

Alberta Hospice Palliative Care Resource Manual

Second edition (2001)

**A project of the Alberta Cancer Board with financial support
provided by the Alberta Cancer Foundation**

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**Compiled by Jose Pereira and Eduardo Bruera
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University of Alberta**

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Introduction

One in three Albertans will be diagnosed with cancer and one in seven will die of the disease. Cancer is one of the largest contributors to causes of death in Alberta and, with our aging population, cancer incidence will continue to increase dramatically in this next millennium. In response to a need for improved access to quality palliative care for all Albertans, the Alberta Cancer Board (ACB) has created the Palliative Care Network Initiative (PCNI). The PCNI works in collaboration with health regions to help them optimize their palliative care services and promote a smoother transition from tertiary level care settings in the province to primary care in regional communities.

Providing ‘seamless’ coordinated palliative service delivery is a helpful goal as the trend continues in healthcare for a greater number of patients, including palliative patients, to be cared for at home. Furthermore, it has been shown that community based, multidisciplinary palliative care positively impacts the quality of life of patients and families as well as reduces overall healthcare costs. With this shift to more community care comes a greater role for primary care physicians and nurses in caring for palliative patients.

Primary care practitioners are well placed to look after these patients, having often known the patients and their families over a long time. They play a key role in coordinating the various palliative care services, providing home visits and accessing specialist palliative care services for the more complex and difficult cases. Furthermore, they are also in a position to monitor the health of other family members.

However, for many primary care practitioners, palliative care is a relatively new and unfamiliar specialty. The nature of primary care is also such that only a small number of terminally ill patients are generally seen annually by any one primary care physician or nurse and therefore it can be difficult to maintain a high level of knowledge and expertise in the field.

This manual is intended as an educational resource to aid primary care practitioners in Alberta to care for their palliative patients. In order to assist regions to use a common language in describing palliative care concepts and programs/services, the PCNI developed this comprehensive patient care resource manual to promote a similar knowledge of palliative care treatment options throughout the province. Many primary care physicians throughout the regions felt that a manual with concise, practical, step-by-step suggestions regarding management strategies of the more common clinical problems was needed. In an attempt to keep this resource practical and concise, detailed debate regarding more controversial issues was minimized.

This manual was developed in consultation with members of the Edmonton and Calgary tertiary palliative care programs as well as primary care physicians practising in rural settings of Alberta. It is primarily intended for distribution in Alberta and the suggestions and management protocols reflect the philosophy and experience of the contributors. Generally, the suggestions do support a philosophy that palliative care necessitates a disciplined and thorough approach with multidimensional assessments, ongoing assessments and a proactive approach. A choice of well-validated, evidenced-based assessment tools for palliative care is listed in Appendix A and referred to throughout this text. However, assessments and management protocols need to be individualized to meet the needs of individual patients and families.

This manual addresses common symptom problems encountered in palliative care. However, palliative care is a much broader discipline than symptom management and one that encompasses a multitude of issues and domains, including existential, psychological and spiritual issues. The overwhelming majority

of patients seen in palliative care programs have advanced cancer. The focus of this manual is therefore palliative care in the context of terminal cancer.

We would like to thank all of our reviewers and contributors for their input. We would especially like to thank the authors of the *Edmonton Aid to Palliative Care*, Drs. J. Pereira and E. Bruera, upon whose original work this provincial resource book is primarily based. Finally, we gratefully acknowledge the authors and editors of *99 Common Questions about Palliative Care* for information included from their text: Patsy Cantwell, Susan MacKay, Karen Macmillan, Sally Turco, Sandy McKinnon, Linda Read Paul, Carleen Brenneis, Beth Perry and Eduardo Bruera.

We would appreciate receiving feedback from our readers as to the usefulness of this manual as an aid to primary caregivers.

PCNI Steering Committee

c/o

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Abbreviations

Routes of Administration

po	oral
pr	rectal
sc	subcutaneous
td	transdermal
IV	intravenous
im	intramuscular

Frequency of Administration

prn	pro re nata/as required
q	quantum/frequency <i>e.g:</i> q4h is every four hours
ATC	around the clock/regularly
BTA	breakthrough analgesia/ rescue dose

Procedures

CT	computerized tomography
MRI	magnetic resonance imaging

Measures

mg	milligram
l	litre
(μ g) mcg	micrograms
U	units
ml	millilitre

Preparations

cap	capsule
tab	tablet
supp	suppository
inj	injection
SR	slow release
IR	immediate release opioid formulation
CR	controlled release opioid formulation

CHAPTER 1: Principles of decision-making in palliative care

Not infrequently, decisions have to be made regarding the active treatment/non-treatment of various metabolic or hematologic abnormalities that are found in patients with advanced cancer. These decisions, which occasionally may be difficult and complex, need to be made within the ethical parameters of beneficence, non-maleficence, justice and respect for the patients autonomy and wishes.

A balance needs to be achieved between aggressive management, with increased treatment- related toxicity, and not using treatments that could have useful symptomatic benefit. Every patient is an individual, with unique needs, wishes, hopes and circumstances. Management protocols, therefore, need to be individualized.

Although the diagnostic or therapeutic procedure will vary for different patients, it is best to follow a disciplined approach to assessment and decision making for each patient, eg: In the case of 3 patients with bowel obstruction, it may be appropriate to perform a colostomy in one patient, insert a gastroenterostomy tube for drainage in the second patient, and the third may require medical management of symptoms with pharmacological modalities only - but the decision making and assessment process is similar.

To individualize the decision-making process, the following steps may be helpful:

Step 1: a) Establish the potential problems and adverse effects of the abnormality that may have an impact on that particular patient's quality of life.

anemia	shortness of breath, lethargy, chest pain
hypercalcemia	somnolence, confusion, thirst
dehydration	confusion, renal impairment,
pathological fracture	immobility, pain
infection	pain, nausea, rigours, delirium
hyponatremia	lethargy, confusion

b) Rank the discomfort associated with a specific problem on the patient's overall symptom complex. For example:

Signs and symptoms of pneumonia including crepitations, cough, dyspnea and fever appear in a terminally ill patient with pancreatic cancer. The only other problems are asthenia and mild abdominal pain. Two months later, the patient's general condition has changed and he now has severe nausea, pain, delirium, and is bedridden. At this point, pneumonia recurs.

The symptomatic discomfort associated with pneumonia will probably be higher in the first situation as compared with the second situation.

Step 2: Establish the potential problems associated with the correction of the abnormality and the potential impact of the correction on the patient's quality of life. For example:

- The inconvenience of transfer to an emergency/acute unit for a blood transfusion.
- Risks and discomfort involved with surgery.

- Discomfort associated with the administration of injections or maintenance of an intravenous line.

Step 3: Balance overall pros and cons of intervention *v.* no intervention for that individual patient

If the benefits versus drawbacks of a certain treatment may not be clear, a therapeutic trial of the treatment could be considered.

Step 4: Develop a consensus with the patient, family and other health care providers regarding the ideal course of action

This may require a number of discussions or a family conference in order to clarify more complex situations.

Tips

Occasionally, a one time therapy needs to be instituted to assess its impact on symptoms, eg:

A patient presents with severe lethargy, somnolence and delirium. Laboratory tests reveal hypercalcemia. Although advanced cancer *per se* can cause the symptoms, a reduction in the blood calcium level using bisphosphonates can result in improvement in cognitive status and behaviour. Therefore, in the absence of a clear history describing the course of both the hypercalcemia and the cognitive status, it may be appropriate to treat the hypercalcemia and carefully monitor the cognition. Future treatment will depend on the ability to improve cognition as a result of controlling hypercalcemia.

Occasionally, patients who were relatively stable, deteriorate very rapidly and proactive management may be warranted, eg:

A patient with pancreatic carcinoma who is cognitively intact and physically active suddenly becomes delirious due to an infection. Under these circumstances it may be justified to treat the problem actively with antibiotics if the caregiver feels that symptoms and quality of life can be improved.

Recommended reading

1. Cherny N, Foley K. Guidelines in the care of the dying cancer patient. In: Cherny N, Foley K, eds. Hematology/Oncology Clinics in North America: Pain and Palliative Care, Vol 10 #1. Philadelphia: W.B. Saunders Company 1996; 261-286.
2. Wilkinson J. Ethical issues in palliative care. In: Doyle D, Hanks G, MacDonald N, eds. Oxford Textbook of Palliative Medicine. Oxford: Oxford University Press, 1993; 5:493-504.
3. Woodruff R. Palliative Care. In: Woodruff R, ed. Palliative Medicine. Melbourne: Asperula Pty Ltd. 1993; 1:3-12.
4. Woodruff R. Principles of Palliative Care. In: Woodruff R, ed. Palliative Medicine. Melbourne: Asperula Pty Ltd. 1993; 2:13-19.

CHAPTER 2: Management of cancer pain

Basic principles of effective pain control

- Pain is a multidimensional construct.
 - A disciplined, multidimensional assessment is essential.
 - Avoid delay in treating.
 - Communicate with the patient, family and other caregivers.
 - Follow a stepped approach that depends on severity.
 - Constant pain requires regular administration of analgesics.
 - Always leave instructions for a “breakthrough dose”.
 - Consider opioids as only one part of the management of total pain.
 - Patients with rapidly changing clinical circumstances, such as terminally ill patients, require ongoing assessments.
-

2.1 Assessment of pain

Failure to assess pain can lead to less than optimal pain control for the patient. Assessments should occur:

- at regular intervals after initiation of the treatment;
- at each new report of pain or change in quality/intensity of pain; and
- at a suitable interval after pharmacological or non-pharmacological interventions.

The goal of the initial assessment is to characterize the pain by location, intensity and etiology. Essential to the initial assessments are:

- a detailed history;
- a physical examination;
- a psychosocial assessment; and
- a diagnostic evaluation.

Assessment of pain requires four steps:

Step 1: Assess whether the pain is being produced by direct or indirect tumour involvement, cancer treatment or whether it is unrelated to the tumour and treatment.

Step 2: Measure the intensity of pain and other symptoms.

Step 3: Assess the multiple dimensions of the expression of pain.

Step 4: Identify poor prognostic factors for pain control.

Step 1: Determine the nature and possible causes of pain

Identifying the etiology of pain is essential to its management. Prompt diagnosis and treatment of these syndromes can reduce morbidity associated with unrelieved pain. In the great majority of patients, the history, physical examination and, occasionally, an x-ray, are adequate to appropriately assess the pain. In most cases, the pain is caused by direct tumour involvement. Psychological, cultural, and chemical addiction factors can further influence a patient’s pain experience.

What are the causes of pain in a patient with advanced cancer?

Direct tumour involvement (78%), which might include:

- bone metastases,
- nerve compression/infiltration,
- hollow viscus, or
- visceral organs.

Related to cancer therapy (19%), which might include:

- surgery,
- radiotherapy, or
- chemotherapy – neuritis.

Pain unrelated to cancer or cancer therapy (3%), which might include:

- post herpetic neuralgia,
- arthritic pain, or
- pain of any kind significantly influenced by a large psychosocial or spiritual component.

Why do we classify pain?

- Assists in understanding the underlying pathology.
- Certain types of pain such as neuropathic pain and incidental pain can be difficult to control and may require higher doses of opioids, trials of different opioids or the addition of appropriate adjuvant analgesics.

Characterize the pain. The following are various clinical presentations of pain.

Nociceptive pain

a) Somatic

- constant or intermittent
- usually gnawing, aching
- occasionally cramping
- well localized

Mechanism: activation of nociceptive receptors, *e.g.*, bone metastases or muscle/soft tissue tumour infiltration.

b) Visceral pain

- constant
- aching, squeezing, cramping
- poorly localized, occ. referred, occasionally well localized

Mechanism: activation of nociceptors, *e.g.*, intra-abdominal metastases liver metastases.

Neuropathic pain

Mechanism: destruction, infiltration, compression of nerve tissue. Neuropathic cancer pain can have two main clinical manifestations.

a) Dysesthetic pain (deafferentation)

- constant burning
- occasionally radiates, *e.g.*, post herpetic pain

b) Neuralgic pain

- paroxysms of lancinating pain
- sharp, shooting pain, *e.g.*, trigeminal neuralgia

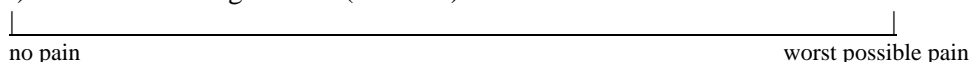
The pathophysiology of neuropathic pain can be very complex. The initial injury to the nervous tissue can occur peripherally, in the central nervous system, or a mixture of both peripheral and central (*e.g.*, brachial plexopathy), but the pain can be propagated and maintained by processes proximal to the initial injury site, including processes in the central nervous system. The autonomic nervous system is also occasionally involved.

Step 2: Measure the pain intensity

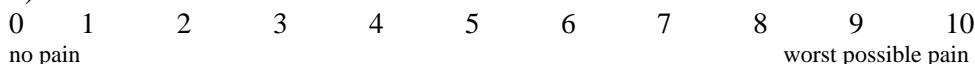
A mainstay of assessment is the patient’s self reporting of the pain intensity. (In patients with significant cognitive impairment, this may not be possible). Clinicians should teach patients and families to use pain assessment tools in their homes. Numerical, verbal or visual analogue scales (0=no pain to 10=worst possible pain) are common. These scales can be used for symptoms other than pain (See Appendix A: Suggested Validated Tools). However, words, fingers of a hand, *etc.*, are all valid and reproducible ways of assessing pain intensity.

Pain intensity scales

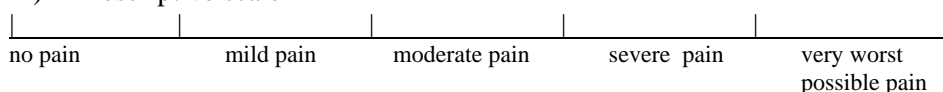
i) Visual analogue scale (0-10 cm)



ii) Numerical scale



iii) Descriptive scale



The usefulness of these scales becomes even more evident when they are used on an ongoing basis for the same patient.

Step 3: Perform a multidimensional assessment

Terminally ill patients need to be assessed regularly since symptoms can change rapidly.

Keep in mind that there are three steps in the pain experience:

Production of pain (nociception)	This occurs at the site of the cancer. This cannot be measured directly and can be different from cancer to cancer, site to site, <i>etc.</i>
↓	
Perception	This occurs at the level of the central nervous system/brain. This component too, cannot be measured and is also subject to the influence of modulation.
↓	
Expression	The expression of pain is the main target of all our assessments and treatment. Two patients with the same level of perception may express dramatically different pain intensity. Therefore, we should not equate the intensity of pain expression directly with nociception. Doing this would be a unidimensional approach that ignores the complexity of the pain experience.

Appropriate pain assessment requires us to consider the multiple dimensions of a certain patient's expression of pain. Fortunately, in most cases, nociception remains the main component of pain. Therefore, most patients are likely to experience excellent pain control if regular analgesics are administered. It is approximately 25% of patients who show limited or no response to regular analgesics that influences of different dimensions on the pain experience are more likely to be operant; in this setting the patient should be reassessed for the presence of poor prognostic factors for pain control.

The components of a multidimensional pain assessment:

<i>Pain syndrome</i>	<p>What type of pain is it?</p> <ul style="list-style-type: none"> • location, radiation, intensity (use scale), triggers • bone pain • visceral pain • neuropathic pain • incidental <p>Are there other symptoms that need controlling?</p>
<i>Drug</i>	<p>What is the dose?</p> <p>Are there indications of tolerance?</p> <p>Are there signs of toxicity?</p> <p>What has been the response to individual opioids?</p> <p>What other treatments have been/are being used for pain relief?</p> <p>Effectiveness?</p>
<i>Patient</i>	<p>Are there underlying metabolic abnormalities (<i>e.g.</i>, renal impairment, hypercalcemia, hepatic encephalopathy, <i>etc.</i>)?</p> <p>Is there significant psychological distress?</p> <p>How has the patient coped previously with life stressors?</p> <p>Is there a history of drug/alcohol addiction?</p> <p>Is the patient cognitively impaired/delirious? (Use screening tools such as Folstein MMSQ to assess cognition)</p> <p>Are there spiritual issues that need to be addressed (<i>e.g.</i>, what is the meaning of pain to the patient?)</p>
<i>Social</i>	<p>How does pain influence the patient's daily living?</p> <p>What are the family and social support systems?</p> <p>Is there severe family dysfunction?</p> <p>Are there financial concerns?</p> <p>Are there cultural issues influencing the illness experience?</p>

Alert!

Back pain that radiates and increases with straight leg raise may indicate a cord compression.

Step 4: Identify poor prognostic factors

The following are ‘red flags’ to alert to the possibility that difficulties may be encountered in trying to control pain.

Poor prognostic factors for pain control

1. Neuropathic pain.
2. Incidental pain (pain severely exacerbated by an incident such as movement, coughing, etc.).
3. Impaired cognitive functioning.
4. Major psychological distress.
5. Positive history of alcohol abuse or drug addiction (indicates poor coping strategies).

Somatization factor

Pain that has a large psychosocial or spiritual component is often referred to as “total pain” or “total suffering.” You should suspect somatization if:

- significant psychosocial or spiritual issues are identified;
- the patient describes pain as “all over” (in absence of physical cause for “all over” pain such as widespread skeletal metastases or accumulation of opioid metabolites);
- pain appears to improve with socialization, physical activity or other distraction, and increases when alone;
- escalating doses of opioids produce toxicity with little or no pain relief; or
- there is a history of somatization under stress.

2.2 Starting a patient on an analgesic

This depends on the severity of the pain. The following steps may be useful.

Mild pain

Start with a non-opioid (*e.g.*, acetaminophen) or a weak opioid (*e.g.*, codeine):

- acetaminophen (325 mg to 650 mg q4hr po and 325 mg to 650 mg q1h prn). (maximum number of acetaminophen tablets: 14-16/day-each tablet being 325 mg).
- codeine 30-60 mg q4hr po regularly and q1hr po prn for rescue doses (codeine can also be given subcutaneously for patients unable to take oral medications).

If the pain persists or worsens:

Optimize the above dose of the analgesic and if this does not improve the pain, switch to a stronger opioid (*e.g.*, oxycodone, morphine):

E.g., If oxycodone is chosen, the starting dose is 5 mg q4h po regularly and 5 mg q1h po prn for rescue doses. The dose of oxycodone is limited by the acetaminophen or acetylsalicylic acid in the medication. (oxycodone 10 mg po = morphine \pm 15-20 mg po).

Moderate to severe pain

Start with a stronger opioid (*e.g.*, oxycodone, morphine or hydromorphone)

If the pain persists or worsens, optimize the opioid dose by increasing the dose progressively. The upper limit is determined primarily by toxicity. If using combination drugs, (*e.g.*, oxycodone with acetaminophen or acetylsalicylic acid), the dose is limited by the risk of acetaminophen or acetylsalicylic acid toxicity.

- If unsuccessful in controlling the pain with the above measures, or if toxicity occurs, switch to a different opioid.
- Adjuvants may be used but *first* optimize the opioids. Note that non-opioid drugs also cause adverse effects. For example, NSAIDs can result in renal impairment or GI effects.

- Where possible, try avoiding polypharmacy.
- Always consider non-drug modalities *e.g.*, radiotherapy for bone pain, surgical repair of a pathological fracture.

2.3 Starting a patient on opioid

Step 1: Initiate opioid

What are the preferred opioids?

We prefer to use the following opiate agonists: codeine, oxycodone, morphine, hydromorphone, fentanyl, and methadone. Their effectiveness is not limited by a ‘ceiling’ with increasing doses. Full agonists, unlike the partial agonists or mixed agonists-antagonists, will also not reverse or antagonize the effects of other full agonists.

Avoid the following opioids

- Meperidine: with chronic use its metabolite (normeperidine) often accumulates and causes neurotoxicity such as delirium and seizures.
- Partial agonists, *e.g.*, buprenorphine. these opioids have less effect than full agonists at opioid receptors. They are also subject to a ceiling effect – *i.e.*, increasing the doses above a specific point does not result in increased analgesia but, rather, in more side effects. Patients taking an opioid agonist (*e.g.*, morphine or hydromorphone) may develop withdrawal problems when buprenorphine is started. When patients are changed from buprenorphine to a full agonist opioid, the action of the agonist opioid will be delayed.
- Mixed agonist-antagonist, *e.g.*, butorphanol, nalbuphine, pentazocine: they block or are neutral with one type of opiate receptor while activating a different opiate receptor. These have a high incidence of psychotomimetic side effects and they may cause withdrawal symptoms when given to patients receiving opioid agonists. Their analgesic effectiveness is also limited by a dose-related ceiling effect.

Starting doses are:

- Morphine 5 mg q4h po regularly and 2.5 or 5 mg po q1h prn for breakthrough pain (BTA).
- Hydromorphone 1mg q4h regularly and 0.5mg (1mg is more practical) q1h po prn for BTA.
- Oxycodone 5mg q4h po regularly and 5mg q1h po prn for BTA.

Over the next few days, *titrate the dose* to achieve good pain control. (More than 3 BTA/day can be an indicator that pain may not be adequately controlled).

To determine the new dose while titrating, add the number of breakthroughs being used in a 24-hour period and add that to the total daily dose. Divide by 6 to get the q4h doses. Alternately, increase the total daily opioid dose by 25-75% depending on the severity of the pain.

Breakthrough doses/rescue doses (BTA): These are an important component of the analgesic strategy since patients may experience pain in between their regularly scheduled opioid doses and will require a rescue dose of opioid to provide relief of this breakthrough pain. Breakthrough doses are generally approximately 5-20% of the total daily dose and are usually ordered q1h on an as-needed basis (prn).

Be sure to inquire about the effectiveness of these doses and titrate them between the 5%-20% daily dose range.

NB: If the patient requires more than three BTA per day, s/he should contact the home care nurse or the attending physician and a further reassessment is necessary.

Route of administration

Oral administration is preferred, as it is convenient and usually effective. When patients cannot take oral medications, other routes should be considered (eg: subcutaneous, rectal, transdermal).

Pitfalls

Do not use a slow-release opioid formulation to start a patient on opioids. These can be difficult to titrate. Because of their long onset and duration, they may be associated with uncontrolled pain or they may accumulate, resulting in toxicity. It is also advisable to avoid controlled-release formulations when switching opioids or in unstable situations.

Step 2: Warn of potential side-effects and treat these

What are common toxicities of the opioids?

General

- nausea
- constipation
- somnolence
- dry mouth (xerostomia)
- pruritus

Neurotoxic

- myoclonus (jerking of limbs or facial muscles)
- hyperalgesia/allodynia
- delirium
- hallucinations
- cognitive impairment

Therefore, warn the patient of:

- increased nausea for the first three to four days;
- increased somnolence for the first three to four days (both of these side effects usually disappear with continued use of the drug);
- constipation.

Provide relief

All patients who develop side effects should be started on the following:

- Antiemetic: Metoclopramide 10 mg po/sc q1hr prn for nausea. If nausea is a problem, regular metoclopramide can be given (*e.g.*, qid or q4hrs) for the first three to four days.
- Laxatives: Use both a stimulant and a stool softener, *e.g.*, senna two tabs po qhs and docusate 100-240 mg po bid to start with. These can then be further increased to ensure a bowel movement at least every 2nd to 3rd day. Avoid bulk laxatives. These patients frequently have anorexia, early satiety and chronic nausea, and are not able to ingest the necessary amounts of liquids for these laxatives to be effective.
-

Explain that the opioid needs to be taken every four hours if immediate release formulations are used.

- The cancer pain is constantly present.
- After four hours, the effect of the opioid diminishes significantly.

NB: If the patient wishes an uninterrupted night's sleep, he or she may try doubling the regular bedtime dose and taking either the regular or breakthrough dose whenever he or she wakes up during the night. The regular regimen would be started again in the early morning on awakening.

Encourage normal activity and good fluid intake

Avoid activities that can be affected by increased somnolence.

Reassure the patient and family.

Ask the patient and family about fears regarding opioids and address these fears if present.

Explain to the patient the difference between physical dependence, addiction, and tolerance

Physical dependence is a normal physiological response to the pharmacological effects of chronic opioid administration. It is only seen when administration of the opioid is abruptly stopped or an antagonist is administered. The withdrawal syndrome is typically characterized by sweating, tremors, agitation, muscle cramps, abdominal cramps, tachycardia, fever and dilated pupils. In some rare instances, patients taking opioids may have their pain alleviated by non-pharmacological measures such as surgery neurosurgery, radiation or anaesthetic procedures. In these cases, the opioids should be reduced at a rate of 15-20% per day rather than being abruptly discontinued.

Addiction (psychological dependence) is a pathologic psychological condition that includes a compulsion to take a specific drug (*e.g.*, opioid) to experience its psychic effects. Several large studies have shown that patients receiving opioids for cancer pain almost never become psychologically dependent, *i.e.*, “addicted” to opioid analgesics.

Tolerance is a normal physiological phenomenon in which increasing doses of an opioid are required over time to produce the same analgesic effect. The mechanism of this is complex but may be related to changes in opioid receptors or drug metabolism. The degree and rate to which tolerance develops varies greatly between different individuals. True tolerance is rare. The most frequent reason for dose escalation remains disease progression. Although true tolerance is rare, it does occasionally occur and, when it does, it can usually be adequately dealt with by using a different opioid.

Cross tolerance between various opioids is not complete and an alternative drug can be substituted if the rate of development of tolerance is a problem or if the patient experiences dose-limiting side effects from one particular opioid. However, for patients with cancer, the most frequent reason for dose escalation is progression of the disease causing increased pain.

Almost all patients with pain from advanced cancer require treatment until death and concerns about physical dependence or addiction are irrelevant. Concern regarding tolerance is not a reason for ‘saving up’ the use of opioid drugs until the terminal phase.

NB: Placebos should not be used in the management of cancer pain.

2.4 Maintaining a patient on an opioid

Patients on opioids will require regular assessments. Assessments L must include monitoring for opioid adverse effects and signs of disease progression. Opioid titrations will be required to manage increased pain resulting from disease progression or opioid tolerance. The appropriate dose is the amount of opioid that controls pain with the fewest adverse effects.

Titration opioids

In most cases, titration involves an increase in opioid dose. Dose increases can either be:

- i) 30-50% increases of the previous dose – *e.g.*, if the previous dose was morphine 120 mg po/day, the new dose, if a 50% increase is decided upon, will be 180 mg/day; or
- ii) the new dose may be determined by the average amount of opioid used as breakthrough doses per 24 hours – *e.g.*, a patient is taking morphine 20 mg po regularly every four hours and has used, on average, five breakthrough doses per day in the previous couple of days. Each breakthrough dose consists of morphine 12 mg po. The total amount of breakthrough opioid is, therefore, 60 mg of po morphine per day. This is then added to the regular dose of 120 mg per day, giving a total daily dose of 180 mg (morphine 30 mg po q4h ATC).

If the pain is severe, a further 20-30% in the total daily dose may be required.

Occasionally, opioid doses may need to be reduced:

- i) if pain improves dramatically as a result of other interventions (*e.g.*, palliative radiotherapy, surgical fixation of a pathological fracture);
- ii) severe sedation due to opioids is accompanied by good pain control; or
- iii) renal impairment is present.

One to three regular opioid doses can be withheld in patients with very severe side effects – *i.e.*, severe sedation, miosis, respiratory depression. If an acute overdose occurs, naloxone may need to be administered if respiratory rate is less than eight per minute.

What is the maximum dose of an opioid agonist?

Contrary to other drugs, such as anticoagulants or anticonvulsants, that have an established safety dose range, the adequate dose of opioid agonist is extremely variable and it should be titrated according to analgesic effects and toxicity, *e.g.*, while one patient may achieve excellent pain control on 5 mg of morphine orally every four hours, another may require 50 mg of morphine every four hours and another 500 mg every four hours. The maximum dose is limited by toxicity and this varies widely from patient to patient.

2.5 Opioid toxicity (myoclonus, delirium, hyperalgesia, hallucinations, intractable nausea)

These occur in patients taking opioids in high doses or for prolonged periods of time or in patients who develop renal impairment. It is postulated that active opioid metabolite accumulation is responsible for some or most of this toxicity.

Management of opioid toxicity

Several strategies have been recommended to manage opioid-related toxicity. These include switching from one opioid to another opioid agonist, hydration, and reducing the opioid dose. Reducing the opioid dose is an option if pain is well controlled and the toxicity is minimal. A combination of rotating to an alternative opioid and hydration is often effective.

Step 1: Hydrate

If oral intake is limited, parenteral hydration may need to be started. We have found hypodermoclysis (subcutaneous hydration) to be a convenient method for parenteral hydration. *E.g.*, hypodermoclysis: N/S @ 80-100 ml/hr (hyaluronidase 150U to each litre is only required if the subcutaneous site leaks significantly. Warn the patient that the site will swell up somewhat but as long as it is not inflamed, the swelling should subside).

The rationale for hydration is that it can correct delirium caused by dehydration and renal impairment which, in turn, causes metabolites to accumulate.

Step 2: Rotate opioids (see “2.7 Opioid Rotations”)

Step 3: Exclude underlying aggravating metabolic factors

E.g., uremia or hypercalcemia.

Step 4: Treat symptoms

E.g., hallucinations/agitation. haloperidol is the drug of choice (see Chapter 5, page 40, on delirium).

NB: Benzodiazepines or other drugs (such as baclofen or clonazepam) are almost never required to treat opioid metabolite induced myoclonus or toxicity. Increased benzodiazepines are only required if the myoclonus is so severe that a generalized seizure appears to be imminent or of the myoclonic jerks are painful.

Tips

In the presence of renal impairment with no clinical signs of opioid toxicity, the opioid dose may need to be decreased because of the probable accumulation of opioid metabolites.

2.6 Opioid rotations

Reasons for switching opioids

- Poor analgesic response to a particular opioid.
- Opioid toxicity
- Use of very high doses of a particular opioid making administration via oral or parenteral route of that opioid impractical. (Maximum concentrations of parenteral formulations are: morphine sulphate: ± 50 mg/ml, hydromorphone: ± 30 mg/ml).

Step 1: Calculate the total daily dose of the opioid

Add the breakthrough doses used in 24 hours to the total of the regular doses used in 24 hours.

Step 2: Use equianalgesic dose ratio tables to calculate the dose of the new opioid (see Table 1, page 20).

NB: Remember that these tables are only guidelines and that close clinical monitoring is required during the switching process.

Step 3: Take into account the lack of complete cross tolerance between opioids

When switching from one opioid to another, decrease the dose of the new opioid by 20-30% because cross tolerance between opioids is not always complete, *e.g.*, a patient may have become tolerant to one of the side effects, such as somnolence, of a particular opioid, but when switched to the equianalgesic dose of another opioid the patient may once again experience initial somnolence.

If a patient has used many breakthroughs in the last 24 hours (four or more) then assess for delirium or profound psychological distress. If these are present, then the dose of the new opioid may need to be reduced by up to 50%.

Step 4: Establish the regular dose

Divide the total daily dose of the new opioid by the number of doses to be given in a day. In the case of immediate-release formulations of opioids which need to be given regularly every 4 hours, the number of daily doses will be 6. Methadone can be given less frequently (often every 8 hours but occasionally every 12 hours or even every 24 hours.)

Step 5: Order breakthrough doses

Order breakthrough doses at 10% of the total daily dose q1h prn. Monitor the effect of these doses. If ineffective, the dose may need to be increased to 20% of the total daily dose. On the other hand, if it is effective but causes significant somnolence, then it may need to be decreased to 5% of the total daily dose.

NB: Patients and family should be warned that if more than three breakthroughs are required per day, they should contact their physician/nurse and be reassessed.

Step 6: Assess regularly

Patients should be followed up on a daily basis during the rotation period and until stable (pain is well controlled; 3 or less breakthroughs are being used per day; and no severe side effects) for at least 48 hours.

Warning

Methadone should be started and titrated under the guidance of a palliative care physician or pain specialist. Parenteral fentanyl should also be used under similar guidance.

NB: The table below is a guideline only. Patient-to-patient variability occurs. Patients should therefore be monitored closely when their opioids are being switched.

Table 1: Equianalgesic dose

Drug	PO Dose	PO:SC/IV Ratio	SC/IV Dose
Morphine	10 mg	2:1	5 mg
Codeine	100 mg	2:1	50 mg
Oxycodone*	5 mg	--	--
Hydromorphone	2 mg	2:1	1 mg
Methadone†	1 mg	--	too irritating
Fentanyl‡ - infusion	--	--	0.05 mg
Fentanyl patch	use chart supplied by manufacturer		
morphine 10 mg po = codeine 100 mg po = oxycodone 5-7.5 mg po = hydromorphone 2 mg po = methadone 1 mg po			

* The equianalgesic dose ratio of morphine to oxycodone is controversial. It appears to be between 1.5:1 and 2:1.

† Many tables quote the equianalgesic dose ratio of morphine to methadone as being 1:1, i.e., morphine 1mg po = methadone 1 mg po. This ratio was determined using single dose studies. In cancer pain, when multiple doses are required, the ratio of morphine to methadone becomes approximately 10:1, i.e., morphine 10 mg po = methadone 1 mg po.

‡ The equianalgesic dose ratio of morphine to fentanyl has not been accurately determined. It appears to be approximately 100:1, i.e., morphine 1 mg sc = fentanyl 10 µ (micrograms) sc. The equianalgesic ratio between parenteral fentanyl and transdermal fentanyl (patch) is also not well described, but appears to be approximately 1:1.

Example of an opioid rotation

A patient who has been taking morphine 40 mg po q4hr regularly around the clock (ATC) develops signs of opioid toxicity (myoclonus, delirium). Five breakthrough doses of morphine, each 24 mg po, have been taken in the last 24 hours. A decision is made to switch from morphine to hydromorphone.

Step 1: Calculate the total of the daily dose of opioid

- $40 \text{ mg} \times 6 = 240 \text{ mg}$ (regularly scheduled opioid doses).
- Add $24 \times 5 = 120 \text{ mg}$ (total breakthroughs) to the above.
- Total daily dose = 360mg of oral morphine.

Step 2: Calculate equianalgesic dose of new opioid

$360 \text{ morphine po} \div 5$ (see “Table 1: Equianalgesic dose”) = 72 mg hydromorphone po per 24 hours.

Step 3: Decrease dose by 20-30%

$72 \text{ mg} - 20\% = 58 \text{ mg}$ hydromorphone in 24 hours.

Step 4: Calculate regular dose

$58 \text{ mg} \div 6 = \pm 10 \text{ mg}$ hydromorphone po q4h ATC.

Step 5: Order PRN breakthrough doses

10% of the total daily dose, therefore 10% of 58 mg = $\pm 6 \text{ mg}$ q1h po prn.

Step 6: The patient should be followed up on a daily basis during the rotation...

... until the patient is relatively stable – pain is well controlled, 3 or less breakthroughs being taken per day, and no severe side effects are present – for at least 48 hrs.

2.7 Controlled release (CR) of opioid formulations

Controlled-release formulations need to be taken at greater intervals than the immediate-release formulations because of the gradual release of opioid systemically. Several opioids are now available in controlled-release formulations:

- codeine (po), oxycodone (pr), morphine (po and pr); and
- hydromorphone (po), fentanyl (td).

When slow release formulations should be used:

- Controlled-release formulations offer patients the convenience of less frequent opioid administration and may, therefore, improve compliance.
- Controlled-release formulations should preferably be used in stable situations where pain is relatively well controlled and the patient is requiring minimal amounts of breakthrough doses/day.
- Opioid naïve patients should preferably not be started on a controlled-release formulation. Initially, an immediate-release formulation should be used to allow for safer and more rapid titration. The opioid can be changed later to a controlled-release formulation when the pain is under good control.
- It is prudent to switch from a controlled-release formulation to an immediate-release formulation when the patient becomes unstable (*e.g.*, delirium, severe pain with rapid escalation of opioid requirement).
- Use controlled-release formulations very cautiously, if at all, in the presence of significant renal impairment (risk of accumulation).

2.8 Switching from an immediate release (IR) formulation to a controlled release (CR) formulation

Switching to codeine, oxycodone, morphine or hydromorphone CR formulations

Step 1: Calculate the total daily dose of the immediate release opioid

This is equivalent to the total daily dose of the controlled-release formulation, *e.g.*, immediate-release morphine 10 mg q4hr po = controlled-release formulation 60 mg/24 hours.

Step 2: Calculate the amount of each individual dose

Divide the total daily dose by the frequency of doses required in 24 hours. This will depend on the specific formulation being used, *e.g.*, morphine is available in controlled-release formulations that require either every 12 hour or every 24 hour administration:

- q12h formulation: morphine 60 mg \div 2 = CR morphine 30 mg q12h po;
- q24h formulation: morphine 60 mg q24h po.

Very occasionally, 8 hourly dosing may be required. However, this is very uncommon.

Step 3: Breakthrough orders

Use an immediate-release formulation, preferably of the same opioid as the controlled-release formulation, to provide break-through analgesia. Breakthrough doses are 10% (5-20%) of the total daily opioid dose:

- If the total daily dose is 60 mg po of morphine, the order for breakthrough dose should be morphine immediate-release: 6 mg po q1h prn for pain.

When starting morphine, hydromorphone, codeine or oxycodone CR formulations that require q12h dosing, no overlap is required between the immediate-release formulation and the CR formulation. Give the first dose of the CR formulation four hours after the last dose of the IR formulation and rely on breakthrough doses for analgesia if pain occurs during the switch over period.

Example of a switch to morphine CR

A patient is taking 10mg of morphine orally every four hours and his/her pain is well controlled. It is decided to switch him/her to a CR formulation.

Step 1: Total daily dose of morphine is 60 mg (10 mg x 6) po.

Step 2: CR should be ordered as morphine CR 30 mg q12h po. 60 mg PO q24h if the q24h formulation is being used.

Step 3: Breakthrough doses should be: IR morphine 6 mg po q1h prn (\pm 10% of the total daily dose).

Switching to transdermal (TD) fentanyl

Step 1: Calculate the total daily dose of quick release opioid

Step 2: Use manufacturer's conversion table to calculate the equivalent dose of transdermal fentanyl (see Appendix G).

Step 3: Give breakthrough orders

Since fentanyl cannot be taken orally, the IR formulation of another opioid (*e.g.*, morphine, hydromorphone or oxycodone) is required for breakthroughs. An alternative approach is to use a parenteral formulation of fentanyl sublingually (especially if there is a significant incidental component to the pain). The dose is limited by the volume required. Volumes exceeding 1.5-2 ml are impractical. If the breakthrough dose requires a volume greater than 2

ml sublingually (parenteral formulation administered SL) then sufentanyl is an option.

Calculate the dose of the breakthrough to be 10% of the total fentanyl daily dose (using the manufacturer's tables), *e.g.*, a 50 mcg/hour patch is equivalent to 135-224 mg of oral morphine/24 hours. Morphine 15 mg po q1h prn would therefore be appropriate as a breakthrough order.

Step 4: Overlap the TD fentanyl with the previous opioid for the first 12 hours

When initiating the patch, it should be overlapped with the regular IR opioid for the first 12 hours (*i.e.*, three scheduled doses of the IR opioid), or one dose of a CR opioid (*i.e.*, q12h formulations and q24h formulations).

Step 5: Initial titration of TD fentanyl

Because of its prolonged action, the transdermal fentanyl dose should only be increased every three days. Rely on the breakthrough doses to provide extra pain relief in the first three days. If more rapid titrations are necessary, they should be done under the guidance of a palliative care physician or pain specialist.

Step 6: The patch should be replaced every three days

Rarely do patients require patches replaced more frequently. Early wearing off of the patch can indicate under-dosing

Example of starting a patient on transdermal fentanyl

It is decided to switch a patient who has been stable on oral morphine 50 mg q4h to transdermal fentanyl.

Step 1: The total daily dose of morphine is, therefore, 300 mg po. According to the manufacturer's table, the equivalent dose of transdermal fentanyl is approximately 75 micrograms per hour. Rescue doses could be in the form of morphine 30 mg po q1h prn (10% of the total daily dose) or hydromorphone 6 mg q1h prn or oxycodone 15 mg po q1h prn.

Step 2: The patch should be applied and the previous opioid formulation be continued for another twelve hours. After twelve hours the previous opioid is discontinued and the patient is left on the transdermal fentanyl and immediate release opioid for breakthroughs.

2.9 Increasing CR opioid dose

Generally, opioid doses need to be gradually increased over time to compensate for disease progression and occasionally for tolerance. The amount of breakthrough doses taken in a 24 hour period can serve as a guide to determine how much to increase the dose of the CR opioid formulation. Alternatively, the dose of the CR formulation can be increased by 25% to 50%. Since CR formulations are available only in certain strengths, the new dose will need to be adjusted to take this into consideration.

The breakthrough dose will also require adjustment (10% of the total daily dose).

2.10 Switching from a CR to an IR opioid formulation

Controlled release formulations may need to be discontinued for various reasons. These may include the following.

- Unstable pain syndrome.
- Opioid toxicity.
- Renal impairment.
- Inability to swallow (if the CR opioid is being taken PO).

Discontinuing morphine, hydromorphone, codeine or oxycodone formulations

Step 1: Calculate the equivalent dose of the IR formulation

E.g., CR morphine 60 mg q12h po = morphine 120 mg/24 hours.

Step 2: Calculate the regular dose and the breakthrough doses of the IR formulation

E.g., morphine 120 mg/24hours = morphine 20 mg q4h ATC with breakthrough of morphine 12 mg q1h prn.

Step 3: Start the regular IR formulation 12 hours after the last CR formulation dose

Rely on breakthrough doses for the first 12 hours.

Discontinuing the fentanyl patch

Step 1: Calculate the equivalent dose of the new IR formulation

Use manufacturer's tables.

Step 2: Calculate the regular dose and the breakthrough doses of the IR formulation

Step 3: Remove the patch and start the regular dose of the new quick release opioid 12 hours later

Use rescue doses of the IR opioid for break-through pain until the regular dose commences. A transdermal reservoir of fentanyl continues to release drug for up to 12-17 hours after removing the patch.

2.11 'Crescendo pain'

Patients occasionally present with sudden exacerbation of their cancer pain. This often results in rapid and, sometimes, massive escalations of their opioid requirement.

If this occurs, look for the following possible causes.

- Complications of the cancer, *e.g.*, pathological fracture, bowel obstruction, and local infection.
- Somatizing: *i.e.*, expressing total suffering (fears, anxiety, existential concerns, *etc.*) as pain.
- Delirium: results in altered expression of pain, often followed by misinterpretation of the delirium induced moaning and groaning as pain.
- Rapid development of tolerance. (This is unusual; tolerance more commonly develops very gradually.)
- Accumulation of opioid metabolites causing hyperalgesia.
- Urinary retention or severe fecal impaction in cognitively impaired patients.

Pitfalls

Avoid rapidly increasing the dose of an opioid in a patient who is either delirious or overtly somatizing (expressing total suffering as pain).

2.12 Alternative routes of opioid administration

- The oral route is the preferred route.
- Occasionally it is necessary to use alternative routes if a patient is unable to take medications orally. Reasons for this can include dysphagia (*e.g.* advanced head and neck cancers) severe delirium, severe obtundation and bowel obstruction.
- Alternative routes include: rectal, subcutaneous, intravenous, transdermal, and via a gastrostomy tube.
- The rectal route is safe, inexpensive and effective. It is probably best avoided in patients with anal/rectal lesions or severe thrombocytopenia.
- The transdermal route is very convenient but not suitable for rapid dose titration. Hence, this route is reserved for when pain is in good control.
- The subcutaneous route is preferred when a parenteral route is required. It is more convenient and just as effective as the IV route. The IV route can be more difficult to maintain.
- Regular intermittent subcutaneous administration of opioids appears to be as effective as continuous administration in the majority of cases.
- Most commonly utilized opioids are available in parenteral formulations. These include codeine, morphine, hydromorphone and fentanyl. In North America, the parenteral formulation of methadone causes too much tissue irritation and is seldom used. Oxycodone is now available in a parenteral formulation.
- When switching from the oral route to the subcutaneous route and vice versa, use equianalgesic dose tables, *e.g.*:
 - morphine 10 mg po morphine 5 mg sc
 - hydromorphone 10 mg po = hydromorphone 5 mg sc
 - codeine 10 mg po = codeine 5 mg sc
- The rectal route is acceptable to some patients and can be useful if the patient is unable to take opioids orally. The following opioids are available in rectal formulations: IR morphine, CR morphine and methadone. Parenteral formulations of most opioids appear to be absorbed rapidly and effectively when administered rectally but the effect may be variable and unpredictable.
- A very small, select group of patients may benefit from opioids administered intraspinaly. Often a local anesthetic (bupivacaine) is added to enhance analgesia.

See Figures 1 and 2 on the following pages for a visual representation of cancer pain management.

Figure 1: Algorithm for cancer pain management

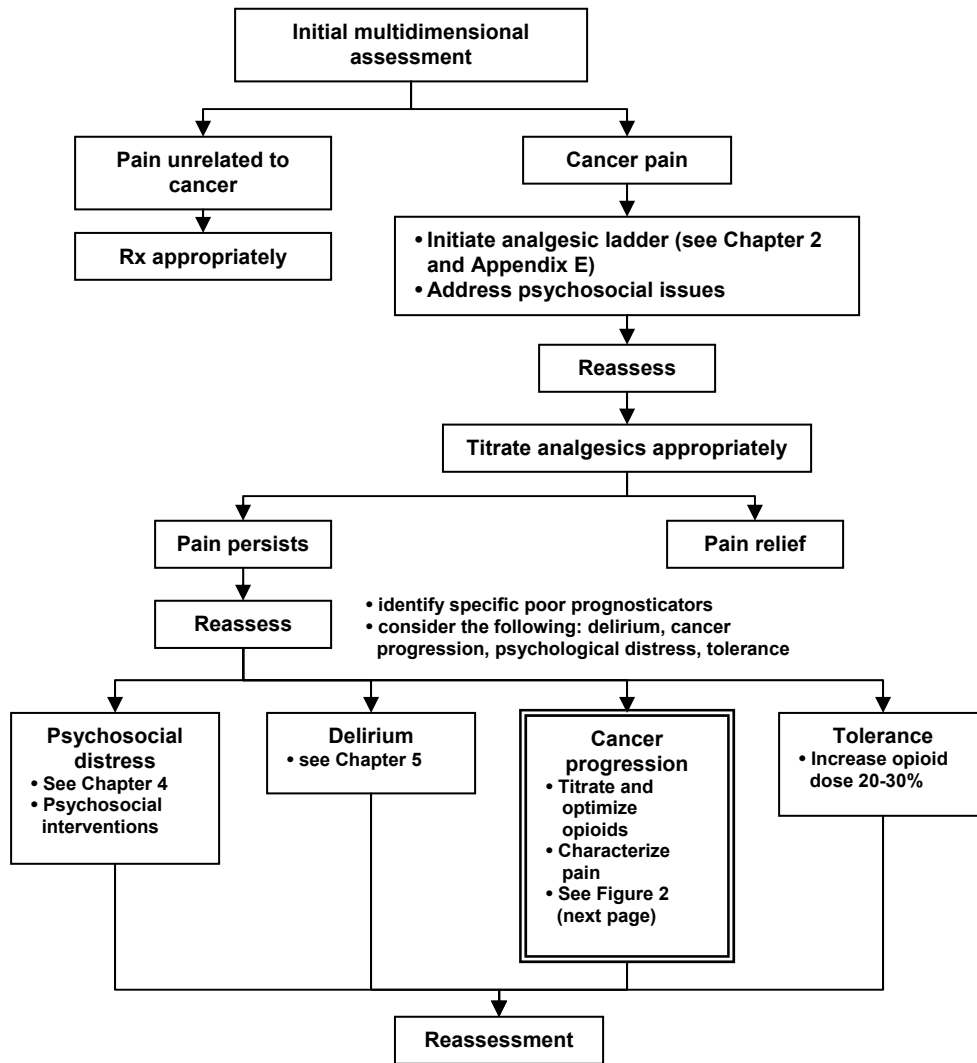
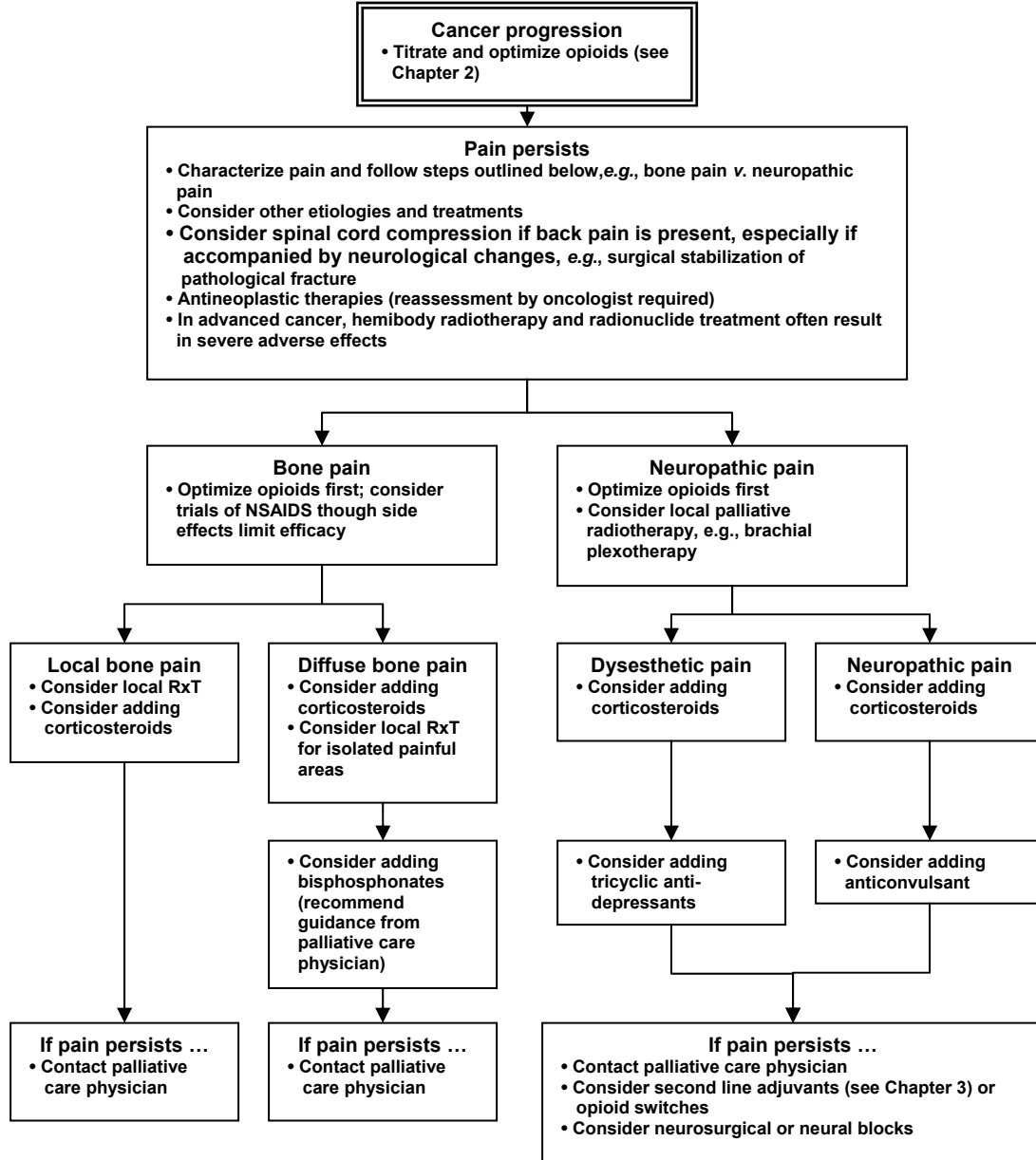


Figure 2: Algorithm for cancer pain management – cancer progression



Recommended reading

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CHAPTER 3: Adjuvant analgesics

Adjuvant analgesics are drugs that have a primary indication other than pain but are analgesic in some painful conditions or are capable of decreasing the side effects of analgesics. They are commonly administered in combination with one of the primary analgesics (*e.g.*, opioids).

3.1 Adjuvant analgesics

Adjuvant analgesics are generally less reliable than the opioids for cancer-related pain and should be considered after opioid treatment has been initiated and optimized. This decreased reliability is reflected by a smaller proportion of treated patients who respond adequately, a higher likelihood of troublesome side effects, or a slower onset of analgesic effect for most drugs. Approximately one-half to two-thirds of patients given an adjuvant achieve at least 50% pain relief from a carefully adjusted dosing regimen, and most patients require many days to achieve a maximal response.

It is not very clear when the optimal time is to add an adjuvant analgesic to an opioid regimen. The timing will depend on various factors, such as the type of pain and the patient's overall disease burden. However, it is prudent to avoid polypharmacy where possible in order to minimize adverse effects. One approach is to first initiate opioid therapy and optimize the regimen by titrating the dose upwards to achieve pain control. The occasional patient may be adequately managed on an adjuvant alone; however, too many patients have insufficient relief and require an opioid. Trials of one or more adjuvant drugs (preferably not concurrent) can then be attempted if opioid therapy alone is proven problematic.

The existence of large inter-individual and intra-individual variability in response to adjuvant analgesics suggests the need for sequential therapeutic trials to identify the most useful drug and dose titration to identify the optimal dose of the drug selected.

See Table 2 on the following pages for some of the most common adjuvant analgesics.

Table 2: Some of the more commonly used adjuvant analgesics

Drug	Indications	Comments	Starting dose	Usual effective dose range
Corticosteroids (c/s)	Bone, visceral, and neuropathic pain	C/S have a range of effects including mood elevation, anti-inflammatory activity, anti-emetic activity and temporary appetite stimulation. They also reduce cerebral and spinal cord edema and are essential in the emergency management of elevated intracranial pressure and epidural spinal cord compression. Adverse effects of long term c/c administration are well known. Amongst the potential early side effects are loss of glucose control, increased risk of infection and acute psychiatric disorders (e.g., mania).	This is empiric. Dexamethasone 2-8 mg tid to qid po or s.c.	This is empiric. After starting the c/s, it needs to be tapered according to clinical effect.
Nonsteroidal anti-inflammatory drugs (NSAID)	Bone pain; various soft tissue, visceral or neuropathic pains	The long term benefits of traditional NSAIDS are limited by adverse effects such as gastrointestinal perforation and hemorrhage, and renal impairment. However, the new COX-2 specific NSAIDS may offer analgesia with decreased incidence of gastro-intestinal and renal adverse effects.	The optimum NSAID and the optimum dose has not been determined for cancer pain.	
Tricyclic antidepressants	Neuropathic pain (dysesthetic type)	Their adjuvant effects often occur at lower doses than are used for the treatment of depression and may be seen within 24-48 hours of initiating treatment. The most widely reported experience has been with amitriptyline. The adjuvant analgesic properties of other antidepressants have not been researched extensively.	Amitriptyline or desipramine 10-25 mg hs po. (a trial of 7-10 days may be necessary while monitoring for adverse effects).	Amitriptyline or desipramine 50-100 mg hs po.
Anticonvulsants	Neuropathic pain (neuralgic type)	These need to be used with caution in patients undergoing marrow-suppressant therapies such as chemo or radiotherapy. Periodic monitoring of complete blood count are recommended.	Carbamazepine: 100 mg bid po Phenytoin: 100 mg TID Gabapentin: an anti-convulsant that can be useful for neuropathic pain (reported to have fewer adverse effects than carbamazepine and dilantin)	Carbamazepine: increase dose over about 2 weeks to a maximum of 400 mg TID (followed by blood levels). Phenytoin: 100 mg TID (followed by blood levels). Gabapentin: starting dose is ±100 mg po tid and this can be titrated over about 2 weeks to a maximum of 3,000 mg per day in 3 divided doses.

Table 2: Some of the more commonly used adjuvant analgesics (cont.)

Drug	Indications	Comments	Starting dose	Usual effective dose range
Oral local anesthetics	Neuropathic pain (dysesthetic type)	Controlled clinical trials have demonstrated efficacy in both lancinating and dysesthetic neuropathic pains. However, they are more frequently indicated for dysesthetic pains. Side effects are common and include gastrointestinal (nausea) and central nervous system side effects (ataxia, tremors, confusion) and are often dose limiting. Patients with a history of heart disease may be at risk for serious adverse effects. Mexilitine is the preferred drug, generally not administered with tricyclics.	Mexilitine: 100 mg q12h po Flecainide: 50 mg q12h po	Mexilitine: increase gradually to a maximum of 300 mg q8h po Flecainide: 100 mg q12h po
Table 2: Some of the more commonly used adjuvant analgesics	Bone pain	See Chapter 9, page 53, on hypercalcemia. Primarily for pain secondary to diffuse, lytic metastatic bone lesions. Appears to be helpful in decreasing the risk of skeletal complications.	See Chapter 9, page 53, on hypercalcemia.	

Other adjuvant analgesics include the following.

NMDA antagonists (e.g., ketamine)

Neuropathic pain, especially those with a hyperalgesic component. Note that methadone appears to have NMDA antagonist properties while ketamine often causes significant psychotic effects.

Baclofen

Neuropathic pain (neuralgic type) painful muscle spasms.

Psychostimulants

Reverses opioid sedation. See Chapter 4 for treatment of depression in cancer patients.

Antibiotics

Infections can worsen pain – especially head and neck cancers.

Clonidine (alpha 2 antagonist)

Refractory neuropathic pain (seldom used).

See Figures 1 and 2, on pages 26 and 27 respectively, for algorithms concerning pain management.

Consider the following before trying an adjuvant

- Optimize the opioid, *i.e.*, titrate up.
- Consider risks *v.* benefits of the adjuvant drug. Many of the adjuvants may cause serious adverse effects. Although most have less serious side-effects, these adverse effects may be severe enough to affect a patient's quality of life. *e.g.*: NSAIDS can cause renal impairment, GI bleeding.
- Tricyclic antidepressants: delirium and other anticholinergic side effects
- Recognize inter-individual and intra-individual variability. Therefore, the response to a certain adjuvant may vary from patient to patient, while one patient may not respond to a specific adjuvant but show good response to another. The response rate (usually partial) varies considerably from one adjuvant to another but is, on average, about 60%. Several trials of different adjuvants, allowing at least 7 to 10 days for each one, may therefore be necessary to determine the optimal adjuvant. During these trials patients need to be monitored closely for potential adverse effects.
- Avoid using more than one adjuvant concurrently.
- The goal should be to obtain adequate analgesia and symptom control without severe adverse effects.

Pitfalls

Do not use benzodiazepines and phenothiazines as adjuvant analgesics; these drugs do not have analgesic properties and may cause significant sedation and delirium. Where possible, avoid polypharmacy.

3.2 Non pharmaceutical methods to control pain

Palliative radiotherapy is often useful for the control of bone pain and for some other pains that are caused by tumour infiltration. Palliative radiotherapy should be considered early, especially if bone involvement is the cause of pain. Often, a single dose of radiotherapy is sufficient.

Orthopedic procedures, *e.g.*, some pathological fractures, especially those of the femur and sometimes the spine, may require surgery to achieve pain control.

Occupational and physiotherapy modalities:

- transcutaneous electronic nerve stimulation (TENS);
- massage therapy;
- relaxation therapy; and
- supports such as collars and slings to immobilize fractures.

Complementary therapies are especially useful for patients who have a high locus of control, anxiety, fatigue, and insomnia, and who are comfortable with these treatments. Such therapies (usually used in conjunction with traditional therapies) include: reiki, therapeutic touch, massage, hypnosis, imagery and acupuncture.

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CHAPTER 4: Mood disorders in patients with cancer

Emotional distress is a normal response to the catastrophic event that a cancer diagnosis represents, especially if the cancer is non-curable. For most, this distress is transient and resolves with time and with general supportive care.

Research has shown that approximately half of the patients diagnosed with cancer or with recurrence of cancer will adjust adequately without symptoms beyond those regarded as normal. The symptoms abate as the crisis resolves. The other half have sufficient psychiatric symptoms to warrant the diagnosis of a psychiatric disorder.

Of the approximately 50% of patients who experience problems that are significant enough meet the criteria of a psychiatric diagnosis: two thirds have an adjustment disorder with or without a depressed or anxious mood. A smaller percentage ($\pm 10\%$ of patients) have depression of such magnitude that it meets the criteria for a major depression - it is so profound that it interferes substantially with the patient's comfort, quality of life, social functioning, and ability to make appropriate treatment decisions. Some patients, $\pm 10\%$, have pre-existing psychiatric problems such as anxiety or personality disorders.

During the terminal stages of the illness, more than 80% of patients develop delirium. Delirium, especially the hypoactive form, is frequently misdiagnosed as depression.

4.1 Management of adjustment disorders

Step 1 History and physical examination (sometimes collateral information from family members or friends is required).

- Previous depressive episodes, or other previous psychiatric diagnoses.
- Substance abuse (including alcohol). This would suggest maladaptive coping techniques, *i.e.*, “chemical coping”.
- Family history of depression and suicide.
- Concurrent stresses, *e.g.*, social, financial, occupational.
- Fears regarding dying and previous experiences with the dying process, *e.g.*, witnessing family members or friends die.
- The meaning of the illness to the patient and his or her understanding of the medical situation (including prognosis).
- Assess suicidal risk.
- Rule out delirium: delirium is more frequent than depression in terminal disease. However, because patients with delirium frequently appear withdrawn or sad, they are frequently misdiagnosed as being depressed.
- How did the patient cope with stressors before?

Step 2: Expressive/supportive therapy

- Make time in a busy office schedule to allow sufficient time to see cancer patients. Schedule near the end of the afternoon clinic if necessary.
 - Repeat follow-ups are necessary.
 - Have a supportive relative or friend accompany the patient whenever possible.
 - Listen to the patient and allow him/her to express his/her feelings (fear, anger, *etc.*). Open
-

ended questions regarding concerns or fears may help patients express themselves, *e.g.*, “what would you say are the main concerns you are having these days?”

- Be non-judgmental.
- Legitimize the difficulty of the situation – the “right” to be upset reduces the fear of being perceived to be “weak” or “inappropriate.”
- Reassurances should be realistic.
- Respect the desire of the patients to maintain hope. Respect too, the defence mechanisms of denial, repression, and regression as long as they do not interfere with diagnostic or therapeutic processes, or with important personal matters that need to be addressed.
- Social supports provided by family, friends, community and religious groups are important. Assess these and, if need be, enlist them.
- Clarify the medical situation and its implications.
- Patient education is vital. Correct misconceptions regarding the illness, treatment or the dying process.
- Reassurances of continued care and interest.

Patients with a high level of anxiety, fatigue or insomnia may benefit from relaxation exercise. Examples of relaxation exercises include:

1. simple touch, massage or warmth
2. slow rhythmic breathing exercises
3. imagery
4. drawing on peaceful, past experiences
5. listening to soothing music

Cognitive distraction and refraining enable patients to learn to monitor and evaluate negative thoughts and replace them with more positive thoughts and images. This psychological technique needs to be taught by a person trained in the technique.

The above measures are usually sufficient to assist the patient to regroup and cope.

Step 3: Pharmacological modalities

- These are not commonly required; when indicated, they should be utilized for a limited time only, with regular reassessments.
- Focus of management should be on psychosocial support.
- Balance the potential benefits against the potential adverse effects of the drugs - remember that patients with advanced cancer are very vulnerable to the side effects of psychoactive medications.
- Medications occasionally used are as follows.
 - For *anxiety*: short acting benzodiazepines, *e.g.*, lorazepam 0.5-1 mg prn or alprazolam 0.25 - 1 mg bid prn. Potential side effects include somnolence, cognitive impairment or aggravation of delirium, increase risk for falls.
 - The emphasis should be on supportive measures rather than pharmacological modalities.
 - Monitor for delirium. It is prudent to discontinue any anxiolytic if delirium is suspected.

4.2 Insomnia

The use of benzodiazepines is discouraged because of the increased risk for falls, cognitive impairment and risk of interactions with other medications. Preferably, the treatment should be focused on non-pharmacological modalities such as relaxation therapy, supportive therapy, etc. If severe insomnia accompanies a major depression, a more sedating anti-depressant can be taken in the evening.

4.3 Major depression

In cancer patients, somatic symptoms (*e.g.*, anorexia, fatigue, insomnia, weight loss) are of little value as diagnostic criteria for depression since they are common consequences of advanced cancer. The diagnosis, therefore, often focuses on psychological symptoms. Diagnostic and screening tools for depression commonly used in the general population are often not very helpful in patients with advanced cancer. It has been suggested that asking a patient the simple question “are you depressed?” can be a useful screening – but not a diagnostic – tool.

Psychological indicators for the presence of a major depression are:

- Profound feelings of worthlessness.
- Profound feelings of guilt.
- Profound anhedonia (no pleasure).
- Profound thoughts of “wishing to die soon.”
- Profound feelings of hopelessness.
- Suicidal ideation.

The symptom of sadness or depressed mood is not equivalent to the syndrome of major depression.

NB: Always assess for suicidal risk.

4.4 Assessing risk for suicide

The following factors increase the risk for suicide:

- Precise, detailed suicidal plan.
- Lack of social support.
- Any other significant life stressors.
- Presence of delirium or mild dementia.
- Any prior suicide attempts or depression.
- Male, aged 15-24 or 50+.

To reduce the risk of suicide:

- Provide a safe environment.
- Work to alleviate all physical and psychosocial suffering and make referrals to appropriate specialists, if necessary.
- Enhance social support from significant others.
- Involve the interdisciplinary team where possible.

4.5 Management of major depression in advanced cancer

Step 1: Look for clinical conditions that may mimic depression and treat these

Delirium (see Chapter 5 on confusion), especially the hypoactive, withdrawn form, can easily be mistaken for a major depression.

Metabolic *E.g.*, hypercalcemia.

Endocrine *E.g.*, hypothyroidism.

Drugs *E.g.*, anticonvulsants, baclofen, beta blockers, corticosteroids tamoxifen, cyproterone acetate.

Step 2: Assess

- Pain and other symptoms, social issues (financial concerns, complex family dynamics), cultural and spiritual issues.
- Past losses and coping strategies.
- History of psychiatric disorders.
- History of drug abuse - including alcohol abuse (a history of this suggests poor coping strategies when faced with life stressors).
- Assess family and social supports.

Step 3: Expressive/support therapy

- Explore fears about the illness and the prognosis.
- Encourage family and social supports.
- Reassurance of your continued care input, and interest.

Step 4: Antidepressants

Antidepressant medication is considered for any patient with significant depression. Monitor for potential adverse effects since these are common and can be troublesome, especially in elderly or frail patients. Presently, the drugs most frequently used in patients with a major depression in advanced cancer are the tricyclic antidepressants and the selective serotonin reuptake inhibitors (SSRIs).

Tricyclic antidepressants

The various tricyclic antidepressants cause varying degrees of sedation, anticholinergic and cardiovascular side effects and different drugs are more suited to certain situations. Patients with accompanying anxiety or insomnia are treated with a sedating antidepressant such as amitriptyline or doxepin while patients with psychomotor retardation require less sedating drugs, such as desipramine. Patients with problems related to urinary retention or intestinal motility need a drug with fewer anticholinergic side effects, such as desipramine or nortriptyline. Generally, desipramine has a better side-effect profile.

Starting doses of the tricyclic antidepressants should be low, 10-25 mg po at bedtime and increased slowly over several weeks. Depressed cancer patients often have a therapeutic response at much lower doses (25-125 mg po) than are usually required in physically healthy patients.

Unfortunately, there is a delay of two to four weeks in the onset of the antidepressant effect of these drugs. In patients with a short life expectancy or with severe depression this period may be too long. Where a rapid antidepressant effect is desired, psychostimulants can be very useful.

Selective serotonin reuptake inhibitors (SSRIs)

These drugs are reported to cause fewer sedative and autonomic side effects than the tricyclic antidepressants. Nausea and increased anxiety may occur. Fluvoxamine has been reported to cause more nausea than others.

Fluoxetine generally has a stimulating effect while sertraline, fluvoxamine and paroxetine are more sedating. However, it must be noted that all SSRIs can cause either somnolence or insomnia/stimulation and that the timing of the dose often has to be tailored depending on the individual's response. This appears to be particularly true of paroxetine.

Fluoxetine has a long half life (several weeks) and its use in these patients is discouraged. The advantages of paroxetine are its short half life and lack of active metabolites.

Table 3: SSRI use in cancer patients

SSRI	Starting does	Usual effective dose
Fluoxetine	10 mg/day po (am)	20 mg/day
Paroxetine	10 mg/day po (am)	20 mg/day
Sertraline (with evening meal)	25-50 mg/day po	0-100 mg/day
Fluvoxamine (at bedtime)	50 mg/day po	100-200 mg/day

Withdrawal syndromes consisting of abdominal cramps and flu-like symptoms have been described following abrupt discontinuation of SSRIs. The symptoms are usually mild and transient. SSRIs may interact with MAO inhibitors, amphetamine derivatives and dextromethorphan to cause a serotonin syndrome which includes mental status changes and agitation. It should also be noted that SSRIs – particularly paroxetine and fluoxetine – are active inhibitors of the enzyme responsible for metabolizing oxycodone and codeine to its active analgesic form. Concurrent use of these opioids and SSRIs can therefore result in decreased pain control.

Psychostimulants

These drugs have been used successfully in the treatment of depression in cancer patients. They have a rapid onset of action and are especially useful in patients with severe psychomotor slowing. Other benefits include:

- energizing effect;
- improved appetite; and
- reduced opioid-induced sedation.

Potential side effects include:

- anxiety;
- insomnia and nightmares;
- psychosis, paranoia; and
- tolerance and physical dependence occurs with prolonged use.

Psychostimulants used include methylphenidate, pemoline and dextroamphetamine.

NB: Hyperactive delirium and/or severe anxiety are contraindications for the use of psychostimulants. Exclude these prior to initiating a psychostimulant.

When initiating a psychostimulant therapy, a test dose is advised. It can be given at 8 am and the patient reassessed 1-2 hours later. If side effects occur after the test dose (psychomotor agitation, hallucinations), discontinue the psychostimulant.

Methylphenidate

Test dose: 5 mg po at 8 am
 Starting dose: 10 mg po at 8 am
 5 mg po at noon

- Avoid psychostimulants after noon to prevent insomnia
- The dose may need to be increased gradually over many days to weeks

- Doses greater than 30 mg per day are seldom required
- Patients can be maintained on psychostimulants for four to eight weeks and two-thirds will be able to be withdrawn from the psychostimulant without a recurrence of the depressive symptoms

Pemoline

In the United States pemoline is available as a chewable tablet and has been used for patients who cannot swallow.

Test dose: 18.75 mg

Starting doses: 18.75 mg at 8 am and at noon.

The dose can then be increased gradually over several days. Typically, patients require less than 75 mg a day.

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3. Massie M, Gagnon P, Holland J. Depression and suicide in patients with cancer. *J Pain Symptom Manage*, 1994; 9(5):325-340.
4. Loscalzo M. Psychological approaches to the management of pain in patients with advanced cancer. In: Cherny N, Foley K, eds. *Hematology/Oncology Clinics of North America: Pain and Palliative Care*, Vol 10 #1. Philadelphia: WB Saunders Company, 1996:139-156.
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CHAPTER 5: Confusion

Neuropsychiatric disorders are frequent complications of advanced cancer. The most common reason for cognitive failure in these patients is delirium. Up to 85% of terminal cancer patients will develop delirium in the last weeks of life. A smaller percentage develop delirium earlier in the course of their illness. Delirium makes assessment of pain and symptoms difficult and is a common cause of distress for patients, families and health care providers.

Delirium presents a “clinical dichotomy” in palliative care. On the one hand, it can be seen to be an expected end-of-life occurrence. On the other hand, 25-45% of episodes (especially those occurring in the pre-terminal phase) are reversible by implementing relatively non-invasive management strategies. One of the clinical dilemmas, therefore, lies in attempting to predict which is an end-of-life episode and which are potentially reversible. If reversible, the patient may still have many weeks and months of good quality-of-life, able to communicate with loved ones and clearly express needs. To complicate this decision-making process, predicting life expectancy can be difficult and often inaccurate. It would therefore be reasonable to approach delirium as a reversible episode unless there are clear signs suggesting death is near or the cause is irreversible, such as with significant hepatic encephalopathy. The management of delirium should be on a “case-by-case” basis.

5.1 Diagnosing delirium

Essential criteria for diagnosing delirium

- Disordered attention and cognition.
- Disturbance of psychomotor behavior (agitation, somnolence, hallucinations, paranoia).
- Acute or subacute onset and fluctuating course.

Clinical subtypes of delirium

- Hyperactive: confusion, agitation, hallucinations, myoclonus (consider this if patient presents with apparently uncontrolled pain).
- Hypoactive: confusion + somnolence ± withdrawn.
- Mixed: features of both above.

Cardinal features that distinguish delirium from dementia in palliative care patients

- *Delirium*: sudden onset, altered level of consciousness, clouded sensorium, occasionally reversible.
- *Dementia*: gradual onset, unimpaired level of consciousness, chronic.

Table 4: Common causes of cognitive impairment in advanced cancer

Drugs	directly:	Opioids, benzodiazepines, antidepressants
	indirectly:	NSAIDs or ACE inhibitors causing renal failure resulting in uremia or opioid metabolite accumulation.
Infection		
Metabolic	<i>E.g.</i> , hypercalcemia, uremia, hepatic failure, hyponatremia	
Dehydration		
Hypoxia		
Brain metastases		

Often the cause of delirium is multifactorial and, occasionally, no specific cause is identified. This should not deter one from looking for underlying causes since appropriate management involves addressing these causes where possible and reversing them when appropriate.

5.2 Management of delirium

Step 1: Assess the patient

- Maintain a high index of suspicion. Use a screening tool on a regular basis to look for cognitive decline or other signs of delirium. The Folstein Mini-Mental State Examination (MMSE), for example, is a well validated screening tool for cognitive impairment. (Appendix A, page 73). Almost one-quarter of delirium episodes are missed by both physician and nurse until late unless such a tool is used. Orientation questions alone – re: person, place and time – do not provide an accurate assessment of cognitive status. Although the MMSE has some deficiencies and does not capture the neuro-behavioural changes associated with delirium, it has been shown to be a useful tool. Other more specific screening and diagnostic tools are available or under development.
- Ask the patient specifically about hallucinations (usually visual and tactile) and assess for paranoid ideation.
- Examine and look for clinical signs of infection, opioid toxicity (myoclonus, hyperalgesia), dehydration, uremia, hepatic encephalopathy, *etc.*
- Order appropriate investigations, *e.g.*, CBC, electrolytes, calcium (with albumin), urea and creatinine, CXR, O₂ sats, *etc.*

Tips to distinguish between pain and delirium

Delirium alters a patient's perception and expression of pain and other symptoms. Delirious patients often moan and groan and look restless. These signs cannot be attributed entirely to pain since they are often manifestations of delirium. We suggest that managing the delirium becomes a priority. Distinguishing delirium-related symptoms and signs from pain control can be challenging.

Step 2: Treat the underlying cause

- *Opioid toxicity*: switch to another opioid; see Chapter 2.6, 'Opioid Rotations,' on page 19.
- *Sepsis*: start antibiotics if appropriate. Obtain consensus from the patient and family where possible.
- *Drugs*: discontinue drugs that would be aggravating the delirium, *e.g.*, tricyclic antidepressants, benzodiazepines.
- *Dehydration*: if a patient is unable to take in enough oral fluids, then consider hypodermoclysis with normal saline at 60-100 mg/hour and reassess daily. If an IV line is already established, hydration can be given intravenously. Hyaluronidase is not routinely indicated unless the site leaks consistently. **Hyaluronidase should not be administered IV.**
- *Hypercalcemia*: see Chapter 9, page 53, on hypercalcemia.
- *Hypoxia*: treat underlying cause and administer O₂.
- *Brain metastases*: cognitive impairment induced by brain metastases may respond, at least temporarily, to corticosteroid therapy.

Step 3: Treat symptoms of delirium

Agitation/hallucinations

- Start haloperidol 1 mg po/sc q8-12hrs and 1 mg q1h po/sc prn for agitation. If the

agitation/hallucinations are severe, higher doses of haloperidol are indicated, eg: haloperidol 2 mg q6-8h sc/po with breakthrough orders of 2 mg q1h sc/po. To bring severe agitation rapidly under control, it may be necessary to give haloperidol more frequently initially *e.g.*, haloperidol 2 mg q30 minutes sc/po prn in the first few hours and thereafter q1h prn. It is appropriate to bring an agitated delirium under control rapidly to prevent patient, family and staff distress.

- If symptoms persist, or worsen, the dose of haloperidol can be increased up to a maximum of 20-30 mg/day.
- **Always assess for the possible occurrence of extra-pyramidal adverse effects or other adverse effects.**
- If symptoms persist after 36-48 hours despite optimal haloperidol doses, an alternative drug, perhaps more sedating, needs to be offered, eg: methotrimeprazine. Starting doses are 6.25 mg to 12.5 mg sc/po q8-12h. This drug can be sedating and the family need to be informed of this. Breakthrough doses for agitation/hallucinations can also be ordered, eg: methotrimeprazine 6.25 mg or 12.5 mg q1h po or sc prn.
- Very rarely is sedation for uncontrolled agitation with midazolam required. When indicated, start a continuous subcutaneous infusion at 1 mg/hour and titrate up to 4 mg/hour (see Chapter 13).

Step 4: Family counseling and discussion with nursing staff

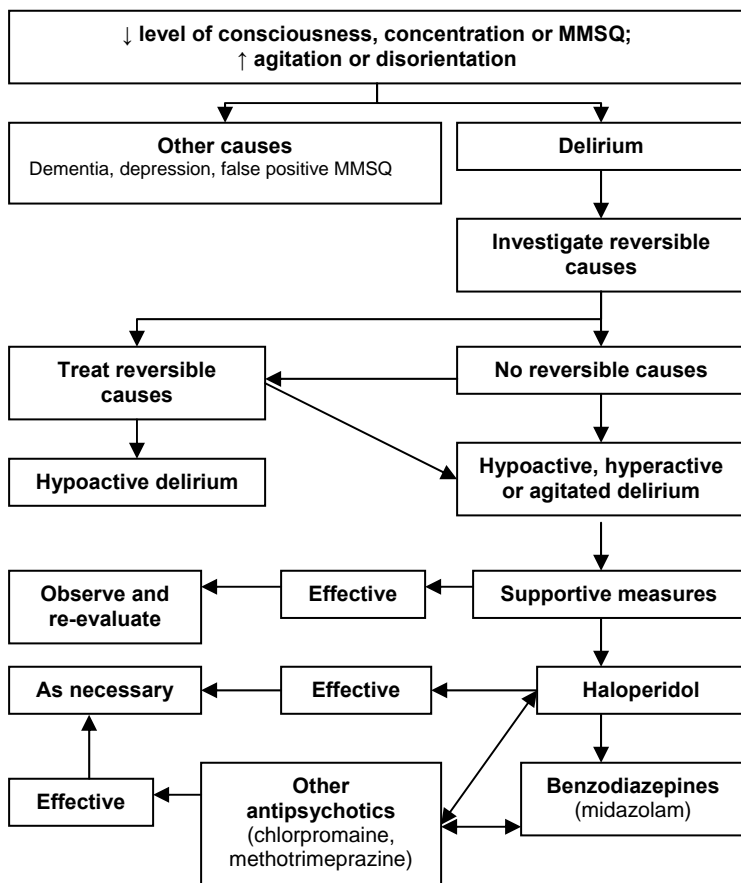
- Confusion and agitation are an expression of brain malfunction. Misinterpretation of delirium-related signs and symptoms as pain can result in inappropriate use of opioids, perhaps even aggravating the agitation.
- The aim of the treatment is comfort rather than life prolongation.
- Good communication will avoid a 'destructive triangle' of poor communication and minimize family and staff distress, as well as dissatisfaction with care.

Pitfalls

- Not recognizing the presence of delirium.
- Diagnosing a hypoactive delirium as depression and treating inappropriately with antidepressants.
- Interpreting agitation and the accompanying moaning and grimacing of a delirium as a direct indication of poor pain control and responding by increasing opioid doses. This is particularly important to remember since in many cases opioids are the cause of delirium and by giving more opioids, one aggravates the situation.
- Not discontinuing drugs that could be causing or aggravating the delirium.
- Occasionally delirium is superimposed on pre-existing dementia. Some medications that are used for symptom control in advanced disease may unmask a pre-existing cognitive problem that was previously unrecognized by the patient's family.
- Urinary retention and constipation in cognitively impaired patients are not an uncommon problem that can increase agitated behavior due to discomfort and inability to communicate the source of discomfort. Catheterization or disimpaction will likely not resolve the delirium but may decrease the agitation.

See Figure 3 on the next page for an algorithm for the treatment of delirium.

Figure 3: Algorithm for management of delirium



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3. de Stoutz N, Tapper M, Fainsinger R. Reversible delirium in terminal ill patients. J Pain Symptom Manage, 1995; 10(3):249-253.
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CHAPTER 6: Constipation

Constipation is a common cause of morbidity in palliative care patients. It affects up to 95% of patients who are taking opioids if not treated prophylactically.

Common causes of constipation

- Poor oral intake or dehydration.
- Malnutrition: autonomic neuropathy related to the anorexia/cachexia/asthenia syndrome of advanced cancer.
- Drugs: opioids, anticholinergic drugs, diuretics, iron, etc.
- Decreased mobility.
- Abdominal tumours.
- Hypokalemia, hypercalcemia.

N.B.: Patients can become constipated even if they are not eating!

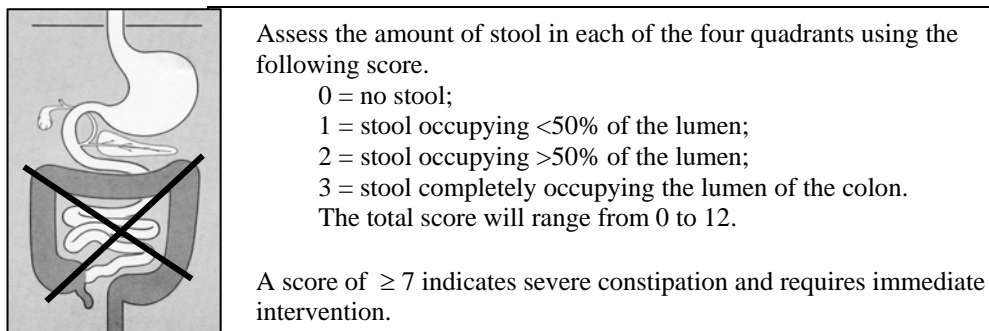
Common complications of constipation

- Abdominal pain and aggravation of cancer pain in patients with abdominal or retroperitoneal malignancy.
- Abdominal distension and discomfort.
- Nausea and vomiting.
- Overflow diarrhea.
- Hemorrhoids and anal fissures.
- Bowel pseudo obstruction.
- Urinary retention.

6.1 Diagnosing constipation

- Suspect constipation in any patient with advanced cancer presenting with, amongst others, one or more of the following: irregular bowel movements, diarrhea, nausea and vomiting, abdominal discomfort and bowel obstruction.
- Perform a digital rectal examination.
- Occasionally a plain abdominal radiograph may assist in the diagnosis.
- A “constipation score” is occasionally very helpful in assessing constipation.
- Using a flat abdominal x-ray, draw two diagonal lines transecting at the umbilicus as shown in Figure 4 below. This divides the abdomen into four quadrants, corresponding to the ascending, transverse, descending and recto sigmoid colons.

Figure 4: Using an abdominal x-ray to calculate a “constipation score”



6.2 Management of constipation

Prevention

- General measures: encourage generous fluid intake (8-10 glasses/day).
- Large amounts of dietary fibre are often poorly tolerated by debilitated patients and should only be increased gradually.
- Encourage exercise as tolerated.
- When starting a patient on an opioid, start laxatives simultaneously. Start with a bowel stimulant and a stool softener eg: senna 1-2 tabs hs. + docusate 100 mg bid po.
- Doses can be titrated upwards so as to achieve a bowel movement regularly (every 1 to 2 days).
- If patients find it difficult swallowing tablets/capsules, senna and docusate come in liquid forms. (Lactulose, 30 ml tid, is an alternative).
- If unable to achieve a bowel movement within 3 days, administer a fleet enema or bisacodyl suppository rectally on day three.

Commonly used doses are:

- senna 2-4 tabs bid, up to qid if necessary; or
- docusate 240 mg tid, up to qid if necessary

Treatment of established constipation (with or without fecal impaction)

Requires the use of enemas and/or suppositories.

- Administer a fleet enema or a bisacodyl suppository. Repeat if unsuccessful.
- If still unsuccessful, administer an oil retention enema followed by a soap suds enema several hours later. (Caution: soap suds enemas may be poorly tolerated by debilitated, frail patients. A high fleet is an alternative in these patients.)
- If the impaction appears to be in the proximal colon, magnesium citrate, up to 250 ml po, may be tried.
- Seldom is manual disimpaction necessary.

Tips

- Always exclude overflow diarrhea secondary to stool impaction when a palliative care patient presents with diarrhea.
- Try to avoid long-term use of osmotic laxatives as they may result in fluid and electrolyte imbalances.
- On rectal examination, consistency of the stool is helpful to guide treatment. In the presence of hard stools, increase stool softeners (*e.g.*, glycerine, docusate). When stools are soft, try bisacodyl or senna.
- When you suspect significant stool impaction and the rectum is empty on rectal exam, a plain abdominal x-ray may be useful. If bowel obstruction is present, treat appropriately.
- For patients unable to take laxatives orally, senna is available in formulations for rectal use. Other effective methods are bisacodyl suppositories (q3d) or fleet enemas (q3d).

6.3 Bowel obstruction

Signs and symptoms

- Nausea and vomiting will occur in almost all patients with complete obstruction.
- Abdominal visceral pain.
- Abdominal distension.
- High pitched or absent bowel sounds.
- Tympanic sounds with percussion of abdomen.
- History of infrequent bowel movements.
- Absence of flatus.

NB: Prokinetic agents such as metoclopramide or cisapride should be avoided in the presence of complete malignant bowel obstruction.

Surgical management

Suitability for surgery should be assessed to justify any surgical intervention. This includes assessing the general condition of the patient, the evidence of mechanical obstruction, reasonable expectation of survival and quality of life.

Surgical interventions vary from aggressive procedures such as resection (\pm colostomy, enterostomy) to less aggressive options such as a percutaneous endoscopic gastrostomy (PEG) tube. Gastrostomy tubes can be helpful to drain gastrointestinal contents when a proximal bowel obstruction is complete and irreversible. A nasogastric (NG) tube may be used temporarily until the obstruction resolves or a gastrostomy tube is inserted.

Medical management

Several medical options are available to help improve the comfort of patients with inoperable obstructions.

- It is important to differentiate between a partial and a complete bowel obstruction. Prokinetic agents may be appropriate in the presence of an incomplete obstruction.
- Prevent dehydration by using hypodermoclysis (1-2 litres of fluid/day).
- Corticosteroids can be used to reduce swelling and inflammation related to peri-tumour edema. Dosages for this are not well studied but ACB uses dexamethasone 6-8 mg sc tid to qid, followed by a tapering regimen.
- To control nausea and vomiting, use dexamethasone 10 mg po/sc bid, then taper to lowest effective dose when response observed. If ineffective, haloperidol 1-2 mg sc q8-12h and q 1h prn. If dexamethasone and haloperidol together are ineffective, try hyoscine butylbromide to reduce GI secretions.
- To reduce GI secretions and severe abdominal cramping related to the obstruction, consider using hyoscine butylbromide 10 mg sc qid or 10 mg /24 hr with continuous infusion. Hyoscine butylbromide is indicated as long as there is a complete bowel obstruction. In the presence of an incomplete obstruction hyoscine would be less appropriate. If the obstruction persists and the patient remains symptomatic, try adding octreotide 50-100 mcg sc bid.
- Although it is not feasible for the long term, in the short term the nasogastric (NG) tube can provide significant relief until the obstruction is overcome or until a PEG tube is inserted.
- Providing mouth care is advised if the patient is NPO.

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3. Fainsinger RL. Integrating medical surgical treatments in gastrointestinal, genitourinary, and biliary obstruction in patients with cancer. *Hematology/Oncology Clinics of North America*, February 1996; 10(1): 173-188.

CHAPTER 7: Hydration

The old biomedical model of patient care insisted on universal hydration (even for terminally ill patients) as a basic standard of medical care. Original hospice models justifiably challenged that extreme approach and promoted the approach that parenteral hydration was not useful in the terminal phase of an incurable illness. However, both approaches, universal hydration and universal non-parenteral hydration, reflect potential biases. Probably a more individualized approach is required. Dehydration can cause delirium and can precipitate prerenal failure. The latter has been associated with opioid related neurotoxicity and other adverse effects, such as nausea and persistent somnolence. Conversely, some patients may not experience problems re: diminished hydration, and appear not to benefit from hydration.

Patients who develop delirium or opioid toxicity may benefit from parenteral hydration if the oral route is not feasible. Parenteral hydration can be administered subcutaneously. This is generally more convenient and perhaps less invasive than the intravenous route. Patients receiving parenteral hydration should be reviewed regularly. Hydration could be discontinued, or the volume could be decreased, if the underlying symptom such as delirium has resolved. Over hydration should also be avoided since palliative patients can require much smaller volumes of fluid than the general population.

In those patients for whom it is felt parenteral hydration is not indicated, one should consider decreasing the opioid doses judiciously if there are indicators of renal impairment or monitor for evidence of early toxicity. This would minimize the risk of distress from severe opioid-related toxicity.

7.1 Hydrating palliative patients

When the decision is made to hydrate a patient, various options are available. Patients who can still take fluids orally are encouraged to do so. From time to time patients are admitted to Palliative Care facilities via acute care units and arrive with intravenous lines in situ. If the line is running well and the patient is severely dehydrated and experiencing problems related to that, then hydration can be continued until the intravenous line is no longer viable or hydration is no longer required.

Hypodermoclysis (see Appendix H, page 82)

Hypodermoclysis is the subcutaneous administration of fluids. It offers certain advantages over the intravenous route:

- easier access;
- can be given at home easily and safely;
- subcutaneous HDC sites can last up to 7 days; and
- can easily be turned off and disconnected, giving the patient more mobility.

7.2 Ordering hypodermoclysis

Hypodermoclysis can be administered in various ways, depending on the clinical situation.

For rehydration

Fluid type: normal saline

Rate: 70-100 ml/hr by continuous infusion

Augmenting fluid intake or maintaining fluid intake

Fluid type: 2/3 1/3

Rate: If by continuous infusion: 40-80 ml/h

If by overnight clysis: 1 litre overnight. This can be done by gravity especially in the home setting.

If by boluses: Boluses of 500 ml each can be given twice daily. Each 500 ml can be run in over 1 hour.

In our experience, hyaluronidase is not universally required to effectively administer fluid subcutaneously. Most hypodermoclyses can be given without hyaluronidase. However, if the site leaks, hyaluronidase can be added to the fluid. 150 units in each litre of fluid is usually adequate. Reactions to hyaluronidase are uncommon. Hyaluronidase is not to be administered intravenously.

Occasionally, mild redness can be seen around the subcutaneous site. If there is no discomfort to the patient, the clysis can be continued. Seldom do more severe reactions occur. When they do, they are characterized by severe swelling, redness and puritus and the hyaluronidase needs to be discontinued. Hypodermoclysis is contraindicated in the presence of a generalized bleeding disorder or severe thrombocytopenia.

Hydrating with edema

A patient with edema has excessive fluid in the interstitial spaces but may have inadequate fluid in the intravascular or intracellular spaces and, therefore, may be in need of additional fluids. Edema is rarely the result of overhydration but is most often the result of tumour blockage of the venous or lymphatic systems or low serum albumin levels related to cachexia

N.B.: It is not useful to treat either of these causes with diuretics. However, hypodermoclysis is discouraged if the patient presents with severe edema.

Monitoring the treatment

Monitor clinical parameters such as urine output, blood pressure, and mental status. Volumes may need to be adjusted regularly. Ensure that the patient is not being over-hydrated.

If the patient is very close to dying, it would be appropriate to discontinue parenteral hydration.

Some patients may only require 1 litre three to four times per week, rather than daily. Our experience has been that smaller volumes (1 litre per day) are often adequate to maintain hydration in terminally ill patients requiring hydration for symptom control.

Monitor the hypodermoclysis sites for reactions or infections.

Tips

Some patients in whom hypodermoclysis is not possible (eg: severe edema) could benefit from fluid via the rectal route (proctoclysis). For details, contact a palliative care physician.

Recommended reading

1. Fainsinger R, Bruera E. The management of dehydration in terminally ill patients. *J Palliat Care*, 1994; 10(3):55-59.
2. Fainsinger R, MacEachern T, Miller M, Bruera E, Spachynski K, Kuehn N, Hanson J. The use of hypodermoclysis for rehydration in terminally ill cancer patients. *J Pain Symptom Manage* 1994; 9(5):298-302.
3. MacDonald N, Fainsinger R. Indications and ethical consideration in the hydration of patients with advanced cancer. In: Bruera E, Higginson I, eds. *Cachexia-Anorexia in Cancer Patients*. Oxford: Oxford University Press. 1996; 7:94-110.
4. Fainsinger RL, Bruera E. When to treat dehydration in a terminally ill patient? *Support Care Cancer* 1997; 5: 205-211.

CHAPTER 8: Dyspnea

Dyspnea is an uncomfortable awareness of breathing. Like pain, it is a subjective sensation, involving both the perception of breathlessness and the patient's reaction to it. It occurs in approximately 30% to 75% of patients with terminal cancer. It occurs more frequently in patients with primary lung cancer than those with pulmonary metastases. It is helpful to ask patients specifically about shortness of breath. Occasionally, although they may have tachypnea and look in distress, they may not feel dyspneic or distressed. The opposite may also occur - patients who are not tachypneic or in apparent respiratory distress may describe feeling very short of breath. Dyspnea is therefore a symptom that needs to be reported by the patient.

The pathophysiology of dyspnea in advanced cancer patients is complex, involving many different factors, central and peripheral chemoreceptors, cortical centres and pulmonary receptors.

Causes of dyspnea

There are multiple etiological factors and these factors are often coexistent. Some of the causes are listed below.

- Pre-existing chronic obstructive lung disease.
- Primary lung cancers.
- Metastatic cancers to the lung, including lymphangitis and carcinomatosis.
- Pleural effusion.
- Infection.
- Pulmonary embolism.
- Tumour-related atelectases or airway obstruction.
- Fibrosis secondary to radiation or chemotherapy
- Elevated diaphragm secondary to ascites, hepatomegaly or phrenic nerve lesion.
- Anxiety.
- Anemia.
- Cardiac causes, such as congestive heart failure, pericardiac effusions or pericarditis.
- In some patients with advanced cancer, particularly those with severe cachexia and asthenia, dyspnea may be a manifestation of profound muscle weakness.

8.1 Treatment of dyspnea

Step 1: Treat the underlying cause if appropriate, e.g.:

Pleural effusion	Drain if clinically significant.
Anemia	Transfusion of packed cells if it is felt that this could improve the dyspnea. Sometimes a therapeutic trial is required to determine this.
Airway obstruction	Radiotherapy is an option. Corticosteroids may be useful (<i>e.g.</i> , dexamethasone 6-8 mg tid to qid). The optional dose is variable.
Lymphangitis carcinomatosis	Corticosteroids may be helpful, <i>e.g.</i> , -8 mg tid to qid.
Pulmonary emboli	Anticoagulate.
Radiation fibrosis	Corticosteroids can be tried.
Pneumonia	Antibiotics.

All treatments can be altered according to the stage of the patient's disease, general condition and the prognosis.

Step 2: General symptomatic measures*Supplemental oxygen*

- If hypoxic, try to maintain O₂ sats >90%. Be cautious when administering O₂ in the setting of severe COPD.
- If O₂ sats <90% on room air:

O₂ by nasal cannula at 1-3 litre/min

- recheck in 20-30 minutes
- titrate up to 6 litre/min if necessary.

O₂ by mask (if nasal cannula not effective, rebreathing or non-rebreathing mask may be necessary.)

- flow rate will need to be adjusted accordingly
- reassess in 20-30 minutes

N.B.: The extent of breathlessness experienced by a patient may or may not directly correlate to the oxygen saturation level. Therefore, rely more on the patient's own assessment of his/her level of dyspnea rather than on the pulse oximeter reading.

N.B.: For patients with COPD, the level of CO₂ in their blood may be chronically elevated and, therefore, does not provide the stimulus to breathe as it does in healthy people. Instead, breathing is stimulated by a low O₂ level and O₂ saturation should be kept at around 90%.

Opioids

- Opioids have been shown to decrease the perception of dyspnea.
- If the patient is already on opioids for pain, breakthrough doses can be ordered for dyspnea as well.
- If on no opioids, morphine can be ordered at doses of 5-10 mg po (2.5-5 mg sc) q4hrs ATC with breakthroughs of 3-6 mg po (1.5-3 mg sc) q1h prn for dyspnea.

Other medications

- Bronchodilators, as needed with or without regular doses may be helpful if there is a significant obstructive component.
- Distraction therapy, relaxation exercises and breathing control techniques can be very helpful, especially if there is a significant anxiety component.
- Sedation is very rarely necessary. Consult a palliative care physician if you are considering it.
- Nebulized opioids do not appear to be generally effective although this remains an area of controversy. Their systemic absorption via this route is limited and erratic. It is felt that in those few patients where it may be of benefit, the benefit results from the systemic absorption of the opioid rather than its local effects on the lung.

N.B.: Maintaining high fowler's position, bed rest, good oral hygiene, and increased ventilation are all easy measures to decrease perception of dyspnea.

Diuretics

Occasionally patients present with episodes of severe pulmonary congestion and accompanying severe dyspnea. A stat dose of furosemide 20-40 mg subcutaneously can be helpful. Diuretics should not be ordered routinely for patients with dyspnea or hypoalbuminemia-

induced edema unless there is a concurrent heart condition requiring diuretics.

Alert

Intubation is not appropriate for palliative care patients.

8.2 Managing cough

Occasionally, opioids alone do not control persistent cough. Sodium cromoglycate inhalations 2 puffs qid, can be of benefit. Some authors have proposed the use of inhaled local anesthetics but the optimum dose has not been well established, the taste can be troublesome and severe allergic reactions can occur to the local anesthetic. Local anaesthetics can decrease gag-reflex, especially in those patients with diminished consciousness. Cough suppressants such as dextromethorphan 30 mg q4h po can be useful for a persistent dry cough, and expectorants can help ease dyspnea associated with a productive cough.

Recommended reading

1. Dudgeon D, Rosenthal S. Management of dyspnea and cough in patients with cancer. In: Cherny N, Foley K, eds. Hematology/Oncology Clinics of North America: Pain & Palliative Care, Vol 10 #1. Philadelphia: WB Saunders, 1996: 157-172.
2. Ahmedzai S. Palliation of respiratory symptoms. In: Doyle D, Hanks G, MacDonald N, eds. Oxford Textbook of Palliative Medicine. Oxford: Oxford Medical Publications. 1993; 4.4:349-377.
3. Hagen NA. An approach to cough in cancer patients. J of Pain and Symptom Management. 1991; 6(4):257-262.

CHAPTER 9: Hypercalcemia

Hypercalcemia is not infrequent in advanced cancer. Up to 40% of patients with breast cancer, lung cancer and multiple myeloma will present with elevated calcium levels. In the majority of cases (80%) the production of parathyroid hormone-like peptide is responsible for the hypercalcemia. A minority of cases are due to direct bone destruction.

Clinical features of hypercalcemia

- Nausea and vomiting.
- Polyuria, polydipsia.
- Dehydration.
- Confusion.
- Lethargy/weakness.
- Somnolence.
- Irritability/agitation.

Adjust the blood calcium according to the blood albumin

Corrected serum calcium = measured serum calcium + $[(40 - \text{measured blood albumin}) \times 0.02]$. *E.g.*, a patient's measured calcium level is 2.4 and the serum albumin is 20. The corrected serum calcium is therefore: $2.4 + [(40 - 20) \times 0.02] = 2.4 + 0.4 = 2.8$.

Hypercalcemia: corrected calcium > 2.65.

N.B.: Consideration should be given to treating hypercalcemia if the patient is symptomatic.

9.1 Treatment of hypercalcemia

Mild hypercalcemia (2.65-2.8)

Step 1: Rehydrate with normal saline

E.g., hyperdermoclysis or IV at 100 ml/h or IV at 100-120 ml/h. This alone is sufficient in a small number of cases.

Moderate to severe hypercalcemia

Step 1: As above

Step 2: Bisphosphonates

Pamidronate 60-90 mg diluted in 500-1000 ml of N/S and given intravenously over four to six hours; or

Clodronate 1500 mg diluted in 500-1000 ml of N/S and given intravenously over four to six hours. It has also been successfully administered over 30 minutes to 1 hour.

Clodronate can be administered safely and effectively via the subcutaneous route. Suggested doses are: Clodronate 1500 mg diluted in 500-1000 ml of N/S and given subcutaneously over four to six hours.

- Assess renal function (urea + creatinine blood levels) prior to administering a bisphosphonate. If renal impairment is present – especially if there is evidence of prerenal failure – hydrate the patient with N/S prior to administering the bisphosphonate. Bisphosphonates may aggravate renal failure.
- Order electrolytes, calcium, urea and creatinine on the third day after administering pamidronate/clodronate to document any improvement and to correlate changes in calcium levels to clinical response.
- Symptomatic hypocalcemia is very rare after treatment with a bisphosphonate.
- Ensure good venous access when pamidronate is being administered.
- Pamidronate must not be administered subcutaneously.
- When effective, calcium levels usually decrease within the first 3 days after administration of a bisphosphonate.
- There appears to be little difference between clodronate and pamidronate; they appear as effective in decreasing the calcium. However, the duration of effect of pamidronate may be more sustained in some patients (average of four weeks) as compared to clodronate (average of two weeks). Clodronate is less expensive than pamidronate.
- Occasionally, a patient with highly elevated calcium levels and severe symptoms is also found to be dehydrated and in pre-renal failure. Calcitonin is a temporary option if a rapid reduction in calcium levels is desired while the patient is being hydrated in preparation for bisphosphonate administration. Calcitonin is administered as 100 U - 200 U tid sc x 3-6 doses.
- Calcitonin results in rapid correction of serum calcium but its effect is not sustained. Therefore, one often needs to follow-up with a bisphosphonate. Repeat the calcium level the day after giving calcitonin.
- In our experience, one-time dose of bisphosphonates are adequate for the treatment of symptomatic hypercalcemia. If the hypercalcemia recurs several weeks later, another dose of the same bisphosphonate (as described above) can be given, especially if the first attempt was successful in decreasing the calcium level. Occasionally, an alternative bisphosphonate can be tried if hypercalcemia recurs.

The main desired outcome in treating hypercalcemia is improvement in symptoms.

It is therefore useful to monitor these clinical outcomes during the course of the treatment. For example, in some cases, cognitive failure may precede the development of hypercalcemia and may therefore not be expected to improve with correction of the calcium. In other instances, the two are co-existent and a therapeutic trial might be required. In case of doubt about implementing therapy, consult a palliative care physician.

Recommended reading

1. Kovacs CS, MacDonald SM, Chik CV, Bruera E. Hypercalcemia of malignancy in the palliative care patient: a treatment strategy. *J Pain Symptom Manage* 1995; 10(3):224-232.

CHAPTER 10: Anorexia and cachexia in advanced cancer

Cancer anorexia/cachexia occurs in 80%-90% of patients with advanced cancer. It results in the loss of appetite and weight and is often accompanied by asthenia (severe fatigue and lethargy). Cachexia appears to be a consequence of both decreased food intake and metabolic abnormalities. Cytokines, induced by interactions between the immune system and the tumour, are largely responsible for the syndrome. Some of the cytokines implicated are tumour-necrosis factor/cachectin, interleukin 1 and interleukin 6. Abnormalities of carbohydrate, protein and lipid metabolism and energy expenditure have been described in association with cachexia. The net result is loss of body protein and fat mass. Some patients with this symptom have demonstrated delayed gastric emptying and other manifestations of autonomic insufficiency, including chronic nausea. Factors that aggravate cachexia and anorexia are altered taste, head and neck malignancies, dysphagia and odynophagia.

10.1 Management of anorexia and cachexia

Step 1: Remove underlying cause

This is rarely possible.

Step 2: Attempt to improve the quality of life

- Relieve nausea.
- Improve appetite where severe anorexia is a major symptom and source of distress for the patient.

Pharmacological management of anorexia

Control nausea with gastrointestinal motility agents, *e.g.*:

- metoclopramide
- domperidone
- cisapride

Corticosteroids, e.g., dexamethasone: 4-10 mg bid po/sc.

Steroids may be of benefit in stimulating appetite, but prolonged use is not recommended. Although the appetite may improve, there is often no concomitant weight gain. The improvement in appetite is temporary, lasting usually less than four weeks. Other possible benefits include an improvement in the general sense of well-being and control of co-existing nausea and pain. If a trial of dexamethasone is successful, continue and taper slowly over the following few weeks. If unsuccessful in improving appetite in the first week, the steroid can be tapered more rapidly. Monitor for potential side effects and complications. The most common on the short term are: infections, poor glucose control and acute psychiatric disturbances such as mania.

Progestational agents, e.g., megestrol acetate, starting at 160 mg/day, available in capsule or in solution.

The dose may be increased up to 480 or 640 mg/day depending upon the response. The appetite stimulating effect of progestational agents lasts longer than corticosteroids. An initial trial of one to two weeks is advisable. Avoid these agents in the presence of a high risk for

thromboembolic episodes (*e.g.*, patients with DVT or pulmonary emboli). A potentially limiting factor for the use of megestrol acetate is its high cost (available in 40 mg/ml solution; capsules are large).

Thalidomide and Omega-3-fatty-acids (and some oils) have recently shown promise but are still undergoing research.

Role of enteral and parental nutrition

The consensus is that aggressive enteral or parenteral feeding is not appropriate for most patients with advanced cancer. Aggressive nutrition has not been shown to improve survival, improve response to antineoplastic therapy or decrease toxicity to antineoplastic therapies. Parenteral nutrition also has serious side effects in 15% of patients (septicemia, electrolyte imbalances) and the total cost often exceeds \$10,000/patient. Some highly selected patients may have limited benefit from parenteral nutrition, especially over the short term and during the perioperative phase. (Eg a patient with a slow growing primary abdominal tumour that has recently undergone intestinal resection; head and neck cancer with dysphagia; and malignant bowel obstruction with a slow growing primary cancer.) Even in these patients, if the cancer is very advanced, there does not appear to be a benefit to parenteral nutrition.

Enteral nutrition, although not generally used, may be helpful where patients who potentially still have many months or perhaps years to live and are unable to swallow. The overall impact on quality-of-life needs to be considered in that aggressive feeding can be unpleasant for patients.

Metabolic abnormalities are usually not reversible by nutritional support.

Step 3: Discuss management strategy with the patient and family

- Improve the patient's and family's understanding of the nature of the problem, treatment limitations and treatment aims.
- Explain that forcing patients to eat will have no positive impact on well-being or survival.
- Encourage favourite foods for comfort and enjoyment of eating. Nutritional value should be of secondary importance in terminally ill patients.
- Emphasize fluids over solids to maintain hydration.
- Alcohol with meals may also help improve appetite.
- Advise families to create the best conditions for eating, (*i.e.* nausea and pain have been addressed, good mouth care, frequent small meals, pleasant setting, etc.)
- Explanation of associated morbidity and proven lack of benefit is often helpful in dissuading most families regarding using parenteral nutrition.

Recommended reading

1. Vigano A, Watanabe S, Bruera E. Anorexia and cachexia in advanced cancer patients. In: Sidebottom E, ed. *Cancer Surveys, Vol 21. Palliative Medicine: Problem Areas in Pain and Symptom Management*, 1994: 99-115.
2. MacDonald N, Alexander R, Bruera E. Cachexia - anorexia - asthenia. *J Pain Symptom Management*, 1995; 10(2):151-155.
3. Vigano A, Bruera E. Enteral and parenteral nutrition in cancer patients. In: Bruera E, Higginson I, eds. *Cachexia - Anorexia in Cancer Patients*. Oxford: Oxford University Press, 1996, 8:110-127.

CHAPTER 11: Stomatitis and xerostomia

Many palliative patients will experience mouth problems at some time during the course of their illness. Stomatitis is characterized by an inflamed oral mucosa that can range from mild inflammation to ulceration that can bleed or become infected. There are many possible causes of stomatitis.

Xerostomia, or dry mouth, is a very common complaint in patients with advanced cancer. In most cases it can be managed adequately with oral sips of water.

Causes of stomatitis

- Infection.
- Medication (eg chemotherapy).
- Radiotherapy.
- Poor dental hygiene.
- Poorly fitting dentures.
- Blood dyscrasias.
- Trauma.

Common causes of xerostomia

- Opioids.
- Other drugs, *e.g.*, anticholinergics.
- Dehydration.
- Radiation.

11.1 Management and treatment of stomatitis

Provide regular mouth care

- Provide before and after meals (if the patient is able to eat) and at bedtime; or routinely with other care, eg q2h turns.
- Ensure dentures are properly fitted.
- Use water soluble lip balms or lubricants, rather than petroleum based products, to keep lips moist.
- Avoid mouthwashes that contain alcohol as they dry the oral mucosa. Many patients prefer to use “soda water” with carbonation or sodium chloride as a cleansing rinse.

N.B.: Although dilute hydrogen peroxide and sodium bicarbonate solutions have been recommended in some literature, we do not recommend them.

Treating symptoms

- If pain is severe, suggest analgesic rinses with xylocaine 2%.
- Treat candidiasis or thrush with nystatin, fluconazole or ketoconazole. Oral medications should be swallowed as the thrush infection may extend into the esophagus.

N.B.: Candidiasis can cause mouth pain, dysphagia, retrosternal pain, nausea and vomiting. All patients on immunosuppressive drugs such as dexamethasone should be examined regularly for thrush.

- Treat herpes simplex; consider acyclovir.
- Treat bacterial infection with antibiotics.
- Treat xerostomia by addressing the cause, when possible (*e.g.*, rehydration, antibiotics), by providing artificial saliva products if useful, and by encouraging frequent sips of water, ice chips, or popsicles.

Dietary suggestions

- Eat soft foods or soften them by adding or swallowing with gravy, sauces, or soups or by chopping, blending, grinding meat and poultry.
- Avoid tobacco, alcohol, spicy foods, extremes in food or fluid temperatures, hard foods, citrus juices.

Tips

For patients suffering from changes in taste caused by chemotherapy, medications, disease, deficiencies in protein, vitamins, or zinc, suggest:

- foods that leave their own taste (*e.g.*, fresh fruit or mints);
- tart foods (*e.g.*, citrus juices, pickles, cranberry juice);
- dairy products, eggs or fish in place of meat; and
- using spices or sauces to enhance food flavour.

11.2 Treatment of xerostomia, or dry mouth

- General measures such as regular oral hygiene, frequent swabbing with moist sponge swabs.
- Saliva substitutes such as Oral-balance Gel.
- Pilocarpine 5 mg po qid (available as tablets) may be considered though, at this stage, it is still being studied in the palliative setting. It has been shown to be useful in radiation therapy - induced xerostomia. It is contraindicated in chronic obstructive airway disease, congestive heart failure, glaucoma, acute iritis, and hypotension.

CHAPTER 12: Chronic nausea

Chronic nausea is a frequent and distressing symptom in patients with advanced cancer. The prevalence of chronic nausea in patients with advanced cancer varies from 20% to 70%. It is often multi causal, and there is increasing evidence to support that it may be a component of the cachexia syndrome of which the manifestations include: 1) anorexia, 2) chronic nausea, 3) asthenia, 4) cachexia and 5) autonomic failure.

Frequent causes of chronic nausea in cancer

- Autonomic failure (gastroparesis).
- Constipation.
- Opioid therapy.
- Bowel obstruction.
- Gastric/duodenal ulcer.
- Other drugs (*e.g.*, SSRIs, NSAIDs).
- Radiation therapy.
- Metabolic abnormalities (*e.g.*, hepatic and renal failure, electrolyte imbalance, hypercalcemia).
- Increased intracranial pressure.
- Delayed chemotherapy induced emesis
- Dehydration.

12.1 Assessment and management of chronic nausea

Step 1: Measure the intensity

Use scales such as the Visual Analogue Scale (VAS) and obtain a history of aggravating and alleviating factors, onset and duration, frequency and description of emesis. Assess the regularity of bowel movements.

Step 2: Review drugs

Drugs such as opioids, SSRIs and some antibiotics cause nausea. Those that are non-essential can be discontinued while others that are essential (such as opioids or SSRIs) may need to be replaced by alternative drugs.

Step 3: Thorough examination

Exclude bowel obstruction, neurological signs suggesting CNS involvement, constipation.

Step 4: Investigations

Further investigations may be helpful, *e.g.*, abdominal x-rays (supine, erect and/or oblique views) where bowel obstruction is suspected or a flat plate AXR if stool impaction is suspected. Renal function and electrolytes may be helpful. Also requisition an augmented CT scan if there are neurological deficits to suggest brain metastases.

Step 5: Attempt to correct suspected underlying causes, *e.g.*:

- Constipation: increased bowel care and prokinetic agents such as metoclopramide ±cisapride if laxatives are ineffective.
- Opioids: rotate opioids if accumulation of opioid metabolites is suspected.
- Raised intracranial pressure: corticosteroids and/or RXT.
- Electrolyte imbalances: correct these.
- Dehydration: hydrate.

Occasionally the underlying causes cannot be specifically identified or addressed.

Step 6: General measures, e.g.:

- Maintain good oral hygiene.
- Eat/drink smaller volume meals at more regular intervals.
- Avoid food odours, *i.e.*, eat cold food.
- Avoid food that is greasy, spicy, or sweet.
- Relax in an upright position after eating.
- Eat in a pleasant environment.

Step 7: Pharmacological measures

Metoclopramide is the drug of first choice. The reasons are:

- It improves gastrointestinal motility.
- It has an antidopaminergic effect on receptors in the gastrointestinal tract and the chemoreceptor trigger zone. Opioids exert their emetic effect mainly via these two mechanisms.

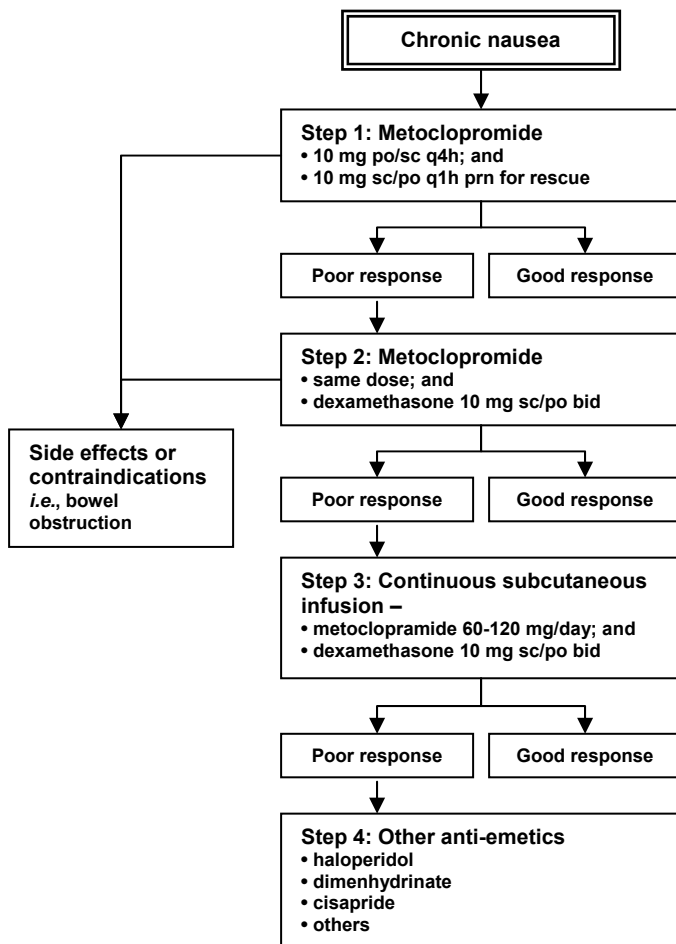
Monitor for possible adverse effects such as extra-pyramidal side effects. These are infrequent but, if they do occur, one may need to switch to an alternative antiemetic. If the nausea persists, consider adding an adjuvant anti-emetic such as a corticosteroid (*e.g.*, dexamethasone 4-6 mg tid po/sc). See Figure 5 on the following page.

Contraindications to metoclopramide include complete bowel obstruction. In the presence of complete bowel obstruction, use haloperidol 1 mg q1hr prn po/sc with or without buscopan 60-90 mg sc in 24 hours in divided doses or continuous infusion.

- Review after a few days – if the nausea settles, consider discontinuing the regular dose and continuing only with rescue orders.
- If metoclopramide results in significant adverse effects, consider motilium. Motilium does not cross the blood-brain barrier and therefore has little risk for extra-pyramidal side-effects. Its effects are primarily on the stomach.
- If there is significant impaired gastrointestinal motility, consider adding cisapride. Cisapride (10 mg po tid to qid) affects both the upper and the lower gastrointestinal tract unlike metoclopramide, which works primarily proximally. Beware of using cisapride concurrently with some antifungals and some antibiotics.

Tips

- The primary mechanism by which opioids cause nausea is via dopaminergic receptors in the chemoreceptor trigger zone of the brain and the gastrointestinal tract. Therefore, the preferred antidote for this is an antidopaminergic agent such as metoclopramide or haloperidol.
- Antihistamines do not have an antidopaminergic effect and are not the agents of choice in treating opioid induced nausea. Furthermore, they can be sedating. Phenothiazines, such as prochlorperazine and chlorpromazine are also sedating and often can result in other adverse effects (*e.g.* anticholinergic side-effects).
- Always exclude constipation in a terminally ill patient presenting with chronic nausea and/or vomiting.
- If dexamethasone is used, taper it to the minimal effective dose as soon as a response is observed.

Figure 5: Algorithm for the management of chronic nausea

12.2 Management of hiccups

Step 1: Remove the underlying cause

Exclude constipation or bowel obstruction as the possible cause. If poor gastrointestinal motility is suspected, then prokinetic agents such as metoclopramide (po or sc) ± cisapride (po) should be trialed and optimized.

Medications such as corticosteroids may also be contributing factors. Consider stopping or decreasing these.

Hiccupping may also be attributed to diaphragm irritation caused by a tumour.

Step 2: Suggested treatments

If hiccupping becomes severe and the underlying cause is not reversible, consider using chlorpromazine, baclofen or nifedipine.

Recommended reading

1. Pereira J, Bruera E. Chronic nausea. In: Bruera E, Higginson I, eds. *Cachexia - Anorexia in Cancer Patients*. Oxford: Oxford University Press. 1996; 2:23-37.
2. Lichter I. Nausea and vomiting in patients with cancer. In: Cherny N, Foley K, eds. *Haematology/Oncology Clinics in North America: Pain and Palliative Care, Vol 10 #1*. Philadelphia: W.B. Saunders, 1996:207-220.

CHAPTER 13: Palliative sedation

The goal of palliative care is to provide pain and symptom relief within the overall context of a person's well being. Most patients obtain relief of pain and other symptoms using the techniques described in earlier chapters of this book. Occasional patients will have pain or other symptoms that appear to be refractory and in this circumstance, sedation can be used so that the individual is no longer experiencing distress. Palliative sedation has been defined as "the intention to induce sleep in a patient with one or more refractory symptoms who is perceived to be close to death". It must be stressed that this powerful palliative intervention should only be used for refractory problems. All appropriate measures to optimally manage the refractory symptom should be implemented and reviewed prior to considering sedation. The most common reason for sedation is severe agitated delirium that does not respond to reasonable attempts at addressing the underlying causes and does not respond to measures mentioned in Chapter 5 of this book. Other less common reasons are dyspnea and pain. The role of palliative sedation for profound spiritual or existential anguish that is not amenable to spiritual, psychological or other interventions is not clear and requires further ethical considerations. It is important to try and differentiate between "difficult" and "refractory" symptoms. Difficult symptoms are clinical situations which could potentially respond within a tolerable time frame to interventions and yet yield adequate relief and preserve consciousness without excessive adverse results. Palliative sedation can be used so that the individual is no longer experiencing distress.

13.1 When should you suspect that palliative sedation may be needed?

If symptoms seem uncontrollable despite repeated efforts and various techniques, palliative sedation may be warranted. In general, a palliative care consultant should review the case before palliative sedation is used.

Patient assessment

Prior to being considered candidates for palliative sedation, patients should be evaluated with a history, physical exam and appropriate diagnostic interventions, such as blood tests or imaging techniques. The patient's family should also be interviewed. Patients and their families should be informed that palliative sedation is not intended to shorten a person's life span and generally does not have this effect. There must be informed consent prior to initiating palliative sedation.

13.2 How to institute palliative sedation

Midazolam is the drug of choice. This benzodiazepine has a relatively short half life and therefore, for the purposes of palliative sedation, generally needs to be administered by continuous infusion. The short half life also allows for rapid dose titration. A subcutaneous or intravenous line can be used. A starting dose of midazolam 1mg/hr by continuous infusion is suggested. This dose may need to be titrated rapidly to effect. In most cases, doses of between 1mg/hr - 7 mg/hr are required. Some suggest using a higher dose of sedative initially in order to obtain sedation as soon as possible. Once deep sedation is induced, the dose should be lowered until the lowest effective dose to maintain sedation has been found. Reassessments of patients are required on a regular basis. In some cases, sedation may be a temporary measure while causes for problems such as delirium are managed.

On rare occasions, these doses may not appear to be adequate. In this event, a reassessment is suggested,

with emphasis on reviewing the causes for the intractable symptom(s). If palliative sedation is indeed indicated, then other sedatives may be used, such as phenobarbital (administered rectally or parenterally). The patient's other medications, such as opioids, should generally be maintained during deep sedation but it may be possible to reduce their dosage. If the respiratory rate becomes low, such as six or less per minute, the opioids should be held and the dose of midazolam can be reduced. Patients should be evaluated to assure adequate ventilation is occurring.

Recommended reading

1. Chater S, Viola R, Paterson J, Jarvis V. Sedation for intractable distress in the dying, a survey of the experts. *Palliative Medicine*, 1998; 12:255-269.
2. Cherny N, Portenoy RK. Sedation in the management of refractory symptoms: guidelines for evaluation and treatment. *J Palliative Care*, 1994; 10:2:31-39.
3. Fainsinger RL, Landman W, Hoskings M, Buera E. Sedation for uncontrolled symptoms in a South African Hospice. *J of Pain & Symptom Manage* 1998; 16(3): 145-152.
4. Fainsinger RL. Case report: Use of sedation by a hospital palliative care support team. *Journal of Palliative Care* 1998; 14(1):51-54.

CHAPTER 14: Emergencies in palliative care

The following are some of the conditions/situations in which a rapid response is required.

- Uncontrolled pain (see “Chapter 2: Management of cancer pain,” page 10).
 - Delirium (see “Chapter 5: Confusion,” page 40).
 - Bowel obstruction (see “Chapter 6: Constipation,” page 44).
 - Spinal cord compression (see below).
 - Seizures (see below).
 - Massive hemorrhage (see below).
-

14.1 Spinal cord compression (SCC)

Spinal cord compression occurs in approximately 5% of patients with cancer. Early diagnosis and treatment is imperative, as the most important determinant of neurological outcome is the degree of neurological impairment at the time of starting therapy. Delay in treatment may leave the patient paralyzed and without bowel and bladder control. About 80% of ambulatory patients will remain so if treatment is prompt, but less than 30% of non-ambulatory patients will be able to walk after treatment again if treatment is not prompt. The majority of SCC occur in the thoracic spine and the majority are caused by extramural tumour.

When to suspect SCC

Pain is the initial symptom in approximately 90% of patients with SCC and this can precede the development of neurological deficit by many days to weeks. Central back pain, aggravated by movement, coughing or straining is a prominent symptom. Occasionally, the pain can worsen when the patient is supine. Nerve root irritation at the site of the vertebral involvement may be the presenting symptom, producing unilateral or bilateral radicular pain. Neurological signs can be overt or discrete, and can consist of progressive weakness and sensory loss, as well as urinary retention and loss of bowel control. Examination may reveal signs of motor weakness, reduced muscle tone, sensory loss or reduced reflexes. Reduced rectal tone can also be present.

Assessment

MRI scanning, when available, is probably the investigation of choice for spinal cord disease.

Myelography has been for a long time the standard investigation used to confirm the diagnosis and plan the treatment but is contraindicated where raised intracranial pressure is present or suspected. CT scanning may provide much of the required information. Plain x-rays as the sole investigation are not recommended since the uncommon situation of extradural metastases not secondary to vertebral involvement may have normal x-rays.

Management of a suspected SCC

- Refer the patient as soon as possible to a centre that will be able to confirm the diagnosis and initiate therapy (radiotherapy, occasionally surgery).
- Initiate dexamethasone as soon as the diagnosis is made or strongly suspected. Various doses are recommended. A conventional starting dose is 8-10 mg three to four times a day.

14.2 Seizures

Seizures occur most frequently in patients with cerebral tumours or meningeal involvement. Less frequent causes are metabolic disturbances, infection, drug toxicity, drug withdrawal or intracerebral hemorrhages.

Management of an active seizure

- Diazepam 10 mg per rectum (using the parenteral solution) or, if there is IV access, diazepam 10 mg IV. An alternative is lorazepam 2 mg sc or midazolam 5 mg sc or IV.

Prophylactic anticonvulsant therapy is generally considered unnecessary for patients with cerebral metastases as only about 20% will experience seizures. The most commonly used anticonvulsants are phenytoin and carbamazepine.

Phenytoin a loading dose of 15-20 mg/kg in divided doses over the first 24 hours is required, followed by 300-400 mg per day. This can be given intravenously or orally. If intravenously, it should not be given more rapidly than 50 mg/min. Toxicity includes sedation, cognitive impairment, ataxia, nystagmus and dysarthria. Tricyclic antidepressants and coumadin can increase serum phenytoin levels, while salicylates or dexamethasone can lower the serum levels.

If carbamazepine or phenytoin are contraindicated, valproic acid can be considered.

Options for patients who are unable to swallow medication, and who experience significant troubles from seizure are:

- Phenobarbital 30-120 mg sc tid (this is sedating); or
- Midazolam 1-4 mg/hr by continuous infusion (very sedating) or
- Phenytoin IV.

14.3 Massive hemorrhage

Occasionally, tumours may infiltrate large vessels and vascular structures, resulting in catastrophic exsanguination. Head and neck cancers are more prone to this. Other causes of hemorrhage can include thrombocytopenia, liver failure, and disseminated intravascular coagulation.

Management

- Anticipate and sensitively warn the family and caregivers.
- Instruct caregivers on measures to take if it occurs.
 - Keep dark towels at hand and apply pressure to the site if the hemorrhage is external.
 - If there is hemoptysis or hematemesis, place the patient on his/her side.
- Maintain administration of regular analgesics.
- It may be prudent to have midazolam at hand for sedation of the patient, *e.g.*, midazolam 2.5 mg - 5 mg sc/IM prn (stat dose). Midazolam can be kept at the bedside in a pre-filled syringe for up to 30 days away from light.
- It is important that a Do Not Resuscitate (DNR) order has been obtained. Copies of the DNR should be kept in the doctor's office, home, and the local ambulance authority.

CHAPTER 15: Supportive care for palliative patients and families

The goal of palliative care is to reduce suffering and optimize quality of life for patients with terminal illnesses and their families. Often the most difficult challenge in palliative care is not controlling physical symptoms, but addressing emotional and spiritual concerns of the patient, family, and other caregivers.

15.1 Patient coping

Patients at high-risk for difficulty adjusting to a palliative diagnosis

- Lack support from at least one loved person.
- Have previous unresolved loss or separation experiences.
- Have a history of early parental death or multiple losses.
- Use, or have used, alcohol or drugs in excess.
- Have not successfully handled stressful experiences in the past.
- Have a history of mental illness (*e.g.*, depression).
- Express severe emotional reactions.
- Express feelings of apathy, hopelessness, despair, self pity, defeat, or helplessness.
- Lack of optimism, self-confidence, and assertiveness.
- Have poor communication or conflict in relationships with family or physician.

Examples of patient coping mechanisms

- Denial
- Keeping busy
- Depression
- Anger, guilt
- Humor
- Crying
- Prayer
- Rationalization

Some mechanisms may help patients adapt to their deteriorating situations. Others, such as coping chemically (using opioids to calm suffering), extreme denial resulting in patients refusing effective treatments, or hostility against family or a caregiver, may be maladaptive and may actually worsen suffering. These coping mechanisms can often be modified with careful and expert counseling.

Suggested strategies to help palliative patients cope

- Support and respect the patient's own coping mechanisms.
 - Find out what has helped coping in the past, what is working now, and what they perceive would help them cope more effectively.
- Help patients express and understand emotions.
- Help maintain or strengthen relationships with significant others.
- Facilitate empowerment.
 - Provide information and involve patients.
 - Support each patient's own strategies for empowerment and allow them choice and control as much as possible.
 - Encourage the patient to adopt a tutoring role when previous roles and responsibilities cannot be maintained.
 - Enhance control over events following death by helping patients arrange affairs, make funeral arrangements, write a will or advanced directive, find ways to keep their memory alive (*e.g.*, video).

- Maintain normalcy
 - Help to maintain the highest level of physical and cognitive function.
 - Help patients stay at home as long as possible.
 - Encourage patients to wear their own clothes and to follow their own routines.

Spiritual needs of palliative patients include:

- having meaning in life;
- sustaining hope;
- maintaining loving relationships with self, others, or a spiritual figurehead;
- giving or receiving forgiveness or acceptance; and
- transcending suffering and connecting with a reality more enduring than the individual self.

N.B.: The essence of spiritual care is “being present” for people as they confront suffering and struggle with spiritual questions. The foundation of spiritual care is the establishment of a trusting, empathetic relationship.

Strategies

To provide spiritual support include watching and listening closely for cues that a patient is comfortable entering into a dialogue about spiritual beliefs and issues and then facilitating the time, space and privacy for spiritual practices and rituals.

15.2 Family coping

Hope

It is important to recognize that each person’s view of reality is different and it is each person’s right to choose what to hope for in accordance with this personal view. It is the responsibility of health practitioners to provide patients and family with information, to the extent that they request it, but it is the patient’s and family’s responsibility and right to also access information from other sources and to determine how they will translate this information into hope.

N.B.: It is not the responsibility of health practitioners to ensure that hope is realistic. People can accept and prepare for death while also holding on to hope. By shattering unrealistic hope, we run the risk of stripping individuals of important ways of coping before they are ready to do so. Health practitioners should listen to patients and families, understand their grounds for hope and reasons for holding onto hope, and assist them in identifying new hopes when they are ready.

Potential indicators of poor family adjustment to a palliative diagnosis

- Inability to function as a cohesive unit.
- Other major stressors require family energy.
- Lack of constancy in a patient’s role performance.
- Lack of positive outside support or willingness to use it.
- Lack of successful past experience in handling stress.
- Inability to perceive a difficult experience as potentially meaningful and growth-producing.
- Closed communication, reluctance to openly express emotions.
- Little or no family participation in care of the dying patient.

Helping families of palliative patients to cope

- Facilitate the expression and understanding of emotion.
- Help maintain and strengthen relationships and communication between family members and the dying patient.
- Help family members differentiate their needs from those of the patient and provide assistance in meeting those needs.
- Help with role reallocation and family reorganization.
- Facilitate understanding of medical information and access to needed resources.
- Be present with family members physically, psychologically, and spiritually.

NB: Family members may each cope differently.

15.3 Cultural considerations

The goal in providing “culture-sensitive” care is to be sensitive and aware of the beliefs, values, traditions and practices of others and to honor them when providing care, even if they are quite different from your own.

Association with a particular cultural, ethnic or religious group may influence:

- expression and meaning of pain and suffering;
- attitude towards disclosure and awareness;
- beliefs about the cause and meaning of illness;
- choice of healer and treatment regimen;
- attitude toward death and dying;
- beliefs about the afterlife, the value of human life, and the body;
- expressions of loss and grief; and
- death rituals including preparation for burial, funeral practices or memorial services, customs for disposing of the body and mourning rites.

The desire to tell or know the truth about illness or death is clearly a **Western cultural value**. Remember that people have the same right “not to know” as they have “to know.”

15.4 Discussing “do not resuscitate” (DNR) orders

The decision regarding resuscitation should be based on:

- the extent of the illness;
- the quality of life;
- potential causes of cardiac or respiratory arrest;
- patient and family preference; and
- setting, as in the case of most palliative care units where patients are required to discuss and accept a DNR prior to admission.

Service providers are encouraged to ask all patients if they have an Advanced Directive or a Living Will. A personal directive is a legal document which gives instructions or names an agent and their authority to make decisions in the event that a person becomes unable to make their own care decisions. Each work setting or organization should have policies and procedures to help service providers implement personal directives. For more information contact the Alberta Government’s Office of the Public Guardian: toll-free dial 310-0000 and ask for (780) 427-7945.

Broaching the topic of DNR with patients and families

- First explore with them their knowledge of the illness and the prognosis. Gently correct any misconceptions, being cautious when denial, unrealistic hope, or a preference for non-disclosure are present.
- Explain that if the disease progresses to the point where breathing or the heart stops beating, efforts at resuscitation (i.e. pressing on the chest, administering drugs, inserting a tube down the throat) will almost always fail.
- If the heart does resume beating, the person will often remain unresponsive, attached to machines in an intensive care unit, and will usually die very shortly afterwards.
- Hence, resuscitation efforts in these circumstances usually results in needless suffering for patients and families and are not recommended.
- Emphasize that the goal of palliative care is to provide comfort, alleviate suffering, enhance quality of life, and promote a peaceful death.
- Explain that, even with a DNR order, any reversible complication that is causing distress will be appropriately treated and symptoms will be managed throughout the course of the illness.

N.B.: Reassure the patient that a DNR order does not mean that all treatment ceases.

15.5 Helping patients and families to prepare for the end-of-life

Teach the family indicators of imminent death.

- Progressive dependence, withdrawal, and detachment.
- Reports of nearing death mystical experiences (*e.g.*, being in the presence of loved ones who have already died, predicting the time of death, *etc.*).
- Physiologic changes.
- Reduced urine output, dark colored urine.
- Changes in patterns and sounds of breathing (periods of apnea or Cheyne-Stokes, possible sound of congestion).
- Progressive coldness, discoloration and mottling.
- Weakening pulse.
- Anxiety, restlessness, confusion, possible hallucinations.
- Fluctuating level of consciousness with gradual decline, accompanied by decreased awareness, dysphagia, and flaccid musculature.

NB: Inform the family that the changes they will observe are usually more distressing for them than for the patient.

Suggestions for families

- Instruct family caregivers in symptom management and comfort measures.
 - turning, changing, washing, massaging, positioning;
 - providing sips of fluid if the patient is able to swallow; and
 - administering analgesics and other medications.
- Ensure family members have access to appropriate professional and support services, needed equipment and supplies.
- Encourage family members to talk to the patient even if the patient appears not to hear or respond; urge the family to tell the patient what he/she meant to them and how he/she will be remembered, give the permission to die, and say their good-byes.
- Encourage gathering of family and friends, touching and grieving.
- Use role modeling to say the words that need to be said and to communicate non-verbally (*e.g.*, “It’s okay to die”, “you will always be loved”).

15.6 Bereavement

Useful times for bereavement follow-up

- Two weeks to one month, for initial contact.
- Three months, often the first crises (extended family leaves and people begin to believe that grievors should be “over it”).
- Six months.
- 11 months to one year, the anniversary of the death.
- Holidays, birthdays, and wedding anniversaries.

Bereavement follow-up can be done by nurses, physicians, volunteers, social workers, psychologists, pastoral care workers, or bereavement coordinators.

Possible strategies for bereavement follow-up

- Attending the funeral or memorial service or holding a memorial service for families at your place of work.
- Making phone calls at the ‘critical times.’
- Providing a card with contact information and resources.
- Making home visits.
- Making referrals for individual or group counseling.
- Providing written/video information.

15.7 Communicating with families at the time of death

- Allow for silence, it is your presence that counts.
- Don’t be afraid to say “I don’t know what to say”.
- Encourage families to express their feelings or to talk about the deceased to whatever extent they desire. As appropriate, share your memories of the deceased.
- It is not helpful to say that you know how they feel.
- Ask the family if they would like time alone with the deceased or if they would like you to stay with them.
- Ask the family if there is anything that they feel needs to be done, offer support as appropriate and follow-through.
- Ascertain special requests regarding treatment of the body after death and honor them if possible.

Be especially aware of the possible need for involvement with bereaved families:

- who have limited support from relatives, friends or community
- who have experienced the death of a child or young adult, a sudden death or a death that leaves a spouse living alone

15.8 The roles that volunteers can play

Volunteers are an important part of the multidisciplinary team approach to the provision of palliative care. Volunteers are able to provide that extra special human touch, which is so important in the physical and emotional support which patients and families need at this time in their lives.

The primary role of the volunteer is to visit with patients for the purpose of providing companionship and support, through listening and sharing, to both the patient and his/her family members. The kind of tasks that volunteers do may vary from one care setting, institution or program to another. Screening and training should be available for Palliative Care Volunteers prior to working directly with patients and families.

Examples of palliative care volunteer tasks

- Sit quietly with patient.
- Filling water jugs.
- Arranging flowers.
- Listening and talking.
- Reading.
- Playing cards.
- Combing hair.
- Backrubs.
- Accompanying individuals on walks.
- Assisting with shopping.
- Assisting with form filling or letter writing.
- Assisting with recreation and occupational therapy.
- Providing support to family members.
- Assisting with the creation of a memory box.
- Communication of patient needs to staff.
- Answering call bells.
- Tidying, restocking the unit.
- Assisting with clerical duties.

APPENDIX A: Validated assessment tools

The regular and frequent measurement of symptoms can improve patient outcomes by increasing staff awareness and by being used as a means to assess patient care. Simple Visual Analogue (VAS), numerical rating, and verbal descriptor scales have proven to be a very effective and reproducible way to measure pain and other symptoms. Despite some shortcomings (*e.g.* some have a uni-dimensional approach), these scales can be universally implemented and regularly applied in all care settings. Their regular application and charting of symptom intensity enables caregivers to assess the impact of therapeutic interventions and also enables the patient to report any changes in the symptom pattern and intensity.

Table 5: A list of validated assessment tools

Tool and authors	Domains covered
<i>McGill Quality of Life Questionnaire</i> Cohen, Mount, Strobel, Bui	Measures existential domain, physical domain and positive contributions to quality of life.
<i>Edmonton Symptom Assessment Scale</i> Bruera, Kuehn, Miller et al	Nine visual analogue scales covering pain, activity, nausea, depression, anxiety, drowsiness, appetite, well-being, shortness of breath.
<i>Palliative Care Core Audit</i> Higginson & Hearn	Ten items measuring pain, general symptoms, patient & family anxiety, information-giving, support from the family, well-being worthlessness, practical issues, with additional space to record main problems.
<i>Support Team Assessment Schedule</i> Higginson, Higginson, McCarthy	17 items including physical symptoms, psychosocial insight, family needs, planning, communication, home services, multi-disc. support.
<i>Symptom Distress Scale</i> McCorckle & Quint-Benoliel	13 items likert scale that indexes the subjective distress experienced by patients caused by either the disease or illness. Covers: nausea, appetite, insomnia, pain, fatigue, bowels, concentration, appearance, breathing, outlook, cough.
<i>European Organization for Research & Treatment of Cancer QLQ-C30</i> Asronson, Ahmedzai, Bergman	30 items made up of 9 multi-item scales: five functional (physical, role, cognitive, emotional, social), 3 symptom scales (fatigue, pain, nausea and vomiting), global health, quality of life, also several single-item measures.
<i>Quality of Well-Being Scale</i> Kaplan	This scale assesses mobility, physical activity, social activity, and 27 symptoms. This scale is unique in that it can summarize a patient's quality of life as a single number.
<i>Memorial System Assessment Scale</i> Portenoy	A verbal rating scale which measures 32 psychological and physical symptoms in terms of the presence, frequency, severity and degree of distress.
<i>Palliative Performance Scale</i> Anderson, Downing, Casorso, Lerch	This updated and modified Karnofsky Performance Scale guides assessment of functional performance. It is divided into 11 categories, measured in 10% decremental levels, differentiated by 5 observable parameters: degree of ambulation, ability to do activities, ability to do self-care, intake, level of consciousness.
<i>Cage Questionnaire</i> J.Ewing	Four well-validated questions that can be used to screen patients for alcoholism and for the risk of coping chemically when stressed. A total of 2 or more positive answers indicates a positive history of alcoholism.
<i>Mini-Mental State Questionnaire</i> Folstein, Folstein & McHugh	This tool is employed extensively for screening cognitive impairment in different populations, including palliative. Measures: orientation to time and place, immediate recall, short memory, calculation, language and constructability. Scores of <23/30 generally indicates impairment.
<i>Calgary Interagency Pain Assessment Tool (CIPAT)</i> Collaborative Project of Active Care, Home Care, TBCC and long-term care centres in Calgary	Comprehensive Pain Assessment tool which can be filled in by patient or health care provider. Involves labeling pain (s) on a diagram, visual analogue scale, and detailed pain history and health care provider's assessment.

The goals of assessment, and the practicality and acceptability of the instrument by palliative patients, must be considered in the selection of assessment tools. Ideally, the tools or questionnaires should be simple and brief in order to encourage compliance by patients and caregivers, and to minimize the burden

on the patient. On the other hand, simplicity and brevity may limit the ability to capture multidimensional impressions of symptoms and quality of life.

Measurement of symptoms and assessment of symptoms are performed for two different reasons. The purpose of measuring symptoms is to quantify the experience, whereas assessment of symptoms critically analyzes information from many dimensions, including physical, psychological, spiritual and social. Once comprehensive assessments, which may include measurement, are done, a plan can be developed and implemented to deal with the symptoms.

Given the complexity of interaction between various physical and psychosocial domains, assessment of palliative patients requires a multi-dimensional approach. Although entire scales exist to measure single symptom domains (*e.g.*, pain), this appendix mostly suggests, as a place to start, several validated tools that each measure several symptom domains. The Mini-Mental State Questionnaire, Cage Questionnaire, and Palliative Performance Scale are added because they are highly validated, brief and simple scales that measure domains often missed by some of the multi-dimensional tools.

An ACCESS database is also available that has been designed to collect demographic, patient and other information, including data from the Edmonton Symptom Assessment Scale, Mini-Mental State Questionnaire and the Cage Questionnaire.

APPENDIX B: Table of equianalgesic doses of opioids

Table 6: Equianalgesic dose

Drug	PO Dose	PO:SC/IV Ratio	SC/IV Dose
Morphine	10 mg	2:1	5 mg
Codeine	100 mg	2:1	50 mg
Oxycodone*	5-7.5 mg	--	--
Hydromorphone	2 mg	2:1	1 mg
Methadone**	±1 mg	--	too irritating
Fentanyl*** - infusion	--	--	50µ
Fentanyl patch	use chart supplied by manufacturer		
morphine 10 mg po = codeine 100 mg po = ±oxycodone 5-7.5 mg po = hydromorphone 2 mg po = methadone 1 mg po			

N.B.: These tables are guidelines. There exists wide ranges in the dose ratio due to inter-individual variability in response to opioids. When switching opioids the doses should be decreased by a 25-30% and the patient should be monitored during the switch-over until they are stable.

** Most tables quote the equianalgesic dose of methadone to morphine as being methadone 1mg po = morphine 1-4 mg po. This ratio was determined using one dose studies. In cancer pain, when the analgesic needs to be administered in regular multiple doses, the ratio of methadone to morphine changes and is closer to methadone 1 mg po = morphine 10 mg po, ie. methadone is approximately 10 times more potent than morphine.

*** The equianalgesic dose of fentanyl to morphine has not been accurately determined. It appears to be 10 micrograms for every 1mg of parenteral morphine. The equianalgesic ratio between parenteral fentanyl and transdermal fentanyl (patch) is also not well described, but appears to be 1:1.

N.B.: Methadone should be started and titrated under the guidance of a palliative care physician or pain specialist. Parenteral fentanyl should also be used under similar guidance.

An interesting characteristic of the equianalgesic dose ratio of morphine and other opioids to methadone is that the ratio changes according to the dose of the previous opioid.

APPENDIX C: Opioid formulations available

Trade names are found in the Canadian Compendium of Pharmaceuticals and Specialties (CPS).

IR = immediate release

CR = controlled release

Codeine

oral, IR	suspension - 5 mg/ml tablets - 15, 30 mg
oral, CR	100, 150, 200 mg
parenteral	30 mg/ml, 60 mg/ml

Oxycodone

oral, IR	oxycodone alone – 5, 10 mg with acetaminophen – 2.5 mg+325 mg acet. 5 mg + 325 mg acet. with ASA – 2.5 + 325 mg ASA 5 mg + 325 mg ASA
rectal, CR	10, 20 mg
oral, CR	10, 20, 40, 80 mg

Morphine

oral, IR	syrup - 1, 5, 10, 20 mg/ml drops - 20 mg/ml, 50 mg/ml tablets - 5, 10, 20, 25, 30, 50 mg
rectal IR	5, 10, 20, 30 mg suppositories
oral, CR	10, 15, 30, 60, 100, 200 mg
oral, once daily CR	20, 50, 100 mg capsules
rectal, CR:	30, 60, 100, 200 mg suppositories
parenteral	0.5 mg/ml, 1 mg/ml, 2 mg/ml, 10 mg/ml 15 mg/ml, 25 mg/ml, 50 mg/ml

Hydromorphone

oral, IR	syrup - 1 mg/ml tablets - 1, 2, 4, 8 mg
rectal, IR	3 mg suppositories
oral, CR	3, 6, 12, 24 mg
parenteral	2 mg/ml, 10 mg/ml, 20 mg/ml, 50 mg/ml

Fentanyl

transdermal, CR	25, 50, 75, 100 micrograms/hour
parenteral	50 micrograms/ml (2, 5, 10, 20 ml vials)

Methadone

oral:	Custom made capsules - in multiples of 5-10 mg. A suspension is available. This is helpful if smaller doses are required. However, it does have a bad taste.
rectal	10 to 600 mg custom made suppositories

APPENDIX D: Examples of drug prescriptions

Various centres may order drugs differently, depending on the formulations, administration devices available and the routes used.

Medical orders for opioids

Example

Date	Time
(drug) _____ mg	every (q) _____ hours ATC (route) and
(drug) _____ mg	every (q) _____ hours prn for breakthrough pain.

ATC = around the clock

Medical orders for subcutaneous opioid injections via the Edmonton Injector (EI)

NOTE: Some problems may be encountered in procuring the 3 ml syringes that are used in the Edmonton Injector.

- Two sizes of bags are used, 20 ml and 50 ml. 20 ml bags are ordered if the patient will be on the EI for only a few days and a 50 ml bag if a longer period is anticipated.
- Concentration of the opioid in each bag is calculated so as to give the patient subcutaneous injections of volumes less than 2 ml at a time.

Example

The following example illustrates the orders for a patient who requires morphine 10 mg sc q4h ATC and 6 mg sc q1h prn. In this case, it is decided to use a 50 ml bag.

Morphine 500 mg in D5W to a total volume of 50 ml (concentration = 10 mg/ml). Give morphine 10 mg (1 ml) sc q4h ATC and morphine 6 mg (0.6 ml) sc q1h prn for breakthrough pain.

Medical orders for hypodermoclysis

Example 1 Continuous Hypodermoclysis.

- Normal saline or 2/3-1/3 at 80 ml/hour by clysis. (Only add 150 U of hyaluronidase to each litre if the site leaks consistently.)

Example 2 Continuous hypodermoclysis at home (If no infusion pump is available.)

- Normal saline by hypodermoclysis. Run by gravity. 1l/24 hours. (Add 150 U hyaluronidase to each litre only if the site leaks consistently.)

Example 3 Twice daily hypodermoclysis boluses. (In the following example, it is decided to administer normal saline in boluses twice a day.)

- Normal saline by hypodermoclysis. Give 500 ml over one hour twice a day. (Precede the first dose with 150 U of hyaluronidase subcutaneously into the same site as the fluid will be administered if the site leaks consistently.)

Example 4 Overnight hypodermoclysis. (In the following example, it is decided to administer fluid in the form of normal saline overnight only, so as not to inconvenience the patient by day.)

- Normal saline by hypodermoclysis. Give 1litre overnight starting at 20h00 hours. (Add 150 U hyaluronidase to each litre if there is consistent leaking at the site.) If the rate can be controlled accurately, 80 ml/hour will give 1 litre overnight.

Medical orders for a continuous subcutaneous infusion of fentanyl

This should preferably be initiated under the guidance of a palliative care physician and an infusion pump is mandatory.

Example In this example, the patient is required to receive 5 micrograms (mcg)/hour of fentanyl by continuous subcutaneous infusion with 10 micrograms q1hrly prn for breakthrough pain.

- Prepare a fentanyl 5 mcg/ml solution diluted in D5W or NS. (For convenience, a total volume of 100 ml of NS with fentanyl can be used.)
- Add 500 mcg of fentanyl to N/S to make up a total volume of 100 ml (Concentration = 5 mcg/ml).
- Run fentanyl at 1 ml/hr (ie. 5 mcg/hour) via an infusion pump and fentanyl 10 mcg (2 ml) q1h prn for breakthrough pain.

N.B.: Avoid mixing the fentanyl in hypodermoclysis fluid.

Check the stability of fentanyl in solution with your pharmacy. Usually it is less than 48 hours once mixed.

Medical orders for a midazolam continuous subcutaneous infusion

Example In the following example, the patient is to receive midazolam at 1 to 4 mg/hour. Prepare a total of 100 ml of NS with 100 mg midazolam (concentration = 1 mg/ml) and run at 1 mg-4 mg/hour (ie. 1 ml to 4 ml) by continuous subcutaneous infusion.

N.B.: Midazolam is incompatible with hyaluronidase.

Medical orders for a metoclopramide continuous subcutaneous infusion

Example In this example, a patient needs to receive 90 mg over 24 hours by continuous subcutaneous infusion.

- Add metoclopramide 90 mg to D5W or NS to make up a total volume of 50 ml.

Solutions are only stable for 48 hours if protected from light or 24 hours if unprotected. The metoclopramide infusion can be piggybacked to a hypodermoclysis.

APPENDIX E: W.H.O. analgesic ladder

Table 7: W.H.O. analgesic ladder

Step 1	Step 2	Step 3
Non-opioid	Weak opioid ± non-opioid	Strong opioid ± non-opioid ± adjuvant
Consider other treatment modalities where possible: radiotherapy, hormonal therapy, palliative chemotherapy, surgery.		
Consider non-pharmacological modalities: physiotherapy, psychotherapy.		
Address all aspects of suffering: physical, psychosocial, cultural and/or spiritual.		

APPENDIX F: Opioid analgesics – pharmacokinetics

Table 8: Opioid analgesics - pharmacokinetics

Drug	Route	Onset of action(in minutes)	Duration of action (in hours)
Codeine IR	po	15-30	4-6
	sc	15-30	4-6
Fentanyl	sc	7-15	1-2
	transdermal	12-17 hours	72
Morphine IR	po	10-90	3-4
	sc	10-30	3-5
Hydromorphone IR	po	30	3-4
	sc	15	3-4
Oxycodone IR	po	10-15	4-6
Methadone	po	15-30	6-12
	pr	15-30	6-12

IR = immediate release

CR = controlled release

APPENDIX G: Fentanyl equianalgesic doses (manufacturer's recommendations)

Table 9: Fentanyl equianalgesic doses

Transdermal fentanyl (micrograms/hour)	Oral morphine (mg/day)	Oral hydromorphone (mg/day)
25	45-134	11-33
50	135-224	34-55
75	225-314	56-78
100	315-404	79-100
125	405-494	Please see manufacturer's tables.
150	495-584	
175	585-674	
200	675-764	
225	765-854	
250	855-944	
275	945-1034	
300	1035-1124	

APPENDIX H: Administering hypodermoclysis

Equipment

- Hypodermoclysis solution as ordered.
- Tape.
- Appropriate tubing.
- Transparent dressing or bandage.
- Winged butterfly needle (23-25 G).
- Alcohol swabs.
- Infusion pump (if needed).

Procedure

1. Explain procedure and answer questions.
2. Wash hands. Assemble and set-up equipment. Flush administration set including winged needle.
3. Put on non-sterile gloves to protect against the possibility of contact with blood.
4. Choose site. See 'Site location' below, under Recommendations.

N.B.: Two sites may be used simultaneously if medications are incompatible when mixed or if the fluid volume ordered is too great for absorption from one site.

5. Cleanse site with alcohol swab. Allow to dry.
6. Insert winged needle. Gently pinch a well defined amount of tissue between your index finger and thumb. Insert needle into the base of the pinch at a 45 degree angle. Bevel up is preferred. The needle should lie in the subcutaneous space, above the underlying fascia. It should move freely in that space.

N.B.: When using the abdomen direct the needle laterally to prevent pinching when the patient sits or bends.

N.B.: If blood return is noted, withdraw the needle. Repeat the procedure using a new needle and an adjacent site.

7. Dress the insertion site. Keep in mind the insertion site must be visible for ongoing inspection and the needle and tubing must be anchored well to avoid displacement. A transparent dressing over the wings of the needle and insertion site with the tubing coiled and secured to the patient's skin with tape works well.
8. Attach administration set to tubing.
9. Insert administration set into pump (if using) and adjust flow. Most infusions can be run by gravity. A pump should only be used if fluid or medication rates must be carefully monitored.
10. Document details.

Recommendations

Hyaluronidase dose

0 units unless there are site absorption problems, then use 150 units to 1 litre of solution increasing to 300 units if necessary. If hyaluronidase is not available for absorption problems, then check the site more often and/or try slowing down the infusion rate. If infusing by gravity, try putting the infusion on a pump or try bolusing.

Site change

Only when necessary (pooling, bruising, unresolved blanching, leaking, redness, pain at the site.) Note: redness needs to be an indication of inflammation rather than of manipulation of the needle or the site (*e.g.*, starting a new site, changing the dressing). At the first sign of inflammation, change the site. If the redness is related to manipulation, leave it but monitor the site more frequently. Sofsets or silastic catheters (small angio-catheters, size 24 or less), can be used in the case of metal allergies or rare absorption problems.

Flush

There is no need to flush between medication if the same medication is going into the same site. Use a separate site for medications that are not compatible (check the medication packaging). If medications are compatible it is not necessary to flush in between the administration of either of them, however, the length of the tubing and volume infusing needs to be considered. The longer the tubing, therefore the larger its volume, the more likely it will be to need to flush the tubing to ensure that the appropriate dose of medication is delivered.

Site location

Ask the individual where the most comfortable site would be for them. All of the following are appropriate site locations: abdomen, chest (avoiding breast tissue), arm, thigh, and scapula. Always be aware about how much the needle placement will affect the individuals mobility, especially joint movement, and how their body ‘folds’. If there is a problem with absorption, select the abdomen or chest. Note: do not use the arm site for hypodermoclysis.

Site preparation

0.5% chlorhexidine or 70% isopropyl alcohol can be used. In case of allergies to the recommended solutions, use povidone iodine. Remember: the preparation solution needs to be dry before inserting the needle.

Site dressing

A clear occlusive dressing is best for the visibility and security of the site, *e.g.*, tegaderm or oposite. The Alberta Cancer Board has created the Palliative Care Network Initiative (PCNI) to assist regions to optimize their palliative care services and programs. The PCNI supports regions in doing this by promoting a ‘common language’ of palliative care for Alberta and by linking regions to available resources and to each other. Available resource linkages include: palliative care programming and service delivery models, palliative care definitions and standards development, educational resources and opportunities, clinical practice tools and guidelines, family caregiver information, other regional and out-of province models and experiences, support services and associations, etc. Please contact:

APPENDIX I: Suggested bowel routine for patients on regular opioids

Stool softeners and bowel stimulants

Must be given regularly, *not* prn, and should be started simultaneously with initiation of opioids.

Usual starting dosages

Senna 1-2 tabs @ hs and docusate 100-240 mg po bid. Adjust dosages and frequencies as needed to ensure the patient has a soft, formed bowel movement every 1-2 days.

Patients often require senna 2-4 tabs bid up to qid prn, and docusate 240 mg tid up to qid prn.

If patients experience diarrhea (*e.g.*, from radiotherapy to the pelvic area or chemotherapy) hold temporarily until diarrhea subsides.

Stimulant suppository (*e.g.*, bisacodyl) and fleet enema

Administer suppository and, if ineffective, give high fleet enema whenever patient does not have a bowel movement for 3 days.

If ...

1. ... suppository and fleet enema are ineffective, repeat.
2. ... still ineffective, high oil retention enema and high fleet.
3. ... still ineffective, soap suds enema (irritating and often poorly tolerated).

NB: Be sure to assess for bowel obstruction *before* initiating aggressive laxative and enema administration. Such therapies are contraindicated in the presence of bowel obstruction, except if obstruction is due to constipated stool.

Lactulose

30ml tid may need to be added to the laxative regime.

Magnesium citrate

Occasionally, magnesium citrate – 1 bottle in 24 hours – may be needed, especially if the flat plate abdominal x-ray shows a large amount of stool in the ascending or transverse colon.

N.B.: One good response to a laxative or enema may not treat the constipation fully. The sigmoid may be clear but the rest of the colon may still be full of stool.

APPENDIX J: Supports for families

The Support Network in Edmonton has a list of bereavement groups and counselors in Edmonton and surrounding areas.

Phone: (780) 482-4636

Alberta Hospice Palliative Care Association (formerly the Palliative Care Association of Alberta) is associated with community level palliative care specific volunteer and support programs throughout Alberta.

E-mail: pcareab@telus.net

Regional and/or community home care offices and Canadian Cancer Society offices are a good source of information on local support services for palliative patients and families.

Homepage: <http://www.cancer.ca/ccs>

Please contact your local health authority for detailed contact information.

The Resource Centre at the Tom Baker Cancer Centre and regional community or associate cancer centres are an excellent source of written and audio-visual information for patients and families.

Phone: (403) 521-3723 (Tom Baker main reception)

On the ACB homepage: http://www.cancerboard.ab.ca/about/about_about_divisions_cancer.html

APPENDIX K: Educational resources and opportunities

Canadian Hospice Palliative Care Association:

CHPCA is active in education for health professionals and volunteers, public awareness and research in palliative care. Written and video resources are available for order.

Phone: (toll-free) 1-800-668-2785

Homepage: <http://www.chpca.net>

Canadian Society of Palliative Care Physicians

This society is active in advocating for issues of relevance to palliative care physicians such as specialist training, remuneration, and CME.

Homepage: <http://www.csppc.ca>

Alberta Hospice Palliative Care Association

AHPCA is a largely voluntary organization that provides linkages between and reports on the activities of regional palliative care services, councils, educational events and promotion/awareness activities.

E-mail: pcareab@telus.net

c/o Pilgrims Hospice Society, 9808 148 Street, Edmonton, AB Canada T5N 3E8

Grant MacEwan Community College Palliative Care Program:

This is a nine course, 30 credit certificate distance-education program for post-diploma degree health care professionals. There is a practical component.

Homepage: <http://www.macewan.ca/web/hcs/palliative/home/index.cfm>

Calgary Regional Palliative and Hospice Care Services

Nurse/physician consultants are available, upon request and identified need, to give presentations to groups of practitioners needing in-services on palliative care. In addition, a Palliative Care Educational Day is offered yearly.

Homepage: <http://www.calgaryhealthregion.ca/commcare/palliative.htm>

Capital Health Authority Regional Palliative Care Program:

Nurse/physician consultants are available, upon request and identified need, to give presentations to groups of practitioners needing in-services on palliative care. Together with the Division of Palliative Care Medicine, University of Alberta, tailored palliative care training programs can be designed for interested practitioners based on each participant's previous knowledge level and schedule.

Homepage: <http://www.caritas.ab.ca/Hospitals/GreyNuns/Default.htm>

Tertiary Palliative Care Unit, Caritas Health Group (Edmonton)

This 14 bed inpatient unit provides acute symptom management for palliative patients as well as opportunities to participate in research and training.

Homepage: <http://www.caritas.ab.ca/Hospitals/GreyNuns/Inpatient+Programs/Default.htm>

Collaborative Palliative Care EdNet Project:

This on-line palliative care educational program will take approximately six to eight weeks. It is case and problem based, and incorporates small group discussion. The technology is user-friendly and extensive support is provided.

Homepage: <http://www.palliative.org/pallcareednet/>

APPENDIX L: Contacts for consultation

Queries and requests can be forwarded to:

Provincial Coordinator, Hospice Palliative Care Network
Medical Affairs and Community Oncology
Alberta Cancer Board
Tom Baker Cancer Centre
1331 - 29 St. NW
Calgary, Alberta CANADA
Phone: (403) 521-3486
Fax: (403) 521-3178
Homepage: www.cancerboard.ab.ca/maco