Analgesic prescribing in palliative care

Pain management requires a multimodal approach involving pharmacological and non-pharmacological strategies. It is important to take a detailed history and examine the patient before prescribing any analgesia. This article focuses on assessment and management of pain in palliative care patients.

Two thirds of cancer patients experience pain and need strong opioids for pain management (National Institute for Health and Care Excellence, 2012). Despite doctors' awareness of this problem there is evidence that pain in advanced disease remains inadequately treated (National Institute for Health and Care Excellence, 2012). Pain is experienced at a similar prevalence in both malignant and non-malignant conditions, something which is often under-recognized in clinical practice (Moens et al, 2014). It is important to remember that patients may experience pain as a result of their palliative condition as well as other existing chronic condition(s). Patients may present with more than one pain simultaneously, requiring a separate assessment and management plan for each one. When managing pain it is essential to consider physical, psychological, social and spiritual elements.

This article covers how to identify the cause of pain, types of pain, the principles of the analgesic ladder and medication for managing persistent and breakthrough pain.

Pain assessment

Assessment and reassessment are key to effective pain management. To tailor treatment selection to patients and their pain, it is essential to diagnose the cause of pain and evaluate treatment efficacy. Pain should be assessed completely before starting or changing analgesia. Patients may have more than one site or type of pain, each of which requires thorough assessment. When considering the cause of pain this may or may not relate to the primary underlying condition.

These components are needed for initial assessment:

- Detailed history taking – to understand the cause and mechanism of pain. Important questions can be remembered by the SOCRATES mnemonic (Site, Onset, Character, Radiation, Associated symptoms, Time factors, Exacerbating and relieving factors, Severity)
- Psychological and spiritual assessment – negative emotions and sleep deprivation can worsen pain. It is essential to know the impact of underlying diagnosis and pain on the patient and family
- Medications history – dose, route, frequency, efficacy, adverse effects, current and previously used medication
- Focused physical examination
- Investigations – recent blood results and scans should be reviewed and new investigations requested judiciously to investigate the cause of pain where there is uncertainty
- Identification of the patient's and family's goals and expectations of pain management.

Types of pain

Identification of the underlying mechanism of pain helps guide treatment. Pain can be divided into various subgroups (National Cancer Institute, 2014). The description of pain given by the patient is very important for assessment and is considered the gold standard of pain assessment (Melzack and Katz, 1994). Pain might typically be described as follows, which helps to determine the cause or type of pain.

- Nociceptive pain (pain caused by damage to tissues) can be either somatic pain – aching, constant, well localized and often worse on movement, or visceral pain – constant and crampy, poorly localized
- Neuropathic pain (pain caused by damage or dysfunction of nerves) which can be sharp, stabbing, shooting or burning.

Breakthrough pain is a transient exacerbation of pain which occurs either spontaneously or secondary to a trigger factor (Davies et al, 2009).

Palliative patients can suffer pain as a result of their disease, treatments, comorbidities or reduced mobility. If pain is related to a chronic condition it may be appropriate to consult chronic pain services as the management strategy is often different.

Assessment tools

There are a variety of validated and reliable pain assessment tools – the most commonly used are the numerical rating scale, the four-point verbal categorical rating scale and the visual analogue scale (*Figure 1*) (Rowbotham and Macintyre, 2003). Pain score should be recorded on every assessment to monitor effectiveness of analgesia.

General considerations in pain management

Treating the underlying cause is the key to successful pain management. In cancer patients anti-cancer treatment such as chemotherapy, radiotherapy or hormonal treatment can be effective in managing pain. Cancer pain may be caused by multiple mechanisms and a combination of treatments may be required to get the maximum pain relief (Twycross et al, 2009).

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Communication is a key part of managing pain. The likely diagnosis and management plan should be agreed with patients. Sometimes explanation itself relieves anxiety and hence, psychological aspects of the pain. It is important to address the patient's concerns such as addiction and tolerance while informing patients of potential medication side effects.

There are various non-pharmacological approaches to manage pain such as complementary therapy, acupuncture and transcutaneous electrical nerve stimulation. However, there is insufficient evidence to be able to routinely recommend these practices (Paley et al, 2011; Hurlow et al, 2012).

Two main formulations of analgesia can be prescribed: regular medication should be prescribed for persistent pain, and 'as required' medication (PRN) should be prescribed for breakthrough pain. The patient must be aware that the PRN analgesia is available. Documentation of use within 24 hours can allow medication to be titrated.

Where possible analgesia should be given orally but where there is difficulty swallowing or concern about absorption it may need to be given via a non-oral route (usually a patch or subcutaneously).

The World Health Organization (1996) analgesic ladder provides a framework for treating pain with analgesia but does not replace individualized treatment plans. The ladder has been used to provide adequate pain control in 96% of patients with renal failure (Barakzoy and Moss, 2006) and 45–100% of cancer patients (Azevedo São Leão Ferreira et al, 2006; Mishra et al, 2009). Analgesia is titrated through the steps when the previous step is no longer adequately controlling the pain (*Figure 2*). For mild pain, start with a non-opioid like paracetamol. If the pain persists a weak opioid such as codeine or tramadol should be added. If the patient continues to have pain with the maximum dose of weak opioid, it should be replaced by a strong opioid. Adjuvants can be added to any step of the ladder depending on the type of pain. Analgesics used in the different steps of the ladder are detailed below.

Figure 1. Pain assessment tools. From Breivik et al (2008).

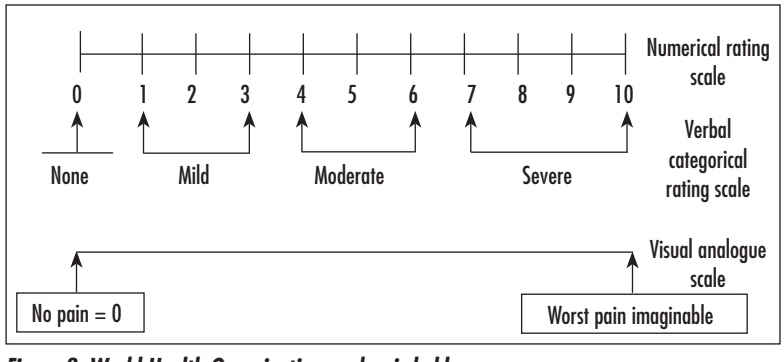
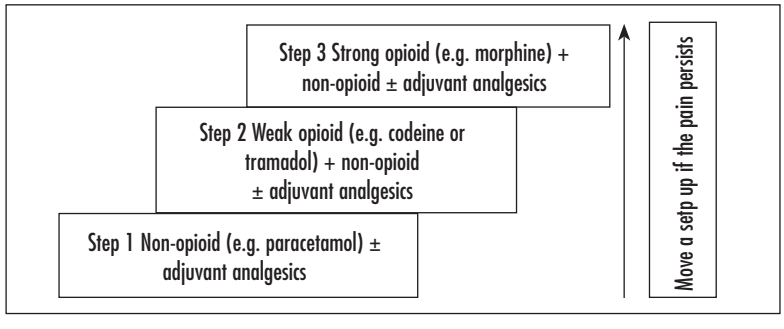


Figure 2. World Health Organization analgesic ladder.



Paracetamol

Paracetamol is an antipyretic with a centrally-acting non-opioid analgesic effect. Its mode of action is not fully understood but it appears to work synergistically with opioids. Dosing should initially be regular but where tablet burden is a concern it could be stopped if there is no definitive benefit after 2 days (Twycross and Wilcock, 2011). Consider dose reduction in patients with risk factors for hepatotoxicity or who weigh less than 50 kg (Twycross and Wilcock, 2011).

Opioids

There are four main opioid receptors: mu (μ), kappa (κ), delta (δ) and opioid receptor like-1 (ORL-1) distributed throughout the body (Twycross and Wilcock, 2011). Opioids act on μ-opioid receptors in the CNS to produce their analgesic effects. Opioids also produce peripheral analgesic action in the presence of local inflammation.

Opioids have different pharmacokinetic properties, bioavailability and metabolism in different patients necessitating individualized opioid selection, dosing and titration (National Institute for Health and Care Excellence, 2012). All opioids may be associated with transient nausea and drowsiness on initiation of therapy, usually resolving within a week, whereas constipation continues throughout. To manage this prescribe regular laxatives and ensure rescue anti-emetics are available (National Institute for Health and Care Excellence, 2012). Patients should be counselled about common adverse effects and impact on activities such as driving.

Weak opioids

Codeine and tramadol are weak opioids and are metabolized via the CYP2D6 enzyme, so can be ineffective in people with slow metabolism (Stamer et al, 2003). CYP2D6 inhibitors (e.g. selective serotonin-reuptake inhibitors) can block biotransformation of both drugs and reduce their analgesic effect (Twycross and Wilcock, 2011).

There are no absolute contraindications to use but metabolites of both agents accumulate in patients with renal impairment and the dose may need to be reduced or alternative opioids used. Tramadol may be less constipating than codeine or morphine but causes more anorexia, dizziness and vomiting and is associated with seizure threshold reduction. Tramadol, fentanyl and some antidepressants may cause serotonin syndrome if used together (Park et al, 2014), so medication should be rationalized and vigilance maintained for adverse effects.

When patients are at the maximum dose (codeine 240 mg, tramadol 400 mg) they should be prescribed PRN

immediate release morphine for breakthrough pain. If two or more doses of PRN morphine are needed within 24 hours, and are effective, move to step three of the ladder. Safe and clinically useful oral dose conversions to morphine are 240 mg codeine:24 mg morphine, and 400 mg tramadol:40 mg morphine (Twycross and Wilcock, 2011). In rapidly escalating pain it is reasonable to go directly from step one to three of the ladder (Maltoni et al, 2005).

Strong opioids

In the absence of renal or hepatic dysfunction National Institute for Health and Care Excellence (2012) guidelines suggest morphine as the first-line opioid with a starting dose of 20–30 mg of a twice-daily modified release preparation in 24 hours. A PRN dose for breakthrough pain (usually 1/6th of the 24-hour morphine dose) should also be prescribed. By monitoring use of PRN doses morphine can be titrated until satisfactory pain relief is obtained without toxicity. When the modified release dose is increased, review the PRN dose as this may need to be increased proportionally. While there is no opioid ceiling dose, escalation of opioid treatment with brief or minimally improved pain control should prompt treatment review.

In frail or elderly patients smaller doses may be used to reduce drowsiness and confusion.

Opioid switching

Switching between strong opioids might be of benefit when there are persistent and unacceptable side effects despite laxatives, anti-emetics and opioid-sparing treatment.

Morphine metabolites accumulate in renal failure which can prolong duration of action and toxicity. Specialist advice should be taken when prescribing opioids in patients with moderate to severe renal or hepatic impairment. When glomerular filtration rate <50 ml/min consider a dose reduction by 75%, or switch to an alternative opioid.

The dose of oral oxycodone is half that of oral morphine but is better tolerated in patients with renal impairment and is used in patients with glomerular filtration rate <50 ml/min. There are no other differences in side-effect profile between morphine and oxycodone although there may be variations between individual patients.

When glomerular filtration rate drops <10 ml/min alfentanil becomes the preferred subcutaneous opioid as it undergoes hepatic inactivation. It requires specialist supervision and continuous subcutaneous infusion because of its high potency and short duration of action.

Transdermal patches containing buprenorphine or fentanyl should not be used as first-line opioids or in unstable pain as a result of their long half-lives and latent periods before pharmacological steady state is reached (National Institute for Health and Care Excellence, 2012). However, they may be useful for patients with an unsafe swallow, poor gastrointestinal absorption, renal failure or poor medicine compliance. Seemingly 'low dose' patches deliver a considerable morphine equivalent dose: fentanyl 12 µg patch = 45 mg oral morphine daily, buprenorphine 20 µg patch = 30 mg oral morphine daily (National Institute for Health and Care Excellence, 2012). Patients with transdermal patches should also have rescue medications prescribed.

Local guidance should be followed when switching opioids as opioid conversion ratios are only ever approximate measures. As pharmacokinetics differ between individual patients and other variables may affect the opioid potency it is impossible to give guidance which will fully apply to every patient. Patients should be closely monitored during the switching phase (Twycross and Wilcock, 2011).

Opioids may be given via continuous subcutaneous infusion when the oral route is compromised. Morphine and oxycodone subcutaneously are approximately twice as potent as their oral equivalents. In the final days of life if patients have a transdermal patch this should be continued and extra opioids prescribed via continuous subcutaneous infusion if required.

Adjuvants

Various adjuvants can be considered at any stage of the analgesic ladder depending on the likely cause of the pain.

Non-steroidal anti-inflammatory drugs

This group inhibits cyclo-oxygenase (COX) which blocks prostaglandin production and reduces inflammation-induced pain (Twycross and Wilcock, 2011). Non-steroidal anti-inflammatory drugs are usually classified depending on their selectivity for COX-1 (present in all cells) and COX-2 (present mainly at sites of inflammation). A Cochrane review (McNicol et al, 2005) showed that non-steroidal anti-inflammatory drugs are more effective than placebo for cancer pain and that there may be a slight benefit to adding non-steroidal anti-inflammatory drugs to opioids. They are particularly effective in pain associated with inflammation and may also be useful for musculoskeletal and neuropathic pain.

As non-steroidal anti-inflammatory drugs can have significant adverse effects the lowest possible dose should be used for the shortest period and use restricted in at-risk patients. The choice of non-steroidal anti-inflammatory drug depends on the side-effect profile in relation to patient risk factors and evidence has changed the recommended choice of non-steroidal anti-inflammatory drug. Low dose ibuprofen has a lower gastrointestinal risk but a significant cardiac risk. Consider co-prescription of a proton pump inhibitor to further reduce the gastrointestinal risk. Naproxen is the non-steroidal anti-inflammatory drug of choice for patients with cardiovascular disease (Trelle et al, 2011). Diclofenac and selective COX-2 inhibitors should be avoided (Coxib and traditional NSAID Trialists' (CNT) Collaboration, 2013). All non-steroidal anti-inflammatory drugs cause renal impairment, so this does not dictate drug choice (Schneider et al, 2006). Consider checking glomerular filtration rate before and 1–2 weeks after non-steroidal anti-inflammatory drug initiation and be aware that estimated glomerular filtration rate can be misleading in patients who have cachexia (Claxton et al, 2010).

Ketorolac is a preferential COX-1 inhibitor which can be given via continuous subcutaneous infusion and therefore may be useful for patients requiring parenteral analgesia. It should only be used under specialist guidance.

Corticosteroids

Dexamethasone is the corticosteroid of choice in palliative care as a result of its predominantly glucocorticoid effect and practicalities of administration. It can be useful for pain resulting from nerve compression or tumour in a confined space (Twycross and Wilcox, 2011). The dose is variable (usually initially ranging from 2–16 mg depending on indication) and should be titrated down to the lowest effective dose where possible. Corticosteroids should be used for the shortest time possible; if there is no improvement in analgesia they should be stopped. A proton pump inhibitor is usually co-prescribed to reduce gastrointestinal risk and capillary blood glucose should be monitored if appropriate.

Neuropathic agents

Much of how we use neuropathic agents is extrapolated from evidence in non-palliative care patients. National Institute for Health and Care Excellence (2013) guidance recommends amitriptyline, duloxetine, gabapentin or pregabalin as first-line agents. If this is not effective then another agent within this group can be tried. Choice of first-line agent may be guided by patient risk factors and consideration of other symptoms which may be treated by a neuropathic agent to reduce tablet burden.

Amitriptyline is a tricyclic antidepressant which blocks re-uptake of serotonin and noradrenaline to cause an analgesic effect. Although not licensed for neuropathic pain it is widely used and sometimes considered the gold standard with a large number of trials showing efficacy (Saarto and Wiffen, 2007). Dosing starts at 10 mg at night and can be titrated up as required depending on efficacy and side effects. Other medication should be reviewed for risk of serotonin toxicity or QT prolongation. Amitriptyline is contraindicated after recent myocardial infarction or new arrhythmia and care should be taken in those with previous arrhythmia, postural hypotension, hepatic dysfunction or epilepsy (reduces seizure threshold). Sedation is the most common side effect: if present the dose can be taken 2 hours before bedtime (Twycross and Wilcock, 2011).

Gabapentin is an antiepileptic which blocks pre-synaptic calcium channels and reduces neuroexcitability. It is licensed for neuropathic pain and there is some evidence for its effectiveness in treating chronic neuropathic pain (Moore at al, 2014). In palliative care patients it is usually started at 100 mg at night, titrated up to three times a day and then upwards in steps of 100 mg. Gabapentin has many other potential indications including seizures, flushes, hiccup and itch (Twycross and Wilcock, 2011).

Pregabalin is another antiepileptic medication with a similar action to gabapentin. It is licensed for peripheral and central neuropathic pain and has evidence of effectiveness in treating both acute and chronic pain (Moore at al, 2009). In frailer patients it may be started at 25 mg twice a day and then titrated up in 25 mg steps. This twice-daily dosing is one of the benefits over gabapentin. Extra care should be taken with gabapentin and pregabalin in patients with renal impairment; amitriptyline is a useful alternative. Pregabalin also has a license for treating generalized anxiety disorder (Twycross and Wilcock, 2011).

Other neuropathic agents, e.g. duloxetine (a serotonin-noradrenaline reuptake inhibitor) or sodium valproate (an anti-epileptic), may be useful when patient characteristics prohibit the use of first-line medication or where they have been ineffective. Two neuropathic agents can be combined for additional effect but avoid using two from a similar class (i.e. two tricyclics, pregabalin and gabapentin).

Skeletal muscle relaxants

Diazepam and baclofen may be used to treat painful muscle spasm and spasticity, often associated with neurological conditions. Diazepam is a gamma-aminobutyric acid (GABA) modulator while baclofen is a GABA agonist. Both reduce neurotransmitter release and therefore muscle spasm. Baclofen may be more appropriate where longer term use is likely to avoid the risk of benzodiazepine dependence. Sedation is the most common side effect with both and patients should be monitored for reduction in voluntary muscle power (Twycross and Wilcock, 2011).

N-methyl D-aspartate receptor-channel blockers

N-methyl D-aspartate (NMDA) receptor channels, when activated, transmit a pain signal (Twycross and Wilcock, 2011). Agents which block this pathway, such as ketamine and methadone, should only be used after specialist advice to treat resistant neuropathic pain.

Bisphosphonates

There is evidence that bisphosphonates are effective for treating bone pain (Wong and Wiffen, 2002). However, there is insufficient evidence to assess relative efficacy of different bisphosphonates in different neoplasms so choice is usually dictated by local policy and patient characteristics.

Topical agents

Topical non-steroidal anti-inflammatory drugs can be useful when managing pain associated with soft tissue trauma. In large quantities they can cause similar systemic effects to systemic non-steroidal anti-inflammatory drugs.

Capsaicin depletes substance P at sensory nerve endings and can be used to treat peripheral neuropathic pain (Twycross and Wilcock, 2011). It is available as a cream (0.025–0.075%) which initially causes a stinging or burning effect when applied. It is also available as an 8% patch which requires specialist application but whose effects can last up to 3 months.

There is some evidence that topical menthol is effective for the treatment of chemotherapy-induced peripheral neuropathy (Storey et al, 2010) and further research is ongoing.

Lidocaine 5% plasters are licenced for post-herptic neuralgia. Up to three plasters can be applied (and cut to size) for relief of localized neuropathic pain. Plasters are applied for 12 hours and then removed to reduce skin reactions. There is a lack of high quality data for their efficacy (Twycross and Wilcock, 2011).

And if you're still struggling…

It is important to know your limitations and get advice from the palliative care team in complex cases.

Although outside the scope of this article do not forget non-drug options in palliative care patients. Anaesthetic interventions such as nerve blocks, intrathecal devices or cordotomy may also be useful in specific patients.

Conclusions

Palliative care patients are a diverse group who may be experiencing pain from a number of different causes. It is important to assess pain carefully and repeatedly to ensure appropriate analgesia. The WHO analgesic ladder remains central to pain management and many patients will require strong opioids. However, it is important not to forget the variety of adjuvant analgesia which is available. **BJHM**

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Azevedo São Leão Ferreira K, Kimura M, Jacobsen Teixeira M (2006) The WHO analgesic ladder for cancer pain control, twenty years of use. How much pain relief does one get from using it? *Support Care Cancer* **14**(11): 1086–93

Barakzoy AS, Moss AH (2006) Efficacy of the World Health Organization analgesic ladder to treat pain in end-stage renal disease. *J Am Soc Nephrol* **17**(11): 3198–203 (doi: 10.1681/ASN.2006050477)

Breivik H, Borchgrevink PC, Allen SM et al (2008) Assessment of pain. *Br J Anaesth* **101**: 17–24 (doi: 10.1093/bja/aen103)

Claxton RN, Blackhall L, Weisbord SD, Holley JL (2010) Undertreatment of symptoms in patients on maintenance hemodialysis. *J Pain Symptom Manage* **39**(2): 211–18 (doi:10.1016/j.jpainsymman.2009.07.003)

Coxib and traditional NSAID Trialists' (CNT) Collaboration (2013) Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* **382**(9894): 769–79

Davies AN, Dickman A, Reid C, Stevens AM, Zeppetella G, Science Committee of the Association for Palliative Medicine of Great Britain and Ireland (2009) The management of cancer-related breakthrough pain: recommendations of a task group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland. *Eur J Pain* **13**(4): 331–8 (doi: 10.1016/j.ejpain.2008.06.014)

Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG (2012) Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst Rev* **3**: CD006276 (doi: 10.1002/14651858.CD006276.pub3)

Maltoni M, Scarpi E, Modonesi C et al (2005) A validation study of the WHO analgesic ladder: a two-step vs three-step strategy. *Support Care Cancer* **13**(11): 888–94

McNicol ED, Strassels S, Goudas L, Lau J, Carr DB (2005) NSAIDS or paracetamol, alone or combined with opioids, for cancer pain. *Cochrane Database Syst Rev* **2**: CD005180 (doi: 10.1002/14651858.CD005180)

Melzack R, Katz J (1994) Pain measurement in persons in pain. In: Wall PD, Melzack R, eds. *Textbook of Pain.* Churchill Livingstone, London: 409–26

Mishra S, Bhatnagar S, Gupta D, Nirwani Goyal G, Jain R, Chauhan H (2009) Management of neuropathic cancer pain following WHO analgesic ladder: a prospective study. *Am J Hosp Palliat Care* **25**(6): 447–51 (doi: 10.1177/1049909108322288)

Moens K, Higginson IJ, Harding R (2014) Are there differences in the prevalence of palliative care-related problems in people living with advanced cancer and eight non-cancer conditions? A systematic review. *J Pain Symptom Manage* (doi: 10.1016/j.jpainsymman.2013.11.009)

Moore RA, Straube S, Wiffen PJ, Derry S, McQuay HJ (2009) Pregabalin for acute and chronic pain in adults. *Cochrane Database Syst Rev* **3**: CD007076 (doi: 10.1002/14651858.CD007076.pub2)

Moore RA, Wiffen PJ, Derry S, Toelle T, Rice AS (2014) Gabapentin for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Database Syst Rev* **4**: CD007938 (doi: 10.1002/14651858.CD007938.pub3)

National Cancer Institute (2014) Pain (PDQ). www.cancer.gov/cancertopics/pdq/supportivecare/pain/HealthProfessional/page2 (accessed 15 February 2014)

National Institute for Health and Care Excellence (2012) Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. www.nice.org.uk/guidance/cg140 (accessed 27 October 2014)

National Institute for Health and Care Excellence (2013) Neuropathic pain – pharmacological management: The pharmacological management of neuropathic pain in adults in non-specialist setting. http://publications.nice.org.uk/neuropathic-pain-pharmacological-management-cg173 (accessed 7 February 2014)

Paley CA, Johnson MI, Tashani OA, Bagnall AM (2011) Acupuncture for cancer pain in adults. *Cochrane Database Syst Rev* **1**: CD007753 (doi: 10.1002/14651858.CD007753.pub2)

Park SH, Wackernah RC, Stimmel GL (2014) Serotonin syndrome: is it a reason to avoid the use of tramadol with antidepressants? *J Pharm Pract* **27**(1): 71–8 (doi: 10.1177/0897190013504957)

Rowbotham DJ, Macintyre PE (2003) *Clinical Pain Management: Acute Pain.* Arnold, London

Saarto T, Wiffen PJ (2007) Antidepressants for neuropathic pain. *Cochrane Database Syst Rev* 4: CD005454 (doi: 10.1002/14651858.CD005454.pub2)

Schneider V, Levesque LE, Zhang B, Hutchinson T, Brophy JM (2006) Association of selective and conventional nonsteroidal anti-inflammatory drugs with acute renal failure: a population-based, nested case-control analysis. *Am J Epidemiol* **164**(9): 881–9

Stamer UM, Lehnen K, Höthker F et al (2003) Impact of CYP2D6 genotype on postoperative tramadol analgesia. *Pain* **105**: 231–8

Storey DJ, Colvin LA, Scott AC et al (2010) Treatment of chemotherapy-induced peripheral neuropathy (CIPN) with topical menthol: A phase I study. *J Clin Oncol* **28**(15): 9129

Trelle S, Reichenbach S, Wandel S et al (2011) Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ* **342**: c7086 (doi: 10.1136/bmj.c7086)

Twycross R, Wilcock A, Toller CS (2009) *Symptom Management in Advanced Cancer*. 4th edn. Radcliffe Medical Press, Abingdon

Twycross R, Wilcock A, eds (2011) *Palliative Care Formulary*. 4th edn. Palliativedrugs.com, Nottingham

Wong R, Wiffen P (2002) Bisphosphonates for the relief of pain secondary to bone metastases. *Cochrane Database Syst Rev* **2**: CD002068 (doi: 10.1002/14651858.CD002068)

World Health Organization (1996) *Cancer Pain Relief*. 2nd edn. World Health Organization, Geneva

KEY POINTS

- Detailed history taking and clinical examination can establish the type and cause of pain so that appropriate pain management strategies can be chosen.
- Consider the impact that pain can have on the patient and take time to explain the likely cause of pain.
- Analgesia should follow the World Health Organization pain ladder with paracetamol as step one and opioids titrated (if effective) to the patient's requirements.
- Opioids should be prescribed both as regular modified release preparations and as required immediate release preparations for breakthrough pain.
- Adjuvant medication should be considered at any stage and specific adjuvants may be more helpful in specific pain syndromes.