moisturiser.
- Add an emollient to bath water and use aqueous cream as a soap substitute.

Topical Agents

- Emollients
- Aqueous cream (1% menthol can be added).
- Crotamiton 10% cream (Eurax) or capsaicin (0.025%) cream for localised itch.
- Topical corticosteroid (mild/moderate potency) once daily for 2-3 days if the area is inflamed but not infected.

Medication

- Antihistamine (stop if no benefit after a few days).
 - Sedating antihistamine if poor sleep is a problem (eg. chlorphenamine, hydroxyzine).
 - Some non-sedating antihistamines can have an antipruritic effect (eg loratadine, cetirizine).
- An antidepressant can help if the patient has associated anxiety or depression.
- Cimetidine 400mg twice daily for itch in lymphoma or polycythaemia. (Check BNF for drug interactions).
- Biliary stenting: may relieve the symptoms of cholestatic jaundice.

Practice points

- Avoid topical antihistamines as they can cause allergic contact dermatitis.
- Systemic treatment is often unnecessary if skin care is improved.

Patient advice points

- Keep nails short and clean. Wear loose clothing, preferably cotton. Keep cool.
- Dry skin by gently patting rather than rubbing; then apply moisturisers.
- Avoid lanolin and perfumed products; try a little baking soda in the bath water.

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Last days of life

Introduction

When all reversible causes for the patient's deterioration have been considered, the multi-disciplinary team agrees the patient is dying and changes the goals of care.

Reversible causes to consider include

• dehydration	• infection	• opioid toxicity
• renal impairment	• hypercalcaemia	• delirium

Clinical signs of dying may include:

Patient is bedbound	Increasingly drowsy or semicomatose
Only able to take sips of fluid	Difficulty swallowing tablets

Management of a dying patient and their family

Plan and document care; consider using a care pathway or checklist.

Team

- Discuss prognosis (patient is dying), goals of care (maintaining comfort) and preferred place of death with the patient and/or family.
- If discharge home is possible, prompt and careful planning are needed. Contact GP, community nurse and occupational therapist urgently.

Medical staff

- Clarify resuscitation status; check DNAR form has been completed. (See: local policy)
 - Reassure the patient and family that full supportive care will continue.
- Discontinue inappropriate interventions (blood tests, IV fluids and medication, vital signs monitoring, frequent blood sugar tests).
- Medication – review at least once daily.
 - Stop any treatment not needed for symptom control.
 - Choose an appropriate route. If able to swallow, consider liquid formulations otherwise change to the subcutaneous or rectal route.
 - Consider need for a SC infusion of medication via a syringe driver/pump.
 - Anticipatory prescribing of as required medication in advance for common symptoms.
- Hydration:
 - Discontinue tube feeding/ fluids if respiratory secretions are present, if there is risk of aspiration due to reduced conscious level, or at the patient's request.
 - Over-hydration contributes to distressing respiratory secretions. Artificial fluids are usually not appropriate, but if indicated can be given subcutaneously overnight. (See: Subcutaneous fluids)

Nursing staff

- Comfort nursing care (pressure relieving mattress, reposition for comfort only), eye care, mouth care (sips of fluid, oral gel), bladder and bowel care.
 - Explain to the family why the nursing and medical care has been altered and what changes to expect in the patient's condition. (See leaflet: What happens when someone is dying)
 - Ward team; record arrangements for contacting the family when the patient deteriorates or dies. Community team; ensure the family/ carers know who to contact when the patient dies.
 - Consider emotional, spiritual/ religious, legal and family needs including those of children.
 - Identify those at increased risk in bereavement and seek additional support.
 - Previous multiple losses or recent bereavement
 - Ambivalent or dependent relationship
 - Living alone and lacking a support network
 - Mental illness, drug or alcohol dependency
 - Dependent children
- (See: Bereavement on website)

Symptom Control in the last days of life

Anticipatory prescribing

All patients should have as required medication for symptom control available.

- **Opioid** analgesic SC, hourly; dose depends on patient, clinical problem and previous opioid.
 - 1/6th of 24 hour dose of any regular opioid.
 - If not on a regular opioid, morphine SC 2-5mg or diamorphine SC 2.5-5mg.
- Anxiolytic sedative: **midazolam** SC 2.5-5mg, hourly.
- Anti-secretory medication: **hyoscine butylbromide** (Buscopan) SC 20mg, hourly.
- Anti-emetic: **cyclizine** SC 25-50mg, 8 hourly or levomepromazine SC 2.5-5mg, 8-12 hourly.

Pain

- Paracetamol or diclofenac (as liquid/ dispersible or rectally).
NSAID benefits may outweigh risks in a dying patient; can help bone, joint, pressure sore, inflammatory pain.

Convert any regular oral morphine or oxycodone to a 24 hour, SC infusion		
eg. oral morphine 30mg	= SC morphine 15mg	= SC diamorphine 10mg
eg. oral oxycodone 15mg	= SC morphine 15mg	= SC oxycodone 7-8 mg

- Fentanyl patches should be continued in dying patients. (See: Fentanyl patches)
For other opioids, see: Choosing & Changing Opioids and/ or seek advice.
- For patient with stage 4-5 chronic kidney disease, see: Last days of life (renal) guideline.
- Breakthrough analgesia, should be prescribed hourly as required:
 - 1/6th of 24 hour dose of any regular opioid orally and subcutaneously.
 - If not on any regular opioid, prescribe morphine SC 2-5mg or diamorphine SC 2.5-5mg.

Agitation / delirium

Anxiety/ distress	midazolam SC 2.5-5mg, hourly, as required	
Confusion/ delirium	haloperidol SC 2.5mg, once or twice daily	
Established terminal delirium/ distress	1 st line	2 nd line
	midazolam SC 20-30mg over 24 hours in a driver/pump + midazolam SC 5mg hourly, as required OR regular rectal diazepam 5-10mg, 6-8 hourly.	midazolam SC 40-80mg over 24 hours in a syringe driver/pump + levomepromazine SC 12.5-25mg, 6-12 hourly, as required. Stop any haloperidol.

Nausea/ vomiting (see: Nausea / Vomiting)

- If already controlled with an oral anti-emetic, use the same drug as a SC infusion.
- Treat new nausea/ vomiting with a long acting anti-emetic given by SC injection or give a suitable antiemetic as a SC infusion in a syringe driver/ pump.

Long acting anti-emetic: haloperidol SC 1mg twice daily or 2.5mg once daily.
levomepromazine SC 2.5mg twice daily or 5mg once daily.

- Doses of antiemetics for use in a SC infusion - See: Subcutaneous medication.
- Persistent vomiting: an NG tube, if tolerated, may be better than medication.

Other guidelines

Subcutaneous medication (prescribing advice and drug compatibility tables)

Choosing & changing opioids Subcutaneous fluids Mouth Care Levomepromazine

End-of-life care in non-cancer illnesses: Renal disease, Liver disease, Heart disease - see website

Breathlessness

- Oxygen is only useful if hypoxic; nasal prongs are better tolerated than a mask.
- A fan or position change can help.

Intermittent breathlessness/ distress	midazolam SC 2.5-5mg hourly, as required &/ or lorazepam sublingual 0.5mg, 4-6 hourly, as required. opioid (2 hourly as required) <ul style="list-style-type: none"> • regular opioid → 25% of the 4 hourly breakthrough analgesia dose of opioid. • no opioid → morphine SC 2mg or diamorphine SC 2.5mg.
Persistent breathlessness/ distress	midazolam SC 5-20mg + morphine SC 5-10mg or diamorphine SC 5-10mg (if no opioid for pain) in syringe driver/ pump.

Respiratory tract secretions

- Avoid fluid overload; assess fluid balance, stop IV/SC fluids and tube feeding. Changing the patient's position may help.
- Intermittent SC injections often work well or medication can be given as a SC infusion.

1st line: hyoscine butylbromide SC 20mg, hourly as required (up to 120mg/ 24hours).

2nd line: glycopyrronium bromide SC 200micrograms, 6-8 hourly as required.

3rd line: hyoscine hydrobromide SC 400micrograms, 2 hourly as required.

Acute terminal events (see: Emergencies in palliative care)

Dying patients occasionally develop acute distress; can be due to:

- Bleeding: haemorrhage from GI or respiratory tract, or external tumour.
- Acute pain: bleeding into a solid tumour, fracture, ruptured organ.
- Acute respiratory distress: pulmonary embolism, retained secretions.

Management

- Prescribe sedation in advance if patient at risk; document and discuss anticipatory care plan with family and key professionals.
- Give midazolam IM 5-10mg into deltoid muscle or diazepam rectal solution 10mg PR (can be given via stoma) or sedate using IV midazolam if IV access available.
- If patient is in pain or has continued respiratory distress despite midazolam, give additional morphine SC or diamorphine SC as required.

Practice points

- Opioid analgesics should not be used to sedate dying patients.
- Sudden increase in pain or agitation; exclude urinary retention, constipation, fracture.
- Subcutaneous infusions provide maintenance treatment only. Additional doses of medication by SC injection will be needed if the patient's symptoms are not controlled.
- Midazolam is titrated in 5-10 mg steps. Up to 5mg can be given in a single SC injection (1ml). Single SC doses can last 2-4 hours. Useful as an anticonvulsant.
- Rectal diazepam solution; longer acting alternative to midazolam given PR or via a stoma.
- Terminal secretions can be controlled in about 60% of cases; fluid overload, aspiration and respiratory infection increase incidence.
- Consider a nicotine replacement patch for heavy smokers.

Resources

Professional

NHS End of life care Programme <http://www.endoflifecare.nhs.uk/eolc>

Liverpool Integrated Care Pathway http://www.mcpcil.org.uk/liverpool_care_pathway

Patient

Patient leaflet on website: What happens when someone is dying.

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Levomepromazine in Palliative Care

Description

A phenothiazine used widely in palliative care to treat intractable nausea or vomiting, and for severe delirium/ agitation in the last days of life.

Preparations

Oral	6mg scored tablet	Named patient preparation. Allow time for pharmacist to order. Disperses well in water.
	25mg scored tablet	Listed in BNF but rarely used in palliative care as too high a dose for most patients.
Injection	25mg/ml 1ml ampoule	Used by subcutaneous injection or continuous subcutaneous infusion.

Indications

- Second line, broad spectrum antiemetic for intractable nausea/ vomiting.
- Potent sedative used to manage severe delirium/ agitation in a dying patient.

Cautions

- Lowers blood pressure and can cause significant postural hypotension in ambulant patients. Check blood pressure before starting treatment and then daily until dose stable. Additive hypotensive effect if combined with other antihypertensives.
- Additive sedative effect if combined with other sedating drugs.
- Liver impairment: dose reduction and careful titration. Inhibits cytochrome P450 metabolism – check BNF for drug interactions.
- Rarely causes prolonged QT interval in cardiac disease or hypokalaemia.
- Parkinsonism, epilepsy (lowers seizure threshold).

Side effects

- Skin irritation at infusion site; add more diluent when preparing syringes.
- Cover syringe containing the infusion as degrades in sunlight (purple colouration).
- Drowsiness, dry mouth, dystonia, neuroleptic malignant syndrome (rarely).

Dose & Administration

- Low doses for nausea/ vomiting and higher doses for delirium/ agitation.
- SC dose is half the oral dose.
- Each dose can last 12-24 hours; once or twice daily SC injection is an alternative to a continuous subcutaneous infusion.

Antiemetic (see: Nausea / Vomiting, Subcutaneous medication)

- Oral starting dose: 3mg once or twice daily.
- SC starting dose: 2.5-5mg (0.1-0.2ml) once or twice daily, or as a continuous SC infusion.
- Usual dose range: 3-25mg / 24 hours.

Sedative: (see: Last days of life)

- Second line added to a benzodiazepine (midazolam SC 30mg/ 24hours or diazepam PR 5mg, 8hourly) if the patient is dying and agitated. Exclude other causes of terminal delirium particularly opioid toxicity, urinary retention. (see: Delirium)
- Injections will be needed to gain control of agitation while a SC infusion takes effect and may be needed if agitation worsens; use 12.5-25mg SC, 6-12 hourly.
- Subcutaneous infusion dose: 25-100mg over 24 hours.

Further information

Palliative Care Drug Information online: <http://www.palliativedrugs.com>

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Compatibility and stability charts for a subcutaneous infusion in a McKinley T34 Syringe Pump

Table 1: Subcutaneous Morphine Infusion

Diluent: Water for injections

- **These are not clinical doses to prescribe. Most patients do not need such high doses. Read the relevant guidelines.**
- Use this table to check for concentrations that are stable.
- Refer to the relevant guidelines to obtain the usual dose range for each of the medications. Use the minimum effective dose and titrate according to response.

Drug Combination	Concentrations of two drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Morphine Sulphate Cyclizine	300mg 150mg	
Morphine Sulphate Glycopyrronium bromide	300mg 1200 micrograms	
Morphine Sulphate Haloperidol	400mg 10mg	
Morphine Sulphate Hyoscine butylbromide	300mg 120mg	
Morphine Sulphate Hyoscine hydrobromide	450mg 1200 micrograms	
Morphine Sulphate Levomepromazine	300mg 100mg	
Morphine Sulphate Metoclopramide	120mg 60mg	160mg 80mg
Morphine Sulphate Midazolam	300mg 30mg	380mg 40mg
Morphine Sulphate Octreotide	400mg 400 micrograms	500mg 500 micrograms
Drug Combination	Concentrations of three drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Morphine Sulphate Cyclizine Haloperidol	40mg 100mg 2.5mg	
Morphine Sulphate Haloperidol Midazolam	100mg 5mg 20mg	130mg 6.5mg 25mg
Morphine Sulphate Hyoscine butylbromide Midazolam	50mg 40mg 60mg	60mg 50mg 75mg
Morphine Sulphate Metoclopramide Midazolam	50mg 30mg 7.5mg	60mg 40mg 10mg
Morphine Sulphate Glycopyrronium Haloperidol	270mg 1200 micrograms 10mg	

Table 2: Subcutaneous Diamorphine infusion in a McKinley T34 Syringe Pump

Diluent: Water for injections

- **These are not clinical doses to prescribe. Most patients do not need such high doses. Read the relevant guidelines.**
- Use this table to check for concentrations that are stable.
- Refer to the relevant guideline to obtain the usual dose range for each of the medications. Use the minimum effective dose and titrate according to response.

Drug Combination	Concentrations of two drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Diamorphine Cyclizine	340mg 150mg	
Diamorphine Glycopyrronium bromide	425mg 1200 micrograms	
Diamorphine Haloperidol	800mg 10mg	
Diamorphine Hyoscine butylbromide	1200mg 120mg	
Diamorphine Hyoscine hydrobromide	1200mg 1200 micrograms	
Diamorphine Ketorolac	90mg 30mg	
Diamorphine Levomepromazine	850mg 100mg	
Diamorphine Metoclopramide	2500mg 85mg	3300mg 110mg
Diamorphine Midazolam	560mg 80mg	720mg 100mg
Diamorphine Octreotide	425mg 900 micrograms	
Drug Combination	Concentrations of three drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Diamorphine Cyclizine Haloperidol	340mg 150mg 10mg	
Diamorphine Haloperidol Midazolam	800mg 7.5mg 65mg	1000mg 10mg 80mg
Diamorphine Hyoscine butylbromide Midazolam	120mg 80mg 20mg	150mg 100mg 25mg
Diamorphine Levomepromazine Metoclopramide	850mg 100mg 50mg	
Diamorphine Levomepromazine Midazolam	850mg 50mg 30mg	1100mg 60mg 40mg

Table 3: Subcutaneous Oxycodone infusion in a McKinley T34 Syringe Pump

Diluent: Water for injections

- **These are not clinical doses to prescribe. Most patients do not need such high doses. Read the relevant guidelines.**
- Use this table to check for concentrations that are stable.
- Refer to the relevant guideline to obtain the usual dose range for each of the medications. Use the minimum effective dose and titrate according to response.
- The concentration of oxycodone injection is 10mg/ml. If the 24hour dose of oxycodone exceeds 60mg, an alternative opioid may be needed for breakthrough pain.

Drug Combination	Concentrations of two drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Oxycodone Cyclizine	Do not mix - Incompatible	Do not mix - Incompatible
Oxycodone Haloperidol	140mg 10mg	
Oxycodone Hyoscine butylbromide	140mg 40mg	180mg 50mg
Oxycodone Hyoscine hydrobromide	130mg 1200 micrograms	
Oxycodone Ketorolac	85mg 30mg	
Oxycodone Levomepromazine	120mg 100mg	
Oxycodone Metoclopramide	80mg 40mg	100mg 50mg
Oxycodone Midazolam	80mg 40mg	100mg 50mg
Oxycodone Octreotide	80mg 400 micrograms	100mg 500 micrograms
Drug Combination	Concentrations of three drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Oxycodone Haloperidol Hyoscine butylbromide	80mg 2.5mg 100mg	100mg 5mg 120mg
Oxycodone Haloperidol Hyoscine hydrobromide	80mg 2.5mg 1000 micrograms	100mg 5mg 1200 micrograms
Oxycodone Haloperidol Midazolam	80mg 2.5mg 15mg	100mg 5mg 20mg
Oxycodone Levomepromazine Hyoscine butylbromide	80mg 20mg 100mg	100mg 25mg 120mg

Table 4: Subcutaneous Alfentanil infusion in a McKinley T34 Syringe Pump

Diluent: Water for injections

- **These are not clinical doses to prescribe. Most patients do not need such high doses. Read the relevant guidelines.**
- Use this table to check for concentrations that are stable.
- Refer to the relevant guideline to obtain the usual dose range for each of the medications. Use the minimum effective dose and titrate according to response.

Drug Combination	Concentrations of two drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Alfentanil Cyclizine	4mg 150mg	5mg 150mg
Alfentanil Glycopyrronium bromide	5.5mg 1200 micrograms	8mg 1200 micrograms
Alfentanil Haloperidol	7.5mg 10mg	10mg 10mg
Alfentanil Hyoscine butylbromide	5.5mg 120mg	8mg 120mg
Alfentanil Hyoscine hydrobromide	7.5mg 1200 micrograms	10mg 1200 micrograms
Alfentanil Levomepromazine	7.5mg 40mg	10mg 50mg
Alfentanil Metoclopramide	2.5mg 60mg	3mg 80mg
Alfentanil Midazolam	3.5mg 50mg	5mg 60mg
Alfentanil Octreotide	6mg 800 micrograms	8mg 900 micrograms
Drug Combination	Concentrations of three drug combinations that are physically stable	
	17ml in 20ml syringe	22ml in 30ml syringe
Alfentanil Haloperidol Midazolam	4.5mg 5mg 35mg	6mg 5mg 45mg
Alfentanil Hyoscine butylbromide Levomepromazine	5mg 120mg 25mg	7.5mg 120mg 25mg
Alfentanil Metoclopramide Midazolam	3mg 35mg 20mg	3.5mg 45mg 30mg
Alfentanil Levomepromazine Midazolam	3.5mg 80mg 30mg	5mg 100mg 40mg

Key references

1. Dickman A: *The syringe driver: continuous subcutaneous infusions in palliative care*. 2nd Edition, 2004. OUP.
2. Palliative care drug information online <http://www.palliativedrugs.com/>

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Mouth Care in Palliative Care

Introduction

Mouth care is a frequently neglected but crucial aspect of palliative care. It maintains self-esteem, and the person's ability to communicate and enjoy food and drinks.

Assessment

- Identify patients at risk of oral problems and plan regular mouthcare: e.g. receiving chemotherapy/radiotherapy, elderly, terminally ill, immunocompromised, nasogastric or PEG tube fed, O₂ therapy, dysphagia, oro-pharyngeal disease.
- Drug history:
 - Anticholinergics (e.g. cyclizine, hyoscine, tricyclics) – increase dry mouth.
 - Bisphosphonates – risk of osteonecrosis of the jaw particularly if teeth/gums are in poor condition.
- Examine thoroughly using a torch and tongue depressor. Remove dentures and ensure privacy. Avoid pain by lubricating cracked lips. Look for signs of dryness, coating, ulceration, infection or tooth decay. Assess for pain.
- Document findings accurately and assess daily or at each visit.

Management

Healthy mouth

- Keep mouth and lips clean, moist and intact; remove plaque and debris.
- Prevent oral infection, tooth decay and halitosis.
- Maintain fluid intake with frequent, small drinks.
- Oral care using a soft, small-headed toothbrush, fluoride toothpaste and water after each meal and at bedtime.
- Gauze on a gloved finger, soaked in water or chlorhexidine 0.2% may be used if the patient is unconscious or unable to tolerate a toothbrush.
- Apply oral gel to dry lips after oral care.
- Dentures should be cleaned and soaked overnight in a cleanser.

Mouthcare if receiving chemotherapy/radiotherapy – key differences:

- Chlorhexidine is not effective and may be harmful.
- Use bicarbonate mouthwash (5ml spoonful dissolved in 1 pint of warm water) 4-6 times daily to keep the mouth clean.
- Avoid antipyretic analgesics (paracetamol, aspirin) if the patient is at risk of neutropenia; can mask fever due to sepsis.

Painful mouth

- Assess cause and treat accordingly.
- Treat painful mucositis with benzydamine hydrochloride 0.15% (Difflam) 15ml, 2-3 hourly for up to 7 days. Dilute 1:1 with water if it stings too much.
- Consider sucralfate suspension.
- Analgesia: soluble paracetamol and/or aspirin gargle. Co-codamol (30/500) or morphine – if more severe pain. (see: Pain management)
- Look for herpes simplex infection and treat appropriately.

Dry/ coated mouth

- Frequent oral care, maintain hydration, review medication.
- Use a moistened soft toothbrush to remove coating.
- Chlorhexidine gluconate 0.2% mouthwash, 10ml used twice daily. Dilute 1:1 with water if it stings. Inhibits plaque formation.
- Cold, unsweetened drinks taken frequently through the day.
- Saliva substitutes or oral gel if other measures insufficient.

Management

Candidiasis

- Chlorhexidine gluconate 0.2%, 10ml twice daily.
- Nystatin suspension 1ml, as a mouthwash then swallowed, 4 times daily for 7-14 days. Give nystatin with any dentures out and at least 30 minutes after chlorhexidine or it becomes inactive.
- Fluconazole (capsules or suspension) 50mg daily for 7-14 days. Check BNF for drug interactions.
- Angular cheilitis can be treated with nystatin suspension. Miconazole gel (topically 4 times daily) can be used to treat cheilitis and oral candidiasis.
- Dentures should be cleaned thoroughly.

Ulcerated mouth

- Identify the cause if possible; exclude infection, dental problems.
- If ulcers are painful, try benzydamine hydrochloride 0.15% (Difflam) 15ml, 2-3 hourly; or a topical steroid (eg. hydrocortisone lozenge or triamcinolone in orabase).
- Use chlorhexidine gluconate 0.2% mouthwash twice daily to prevent and treat infection.
- If persistent mucositis, consider sending swab for culture.
- Treat herpetic ulcers on the lips with topical aciclovir; use oral aciclovir for herpes infection in the mouth.
- Treat anaerobic (foul smelling) lesions or gingivitis with oral metronidazole.

Practice point

- Refer to a dentist if pain or ulceration is related to teeth or dentures.

Patient / carer advice points

- Regular toothbrushing and dental hygiene are essential. Visit a dentist regularly.
- Avoid sugary drinks. Try sugar free chewing gum.

Resources

Patient

Patient leaflet on website: Managing a dry or sore mouth.

Key references

1. Davies A, Finlay I. *Oral Care in Advanced Disease*: OUP 2005, Oxford
2. De Conno. Mouth care. In *Oxford Textbook of Palliative Medicine*. 3rd Edition 2004, p673-687
3. Gillam JL, Gillam DG. The assessment and implementation of mouth care in palliative care: a review. *The Journal Royal Society Promotion of Health* 2006; 126(1): 33-37

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Naloxone in Palliative Care

Description

Antagonist for use in severe opioid induced respiratory depression.

Preparation

- 400 micrograms/ml injection (1ml ampoule).

Indications

- Reversal of life-threatening respiratory depression due to opioid analgesics, indicated by:
 - A low respiratory rate < 8 respirations/minute.
 - Oxygen saturation <85%, patient cyanosed.

If less severe opioid toxicity

- Omit next regular dose of opioid; review analgesia.
- Monitor the patient closely; maintain hydration, oxygenation.

Cautions

- Naloxone is not indicated for opioid induced drowsiness and/or delirium that are not life threatening.
- Naloxone is not indicated for patients on opioids who are dying.
- Patients on regular opioids for pain and symptom control are physically dependent; naloxone given in too large a dose or too quickly can cause an acute withdrawal reaction and an abrupt return of pain that is difficult to control.
- Patients with pre-existing cardiovascular disease are at more risk of side effects.

Side effects

Opioid withdrawal syndrome: anxiety, irritability, muscle aches; nausea and vomiting; can include life-threatening tachycardia and hypertension.

Dose & Administration

Small doses of naloxone by slow IV injection improve respiratory status without completely blocking the opioid analgesia.

- Stop the opioid.
- High flow oxygen, if hypoxic.
- Dilute 400 micrograms naloxone (1 ampoule) to 10ml with sodium chloride 0.9% injection in a 10 ml syringe.
- Administer a small dose of 80 micrograms (2ml of diluted naloxone) as a slow IV bolus. Flush the cannula with sodium chloride 0.9%.
- Give 80 microgram (2ml) doses at 2 minute intervals until the respiratory rate is above 8. Flush the cannula between the naloxone doses.
- Patients usually respond after 2-4ml of diluted naloxone with deeper breathing and an improved conscious level.
- A few patients need 1-2mg of naloxone. If there is little or no response, consider other causes (e.g. other sedatives, an intracranial event, acute sepsis, acute renal failure causing opioid accumulation).
- Closely monitor respiratory rate and oxygen saturation. Further doses may be needed. The duration of action of many opioids exceeds that of naloxone (15-90 minutes) and impaired liver or renal function will slow clearance of the opioid.

Dose & Administration

Prolonged or recurrent, opioid induced respiratory depression:

- If repeated naloxone doses are required, start a continuous intravenous infusion of naloxone via an adjustable infusion pump.
 - Add 1mg of naloxone (= 2.5ml of 400 micrograms/ml naloxone injection) to 100ml of sodium chloride 0.9% to give a concentration of 10 micrograms/ml.
 - Calculate the dose requirement per hour by totalling the naloxone bolus doses and dividing by the time period over which all the doses have been given.
 - Start the IV infusion of naloxone at **half** this calculated hourly rate.
 - Adjust the naloxone infusion rate to keep the respiratory rate above 8 (do not titrate to the level of consciousness).
 - Continue to monitor the patient closely.
 - Continue the infusion until the patient's condition has stabilised.
- Additional IV boluses may need to be given using naloxone diluted in sodium chloride 0.9% as above.

If in doubt, seek advice

- Seek and treat the precipitating cause(s) of the opioid toxicity.
- Review the regular analgesic prescriptions.

Good Practice Point

- Naloxone should be available in all clinical areas where opioids are used. (National Patient Safety Agency)
- Naloxone is also available in disposable, pre-filled syringes. These doses may be too high for patients on regular opioid analgesics.

Resources

Professional

Palliative Care Drug Information online <http://www.palliativedrugs.com/>

Community use

- Naloxone may be administered IM when IV access is not immediately available
- 100 micrograms (0.25ml) naloxone IM should be given and repeated after five minutes if there is no improvement with the first dose.
- An IV line should be sited as soon as possible.

Key references

1. Twycross R, Wilcock A. *Palliative Care Formulary* (3rd Edition) 2007, Palliativedrugs.com Ltd., Nottingham
2. National Patient Safety Agency. Safer practice notice 2006/12
3. Adult Emergencies Handbook. NHS Lothian: University Hospitals Division.
4. Electronic Medicines Compendium. www.medicines.org.uk/naloxone <http://emc.medicines.org.uk/emc/industry/default.asp?page=displaydoc.asp&documentid=647> 18/6/07
5. Lothian Joint Formulary. Section 15.1.7. www.ljf.scot.nhs.uk

Nausea / Vomiting in Palliative Care

Introduction

Common, distressing symptoms that can be controlled with careful assessment of underlying causes, and selection of appropriate medication and route of administration.

Assessment

Seek and treat any reversible causes including:

• medication	• constipation	• gastric irritation	• coughing
• hypercalcaemia	• uraemia	• gastroenteritis	• infection

Management

Choice of drug is based on likely cause(s), side effect profile and route of administration of antiemetics, and patient's condition/ prognosis. Drug doses and prescribing advice - see chart.

Clinical picture	Possible cause(s)	Treatment
<ul style="list-style-type: none"> • Intermittent vomiting that relieves nausea. • Early satiety. • Audible splash, and frequent small vomits if fluid retained in flaccid stomach. • Other autonomic features (eg syncopal episodes, postural hypotension). 	Impaired gastric emptying: <ul style="list-style-type: none"> • Locally advanced cancer (stomach, pancreas, liver metastases, gross ascites) • Morphine, anticholinergics • Gastroenterostomy • Autonomic neuropathy (diabetes, alcoholism, chronic kidney disease, coeliac plexus infiltration, paraneoplastic syndrome, Parkinson's disease) 	Prokinetic antiemetic: <ul style="list-style-type: none"> • metoclopramide • domperidone • dexamethasone (extrinsic compression/ obstruction from tumour, diffuse gastric tumour) • proton pump inhibitor (gastric irritation, reflux)
<ul style="list-style-type: none"> • Dysphagia, pain, regurgitation, coughing. 	Regurgitation: <ul style="list-style-type: none"> • Obstruction/ compression of oesophagus 	<ul style="list-style-type: none"> • dilatation, stent, laser • dexamethasone
<ul style="list-style-type: none"> • Persistent nausea, little relief from vomiting. 	Chemical/ metabolic: <ul style="list-style-type: none"> • Medication (opioids, antibiotics, SSRI antidepressants, digoxin) • Extensive cancer • Sepsis • Renal or liver impairment • ↑ calcium, ↓ magnesium, ↓ sodium 	<ul style="list-style-type: none"> • haloperidol • metoclopramide • levomepromazine
<ul style="list-style-type: none"> • Intermittent vomits that may relieve nausea. • Colic in mechanical obstruction. • Constipation. 	Bowel obstruction: <ul style="list-style-type: none"> • Mechanical obstruction • Peristaltic failure (autonomic neuropathy or carcinomatosis) 	Medical management if surgery not appropriate. See: Bowel Obstruction
<ul style="list-style-type: none"> • Worse in the morning. • Headache. • Neck stiffness. 	Cerebral disease: <ul style="list-style-type: none"> • Compression/ irritation by tumour • Raised intracranial pressure • Anxiety 	<ul style="list-style-type: none"> • cyclizine • add dexamethasone
<ul style="list-style-type: none"> • Worse on movement. • Vertigo, deafness if ear pathology. 	Vestibular system: <ul style="list-style-type: none"> • Motion sickness • Base of skull, brainstem disease 	<ul style="list-style-type: none"> • prochlorperazine • cyclizine • hyoscine hydrobromide • levomepromazine
	Chemotherapy/ radiotherapy:	<ul style="list-style-type: none"> • Seek specialist advice
<ul style="list-style-type: none"> • Review possible causes/ previous treatment. 	Unknown or multiple causes: <ul style="list-style-type: none"> • Broad spectrum treatment using single or multiple drugs. 	<ul style="list-style-type: none"> • metoclopramide and/or levomepromazine • or cyclizine + haloperidol • add dexamethasone

Practice points

- Even if the patient is not vomiting, ask about nausea (often not reported).
- Mechanisms of nausea/ vomiting are complex and multiple pathways are affected; a pragmatic approach selecting the antiemetic most likely to be effective and then a second drug or drugs is often effective.
- Avoid combining drugs with a similar mode of action or side effect profile; and do not combine prokinetics with anticholinergics.
- If patient is vomiting or if oral absorption is in doubt, use the subcutaneous route or rectal route. (see: Subcutaneous medication)
- Prescribe the antiemetic regularly and as required starting with the lowest dose.
- Review the treatment and response every 24 hours until symptoms are controlled.
- Continue to review antiemetic use regularly. Stop if underlying cause has resolved.
- Nausea can usually be fully controlled; vomiting about once a day may be acceptable in bowel obstruction.
- Good mouth care is essential in patients with nausea/ vomiting. (see: Mouth Care)
- Many antiemetics are used outside their marketing authorisation in palliative care, including by the subcutaneous route; this is supported by extensive clinical experience. Palliative medicine specialists occasionally recommend other regimens. This should be clearly documented in the patient's notes. (see: Medication outside marketing authorisation on website).

Patient/ carer advice points

- Make sure the patient knows if the antiemetic is to be taken regularly or as needed; explain the treatment and plan review.
- Offer dietary advice; small, frequent meals may be better.
- Avoid strong smells, and any nausea triggers.
- Acupuncture/ acupressure has been used for nausea in chemotherapy or surgery.

Resources

Professional

Palliative Care Drug Information online: <http://www.palliativedrugs.com/>

Patient

Patient leaflet on website: Managing sickness & vomiting

Key References

1. Wood GJ. Management of intractable nausea and vomiting in patients at the end of life. *JAMA* 2007; 298(10):1196-1207
2. Stephenson J. An assessment of aetiology based guidelines for the management of nausea and vomiting in patients with advanced cancer. *Support Care Cancer* 2006; 14:348-353
3. Glare P. Systematic review of the efficacy of antiemetics in the treatment of nausea in patients with far-advanced cancer. *Support Care Cancer* 2004; 12: 432-440
4. Kennett A. An open study of methotrimeprazine (levomepromazine) in the management of nausea and vomiting in patients with advanced cancer. *Support Care Cancer* 2004; 13: 715-721
5. Mannix K. Palliation of nausea and vomiting. *CME Cancer Medicine* 2002;(1):18-22
6. Bentley A. Management of nausea and vomiting using clinical pictures. *Palliative Medicine* 2001; 5:247-253

Antiemetic information chart

Drug	Oral dose range	As required dose	24 hour SC dose range	Prescribing notes
Cyclizine	25-50mg, 8 hourly	25-50mg oral or SC, 8 hourly	100-150mg	<ul style="list-style-type: none"> Anticholinergic antihistamine. Slows peristalsis in GI tract; acts directly on vomiting centre. Side effects: dry mouth, urinary retention, blurred vision; also hypotension, extrapyramidal effects, confusion.
Domperidone	10-20mg, 6-8 hourly (tablet / suspension)	10mg oral	---	<ul style="list-style-type: none"> Prokinetic action in GI tract; blocked by anticholinergics. Lower risk of extrapyramidal side effects than metoclopramide. Available as 30mg suppository; dose 30-60mg PR twice daily.
Metoclopramide	10-20mg, 6-8 hourly (tablet / suspension)	10mg oral 5mg SC 5-10mg IM	20-120mg	<ul style="list-style-type: none"> Central and peripheral actions. Prokinetic action in GI tract; blocked by anticholinergics. Extrapyramidal side effects (caution in those < 20 years). Injection is 5mg/ml so give larger as needed doses IM not SC.
Haloperidol	0.5-1.5mg, nocte or bd	0.5-1.5mg oral 1mg SC, 12 hourly	2.5-5mg	<ul style="list-style-type: none"> Main action is dopamine blockade; avoid in Parkinson's disease. Can cause extrapyramidal side effects (eg apathy, withdrawal) especially at higher doses for over 1-2 weeks. Once daily SC dose can be used as alternative to SC infusion.
Levomepromazine	3-6mg, nocte or bd	3mg oral, 2.5mg (0.1ml) SC, 8-12 hourly	5-25mg	<ul style="list-style-type: none"> Phenothiazine with a broad spectrum of action. Use low doses to avoid sedation and hypotension. 6mg scored tablet is available on named patient basis; tablet disperses well in water. (see: Levomepromazine on website) SC dose is half the oral dose; a dose can last 12-24 hours.
Hyoscine butylbromide (Buscopan)	Poor absorption	20mg SC, hourly	40-120mg	<ul style="list-style-type: none"> Anticholinergic. Slows peristalsis and reduces secretions in GI tract. Less central side effects than hyoscine hydrobromide.
Hyoscine hydrobromide	No oral preparation	400 micrograms SC, 2 hourly	400-1200 micrograms	<ul style="list-style-type: none"> Anticholinergic. Slows peristalsis and reduces secretions in GI tract. Side effects: dry mouth, drowsiness, confusion. Available as topical patch (1mg/ 72 hours)
Prochlorperazine	5-10mg, 8 hourly	5-10mg oral, 12.5mg IM	Not used SC (too irritant)	<ul style="list-style-type: none"> Used for motion sickness, post-operative vomiting. Buccal tablet 3mg once or twice daily is available.
Dexamethasone	4-16mg		4-16mg	<ul style="list-style-type: none"> Adjuvant antiemetic; oral dose the same as SC/IM dose. Best given in the morning to maintain diurnal rhythm. Monitor for side effects. Review and reduce to lowest effective dose or stop.
5HT ₃ antagonists	See BNF/ Formulary for drugs and doses			<ul style="list-style-type: none"> Constipating; proven value in oncology

Oral Morphine

Other names: Oramorph® liquid (immediate release or quick acting morphine)
Sevredol® tablets (immediate release or quick acting morphine)

Modified release morphine:

MST Continus® tablets or granules (12 hourly, long acting morphine)
Zomorph® capsules (12 hourly, long acting morphine)
Morphgesic® SR tablets (12 hourly, long acting morphine)
MXL® capsules (24 hourly, long acting morphine)

There are different forms of morphine and different brands – check the name of the medicine on the box.

Q. What is morphine used for?

A. Morphine is used for moderate to severe pain, and to help breathlessness. Quick acting morphine starts to work after about 30 minutes and usually lasts for about 4 hours. It is used to control breakthrough pain as it works quickly. It may be given in regular doses when your doctor is working out how much morphine is needed to control your pain.

Long acting morphine is used to control on-going pain and is taken regularly.

Q. Isn't morphine only used for patients who are at the end of life?

A. NO. Morphine is given for different sorts of severe pain. This may be as a result of cancer, heart disease or other illnesses. Treatment with morphine may be needed to allow you to continue having as comfortable a life as possible. You will be able to go on taking morphine for as long as you need to. The effects do not wear off with time and the dose can be increased if needed.

Q. When do I take it?

A. Quick acting morphine is sometimes taken regularly every 4 hours. An extra dose can be taken if the pain comes back between the regular doses or if you are taking long acting morphine to control your pain. Wait about 30-60 minutes after taking the extra dose of quick acting morphine. If you still have pain take a second dose. If you need more than 2-3 extra doses of quick acting morphine in a day, tell your doctor or nurse.

Long acting morphine is taken every 12 hours to control pain. When you are at home, take your morning dose when you wake up and then the evening dose about 12 hours later. There is one type of long acting morphine (MXL®) that is taken once every 24 hours.

Do not stop taking morphine suddenly.

Q. What do I do if I forget to take a dose?

A. Take a dose as soon as you remember. Do not take a double dose to make up for the missed one. If you are sick and bring up the medicine, repeat the dose as soon as you feel better.

Q. Are there any side effects from taking morphine?

A. Sleepiness

This is most common when you first take morphine or when the dose is increased. It should improve after a few days.

Constipation

This is a very common side effect. It is important to drink plenty of fluids and always take a laxative regularly as prescribed by your doctor. The dose of laxative can be increased or reduced to make sure you pass a soft motion regularly.

Sickness

If you feel sick when you first start to take morphine, try taking it with food. Your doctor may need to give you some anti-sickness medicine for a few days until the sickness goes away.

Q. Will I become addicted to morphine and unable to stop taking it?

A. NO. If you no longer need to take morphine, your doctor will reduce the dose gradually.

Q. Will morphine always relieve my pain completely?

A. Although morphine is a very good pain killer, it is not helpful for all types of pain. Other treatments may be needed and suggested by your doctor or nurse.

Q. What do I do if I get pain between the regular doses of morphine?

A. If the pain is mild, paracetamol may help. (Do not take more than 8 paracetamol tablets in 24 hours). If it is more severe you should take a dose of quick acting morphine (see above). If you need more than 2-3 extra doses in a day, tell your doctor or nurse.

Some people find that doing certain things like having a bath or going for a walk brings on the pain. Your doctor or nurse may suggest you try taking a dose of quick acting morphine before you start doing something that brings on the pain.

Q. How will I know if the morphine is not going to work for some of my pain?

A. You may still have pain despite taking bigger doses of morphine and may feel unwell in one or more of these ways:

- more sleepy than usual
- feeling sick more of the time
- restlessness or jumpiness
- bad dreams

Do not worry if this happens. Tell your doctor or nurse. Your doctor may reduce your dose of morphine and suggest other treatments to help the pain.

Q. Can I drive?

A. You may be able to drive but you must discuss this with your doctor.
(Patient information leaflet: Strong pain killers and Driving).

Q. Can I drink alcohol?

A. A small glass of wine, beer, sherry or whisky may help you feel better and improve your appetite. It is best to avoid taking more than this as you may become too drowsy.

(Discuss this leaflet with your doctor or nurse who will answer any questions you may have)

Oral Oxycodone

Other names: Oxynorm® capsules (immediate release or quick acting oxycodone)
 Oxynorm® liquid (immediate release or quick acting oxycodone)
 Oxycontin® tablets
 (modified release or 12 hourly, long acting oxycodone)

There are different forms of oxycodone – check the name of the medicine on the box.

Q. What is oxycodone used for?

A. Oxycodone is used for moderate to severe pain. Quick acting oxycodone starts to work after about 30 minutes and usually lasts for about 4 hours. It is used to control breakthrough pain as it works quickly. It may be given in regular doses when your doctor is working out how much oxycodone is needed to control your pain.

Long acting oxycodone is used to control on-going pain and is taken regularly.

Q. Isn't a pain killer like oxycodone only used for patients who are at the end of life?

A. NO. Oxycodone is given for different sorts of severe pain. This may be as a result of cancer, heart disease or other illnesses. Treatment with oxycodone may be needed to allow you to continue having as comfortable a life as possible. You will be able to go on taking oxycodone for as long as you need to. The effects do not wear off with time and the dose can be increased if needed.

Q. When do I take it?

A. Quick acting oxycodone is sometimes taken regularly every 4-6 hours. An extra dose can be taken if the pain comes back between the regular doses or if you are taking long acting oxycodone to control your pain. Wait about 30-60 minutes after taking the extra dose of quick acting oxycodone. If you still have pain take a second dose. If you need more than 2-3 extra doses of quick acting oxycodone in a day, tell your doctor or nurse.

Long acting oxycodone is taken every 12 hours to control pain. When you are at home, take your morning dose when you wake up and then the evening dose about 12 hours later.

Do not stop taking oxycodone suddenly.

Q. What do I do if I forget to take a dose?

A. Take a dose as soon as you remember. Do not take a double dose to make up for the missed one. If you are sick and bring up the medicine, repeat the dose as soon as you feel better.

Q. Are there any side effects from using oxycodone?

A. Sleepiness

This is most common when you first take oxycodone or when the dose is increased. It should improve after a few days.

Constipation

This is a very common side effect. It is important to drink plenty of fluids and always take a laxative regularly as prescribed by your doctor. The dose of laxative can be increased or reduced to make sure you pass a soft motion regularly.

Sickness

If you feel sick when you first start to take oxycodone, try taking it with food. Your doctor may need to give you some anti-sickness medicine for a few days until the sickness goes away.

Q. Will I become addicted to oxycodone and unable to stop taking it?

A. NO. If you no longer need to take oxycodone, your doctor will reduce the dose gradually so that you stop taking it without problems.

Q. Will oxycodone always relieve my pain completely?

A. Although oxycodone is a very good pain killer it is not helpful for all types of pain. Other treatments may be needed and suggested by your doctor or nurse.

Q. What do I do if I get pain between the regular doses of oxycodone?

A. If the pain is mild, paracetamol may help. (Do not take more than 8 paracetamol tablets in 24 hours). If it is more severe you should take a dose of quick acting oxycodone (see above). If you need more than 2-3 extra doses in a day, tell your doctor or nurse.

Some people find that doing certain things like having a bath or going for a walk brings on the pain. Your doctor or nurse may suggest you try taking a dose of quick acting oxycodone before you start doing something that brings on the pain.

Q. How will I know if the oxycodone is not going to work for some of my pain?

A. You may still have pain despite taking bigger doses of oxycodone and may feel unwell in one or more of these ways:

- more sleepy than usual
- feeling sick more of the time
- restlessness or jumpiness
- bad dreams

Do not worry if this happens. Tell your doctor or nurse. Your doctor may reduce your dose of oxycodone and suggest other treatments to help the pain.

Q. Can I drive?

- A. You may be able to drive but you must discuss this with your doctor.
(Patient information leaflet: Strong Pain Killers and Driving).

Q. Can I drink alcohol?

- A. A small glass of wine, beer, sherry or whisky may help you feel better and improve your appetite. It is best to avoid taking more than this as you may become too drowsy.

(Discuss this leaflet with your doctor or nurse who will answer any questions you may have)

Oxycodone in Palliative Care

Description Potent, synthetic opioid analgesic; used second line.

Preparations

Oral	Immediate release oxycodone OxyNorm ® capsules OxyNorm ® liquid	5mg, 10mg, 20mg 1mg/ml, 10mg/ml
	Modified release (long acting) oxycodone OxyContin ® tablets	5mg, 10mg, 20mg, 40mg, 80mg
Injection	Oxycodone injection OxyNorm ® injection	10mg/ml, 20mg/2ml

Indications

- **Second line** oral and injectable analgesic for moderate to severe opioid responsive pain in patients unable to tolerate oral morphine, subcutaneous morphine or diamorphine due to persistent side effects (eg sedation, confusion, hallucinations, itch).
(See: Pain management, Choosing & Changing opioids)

Cautions

- Immediate release, modified release and injection preparations have similar names. Take care when prescribing, dispensing or administering oxycodone.
- Frail or elderly patients need smaller doses less frequently and slower titration.
- **Liver impairment:** reduced clearance.
Avoid in patients with moderate to severe liver impairment.
- **Renal impairment:** reduced excretion.
Titrate slowly and monitor carefully in mild to moderate renal impairment.
Avoid in chronic kidney disease stages 4-5 (eGFR <30ml/min).

Drug interactions

No clinically significant interactions.

Side effects

- Opioid side effects similar to morphine - monitor for opioid toxicity.
- Prescribe a laxative and an antiemetic as needed (eg metoclopramide).

Dose & Administration

- Immediate release oral oxycodone:
Prescribe 4-6 hourly regularly and use the same dose as required for breakthrough pain.
- Modified release (long acting) oral oxycodone:
 - o Prescribe 12 hourly, with 1/6th of the 24 hour dose as immediate release oral oxycodone for breakthrough pain.
 - o Biphasic action; a rapid release is followed by a controlled release phase. If the patient has pain when the dose of modified release (long acting) oxycodone is given, wait an hour before giving a breakthrough dose of immediate release oxycodone.

Dose & Administration

- Oxycodone injection:
 - o Continuous subcutaneous infusion in a syringe driver or pump over 24 hours.
 - o In addition, prescribe 1/6th of the 24hour infusion dose subcutaneously, 1-2 hourly as required for breakthrough pain.
 - o If the infusion dose is greater than 60mg / 24 hours, use another opioid for breakthrough injections (low concentration of oxycodone preparation limits dose for SC injection to 10mg in 1ml).
 - o Diluent: water for injection.
 - o Dose conversions are given below.
- Stability and compatibility – see: Subcutaneous medication chart.

Dose Conversions

- Oxycodone is approximately twice as potent as morphine.

Oral morphine 60mg	≈ oral oxycodone 30mg	≈ subcutaneous oxycodone 15mg
Subcutaneous morphine 30mg		≈ subcutaneous oxycodone 15mg
Subcutaneous diamorphine 20mg		≈ subcutaneous oxycodone 15mg

- As with all opioid conversions, these are approximate doses.
- Dose conversions should be conservative and doses rounded down.
- Monitor the patient carefully so that the dose can be adjusted if necessary.
- If the patient has opioid toxicity, reduce the dose by 1/3rd when changing opioid.
(See: Choosing & Changing opioids)

Resources

Professional:

Palliative Care Drug Information online: <http://www.palliativedrugs.com/>

Patient:

Patient leaflet on website: Oxycodone

Discharge planning / Community use

- The unscheduled care service should be informed that the patient is receiving this second line opioid in a syringe driver or pump.
- The Community Pharmacy Palliative Care Network stocks a limited supply of oral and injection preparations of oxycodone for emergency use.

Key references

1. Shah S, Hardy J. Oxycodone: a review of the literature. *European J Palliative Care* 2001; 8: 93-96
2. Smith M et al. Oxycodone has a distinctly different pharmacology from morphine. *European J Pain* 2001; 15 (Suppl A): 135-136.
3. Mucci-LoRusso P et al. Controlled release oxycodone compared with controlled release morphine in the treatment of cancer pain: a randomised, double blind parallel group study. *European J Pain* 1998; 2: 239-249

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Pain Assessment for People with Cognitive Impairment / Communication Difficulties

Aims

- Involve the patient as much as possible in the assessment and management of their pain.
- Use a team approach; involve the family, staff and carers who know the patient well.
- Assess each pain separately and identify the likely cause(s).
- Assess the impact of the pain on the patient and family.
- Make a diagnosis and explain this to the patient and family.
- Agree a pain management plan.

1. Is pain the main cause of the patient's distress?

2. Is the pain severe and overwhelming?

3. Can the patient participate in the assessment?

4. Is there a carer, friend or staff member who knows the patient and can help with assessment?

Pain is often poorly assessed and inadequately managed in people with dementia, learning disabilities or a stroke.

Seek advice

Exclude other problems

- fear, anxiety or disorientation/ isolation
- other physical symptoms – eg constipation
- delirium or chronic confusion
- stress related behaviours

Immediate treatment may be required before further assessment

Adjust the dose of analgesia to take account of recent analgesic use. **Seek advice**

Enhance verbal and non-verbal communication

- Allow plenty of time.
- Use sensory aids where needed- hearing aid, glasses, signing, visual tools.
- Minimise distractions – noise, bright lights, activity.
- Use the person's preferred name at the start of each question to hold their attention and focus.
- Use simple language; short sentences.
- Repeat questions; check understanding.
- Consider using pictures – body maps, photographs, illustrated booklets.

Find out

- How the patient usually behaves when comfortable.
- How the patient usually expresses themselves when in pain.
- If the patient has had previous pain problems due to a long term condition (e.g. arthritis).
- About any non-drug treatments used for pain relief and medications currently or previously used, including their effectiveness and any side effects.

Actions

- Record your assessment; consider using a behavioural tool (eg. Abbey, Doloplus 2, DisDAT)
- Different pains may require different interventions. The management of distress related behaviour is important. (See: Pain management)
- Decide if the Adults with Incapacity Act is needed to cover treatment. (See guideline on website)
- Discuss management with patient / carers. A trial of analgesics and / or non-drug treatments may be appropriate. If opioids are required, discuss any concerns regarding their use.
- Agree goals for pain relief and a monitoring plan.

Reassess regularly

See website for references and online resources including behavioural pain assessment tools.

<http://www.palliativeguidelines.scot.nhs.uk>

Pain Assessment – Five Key Questions

Aims

- Obtain the patient’s own description and assessment of their pain. Most patients have more than one pain.
- Assess each pain separately and identify the likely cause(s).
- Assess the impact of the pain on the patient and family.
- Make a diagnosis and explain this to the patient and family.
- Agree a pain management plan.

1. Is the pain severe and overwhelming

2. What is the pain like?

3. What is causing the pain?

4. Is it a specific type of pain?

5. Are other factors adding to the distress?

Actions

- Record your pain score and assessment. Use a pain assessment tool.
- Different pains may require different interventions to control them. (see: Pain management)
- Discuss management with patient / carers. If opioids are prescribed, discuss any concerns about their use (e.g. addiction, side effects, tolerance, hastening death)
- Agree goals for pain relief; and a monitoring plan.

Reassess regularly

Immediate treatment may be required before further assessment.

Adjust the dose according to current analgesic use.

Seek advice

Ask about

- **Site / radiation** - body diagrams can help
- **Character** - a list of descriptive words may help
- **Intensity / severity** - a rating scale can help
- **Timing**
- **Exacerbating factors**
- **Relieving factors** (including medication)
- **Effect on function / sleep**

Use a structured pain assessment tool to make a full assessment and record of the patient’s pain.

Disease?

e.g. direct invasion by cancer; distension of an organ; pressure on surrounding structures.

Treatment?

e.g. constipation with opioids; chemotherapy neuropathy; mucositis; late onset pain following radiotherapy.

Debility?

e.g. pressure sores.

Other unrelated pathology?

e.g. arthritis; cervical spondylitis, osteoporosis, vascular disease, neuropathy.

Bone Pain

Worse on pressure or stressing bone, or weight bearing.

Nerve Pain

Burning / shooting / tingling / jaggling, altered sensation / dermatomal distribution.

Liver Pain

Hepatomegaly, right upper quadrant tenderness.

Episodic/ incident pain

Sudden onset pain occurring spontaneously or with movement; can be severe but may be very short lived.

Raised intracranial pressure

Headache (and/or nausea) worse with lying down, more often present in the morning.

Colic

Intermittent, cramping pain

Consider adjuvant therapies

(see: Pain management)

- Anxiety / depression.
- Other psychological factors e.g. fear, ‘unfinished business’.
- Other physical symptoms e.g. nausea, breathlessness.
- Family / carer distress.

Pain Management in Palliative Care

STEP 1: Mild Pain

PARACETAMOL or **NSAID** +/- **OTHER ADJUVANT**
1g, qds (if not contraindicated)

Assess pain fully before treatment (Pain Assessment).
Ask the patient regularly about their pain.
Record pain scores. Use a pain assessment tool.

STEP 2: Mild to Moderate Pain

OPIOID + **PARACETAMOL** or **NSAID** +/- **OTHER ADJUVANT**
codeine 30-60mg, qds or dihydrocodeine 30-60mg, qds 1g, qds (if not contraindicated)

Use a combined preparation
eg. **co-codamol 30/500**,
2 tablets, qds

Prescribe regular analgesia for continuous pain.

Discuss and resolve any concerns about taking opioids.

STEP 3: Moderate to Severe Pain

OPIOID + **PARACETAMOL** or **NSAID** +/- **OTHER ADJUVANT**
(if not contraindicated)

Stop any step 2 opioid		Seek advice: ♦ Severe pain. ♦ Pain not responding to treatment. ♦ Dose of opioid has increased rapidly but patient is still in pain. ♦ Episodes of acute severe pain. ♦ Pain worse on movement.	
Codeine or dihydrocodeine 60mg qds ≈ 30mg oral morphine / 24hours			
<table border="1"> <tr> <td>If titrating with immediate release oral morphine prescribe 5mg, 4 hourly and as required for breakthrough pain.</td> <td>If starting with modified release oral morphine prescribe 10-15mg, 12 hourly and immediate release morphine 5mg as required for breakthrough pain.</td> </tr> </table>	If titrating with immediate release oral morphine prescribe 5mg, 4 hourly and as required for breakthrough pain.		If starting with modified release oral morphine prescribe 10-15mg, 12 hourly and immediate release morphine 5mg as required for breakthrough pain.
If titrating with immediate release oral morphine prescribe 5mg, 4 hourly and as required for breakthrough pain.	If starting with modified release oral morphine prescribe 10-15mg, 12 hourly and immediate release morphine 5mg as required for breakthrough pain.		
Use lower doses and increase dose more slowly if patient is frail, elderly or has renal impairment. See: Choosing & Changing Opioids for second/ third line opioids.			

Regular laxative

- Senna or bisacodyl plus docusate
- Movicol
- Co-danthramer (if prognosis limited)

Antiemetic

- Metoclopramide
 - Haloperidol
- Prescribe as required for 5-10 days.

Breakthrough pain

- Prescribe immediate release morphine at 1/6th of the regular 24 hour oral morphine dose, as required.
- Assess 30 - 60 minutes after a breakthrough dose.
- If pain persists → give a second prn dose.
- If pain is still not controlled → **seek advice**.
- Change breakthrough dose if regular dose changes.

Movement/ incident related or episodic pain

Can be difficult to manage; a dose of short acting opioid before moving or when pain occurs may help.
→ **seek advice**.

Adjuvant therapies

NSAID: for bone pain, liver pain, soft tissue infiltration, or inflammatory pain (side effects: GI ulceration/ bleeding [consider PPI], renal impairment, fluid retention).

Antidepressant or anticonvulsant: for nerve pain. Start at low dose; titrate slowly. Check BNF for prescribing information. No clear difference in efficacy.

- amitriptyline (side effects: confusion, hypotension).
- gabapentin (side effects: sedation, tremor, confusion; reduce dose if renal impairment).
- carbamazepine (drug interactions – check BNF).

Steroids: dexamethasone
16 mg/day for raised intracranial pressure.
12mg/day for nerve pain; 4-8 mg/day for liver pain.
Give in the morning; reduce to lowest effective dose.

TENS, nerve block, radiotherapy, surgery, bisphosphonates, ketamine (specialist advice).

Dose titration for STEP 3

- Increase regular oral morphine dose each day in steps of about 30% (or according to breakthrough doses used) until pain is controlled or side effects develop.
- Increase laxative dose as needed.

Convert to modified release morphine when stable

- Divide 24 hour dose of immediate release morphine by 2.
- Prescribe as modified release oral morphine, 12 hourly.
- Prescribe breakthrough analgesia at correct dose (1/6 of 24 hour morphine dose).

Subcutaneous (SC) analgesia

- Usually given in a syringe driver/ pump over 24 hours
- Calculate the 24 hour dose of oral morphine.
- **Convert this to SC morphine or SC diamorphine**
Oral morphine 30mg ≈ SC morphine 15mg
Oral morphine 30mg ≈ SC diamorphine 10mg
- Prescribe 1/6th of the 24 hour SC opioid dose as required, SC for breakthrough pain.

Opioid toxicity → seek advice

- Increasing drowsiness/ sedation.
- Vivid dreams / hallucinations/ delirium.
- Muscle twitching / myoclonus / jerking.
- Abnormal skin sensitivity to touch.
- Reduce opioid dose by 1/3, ensure patient is well hydrated; review and re-titrate analgesia.
- Consider adjuvant therapies and/or alternative opioids.

Further reading: SIGN 106 - Cancer Pain Guideline

Renal Palliative Care – Last Days of Life

Introduction

- Guideline for patients with stage 4-5 chronic kidney disease (eGFR <30ml/min).
- Other relevant guidelines: Last days of life, Subcutaneous medication, Alfentanil, Fentanyl.
- Survival after renal dialysis withdrawal is usually about 7-10 days, but some patients with residual renal function may live much longer and need continuing care.
- If a patient is likely to stop dialysis soon, plan end-of-life care in advance.

Assessment

Diagnosis of the terminal phase can be difficult. Reversible causes of deterioration include hypercalcaemia, infection, and opioid toxicity. Clinical signs include:

- bed-bound and drowsy or semicomatose.
- only able to take sips of fluid/ difficulty swallowing tablets.
- poor tolerance of renal replacement therapy.

Management

Plan and document care of the patient and family; consider using a care pathway or checklist.

- Discuss prognosis (patient is dying), goals of care (maintaining comfort), and preferred place of death with patient and/or family.
- Clarify resuscitation status; check DNAR form has been completed. (See: local policy)
 - Reassure the patient and family that full supportive care will continue.
- Stop unnecessary investigations and monitoring (BP, pulse, temperature).
- Discontinue medication not needed for symptom control, and review daily.

Some patients may still benefit from oral diuretics, adjuvant analgesics, bicarbonate.
- If able to swallow, consider liquid formulations. Otherwise use the SC or rectal route.
- Offer oral fluids, maintaining any fluid restriction; stop IV/IM/SC fluids.
- Comfort nursing care (pressure relieving mattress, reposition for comfort only), eye care, mouth care (sips of fluid, oral gel), bladder and bowel care.

Anticipatory prescribing

All patients should have as required medication for symptom control available:

- Opioid analgesic: **alfentanil** SC hourly (100-250micrograms, if not on a regular opioid).
- Anxiolytic sedative: **midazolam** SC 2.5-5mg, hourly.
- Anti-secretory medication: **hyoscine butylbromide** (Buscopan) SC 20mg, hourly.
- Anti-emetic: **haloperidol** SC 0.5-1mg, 12 hourly or levomepromazine SC 2.5-5mg, 8-12 hourly.

Pain (see dose conversion chart below)

- Paracetamol or an NSAID (benefits may outweigh risks in a dying patient) can help bone, joint, pressure sore, inflammatory pain.
- **Alfentanil** and **fentanyl** are the opioids of choice – no renal excretion of parent drug or metabolites.
 - o Morphine / diamorphine are renally excreted as is oxycodone to a lesser extent; these opioids accumulate and can cause significant toxicity with repeated doses.
 - o A single dose can be given if the patient is not opioid toxic while a supply of alfentanil or fentanyl is obtained.
- No regular opioid: alfentanil SC 100-250micrograms hourly, as required.
- Fentanyl patch: continue patch, use correct SC alfentanil dose for breakthrough pain.
- Other opioids should be converted to a subcutaneous infusion of alfentanil in a syringe driver/ pump with the correct SC alfentanil dose, hourly as required (see chart).

Myoclonus or muscle stiffness/ spasm: midazolam SC infusion, 5-20mg over 24 hours.

Anxiety/distress: midazolam SC 2.5-5mg, hourly, as required.

- Try to address psychological and family concerns causing patient anxiety.

Breathlessness

- May be due to pulmonary oedema, acidosis, anxiety or lung disease.
- Oral diuretic if able to swallow. Avoid fluid overload; consider ultrafiltration.

Intermittent breathlessness/ distress	midazolam SC 2.5mg hourly, as required &/ or lorazepam sublingual 0.5mg 8 hourly, as required. alfentanil SC hourly, as required. - fentanyl patch or alfentanil infusion: see chart for dose. - no regular opioid: alfentanil SC 100-250micrograms.
Persistent breathlessness/ distress	midazolam SC 5-20mg + alfentanil SC 500 micrograms (if no opioid for pain) via a syringe driver or pump.

Respiratory tract secretions

1st line: hyoscine butylbromide SC 20mg, hourly as required (up to 120mg/ 24hours).

2nd line: glycopyrronium bromide SC 100micrograms, 6-8 hourly as required.

Nausea / vomiting (see: Nausea / Vomiting, Subcutaneous medication)

- Nausea is common due to uraemia and co-morbidity.
- If already controlled with an oral anti-emetic, continue it as a subcutaneous infusion or use a long acting anti-emetic: haloperidol SC 0.5-1mg twice daily or 1-2.5mg once daily.
levomepromazine SC 2.5mg twice daily or 5mg once daily.
- Treat persistent nausea with levomepromazine SC 5-12.5mg once or twice daily or use 5-25mg over 24 hours in a syringe driver/ pump.

Delirium

- Common and may worsen as uraemia increases; needs active management

Mild delirium/ hallucinations	Haloperidol SC 2.5mg, once daily	
Established terminal delirium/ distress	1 st line midazolam SC 20-30mg over 24 hours in a driver/pump + midazolam SC 5mg hourly, as required OR regular rectal diazepam 5-10mg, 6-8 hourly.	2 nd line midazolam SC 40-80mg over 24 hours in a syringe driver/ pump + levomepromazine SC 12.5-25mg, 6-12 hourly, as required, stop any haloperidol.

Practice points

- Opioid analgesics should not be used to sedate dying patients.
- Avoid renally excreted opioids (codeine, dihydrocodeine, morphine, diamorphine, oxycodone).
- Subcutaneous infusions provide maintenance treatment only; additional SC doses of medication will be needed if the patient's symptoms are not controlled.
- Midazolam is titrated in 5-10 mg steps. Up to 5mg can be given in a single SC injection (1ml). Single SC doses can last 2-4 hours. Useful as an anticonvulsant.
- A marked increase in pain in the dying patient is unusual; reassess and seek advice.
- As uraemia worsens, the patient may become more agitated and need an increased dose of midazolam, and in some cases additional levomepromazine.

Resources

Professional

NHS End of life care Programme <http://www.endoflifecare.nhs.uk/eolc>

Liverpool Integrated Care Pathway http://www.mcpcil.org.uk/liverpool_care_pathway

Patient

Patient leaflet on website: What happens when someone is dying.

Key references

1. Bunn R, Ashley C. *The renal drug handbook* Oxford, Radcliffe Medical Press 2004
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3. Dean M. Opioids in renal failure and dialysis patients. *J Pain Symptom Management* 2004; 28(5): 497-504

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

A guide to opioid doses for dying patients with acute renal impairment or stage 4-5 chronic kidney disease (GFR < 30ml/min)

- Use this chart as a **guide**. The doses are **approximate** and not exact equivalent doses.
- Always prescribe an appropriate opioid drug and dose for breakthrough pain.
- Avoid renally excreted opioids (codeine, dihydrocodeine, morphine, diamorphine, oxycodone)
- Check the information about individual drugs: see Fentanyl patch, Alfentanil.
- Reduce the dose by up to 30% when changing opioid if the patient is opioid toxic, frail or elderly and re-titrate.
- Particular care is needed when changing between opioids at higher doses or when the dose of the first opioid has been rapidly increased as these patients are at greater risk of adverse effects.

Monitor the patient carefully; if in doubt – seek advice

Change to alfentanil or fentanyl →									Opioids of choice in moderate to severe renal impairment		
Morphine ¹			Diamorphine ¹		Oxycodone ¹			Alfentanil ^{2,3} injection		Fentanyl patch ⁴	
4 hourly oral dose	24 hour total oral dose	24 hour total SC dose	4 hourly SC dose	24 hour total SC dose	4 hourly oral dose	24 hour total oral dose	24 hour total SC dose ¹	SC as required dose, hourly, in micrograms	24 hour SC driver/ pump dose	Patch strength micrograms/ hour	
2 - 3mg	15mg	7 - 8mg	1mg	5mg	1 - 2mg	7 - 8mg	5mg	100-200	500 micrograms	Do not use	
5mg	30mg	15mg	2mg	10mg	2 - 3mg	15mg	7 - 8mg	200-250	1mg (1000 micrograms)	12	
10mg	60mg	30mg	2.5mg	20mg	5mg	30mg	15mg	300-500	2 mg	25	
15mg	90mg	45mg	5mg	30mg	7 - 8mg	45mg	20mg	500	3 mg	37	
20mg	120mg	60mg	7.5mg	40mg	10mg	60mg	30mg	Seek advice	4mg	50	
30mg	180mg	90mg	10mg	60mg	15mg	90mg	45mg	Seek advice	6mg	62	
40mg	240mg	120mg	10mg	80mg	20mg	120mg	60mg	Seek advice	Seek advice	75	

¹ If it is not possible to obtain alfentanil, a single 4 hourly dose of morphine SC, diamorphine SC or oxycodone SC may be given as an interim measure but should not be repeated. A continuous subcutaneous infusion should not be used.

² Alfentanil clearance is reduced in liver impairment; reduce dose and titrate.

³ Alfentanil is supplied as 500micrograms/ ml. If higher SC breakthrough doses or a SC infusion dose over 6mg are needed – seek advice.

⁴ Fentanyl is approximately four times more potent than alfentanil and longer acting. Fentanyl clearance may be reduced in severe liver impairment, and it can accumulate in chronic kidney disease.

Fentanyl SC injections can be used for breakthrough symptom control if alfentanil is ineffective due to its short duration of action.

The low concentration of the fentanyl preparation limits the SC injection dose to a maximum of 50 micrograms (1ml).

Fentanyl SC 50 micrograms is approximately equivalent to alfentanil SC 200-250 micrograms. **Seek advice.**

Compatibility Table: Subcutaneous Alfentanil Infusion in a Syringe Driver

Diluent: Water for injections

- **These are not clinical doses to prescribe. Most patients do not need high such doses. Refer to the prescribing guide above.**
- Use this table to check for concentrations that are stable.
- Read the guideline: Subcutaneous infusion of medication in Palliative Care.
- Use the minimum effective dose and titrate according to response.

Drug Combination	Maximum concentrations of two drug combinations that are physically stable	
	14ml in 20ml syringe	17ml in 30ml syringe
Alfentanil Cyclizine	3mg 100mg	4mg 150mg
Alfentanil Glycopyrronium bromide	4mg 1100 micrograms	5.5mg 1200 micrograms
Alfentanil Haloperidol	6mg 10mg	7.5mg 10mg
Alfentanil Hyoscine butylbromide	4.5mg 90mg	5.5mg 120mg
Alfentanil Hyoscine hydrobromide	6mg 1200 micrograms	7.5mg 1200 micrograms
Alfentanil Levomepromazine	6mg 35mg	7.5mg 40mg
Alfentanil Metoclopramide	2.5mg 45mg	2.5mg 60mg
Alfentanil Midazolam	3mg 40mg	3.5mg 50mg
Alfentanil Octreotide	5mg 700 micrograms	6mg 800 micrograms

Drug Combination	Maximum concentrations of three drug combinations that are physically stable	
	14ml in 20ml syringe	17ml in 30ml syringe
Alfentanil Haloperidol Midazolam	3.5mg 5mg 30mg	4.5mg 5mg 35mg
Alfentanil Hyoscine butylbromide Levomepromazine	4mg 90mg 20mg	5mg 120mg 25mg
Alfentanil Metoclopramide Midazolam	2mg 30mg 20mg	3mg 35mg 20mg
Alfentanil Levomepromazine Midazolam	3mg 65mg 25mg	3.5mg 80mg 30mg

Symptom control in patients with chronic kidney disease/ renal impairment

Introduction

- This guideline covers modifications to standard symptom control that are recommended in patients with chronic kidney disease or acute renal impairment.
- Renal impairment is common in patients with diabetes, cardiovascular disease or cancer (from disease or treatment eg. chemotherapy, obstructive uropathy, myeloma).
- Symptom control is complicated by delayed drug clearance, dialysis effects and renal toxicity associated with commonly used medication (eg. NSAIDs).
- 50% of dialysis patients have pain. Depression and other symptoms are common.

Assessment

Chronic kidney disease (CKD)		
CKD stage 1	Normal renal function	
CKD stage 2	Mild impairment (eGFR 60-89 ml/min)	Asymptomatic
CKD stage 3a	Moderate impairment (eGFR 45-59 ml/min)	Asymptomatic
CKD stage 3b	Moderate impairment (eGFR 30-44 ml/min)	Anaemia, fatigue, muscle cramps
CKD stage 4	Severe impairment (eGFR 15-29 ml/min)	In addition: anorexia, nausea, insomnia, neuropathy, gout
CKD stage 5	End stage renal disease (eGFR < 15 ml/min)	In addition: itch, headache, cognitive impairment; death

- Pain is common and associated with many of the complications of advanced CKD.
- Look for multiple types of pain and/or other symptoms due to:
 - renal disease (polycystic kidneys, liver cysts, amyloid).
 - co-morbidity (diabetes, vascular disease, angina).
 - dialysis (abdominal pain in peritoneal dialysis, headache, fistula problems).
 - other pathology (cancer, osteoarthritis).
- Pain in patients with chronic kidney disease:
 - Musculoskeletal pain.
 - Muscle spasm, cramps, restless leg syndrome.
 - Osteoporosis.
 - Renal osteodystrophy.
 - Osteomyelitis, disc infection.
 - Carpal tunnel syndrome.
 - Neuropathic pain – renal or diabetic peripheral neuropathy.
 - Ischaemic pain – peripheral vascular disease, vasculitis.
 - Calciphylaxis – complex pain caused by tissue ischaemia due to calcification of small vessels/ subcutaneous tissue.
- Identify chronic pain (needs regular analgesia) and any intermittent/ episodic pain as this often needs managed separately with short acting analgesics/ non-drug measures. (see: Pain management, Pain assessment)
- Some drugs will be cleared by dialysis; an extra dose during or after dialysis may be needed.
- Patients are often on multiple drugs with a high risk of interactions/side effects.

Management

- Much of the advice in the palliative care guidelines is applicable to patients with renal disease. See table for renal prescribing advice.
- There is another renal palliative care guideline: Last days of life (renal).
- Choice and dose of opioids depends on the degree of renal impairment.
- Mild renal impairment; use lower starting doses of renally excreted opioids (codeine, dihydrocodeine, morphine, diamorphine, oxycodone) and slower titration.
- Stages 3-5 chronic kidney disease; use a modified WHO analgesic ladder (see page 2).

Pain management in renal disease

STEP 1: Mild Pain

Paracetamol +/- adjuvant analgesic
1g, qds

Assess pain fully before treatment.
Ask the patient regularly about their pain.
Record a pain score.
(See: Pain management, Pain assessment)

STEP 2: Mild to moderate pain

Paracetamol + low dose opioid or nefopam +/- adjuvant analgesic

- Nefopam is a moderately potent, non-opioid – reduce dose if GFR < 60ml/min.
- Low dose oxycodone or tramadol can be used if GFR > 30ml/min – reduce dose and frequency, monitor closely for side effects (drowsiness, hallucinations, confusion).

STEP 3: Moderate to severe pain

Paracetamol + selected opioid +/- adjuvant analgesic

- Fentanyl patch – opioid of choice for stable pain; well tolerated, not renally excreted or removed by dialysis. Can accumulate with longer term use; monitor and adjust dose. Nefopam is used for breakthrough pain or an oral opioid as in step 2.
- Alfentanil injection – used as a SC injection, sublingually, or as a subcutaneous infusion. (see: Fentanyl patches, Alfentanil)
- Methadone – titration complex so only use on specialist advice.

Adjuvant analgesics (for prescribing advice see table below)

Antidepressant or anticonvulsant: for nerve pain

Start at a low dose; titrate slowly. No clear difference in efficacy.

- amitriptyline (side effects: confusion, hypotension, dry mouth)
- gabapentin (side effects: sedation, tremor); adjust dose for renal function
- sodium valproate • carbamazepine • clonazepam

Ketamine: complex neuropathic pain including calciphylaxis
(see: Ketamine on website)

Seek advice:

- ◆ Severe pain.
- ◆ Pain not responding to treatment.
- ◆ Dose of opioid has increased rapidly but patient is still in pain.
- ◆ Episodes of acute severe pain.
- ◆ Pain worse on movement.

Symptom control in renal disease (see prescribing advice tables)

- Depression – common and underdiagnosed. (see: Depression)
 - SSRI antidepressant (eg sertraline) is often used.
- Dialysis associated symptoms (hypotension, nausea, cramps, fatigue) – review dialysis prescription.
- Hiccups – (see: Hiccup)
 - Treat any other underlying cause eg gastro-oesophageal reflux.
 - Prokinetic antiemetic (metoclopramide or domperidone).
 - Baclofen – adjust dose for renal function.
- Itch – common and distressing. (see: Itch)
 - Good skin care with regular use of emollients +/- antihistamine.
 - Ondansetron has been used for intractable uraemic itch; 4-8mg twice daily.
- Nausea/ vomiting – assess likely cause (see: Nausea/ vomiting).
 - Gastric stasis is common – treat with metoclopramide (short term) or domperidone
 - Levomepromazine is a useful broad spectrum antiemetic; use low doses and monitor for hypotension.
 - Cyclizine worsens dry mouth in patients on fluid restriction.
- Restless leg syndrome – affects 20-40% of uraemic patients.
 - Clonazepam orally starting at 0.5mg nocte.
 - Gabapentin 100-300mg nocte (adjust dose for renal function).
- Other common symptoms include anorexia, constipation and fatigue – see relevant palliative care guidelines.

Prescribing advice for palliative care patients with chronic kidney disease/renal impairment – Part 1

For further information see: other Palliative Care Guidelines & Last days of life (renal) guideline

Drug	Renal Impairment			Dialysis Clearance		Comments
	Mild: GFR 60-89 ml/min	Moderate: GFR 30-59 ml/min	Severe: GFR 15-29ml/min	HD	PD	
Paracetamol	Normal starting dose	6 hourly dosing	6-8 hourly dosing	Cleared	No	Safe non-opioid
NSAIDs	50-75% normal dose CAUTION	AVOID	AVOID	No	No	Nephrotoxic, ↑ risk of GI bleed (platelet dysfunction). Only used when patient is dying.
Codeine/ dihydrocodeine	Normal starting dose (monitor closely)	AVOID or use small dose and titrate slowly	AVOID codeine Dihydrocodeine: v small dose, slowly titrated	Unknown	Unknown	Metabolites accumulate. Reports of severe toxicity in CKD stage 4/5.
Tramadol	Normal starting dose	50 -100mg, 12 hourly (Max 200 mg / 24 hrs)	CAUTION	Yes	Unknown	Use 50mg, 12 hourly for dialysis patients. Risk of confusion/ delirium.
Nefopam	30-60mg, 8 hourly	30mg, 6-8 hourly	30mg, 8 hourly	Unlikely	Unknown	Can accumulate if on dialysis. Full dose ≈ fentanyl 12 microgram patch.
Morphine/ diamorphine	75% normal dose	50% normal dose, 6 hourly	AVOID or use very small doses and monitor closely – seek advice	Yes Occasionally used as post dialysis dosing.	No	CNS depot clears slowly in HD. Metabolites accumulate in PD. Single dose post HD can be used. Monitor closely.
Oxycodone (see: guideline)	Normal starting dose	50-75% normal dose, reduce dose frequency to 8 hourly	AVOID or use very low dose & monitor	Unknown	Unknown	↑ half life, and ↓ excretion of metabolites. Avoid modified release preparation.
Fentanyl (see: guideline)	Normal starting dose	75% normal dose	50% normal dose	No	No	Can accumulate after longer term use; monitor and adjust dose.
Alfentanil (see: guideline)	Normal starting dose	Normal starting dose	Normal or reduced starting dose	No	No	Short acting.
Methadone	Normal starting dose	Normal starting dose	50% normal dose	No	No	Seek specialist advice re dose and titration.
Metoclopramide	Starting dose (10mg, 8 hourly)	75% dose, 8 hourly	50% dose, 8 hourly	Yes	No	Reduced clearance; more risk of extrapyramidal side effects.
Domperidone	Starting dose (10mg, 6-8 hourly)	Normal starting dose	Normal starting dose	Unknown	Unknown	
Cyclizine	Starting dose (25mg, 8 hourly)	Normal starting dose	Normal starting dose	Unknown	Unknown	Dry mouth. More CNS side effects. Hypotension, tachyarrhythmias reported.
Haloperidol	Starting dose (1mg, nocte)	Normal starting dose	50% normal dose	No	No	Lowers seizure threshold, ↑risk cardiac arrhythmias, may accumulate.
Levomepromazine	Starting dose (3mg, nocte)	Start low & titrate	Start low & titrate	Unknown	Unknown	Sedation at higher doses. Causes hypotension. Lowers seizure threshold.
Ondansetron/ Granisetron	Normal starting dose	Normal starting dose	Normal starting dose	No	Unknown	May help itch, constipating.

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Palliative Care Guidelines: Renal Palliative Care
Antiemetics

Prescribing advice for palliative care patients with chronic kidney disease/ renal impairment – Part 2

For further information see: other Palliative Care Guidelines & Last days of life (renal) guideline

Drug	Renal Impairment			Dialysis Clearance		Comments
	Mild: GFR 60-89ml/min	Moderate: GFR 30-59 ml/min	Severe: GFR 15-29 ml/min	HD	PD	
Diazepam	Normal starting dose	Start lower	Start lower & titrate	No	No	Used for insomnia, anxiety and muscle spasm/ myoclonus. Start lower and titrate dose for all benzodiazepines. Metabolites excreted renally and protein binding is reduced.
Lorazepam	0.5mg, 6 hourly or nocte	Start lower	Start lower & titrate	No	Unlikely	
Midazolam SC	2.5mg, 1-2 hourly	Start lower	Start lower & titrate	No	Unlikely	
Temazepam	Normal starting dose	Max dose 20mg	Max dose 10mg	No	Unknown	
Clonazepam	0.5mg, nocte	Start low dose & titrate	Lower dose & titrate	No	Unknown	
Gabapentin	300mg, 12 hourly	300mg nocte	300mg alternate days. If on dialysis, only after it.	Yes; 300mg post HD	Probable	Parent drug accumulates. Withdraw gradually, over a week.
Sodium valproate	Starting dose 100-200mg, 12 hourly	Normal starting dose	Normal starting dose	No	Unknown	Well tolerated, avoid if liver disease. Titrate slowly .
Carbamazepine	Starting dose 100-200mg, 12 hourly	Normal starting dose	Normal starting dose	No	No	Drug interactions.
Amitriptyline	Starting dose 10mg, nocte	Normal starting dose	Normal starting dose	No	No	Drug interactions, side effects, and contraindications can limit use. Titrate slowly.
Citalopram	Normal starting dose	Normal starting dose	Use with caution	No	No	Check BNF for drug interactions (eg. with tramadol). Start at lowest dose and titrate carefully in CKD stages 4/5.
Sertraline	Normal starting dose	Normal starting dose	Normal starting dose			
Mirtazapine	Normal starting dose	Normal starting dose	Start at low dose and monitor closely.			
Baclofen	5mg, 8 hourly	5mg, 12 hourly	5mg, daily		Unknown	Withdraw gradually.
Ketamine oral or SC (see guideline on website)	Starting dose orally 5-10mg, 6 hourly	Normal starting dose	May be tolerated in standard doses but start at low dose and monitor closely.	No	Unknown	Little information available. Less than 2-3% of ketamine is excreted unchanged. Can accumulate. Seek specialist advice.
Ranitidine	Normal starting dose	Normal starting dose	50-100% dose	Yes	Unknown	Accumulates.
Fluconazole	Normal starting dose	Normal starting dose	50% dose	Yes	Yes	
Hyoscine butylbromide (Buscopan) SC	20mg SC, 1-2 hourly	Normal starting dose	Normal starting dose	Unknown	Unknown	Use for respiratory secretions, bowel colic, bladder spasms.

Palliative Care Guidelines: Renal Palliative Care
 Benzodiazepines
 Adjuvants
 Anti-depressants
 Other

SIGN 103 recommends that creatinine clearance estimated by the Cockcroft-Gault formula be used for drug dosing as published recommendations are based on this prediction equation for GFR. The tables are a guide to dose adjustments. Each patient should be assessed and monitored individually.

Measuring renal function

- Prediction equations are more accurate than serum creatinine or 24-hour urine creatinine clearance.
- The equations are affected by age, sex and weight so are less reliable in older people and those with cachexia, obesity or oedema.
- eGFR is reported in routine laboratory results but is less accurate at values of > 60ml/ min.
- Cockcroft-Gault formula is recommended in drug manufacturer's information.

$$\text{GFR (ml/min)} = \frac{(140 - \text{Age}) \times \text{IBW (kg)} \times 1.23 \text{ (if male)} \times 1.04 \text{ (if female)}}{\text{serum creatinine (micromoles/l)}}$$

Ideal Body Weight (IBW) is recommended for the calculation particularly if the patient is oedematous or obese.

= male 50 + 2.3kg per inch over 5 feet

= female 45.5 + 2.3kg per inch over 5 feet

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Subcutaneous infusion of medication in Palliative Care

Introduction

- Portable devices are frequently used in palliative care to deliver a continuous subcutaneous infusion of medication over 24 hours. Check which device is used in your area.

Indications

Patient is unable to take medication orally due to:

- Persistent nausea and/ or vomiting.
- Dysphagia.
- Bowel obstruction or malabsorption.
- Reduced level of consciousness, such as in the last days of life.

General information

- Use your local protocol for setting up a syringe driver or syringe pump.
- The table below contains information about preparations, dose ranges and indications for single drugs that can be given by subcutaneous infusion for symptom control in palliative care.

Compatibility tables

- The tables contain information about the stability and compatibilities of drug combinations that are given in a subcutaneous infusion in palliative care.
- **The compatibility charts should not be used to guide prescribing. They do not contain clinical dose information.** Read the relevant sections of the palliative care guidelines for the symptom(s) being treated when choosing the correct dose to prescribe.
- Use the correct compatibility tables for the infusion device in use in your area. Compatibility tables are available for a syringe driver and for the McKinley T34 syringe pump for:
 - Morphine and one or two other drugs
 - Diamorphine and one or two other drugs
 - Oxycodone and one or two other drugs
 - Alfentanil and one or two other drugs
- Drugs, doses or combinations other than those listed in the compatibility charts are used occasionally on the recommendation of a palliative care specialist. Any recommendation given by the palliative care specialist should be documented clearly in the patient's notes.

Practice Points

- A continuous subcutaneous infusion of medication aims to maintain symptom control. If the patient has uncontrolled symptoms before the infusion is started or during the infusion period, give breakthrough doses of medication as required.
- Prescribe the medication for subcutaneous infusion and the diluent (usually water for injection). The infusion is usually given over 24 hours.
- Prescribe the correct breakthrough dose, as required, for each medication in the infusion but avoid a volume over 1ml for subcutaneous bolus injection.
- Prepare a new syringe every 24 hours.
- Protect the syringe from direct light.
- Check the syringe regularly as per local protocol for precipitation, cloudiness, particles, colour change; make sure it is running to time. Check the line, connection and cannula regularly.

Single drugs used in a subcutaneous infusion in Palliative Care

Diluent: water for injections

Single agent	Indications and dose range	Comments
MORPHINE 10mg, 30mg in 1ml 60mg in 2ml	Indications: opioid responsive pain, breathlessness. Dose: See Choosing & Changing opioids	<ul style="list-style-type: none"> 1st line opioid analgesic.
DIAMORPHINE 10mg, 30mg, 100mg, 500mg powder ampoules	Indications: opioid responsive pain, breathlessness. Dose: See Choosing & Changing opioids	<ul style="list-style-type: none"> Can be diluted in a small volume. Preferred for high opioid doses.
OXYCODONE 10mg in 1ml 20mg in 2ml	Indications: opioid responsive pain, breathlessness. Dose: See Choosing & Changing opioids	<ul style="list-style-type: none"> 2nd line opioid analgesic if morphine/diamorphine not tolerated.
ALFENTANIL 1mg (1000micrograms) in 2ml, 5mg in 10ml	Indications: opioid responsive pain, breathlessness. Dose: See Choosing & Changing opioids	<ul style="list-style-type: none"> 3rd line opioid; seek specialist advice. 1st line in stages 4 /5 chronic kidney disease.
Antiemetics		
CYCLIZINE 50mg in 1ml	Indications: nausea and vomiting (bowel obstruction or intracranial disease). Dose: 50-150mg / 24 hours	<ul style="list-style-type: none"> Anticholinergic; reduces peristalsis. Can cause redness, irritation at site. Do not mix with oxycodone or hyoscine.
METOCLOPRAMIDE 10mg in 2ml	Indications: nausea and vomiting (gastric stasis/outlet obstruction, opioid) Dose: 20-120mg / 24 hours	<ul style="list-style-type: none"> Prokinetic. Avoid if complete bowel obstruction or colic.
HALOPERIDOL 5mg in 1ml 10mg in 2ml	Indications: opioid or metabolic induced nausea, delirium. Dose: 2.5-5mg / 24 hours	<ul style="list-style-type: none"> Long half life: can also be given as a once daily SC injection.
LEVOMEPRMAZINE 25mg in 1ml	Indications: complex nausea, terminal delirium/ agitation. Dose: 5-25mg / 24 hours - antiemetic. Dose: 25-100mg / 24 hours - terminal sedation.	<ul style="list-style-type: none"> Lowers blood pressure. Long half life: can be given as a once or twice daily SC injection. See: Levomepromazine.
Anticholinergics for chest secretions or bowel colic		
HYOSCINE BUTYLBROMIDE (Buscopan) 20mg in 1ml	Indications: chest secretions, bowel obstruction (colic, vomiting). Dose: 40-120mg / 24 hours	<ul style="list-style-type: none"> 1st line; non-sedative.
GLYCOPYRRONIUM 200 micrograms in 1ml 600 micrograms in 3ml	Indications: chest secretions or colic. Dose: 600-1200 micrograms /24 hours	<ul style="list-style-type: none"> 2nd line; non-sedative. Longer duration of action than hyoscine.
HYOSCINE HYDROBROMIDE 400 micrograms in 1ml 600 micrograms in 1ml	Indications: chest secretions. Dose: 400-1200 micrograms / 24 hours	<ul style="list-style-type: none"> 2nd line; sedative. Can precipitate delirium.
Sedative		
MIDAZOLAM 10mg in 2ml (preferred) 10mg in 5ml	Indications: anxiety, muscle spasm/ myoclonus, seizures, terminal delirium/ agitation. Dose: titrate according to symptoms and response.	<ul style="list-style-type: none"> Anxiolytic (5-10mg/ 24 hours). Muscle relaxant (5-20mg/ 24 hours). Anticonvulsant (20-30mg/ 24 hours). 1st line sedative (20-80mg / 24 hours).
Other medication occasionally given by SC route in palliative care		
DEXAMETHASONE 4mg in 1ml	Indications: bowel obstruction, raised intracranial pressure or intractable nausea and vomiting. Dose: 2-16mg / 24 hours	<ul style="list-style-type: none"> Subcutaneous dose is the same as oral. Available as different dose formulations so check preparation. Can be given as a daily SC injection (in the morning). Given as a single drug infusion, mixes poorly.
KETOROLAC 10mg in 1ml 30mg in 1ml	Indication: bone/ inflammatory pain if patient in last days of life. Dose: 10- 30mg / 24 hours	<ul style="list-style-type: none"> Specialist supervision only. Give an oral PPI if still able to swallow. Long half life particularly in frail patients; can be given as a twice daily SC injection.
OCTREOTIDE 200micrograms/ml (5ml multi-dose vial)	Indications: intractable vomiting due to bowel obstruction, fistula discharge. Dose: 300-900 micrograms / 24 hours	<ul style="list-style-type: none"> Some formulations very expensive. Potent antisecretory agent. Does not treat nausea. Limit fluid intake to 1-1.5 litre/ 24 hours.

Subcutaneous Fluids in Palliative Care

Introduction

Artificial hydration is occasionally indicated in palliative care. Before fluids are started, the goals of this treatment must be clarified by the healthcare team, discussed with the patient and family, and then reviewed regularly.

Preparations

Sodium chloride 0.9%	500ml or 1 litre	500-1500ml can be given subcutaneously over 24hours.
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Indications for artificial hydration

- Patient has persistent symptoms due to dehydration that are not responding to other management options (eg. intractable nausea, marked postural hypotension).
- Dehydration is contributing to poor renal clearance of opioids (eg. morphine, diamorphine) that are causing symptoms of toxicity such as delirium. The opioid dose and general pain management should also be reviewed.
- The subcutaneous route (SC) can be used if it can meet the patient's fluid requirements in the short term when oral intake is inadequate and maintaining an intravenous line is difficult or inappropriate.

Cautions / contraindications

- If a patient is imminently dying, hydration will not improve survival or symptom control and increases the risk of distressing respiratory secretions.
- Fluid overload, ascites, peripheral oedema due to hypoalbuminaemia.
- Patients on fluid restriction or at risk of fluid overload (heart failure, haemodialysis).
- Site problems due to tissue or skin disorders, thrombocytopenia or coagulopathy.
- Intravenous hydration is more effective in some situations (eg hypercalcaemia, hypovolaemia, acute renal failure).

Dose and administration: See local protocol.

- An overnight SC infusion of 500ml will often meet baseline fluid requirements.
- Choose a suitable site: abdominal wall, thigh or chest wall.
- Avoid areas with skin damage/ disease, oedema or lymphoedema, scarring or previous radiotherapy, near a stoma or a mastectomy scar.
- Fluids are infused by gravity feed; 500ml can be given over 8-12 hours.
- Check site daily and rotate at least every 48 hours to minimise tissue damage.
- Re-site the infusion if there is fluid leakage from the site or significant local pooling of fluid consistent with poor absorption.

Practice points

- Artificial hydration will not improve a dry mouth or associated thirst and is never a substitute for good mouth care. (see: Mouth Care)
- In the last days of life, artificial fluids and feeding that have been started previously should be reviewed and usually discontinued. (see: Last days of life)
- Maintaining hydration can be an emotive issue for families and their concerns need to be addressed sensitively when decisions are being made about artificial hydration and nutrition. (See patient leaflet on website: What happens when someone is dying)

Key reference

Campbell C. *Artificial nutrition and hydration*. National Council for Palliative Care /Association for Palliative Medicine. 2007 London. National Council for Hospice & Palliative Care Services.

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Seizures in Palliative Care

Introduction

- Seizures (generalised or partial) occur in 10-15% of palliative care patients most often due to primary or secondary brain tumours, cerebrovascular disease, epilepsy, or biochemical abnormalities (eg. low sodium, hypercalcaemia, uraemia).
- An advance care plan is needed if the patient wishes to avoid hospital admission.

Assessment

- Exclude other causes of loss of consciousness or abnormal limb/ facial movement. (eg vasovagal episode (faint), postural hypotension, arrhythmia, hypoglycaemia, extrapyramidal side effects from dopamine antagonists, alcohol).
- Find out if the patient has had previous seizures or is at risk - history of epilepsy, previous secondary seizure, known cerebral disease.
- Is there a problem with usual antiepileptic drug therapy – unable to take oral medication, drug interactions – check BNF (eg.corticosteroids reduce the effect of carbamazepine, phenytoin).

Management

Acute seizure management

- Put the patient in the recovery position; move any objects that might cause injury.
- If seizure does not resolve quickly, anticonvulsant medication is needed.

Treatment options

- In hospital, diazepam (emulsion) IV in 2mg bolus doses up to 10mg or lorazepam 4mg by slow IV injection are used.
- Diazepam rectal solution 10-30mg given PR or via a stoma.
- Midazolam SC 5mg, repeated after 5 minutes.
- Buccal midazolam 10mg can be given using the parenteral preparation or the buccal liquid (special order product).

Persistent seizures

- IV phenytoin is used in hospital settings.
- Phenobarbital can be given as 100mg IM bolus dose followed, if needed, by a subcutaneous infusion of phenobarbital 200-400mg diluted in water for injection over 24 hrs. Seek advice from a palliative care specialist.

Chronic seizure control

- Most patients with a structural cause for seizures benefit from treatment.
- Follow SIGN guideline recommendations. Check BNF for drug interactions.
 - o Partial or secondary generalised seizures
 - sodium valproate, carbamazepine or lamotrigine.
 - o Primary generalised seizures – sodium valproate or lamotrigine.
- Dying patient unable to take oral medication - antiepileptics have a long half life so additional anticonvulsant treatment may not be needed.
 - o Midazolam SC 5mg or diazepam rectal solution PR 10mg, if required.
 - o Midazolam SC 20-30mg infusion over 24 hrs can be used as maintenance therapy.

Practice points

- Phenytoin is no longer a first line drug for chronic seizure control. It interacts with many drugs, and is prone to cause side effects including sedation in palliative care patients.

Professional resource

SIGN Guideline 70 (Epilepsy in Adults): <http://www.sign.ac.uk/>

Spinal Cord Compression

Definition

Malignant spinal cord compression occurs when the dural sac and its contents are compressed at the level of the cord or cauda equina.

- It affects about 5% of patients with cancer. Lung, breast, and prostate cancer are the commonest causes but it occurs in other cancers.
- Cord compression can be the initial presentation of cancer.
- Late diagnosis is common causing permanent loss of function and significant morbidity.

Assessment

- Consider cord compression in any patient with cancer.
- Thoracic cord compression is commonest but any part of the spine and multiple sites can be affected.
- Sites of pain and level of compression do not always correlate; X-rays and bone scans can be misleading.
- **Key signs and symptoms**
 - New, progressively severe back pain (particularly thoracic).
 - New spinal nerve root pain (burning, shooting, numbness) – may radiate down anterior or posterior thigh (like sciatica), or like a band around the chest or abdomen.
 - Coughing, straining or lying flat may aggravate pain.
 - New difficulty walking or climbing stairs; reduced power (motor weakness), sensory impairment or altered sensation in limbs.
 - Bowel or bladder disturbance - loss of sphincter control is a late sign with a poor prognosis.
- A full neurological examination should be done but may be normal initially.
- MRI is the correct investigation - images the whole spine.

Cauda equina syndrome

Compression of lumbosacral nerve roots below the level of the cord itself results in a different clinical picture.

- New, severe root pain affecting low back, buttocks, perineum, thighs, legs.
- Loss of sensation often with tingling or numbness in the saddle area.
- Leg weakness, often asymmetrical.
- Bladder, bowel and sexual dysfunction – occur earlier than in cord compression. Loss of anal reflex.

Management

- **Emergency referral is essential** – see local protocol for your NHS Board.
- High dose **dexamethasone**, unless contraindicated, should be started as soon as a diagnosis of cord compression is suspected: 16mg orally and then daily in the morning. Withdraw gradually after radiotherapy treatment.
- If clinical suspicion of spinal instability, transport as a spinal injury.
- Pain control – see Pain Management.
- If there is complete paraplegia and loss of sphincter control, radiotherapy may improve pain control but is unlikely to restore function.
- Patients with residual disability need a full multidisciplinary assessment and continuing supportive care including physiotherapy, occupational therapy, pressure area care, bladder and bowel care; social care, psychological and family support.

Further reading: <http://www.palliativecareguidelines.scot.nhs.uk>

Sweating in Palliative Care

Introduction

Excessive sweating occurs in about 16% of patients with advanced cancer, occurs more at night and may need a change of clothes and/ or bedding.

Assessment

There are multiple causes including:

- Infection (check patient is not at risk of neutropenic sepsis)
- Lymphoma
- Disseminated cancer (particularly with liver metastases)
- Medication
 - SSRI (selective serotonin reuptake inhibitor) antidepressants
 - hormone therapies (tamoxifen, aromatase inhibitors, gonadorelin analogues)
- Endocrine
 - oestrogen deficiency (natural or treatment related menopause)
 - androgen deficiency (surgical or hormone treatment)
 - hypoglycaemia
 - hyperthyroidism
- Alcohol withdrawal
- Autonomic neuropathy

Management

- Treat any underlying cause, including infection (if appropriate).
- Reduce room temperature, remove excess bedding, increase ventilation, use a fan.
- Wear loose cotton clothing, cool with tepid sponging.
- Maintain fluid intake to avoid dehydration.
- Review medication and prescribe an alternative if possible.

Medication

Sweating with pyrexia:

- Paracetamol 1g, 6 hourly.
- Non-steroidal anti-inflammatory drug.

Sweating without pyrexia (associated with tumour):

- Non-steroidal anti-inflammatory drug or dexamethasone 1-2mg daily.
- Antimuscarinic (amitriptyline 10-50mg nocte, levomepromazine 3-6mg nocte) (see: Levomepromazine).
- Cimetidine 400-800mg once daily. (Check BNF for drug interactions).

Sweating with hormone insufficiency:

- Seek advice from an oncologist about hormone replacement therapy.

Resources

Cancerbacup leaflet: <http://www.macmillan.org.uk>

Key references

1. Watson M et al. *Oxford Handbook of Palliative Care* Oxford University Press. 2005; 291-293.
2. Pittelkow M. Sweating. In *Oxford Textbook of Palliative Medicine*. 3rd Edition 2004, p581-585.
3. Twycross R, Wilcock A. *Symptom Management in Advanced Cancer*. Third Edition. Radcliffe Medical Press. 2001; 312-315.