

Palliative care

Introduction



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Palliative care is an approach that improves the quality of life of patients and families facing the problems associated with life-threatening illness (WHO definition). This involves a holistic assessment of patients needs and effective symptom control is an important part of this. Palliative care may extend for many months and is not confined to the final days of life. This tutorial briefly describes the management of some commonly encountered symptoms in adults.

Watch [this video](#) which gives the **patient's perspective** and that of her partner, on the impact that good palliative care has on her quality of life.

You might also like to listen to this [interview](#) with a **palliative care consultant** in Lancashire, who summarises for patients the role of the palliative care team in improving the lives of people with a life-limiting illness. Another [video interview](#) with a **specialist nurse** in a community hospice explains what it is like to work in palliative care.

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WHO pain 'ladder'

Pain is a complex phenomenon. It has been shown that people with advanced disease have many different pains and several factors can influence their pain, such as anxiety. It is important to diagnose the cause and severity of each pain before choosing treatment. This is in part because some pain responds only partially or poorly to opioids (e.g. neuropathic pain).

The World Health Organisation Guidelines (WHO) on the management of cancer pain recommend the use of analgesia 'by mouth, by the clock and by the analgesic ladder'. It describes three types of analgesic:

- **Non-opioids** are essentially NSAIDs and paracetamol.
- **Opioids** range from weak ones (e.g. codeine, dihydrocodeine) to strong (e.g. morphine, oxycodone).
- **Adjuvants** help to relieve pain in certain *specific* circumstances (e.g. dexamethasone for bone pain, amitriptyline for neuropathic pain).



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Patients should continue to take oral medication for as long as possible, prescribed at regular intervals, according to the WHO three-step analgesic ladder shown below. Patients should start on the step of the ladder most appropriate to their level of pain. If a drug fails to relieve the pain, patients should move up one step rather than across the ladder (e.g. don't swap from codeine to dihydrocodeine). Consider the additional use of adjuvants at all steps, and continue with regular paracetamol and NSAIDs at each step if effective and safe.

Step 1	Mild pain	Paracetamol, NSAIDs +/- adjuvants
Step 2	Mild to moderate pain	Paracetamol, NSAIDs, +/- adjuvants Weak opioids (e.g. codeine)
Step 3	Moderate to severe pain	Paracetamol, NSAIDs, +/- adjuvants Strong opioids (e.g. morphine)

Step one: *Regular* paracetamol is the first line analgesic for patients with mild pain. NSAIDs are especially valuable in patients with an inflammatory component to their pain (e.g. bone pain), but come with side effects that need to be taken into account. The combination of both paracetamol and an NSAID can be particularly effective.

Step two: There is some debate about the need for step two of the WHO ladder, and there is no pharmacological need to prescribe a weak opioid before progressing to a strong opioid.



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However, in some situations weak opioids may provide sufficient analgesia; and in others it may be helpful to include step two to help manage the beliefs held by some patients about the use of strong opioids. If regular paracetamol has helped to control a patient's pain, then compound paracetamol-opioid preparations may be prescribed if they contain therapeutic doses of opioid (e.g. co-codamol 30/500).

If step two is omitted then the patient will need to be started on a lower dose of a strong opioid.

Step three: Morphine is often the strong oral opioid of choice for the management of severe pain. The combined use of regular modified-release and 'when required' immediate-release morphine allows effective symptom control for most patients. There is no maximum morphine dose as long as it is titrated carefully, and that increased doses give increased pain relief without unacceptable side effects.

Opioids for pain

Often patients are initially managed on a regular dose of an 'immediate-release' morphine product such as Oramorph every four hours. When pain control is stable, they are then switched to a modified-release version that is given once or twice daily. The initial dose of modified-release morphine can be calculated by adding up the total amount of oral morphine over 24 hours. This includes regular four hourly doses plus any 'when required' doses prescribed for breakthrough pain.

For example, a patient, Paul, has required 10mg oral morphine solution every four hours with two 10mg 'when required' doses, for a few days. His 24-hour morphine requirement is 80mg.

His starting dose of modified-release morphine would be 40mg every 12 hours or 80mg every 24 hours.

The BNF advises that the first dose of the modified-release preparation can be given with the last dose of the oral solution, or within 4 hours of it. However, in practice there might need to be more of an overlap while the modified release preparation starts to work. Immediate-release morphine should continue to be prescribed 'when required' for breakthrough pain. The 'when required' dose should be about one-sixth to one-tenth of the total daily dose of modified-release morphine.



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For our patient Paul on modified-release morphine sulphate 40mg every 12 hours, the 'when required' dose of immediate-release morphine would be around 10mg every 4 hours.

If a patient becomes unable to swallow, a change in route of administration should be considered. Morphine is often the preferred parenteral opioid via e.g. subcutaneous 24-hour syringe drivers. Fentanyl is a useful alternative that can be given as a transdermal patch. Guidance on conversion between oral morphine and other opioids is given in most palliative care resources. Interpret dose conversion factors with care as they are only approximations, and there is a great deal of inter-patient variability.



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Anticipation and management of the side effects of analgesics is an important part of optimising therapy. Nausea and vomiting, sedation and constipation are the most common side effects observed in patients taking opioids. However nausea and vomiting are usually transient and improve after 5-7 days. Patients should take long-term laxatives regularly to minimise the risk of constipation.

Nausea and vomiting

As with pain, there are many causes of nausea and vomiting (e.g. constipation, severe pain, hypercalcaemia, intestinal obstruction, drugs). It is important to identify the most likely cause as this determines the treatment.

At least four different neurotransmitter receptors have been isolated in the areas of the brain that regulate vomiting. Antiemetics can be categorised according to their pharmacological group, effect on a specific neurotransmitter, or likely site of action.

When initiating an antiemetic, the patient should be reviewed every 24 hrs; it may be necessary to substitute the antiemetic or add in another drug from a different class (e.g. haloperidol and cyclizine work in different ways). A single drug is normally sufficient to control symptoms but using two drugs from different groups may be required in resistant patients. Remember to think laterally when using combination antiemetic therapy; don't use drugs that may antagonise one another (e.g. cyclizine inhibits the prokinetic actions of metoclopramide). Adjuvant agents such as corticosteroids may be helpful.

The oral route is suitable for prophylaxis where there is mild nausea and vomiting; non-oral routes should be used for moderate to severe symptoms.

In practice cyclizine, haloperidol or a prokinetic such as metoclopramide or domperidone are often used as first-line antiemetics. Levomepromazine is also used as an antiemetic in palliative care. You do need to be careful about the contraindications to each antiemetic, and assess their relevance to the individual patient.

Other symptoms

Constipation

This is a common symptom in patients with terminal illness due to loss of appetite, dehydration, immobility, drugs, and disease involving the gastrointestinal tract. Patients on morphine and other constipating drugs should be prescribed regular prophylactic laxatives. Regular administration of a faecal softener and a peristaltic stimulant is often recommended. The dose should be titrated to enable patients to pass a stool easily every one to three days.

Diarrhoea

Diarrhoea is less common than constipation in patients with terminal illness. The diagnosis must be made carefully to exclude 'overflow diarrhoea' which is liquid faecal matter seeping past impacted faeces. Common causes of diarrhoea include excessive laxative use, side effects of drug therapy (e.g. chemotherapy, antibiotics), infections (e.g. *C. difficile*) and initiation of enteral feeds.



Agents such as loperamide and codeine may provide symptomatic relief. Treatment for specific conditions includes octreotide for diarrhoea caused by carcinoid tumours.

Dyspnoea

Dyspnoea is an unpleasant sensation of being unable to breathe easily. It is common in patients with advanced disease. It is important to ensure that any underlying co-morbidities, such as COPD, are optimally managed. Opioids can help to relieve the sensation of breathlessness and tend to be more beneficial in patients who are breathless at rest. Often lower doses are required compared with pain, for example starting with immediate-release morphine 2.5mg every four hours and titrating according to response. Benzodiazepines can be used in the management of breathlessness associated with anxiety.



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Confusion

This may be managed by treating the underlying cause e.g. hypercalcaemia. If this fails, consider antipsychotics such as haloperidol or olanzapine. In terminal restlessness midazolam, levomepromazine and haloperidol may be administered as continuous subcutaneous infusions via syringe drivers.

Excessive respiratory secretions

These can be reduced by subcutaneous injection of hyoscine hydrobromide, hyoscine butylbromide or glycopyrronium bromide. However, hyoscine hydrobromide crosses the blood-brain barrier and is often not used as a first-line antisecretory unless sedation is desirable.

Intestinal obstruction

Intestinal obstruction occurs when there is a partial or complete obstruction of the gut lumen and/or peristaltic failure. The patient may suffer a range of symptoms depending upon the severity and location of the obstruction, but they may include vomiting, constipation, constant abdominal pain and colic.

Choosing appropriate medicines to manage these problems is sometimes difficult due to their effects on gut motility. For example, as a prokinetic, metoclopramide may be helpful in a patient with nausea and vomiting who has gastric stasis, but it couldn't be used if the patient also has colic because it might make it worse. Morphine may be helpful for constant abdominal pain, but if the patient also has peristaltic failure then an agent with a lower risk of constipation such as fentanyl should be considered.

Erratic or poor oral absorption of medicines may also present a problem in patients with intestinal obstruction, and the use of non-oral options may be necessary such as patches or syringe drivers.

Syringe drivers

A syringe driver is a small portable battery operated pump that administers drugs subcutaneously by continuous infusion. It is not something that is used by every patient in palliative care, but it can be very useful. Syringe drivers are indicated when other routes become inappropriate or difficult. They are generally programmed to deliver their contents over 24 hours.



Morphine, midazolam, cyclizine and glycopyrronium are common examples of drugs given in this way, but not all medicines are suitable to be administered via a syringe driver. For example an injection needs to be formulated in a relatively small volume to be given via this route. In addition, products that are irritant (e.g. prochlorperazine, diazepam) are less suitable because

of the risk of injection site reactions. Similarly, products that are very acidic or very alkaline may also increase the risk of local irritation.

Most medicines given via continuous subcutaneous infusion are **not licensed** to be given in this way, and mixing them with other medicines in a syringe driver is also unlicensed. However it is common practice in a palliative care setting, and sometimes up to 5 medicines may be given using a single device.

The risk of incompatibility generally increases with the number of drugs, and compatibility information should always be consulted **before** medicines are mixed in a syringe driver (see Information sources, below). If you can't find data for the combination you have been asked about then remember that medicines with a long half-life might not need to go in the syringe driver, and could potentially be given as a once or twice daily subcutaneous injection (e.g. dexamethasone, haloperidol). You can also refer back to the Injection Compatibility topic on [Reducing risk](#) for some more troubleshooting tips.

Water for injection is the preferred **diluent** in the UK because there are more compatibility data for commonly used medicines. Also it is less likely to cause compatibility problems compared to sodium chloride 0.9% which can produce unpredictable results with cyclizine, and higher doses of diamorphine and haloperidol. However sodium chloride 0.9% is isotonic, and so (in theory) is less likely to cause infusion site reactions than water for injection. In practice though, because the volumes involved are low and the rates of administration are slow, site reactions are not usually a problem with water.

The **final volume** of a syringe (volume of drug + volume of diluent) may depend upon the brand of syringe driver and the time over which it is to be administered. Generally the more dilute the contents are, the lower the risk of compatibility problems and injection site reactions. Sometimes the final volume of the syringe may be too large to fit into the device and you may need to consider using more concentrated formulations or halving the volume and giving the infusion over 12 hour periods.

Finally, once set up, the infusion should be **monitored every four hours** to check for precipitation or discolouration and to ensure that the syringe driver is running at the correct rate.

Watch [this video](#), presented by a specialist nurse in Oxfordshire, which shows how one brand of syringe driver is set up. This may not be the brand you use locally, so the detailed instructions may differ in your hospital, but the video does show the range of operational capabilities of a syringe driver.



Suggested questions



You may be asked about a range of clinical problems in the palliative care setting, but many will relate to symptom control or compatibility of medicines in syringe drivers.

If you are asked about **symptom control** then the indication may be obvious, but ask about the likely cause, and establish what the patient has tried already. You will also usually need to find out what other medicines the patient is taking, and their other significant medical problems. You'll need to know whether they are able to take medicines orally, and if they can't what other routes are available (so the intramuscular and rectal routes may be unsuitable if they have low platelets for example).

If you are asked about **mixing medicines in a syringe driver** then you'll need to find out the dose of each medicine and the diluent and volume (if known). Even experienced Palliative Medicine consultants check compatibility.

Information sources

The BNF has a useful section on [prescribing in palliative care](#) that covers the management of a range of symptoms including pain, constipation, nausea and vomiting, and restlessness and confusion. It also includes an opioid conversion guide, helpful information about switching between fentanyl and buprenorphine patches and oral morphine and guidance on using syringe drivers.



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The **Palliative Care Formulary** is a detailed guide to prescribing medicines in the palliative care setting. It is available on the palliativedrugs.com website which also has lots of other useful resources including a database of drug compatibility in syringe drivers and a discussion forum for healthcare professionals. [Palliative Care Matters](#) is an alternative website to support clinical decision-making in palliative care and also includes a compatibility database and links to a range of guidelines.

Andrew Dickman and Jennifer Schneider's book [The Syringe Driver](#) is only available in paper form, but is a comprehensive guide to administering and mixing medicines in syringe drivers. The section on individual drugs at the beginning of the book brings together lots of really helpful information in one place.

There are a range of helpful [Clinical Knowledge Summaries](#) on the topic including pain, secretions, dyspnoea and cough.

Remember to check if you have any **local guidelines** from your palliative care team.

There's a **Medicines Q&A** from UKMi specifically about opioid conversions in the palliative setting which goes into more detail than other resources. Find it on the [SPS website](#).

Be careful about conducting a general internet search on this subject. If you do, you may like to look at our brief guide to [evaluating websites about medicines](#).

Next steps in learning...



CPPE has resources to support your learning and practice in palliative care that you can find by entering 'palliative' into the search box on the [CPPE website](#). In particular, look at:

- [Palliative Care focal point](#) is a distance learning package that focuses on symptoms and management associated with conditions requiring palliative care management.
- [Palliative care \(2nd Edition\) distance learning](#) is a programme which will help you deliver high quality palliative care including advice to support patients, their family, and carers.
- [Dealing with difficult discussions](#) is an e-learning programme looking at discussions that you or a patient may not find easy.

In addition, you might like to look at these resources:

- NICE has published a Clinical Guideline on [Strong Opioids for Adults](#) in palliative care.
- Explore the valuable range of information provided for the public in Scotland about palliative care by [NHS Inform](#).