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# Until the chemist opens

## Palliation from the doctor's bag

### BACKGROUND

People with a life limiting illness may have unpredictable exacerbations of their symptoms requiring after hours care by general practitioners using medications that are readily accessible. All doctors are provided with injectable 'doctor's bag' emergency drugs for use in such a crisis.

### OBJECTIVE

This article aims to: identify which medications from the doctor's bag can be used in the palliative care crises that are most frequently encountered, present the best possible evidence for these indications, and to provide GPs caring for palliative care patients after hours with management strategies so, whenever appropriate, they can continue to be managed at home.

### DISCUSSION

The clinical context, including disease trajectory and patient and caregivers' wishes, must be assessed in palliative care crises. Having excluded reversible problems, symptoms can be treated using doctor's bag medications. Attention must be given to route of administration, duration of effect, and appropriate doses for effective palliation.

**Australian general practitioners treat a median of 5–7 palliative patients each year<sup>1</sup> – a small part of their total clinical practice. However, it is care that patients and their families value greatly and, if done well, stands out in people's minds as a very special encounter. Patients with end stage disease may have unpredictable crises requiring emergency assessment and treatment after hours. Frequently encountered acute problems may include nausea, vomiting, dyspnoea, delirium and pain, which occur in many life limiting illnesses including cancer, HIV/AIDS, end stage organ failure and neurodegenerative diseases such as multiple sclerosis or motor neurone disease.**

Decision making as the end of life approaches can be challenging. Patients may no longer want active investigation and management, or may be unrealistic about what is still achievable, especially at home. Assessment of the patient's disease trajectory and potentially reversible pathologies may be difficult in the after hours setting. Nonetheless, the clinical imperative is to relieve acute, distressing symptoms, and offer the possibility of appropriate management at home if the patient and caregiver wish, and when appropriate.

The doctor's bag contains injectable emergency medications, some of which have off-license but well accepted indications for palliative care, that can provide excellent symptom control (*Table 1, 2*). Appropriate use of these medications for palliation in a crisis requires consideration of route of administration, appropriate doses, knowledge of the duration of effect, and of adverse effects relevant in the emergency setting. The preferred parenteral route of administration for palliative medications is subcutaneous. It is worthwhile to carry subcutaneous butterfly needles in the emergency bag as inserting a butterfly for repeated doses is less traumatic for the patient. Suggested dosages are taken, wherever possible, from the *Therapeutic guidelines* for palliative care.<sup>2</sup>

### Nausea and vomiting

Nausea and vomiting are common, unpleasant symptoms in patients with cancer and other end stage diseases. Assessment aims to identify an underlying cause. Causes may relate to the disease process (eg. cerebral metastases), to treatment (eg. chemotherapy), or be unrelated (eg. gastroenteritis).<sup>3</sup> It is often multifactorial. Assessment should focus on distinguishing potentially reversible presentations

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requiring more urgent attention (eg. bowel obstruction, raised intracranial pressure) from those that can be managed symptomatically pending further review. It also guides medication choice. For example, prokinetic effects of metoclopramide are helpful in gastric stasis but are likely to worsen vomiting and colicky pain in complete gastrointestinal obstruction.<sup>4</sup> Unheralded vomiting suggests the possibility of cerebral metastases or very high bowel obstruction, and steroids may be appropriately used<sup>5,6</sup> (*Table 3*).

The doctor's bag carries several drugs with antiemetic activity: metoclopramide, prochlorperazine, chlorpromazine, haloperidol, dexamethasone, hydrocortisone, and promethazine. Parenteral forms can be administered subcutaneously rather than intramuscularly except prochlorperazine and chlorpromazine, which may only be given intravenously or intramuscularly.

### Dyspnoea

Dyspnoea may be insidious, often worsens as

death approaches, and in some patients no reversible causes will be identifiable (*Table 4*). Several randomised controlled trials using oral or parenteral opioids for dyspnoea in people with a range of life limiting illnesses have shown beneficial effect.<sup>7,8</sup> Pain and dyspnoea are potent stimulants of respiratory drive; by modulating the respiratory drive, morphine lessens distress associated with severe dyspnoea, reducing respiratory effort without changing respiratory rate.<sup>9</sup> Benzodiazepines are sometimes recommended to treat

**Table 1. Doctor's bag medications and their indications for palliation**

Medication and form	Palliative care indication
Adrenaline Injection 1 mg/mL (1 in 1000)	Malignant bleeding
Atropine Injection 600 µg in 1 mL	Noisy breathing/terminal secretions ('death rattle')
Chlorpromazine Injection 50 mg in 2 mL OR Haloperidol Injection 5 mg in 1 mL	Nausea Delirium/acute confusional state
Dexamethasone Injection 4 mg in 1 mL OR Hydrocortisone Injection 100 mg in 2 mL or 250 mg in 2 mL	Central causes of nausea and vomiting, raised intracranial pressure, malignant spinal cord compression, neuropathic pain or other poorly controlled pain, superior vena cava obstruction, dyspnoea caused by lymphangitis
Diazepam Injection 10 mg in 2 mL	Agitation and restlessness, myoclonus, seizures, muscle spasm anxiety from dyspnoea or other difficult symptoms
Metoclopramide Injection 10 mg in 2 mL OR Prochlorperazine	Nausea
Morphine Injection 15 mg in 1 mL OR 30 mg in 1 mL	Pain Dyspnoea, acute pulmonary oedema
Promethazine Injection 50 mg in 2 mL	Nausea (vestibular type in particular) Itch

anxiety associated with refractory dyspnoea in the terminally ill.<sup>10</sup> Their use can only be extrapolated from their anxiolytic role and have not been formally studied in this setting.

Patients with lymphangitis carcinomatosa present with severe dyspnoea which may progress rapidly, often unrelieved by oxygen or morphine. It is most often seen in breast, lung and gastric cancers. Steroids may be tried in this situation.<sup>6</sup>

Noisy respirations at the end of life ('death rattle') may upset the caregivers of a dying

person. Anticholinergic medications are traditionally used, as an extension of their use in anaesthesia for managing airway secretions. The side effect profile of atropine can be distressing to a conscious patient (dry mouth, tachycardia, urinary retention). It may worsen confusion and delirium, because it crosses the blood-brain barrier. Repositioning the patient may be almost as beneficial.<sup>11</sup>

### Delirium/acute confusional states

Delirium is common in patients approaching

the end stage of life limiting illnesses, is underdiagnosed, and is associated with poor prognosis.<sup>12</sup> A simple tool for the detection of delirium is the Confusion Assessment method (Table 5). Delirium is often multifactorial and less than half of cases occurring at the end of life are reversible.<sup>13</sup> Delirium is distressing for patients, families and caregivers. It may be hyperactive (two-thirds), hypoactive, or both, and is characterised by fluctuating poor concentration, confusion, and easy distractibility, making assessment of other

Mode of action	Comment
Vasoconstriction	Can be used topically (ie. adrenaline soaked gauze) for small volume bleeding at superficial sites otherwise difficult to control (eg. fungating wounds)
Anticholinergic – may reduce bronchial secretions	Side effects of atropine can be distressing for conscious or semiconscious patients. Terminal secretions do not always require treatment. Treatment is often ineffective once secretions are well established. Repositioning may reduce breathing noises
Antipsychotic with antiemetic action via dopamine antagonism at the chemoreceptor trigger zone	Haloperidol preferred as it can be given subcutaneously and is less sedating than chlorpromazine, and (unlike metoclopramide) has no prokinetic effect
Corticosteroids – act to reduce malignant inflammation and cytokine production, reduce perineural oedema, mechanism of antiemetic effect not known	Dexamethasone is the more commonly used drug for these indications, but equipotent dose of hydrocortisone is a reasonable alternative. High dose dexamethasone (16 mg daily) may prevent long term neurological consequences of some spinal cord compressions if started immediately. If active treatment of cord compression or raised intracranial pressure is appropriate, it should be instituted without delay and further investigations urgently arranged
Benzodiazepine – GABA agonist, effective as anticonvulsant, muscle relaxant and anxiolytic	Benzodiazepines can worsen delirium. If delirium is suspected an antipsychotic should be used in preference to a benzodiazepine initially. Myoclonus suggests renal or hepatic encephalopathy or neuroexcitatory effects of medications including accumulating opioid metabolites. Further investigation may be appropriate depending on the stage of the patient's disease. Benzodiazepines may precipitate or worsen hepatic encephalopathy due to cirrhotic liver disease
Antiemetics which act by dopamine antagonism at the chemoreceptor trigger zone; metoclopramide	Metoclopramide is preferred as it can be given subcutaneously; contraindicated in suspected high bowel obstruction is also prokinetic and increases tone in the gastro-oesophageal sphincter
Opioid agonist – mode of action in relieving dyspnoea not known, may act by modulating ventilatory drive centrally	Morphine has been shown to relieve dyspnoea in end stage respiratory disease and should not be withheld from distressed patients because of underlying lung disease. Nebulised morphine has not been shown to be effective <sup>18</sup> – the parenteral route is most appropriate in an emergency
Antihistamine – acts on vestibular apparatus and vomiting centre by H1 receptor antagonism	Sedating effects of promethazine can also be beneficial in contributing to symptom control for selected patients. Considerable patient variability in response

**Table 2. Suggested emergency management strategies for acute symptom control and palliation from the doctor's bag****Nausea and vomiting**

- Metoclopramide 10–20 mg subcutaneously, dose may be repeated if necessary, up to 120 mg over 24 hours OR
- Haloperidol\* 0.5–2.5 mg subcutaneously, up to 5 mg over 24 hours OR
- Promethazine 10–25 mg subcutaneously, up to 100 mg over 24 hours
- Suspected central causes of vomiting: dexamethasone 8–16 mg subcutaneously as a single dose

**Dyspnoea**

- Opioid naïve patient: morphine 1–2 mg subcutaneously, repeat half hourly if needed
- Patients on regular opioids: morphine, statim dose should be calculated based on 30–50% increase on the fourth hourly dose of opioid<sup>1</sup>
- Persistent distress unrelieved by morphine: diazepam 2–5 mg intravenously, repeated half hourly if needed until agitation settles

**Delirium**

- Haloperidol 2.5–5.0 mg subcutaneously,<sup>2</sup> titrate at half hourly intervals up to 15 mg in 24 hours OR
- Chlorpromazine 10–25 mg intravenously, titrate at half hourly intervals, up to 100 mg in 24 hours is a more sedating option
- If the patient is agitated, distressed, and/or a risk to themselves or their caregivers, sedation may be required in addition to antipsychotic medication
- Diazepam 2.5–10.0 mg intravenously,<sup>2</sup> repeated in half an hour if needed, until sedation is achieved

**Pain**

- Opioid naïve: morphine 1.0–2.5 mg subcutaneously (frail, elderly) or 2.5–5.0 mg subcutaneously as an initial dose. In a crisis, the patient should be frequently reviewed and the dose titrated up or down by 30–50% according to effect
- On opioids already, experiencing an acute exacerbation that is likely to be opioid sensitive: increase background and breakthrough doses of opioid by 30–50% and convert to parenteral morphine<sup>3</sup>

1. On opioids already, with an acute change less likely to be opioid sensitive (eg. visceral or neuropathic pain): a single dose of dexamethasone 4–16 mg subcutaneously can be added to opioid

2. Use lower end of dose range initially in those who are medication naïve, the frail and elderly to minimise side effects

3. Breakthrough doses are one-sixth to one-twelfth of total daily dose. Conversion from oral to parenteral morphine is based on oral bioavailability of 30–50%. Parenteral doses must therefore be calculated as half to one-third of the oral morphine dose

symptoms with a subjective component difficult (eg. pain or dyspnoea). Confusional states most likely to be reversible at the end of life are those related to medications, sepsis, dehydration, and treatable metabolic abnormalities such as hypoxaemia.<sup>13</sup>

Haloperidol is the first line medication for treating delirium and can be given subcutaneously.<sup>14</sup> Benzodiazepines have no primary role in treating delirium and may worsen it.<sup>15</sup> However, severe agitated delirium occurring in the last hours to days of life sometimes requires a sedating antipsychotic and the addition of a benzodiazepine, which may act synergistically.

**Pain**

Palliative care patients with significant pain will require a strong opioid for adequate symptom relief. The doctor's bag contains injectable morphine and tramadol. Morphine is the preferred medication for palliation (Table 6).<sup>16</sup> Most doctors are familiar with

morphine use, and treatment of acute pain in the opioid naïve patient. Difficulties arise with assessing opioid needs in patients already using regular opioids who have escalating

pain, especially in calculating an appropriate crisis dose when the usual medication is different, or is taken by a different route (eg. transdermal fentanyl patch, methadone, or oral

**Table 3. Bowel obstruction – an emergency management strategy from the doctor's bag****Assessment**

Often partial/subacute rather than complete. Symptoms vary depending on level and completeness of obstruction. Gastric splash suggests high level of obstruction. Bulky hepatomegaly can sometimes cause gastric outlet obstruction

**Management**

Aim is to reduce gastric secretions, pain, nausea and vomiting, and inflammation at site of obstruction, using parenteral medications. A combination of medications usually needed for optimal comfort. Overhydration (>1 L/day) should be avoided as it increases volume of gastrointestinal secretions. Effective medical management is usually possible without use of nasogastric drainage in end stage disease

**Medications**

Haloperidol 0.5–5.0 mg subcutaneously is the most appropriate antiemetic as it will not worsen colicky pain (0.5–2.5 mg in the frail elderly)

Dexamethasone 8–16 mg subcutaneously reduces peritumour oedema and nausea, has been shown to speed resolution of malignant bowel obstruction

Parenteral opioid should be titrated for analgesia

sustained release preparations of oxycodone, morphine or tramadol). These patients are often undertreated in an acute pain crisis. A

30–50% increase in the total daily dose and also in the breakthrough dose of a patient on regular opioids is generally safe, and a

conversion table can be consulted for the conversion to parenteral morphine.<sup>2</sup>

Corticosteroids can be helpful in patients with pain due to acute nerve compression, visceral distension, raised intracranial pressure and soft tissue infiltration.<sup>6,17</sup> Dexamethasone can be given subcutaneously. In a crisis an immediate dose is appropriate, however ongoing steroids should not be given after midday as they have the potential for significant sleep disturbance.

### General considerations

Patients with end stage disease may progress into organ failure, and be frail and cachexic. Many are also elderly. Dose selection should take these factors into account, often starting at the lower end of the dose range. Arranging to review the effect of the initial dose and titrate medications is the safest way to assure good symptom control.

### Conclusion

Some exacerbations may be intermittent or self limiting, but new symptoms can also herald progression of disease and sometimes the onset of the terminal phase. Patients and their families often have clear ideas about where they wish care to be provided at this time. For some people with a good level of function and an acute, unexpected deterioration, transfer to a hospital for investigation and management may be appropriate. For others, it may result in needless hospitalisation for a problem that could have been effectively managed in the community setting. The option of care at home is often gratefully received, and good emergency symptom control contributes to this being a possibility. The challenging aspect of patient assessment as death approaches however is in judging the disease trajectory, and helping people weigh up the benefits and burdens of medical interventions that might be offered for potentially reversible symptoms, so they can make their own choices.

Most palliative care services provide advice around the clock and can assist general practitioners. Referral for acutely uncontrolled symptoms allows urgent follow up from the local palliative care team for ongoing

**Table 4. Possible causes of dyspnoea in terminally ill patients**

**Related to the disease**

- Lung tumour or metastases
- Lymphangitis carcinomatosa
- Pleural or pericardial effusion
- Cardiac tamponade
- Superior vena cava obstruction
- Pulmonary embolism
- Muscle weakness
- Anaemia
- Psychological distress

**Related to treatment of the disease**

- Chemotherapy induced lung injury (eg. bleomycin, taxanes)
- Radiation pneumonitis (a late effect – months to years)

**Comorbid or intercurrent problems**

- Congestive cardiac failure
- Exacerbation of chronic obstructive pulmonary disease
- Pneumonia
- Multifactorial

**Table 5. The Confusion Assessment method<sup>19</sup>**

Feature	Assessment
1. Acute onset and fluctuating course	Usually obtained from a family member or nurse and shown by positive responses to the following questions: 'Is there evidence of an acute change in mental status from the patient's baseline?' 'Did the abnormal behaviour fluctuate during the day, ie. tend to come and go, or increase and decrease in severity?'
2. Inattention	Shown by a positive response to the following: 'Did the patient have difficulty in focusing attention, eg. being easily distracted or having difficulty keeping track of what was being said?'
3. Disorganised thinking	Shown by a positive response to the following: 'Was the patient's thinking disorganised or incoherent such as rambling or irrelevant conversation, unclear or illogical ideas, or unpredictable switching from subject to subject?'
4. Altered level of consciousness	Shown by any other than 'alert' to the following: 'Overall, how would you rate this patient's level of consciousness?' Normal = alert Hyperalert = vigilant Drowsy, easily aroused = lethargic Difficult to arouse = stupor Unarousable = coma

The diagnosis of delirium requires the presence of 1 and 2 plus either 3 or 4

**Table 6. Choice of parenteral opioid from the doctor's bag for palliation in a crisis**

	<b>Advantages</b>	<b>Disadvantages</b>
<b>Morphine</b>	<p>May be given subcutaneously</p> <p>Is also effective for dyspnoea</p> <p>Clinical effect lasts 3–4 hours</p> <p>Upper dose only limited by side effects, and considered titration minimises these effects</p> <p>Can be used to initiate continuing analgesia with regular oral or ongoing subcutaneous morphine (regularly or by continuous infusion)</p>	<p>If there is a history of intolerance, give with an antiemetic. Avoid if possibility of hypersensitivity</p> <p>Renally cleared – dose reduce in renal failure</p>
<b>Tramadol</b>	<p>Can be used if morphine sensitivity or intolerance</p> <p>Acts via serotonin and noradrenaline reuptake, therefore may have a role in complex and neuropathic pain</p> <p>Duration of effect 6–9 hours</p>	<p>Has an upper ceiling on dose, therefore not the ideal agent for palliation</p> <p>Dose reduce in renal failure, hepatic failure, and in the elderly</p> <p>Potential interaction with other analgesics, antidepressants and serotonergic agents – may precipitate seizures or serotonergic syndrome</p>

management, and additional support for those caring for dying people at home.

Conflict of interest: none.

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