Recognising when a patient is soon to die can be complex. In the final days of life the patient will almost certainly be physically wasted and weak. He or she is likely to be bedbound, becoming increasingly drowsy and disorientated with a limited attention span. This article discusses the control of various symptoms that occur at the end of life and common medicines management issues that arise.

Stopping medicines

Drugs that offer long-term survival benefits are of little advantage to someone with a prognosis of months or weeks and these medicines should be reviewed regularly. When a patient enters the final days of life all unnecessary medicines should be stopped and only essential medicines (eg, analgesics, antiemetics, anxiolytics and anticonvulsants) continued.

Delivery of medicines

Dysphagia usually occurs and swallowing tablets can become a problem with little food and drink intake. Continuous subcutaneous infusion (CSCI) via a syringe driver is a common method of drug delivery at the end of life. This route is preferred because it is:

- Less invasive than intravenous administration
- Less painful and more predictable than intramuscular administration
- Quicker than transdermal administration to titrate drug doses

A syringe driver is a small portable infusion device that delivers medicine at a set rate. Older devices, such as the Graseby pump, deliver medicine at rates set in millimetres per unit time, and require a manual calculation to determine the correct rate of administration for the dose prescribed. Newer devices calculate the rate in terms of millilitres per unit time and do not require this calculation — reducing the risk of errors.

In 2010 the National Patient Safety Agency recommended the use of newer millilitre-based devices (such as the McKinley T3) over older devices. Mixing two or more medicines in a syringe driver is commonplace in palliative care because patients will often need treatment for more than one symptom. However, certain drugs may be incompatible and cause problems when mixed. There are reference sources available that provide information on the compatibility of drug combinations, eg, the Syringe Driver Survey Database.

Symptom control

Although it can be difficult to predict how and when a patient's condition will deteriorate, there are common symptoms that can worsen in the last few days of life (eg, pain, nausea, agitation and bronchial secretions).
Anticipatory prescribing of medicines ensures that, should these symptoms develop, treatments are available for administration without delay wherever the patient is being cared for.

Common symptoms experienced in the dying phase are described below and various disease-specific considerations are summarised in Box 1.

**Pain** Parenteral administration of a strong opioid, such as diamorphine or morphine, is routinely used for pain control at the end of life. Administration by CSCI allows the patient continuous pain relief. Additional subcutaneous doses can be prescribed for breakthrough pain, usually one sixth of the total 24-hour dose, and can be given as frequently as needed. The CSCI dose should be reviewed, and the dose titrated if necessary, on a daily basis.

Transdermal patches containing fentanyl or buprenorphine should be continued for patients who are established on them if there is insufficient time to change them to a new regimen. Appropriate breakthrough pain relief should also be prescribed in the form of a subcutaneous injection of a strong opioid. Some patients using transdermal patches may need additional analgesia by CSCI, yet some GPs and district nurses may be reluctant to use two different methods of administering a strong opioid to one patient despite it being a safe and fast way to achieve adequate pain control. The required dose should be equivalent to the total amount of additional breakthrough pain relief the patient needed over the previous 24 hours to control his or her pain. A new breakthrough pain relief dose will therefore need to be determined and the intended continued use of the patch should be documented.

If the decision is made to remove the patch and continue the patient on a strong opioid alone via CSCI, the time it takes for blood concentrations of the drug to decline following removal of the patch should be considered (see Box 2, p324).

**Nausea and vomiting** Various factors influence the choice of antiemetic for the dying patient and considerations to determine the best approach include:

- The cause of the nausea and whether it is preventable
- The available route of administration
- Which antiemetics have worked previously
- Identification of side effects that need to be avoided

Cyclizine (150mg/24h by CSCI or 50mg when required up to three times a day) and haloperidol (5–10mg/24h by CSCI) can be used to control nausea and vomiting. Levomepromazine (6.25–25mg/24h by CSCI or 6.25–12.5mg when required) is a useful option for refractory nausea and vomiting. Prokinetic drugs can be useful for patients with gastric stasis.

**Restlessness and agitation** Certain factors may precipitate restlessness and agitation in dying patients (e.g., pain, anxiety, urinary retention) and efforts should be made to prevent these. If agitation is still present, or no

**Box 1: Disease-specific considerations**

**Breathlessness** Breathlessness is commonly experienced in patients with conditions such as lung cancer, chronic obstructive pulmonary disease, motor neurone disease and heart failure. Patients who are persistently breathless and distressed may benefit from a continuous subcutaneous infusion (CSCI) of morphine (5–10mg/24h) and/or midazolam (2.5–5mg/24h).

**Seizures** Patients with a primary or secondary brain tumour and those with a previous history of seizures may be at an increased risk of having seizures at the end of life. Patients should be managed with oral therapy until they are no longer able to swallow — following this midazolam (20–40mg/24h) can be administered by CSCI to control symptoms.

**Raised intracranial pressure** Intracranial malignancy can raise intracranial pressure and lead to cerebral oedema, which can cause severe headache and agitation. This is commonly treated with moderate-to high-dose oral corticosteroids. In most cases, oral corticosteroids are stopped when the patient becomes moribund and can no longer swallow. Refractory seizures may be at an increased risk of having seizures at the end of life. Patients should be managed with oral therapy until they are no longer able to swallow — following this midazolam (20–40mg/24h) can be administered by CSCI to control symptoms.

**Major haemorrhage** Bleeding is a risk in patients with advanced cancer (more commonly in lung, upper-gastrointestinal, head and neck). The risk of haemorrhage can be increased by the proximity of tumours to major blood vessels, presence of fungating wounds and factors that reduce coagulation. In the event of an acute terminal bleed, subcutaneous or buccal midazolam can be given to relax the patient.

**Renal impairment** Impaired renal function in the dying patient may cause accumulation of drugs and their metabolites, leading to toxicity. This can affect the drug choice for symptom control at the end of life; in particular the use of opioids should be reviewed carefully. The national Liverpool care pathway renal steering group provides guidance on medicines management and the control of disturbing symptoms in patients with advanced chronic kidney disease in the final days of life. Morphone and diamorphine are metabolised to morphine-3-glucuronide and excreted via the kidneys; they should be avoided in renal impairment. Fentanyl and alfentanil are extensively metabolised by the liver and so are the preferred choices of opioid in renal impairment; however, because of their short duration of action the use of these drugs for breakthrough pain is limited. Oxycodone is eliminated primarily by the liver with 10% excreted unchanged in the urine. Although the drug should be avoided in stage 5 chronic kidney disease, it can be used with caution in less severe renal impairment.
clear cause can be identified, it may be appropriate to sedate the patient.

Midazolam, can be given by CSCI (3–30mg/24h) or when required (2.5–5mg), titrating the dose to response. Some patients may need higher doses; however, this increases the risk of disinhibition and paradoxical agitation.

Other medicines that are commonly used include haloperidol (2.5–10mg/24h by CSCI or 1.5–2.5mg when required) and levomepromazine (12.5–75mg/24h by CSCI or 6.25–12.5mg when required). Both of these medicines can be useful when nausea and vomiting are also present.

**Respiratory tract secretions**
In the last days of life progressive muscle weakness can prevent patients from coughing or swallowing effectively. An inability to clear secretions in the upper respiratory tract causes noisy or bably breathing.

Although it is common clinical practice to treat this symptom, the evidence to support doing so is lacking. Hyoscine butylbromide can be given subcutaneously as required (20mg) or by CSCI (60–120mg/24h). Hyoscine hydrobromide (400µg as a single dose or 1.2–2.4mg/24h by CSCI) can also be used but is more sedating than hyoscine butylbromide. Glycopyrronium bromide is another alternative although it is sometimes difficult to obtain.

### Palliative Care

**Lifelong Learning questions**

**How to undertake continuing professional development**

Answers from the October module

**Clostridium difficile**

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**Questions**

This month’s Lifelong Learning questions are based on the CLINICAL FOCUS articles on palliative care, which were commissioned from independent authors. The information in the Box (below) is there to help you identify knowledge gaps and undertake continuing professional development. This online module will close on 31 January 2013.

**Answers**

When you have completed the online module, your answers will be submitted for marking and Clinical Pharmacist will send you a certificate and your results by email within two weeks of the module closing. Please do not hesitate to contact us if you have technical problems with the module.

E: clinicalpharmacist@pharmj.org.uk

Our CLINICAL FOCUS articles and the online Lifelong Learning modules can help you plan and record your CPD.

**Reflect on your gaps in knowledge**

- What kind of input can clinical pharmacists have into end-of-life care?
- Which medicines are used for the relief of symptoms in the final days of life?

**Act to enhance your practice**

- Read the CLINICAL FOCUS articles in this issue (pp317–24)
- Test your knowledge by completing the questions at www.clinicalpharmacist.com

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