Pain Management

Gregory Sund, Matthew Kynes

Introduction

The World Health Organization estimates that 5.5 billion people do not have access to treatments for moderate to severe pain. The majority of these people live in low- and middle-income countries. As the availability of surgical services increases in these settings, the need for treatments for moderate to severe perioperative pain will also increase. The barriers to improving access to treatment for pain are numerous and include low prioritization of pain relief by both the patient and the healthcare provider, lack of understanding regarding therapies, misconceptions about opioid addiction, lack of reliable supply chains for analgesics, and lack of understanding regarding the physical, social and emotional harms of poorly controlled pain.

Despite these obstacles, it has been shown that improvements in pain management are possible, even in low-resource settings. In recent years there has been growth in both research and advocacy related to pain management in austere settings. However, without access to pain management education these efforts will be wasted. Essential Pain Management (EPM) is one example of a step toward improving access to education in pain management. EPM was developed in 2010 as a short course (one to two days) to be delivered to healthcare providers of different cadres to equip these providers with the necessary tools to recognize, assess and treat pain, especially in low-resource settings. This course has now been translated into seven languages and delivered in over 60 countries worldwide. Today an on-line version exists and is freely available at https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management.

The harms of poorly controlled pain, including perioperative pain, are numerous. Uncontrolled pain leads to activation of the sympathetic nervous system which can lead to hypertension and myocardial stress. Chest wall and abdominal pain can lead to shallow breathing causing atelectasis. Patients who are in severe pain will be less likely to ambulate, increasing the risk of thrombotic complications. Severe pain will also lead to disturbances in sleep patterns and poor appetite. At a more personal level, pain is closely linked to depressed mood and social stress. All of these complications inevitably lead to increased duration of hospitalization and increased cost of healthcare.

Finally, there is a growing body of evidence that suggests that poorly controlled surgical pain can lead to the development of chronic pain (pain at the site of incision which continues for greater than three months). For all of these reasons and many more, we believe that recognizing, assessing and treating perioperative pain is of great importance in the surgical care of patients in any setting.

Pathophysiology

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” This definition highlights several important points. First, the pain pathways are intricately linked to the cortical emotional centers of the brain. Pain can contribute to anxiety and depression which can, in turn, worsen pain. Second, tissue damage does not need to be obvious for a patient to be suffering from pain. Pain is a subjective experience, and it is never the job of the healthcare provider (surgeon, nurse, anesthetist) to assume that a patient is or is not in pain.

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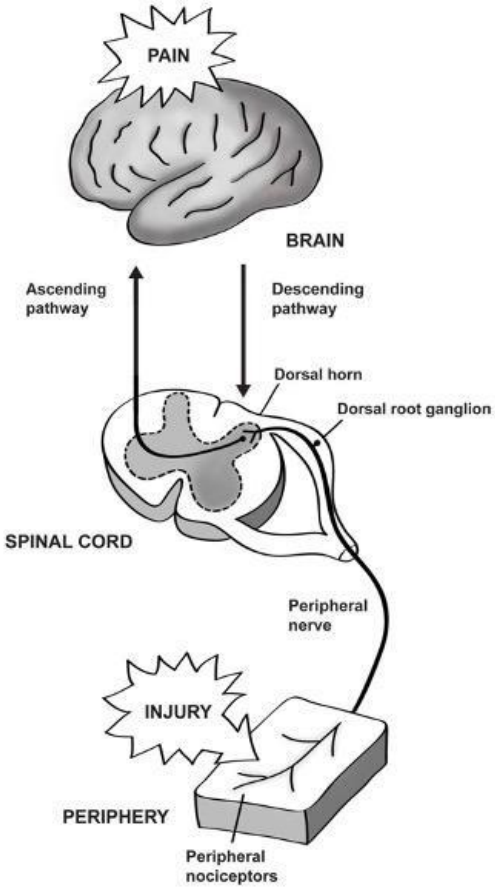
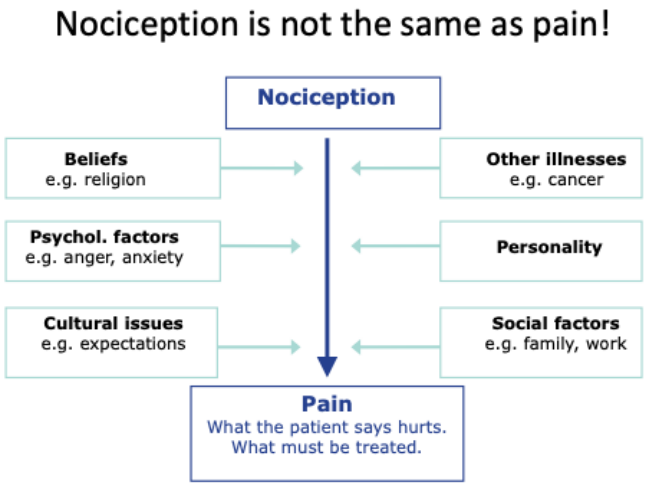


The pain pathway. From "Essential Pain Management" https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management Used with permission.

The pain pathways are illustrated above. Pain begins with the activation of nociceptors by a noxious stimulus (e.g., a surgical incision). This triggers the transmission of pain impulses through A delta and C sensory nerve fibers to the dorsal horn of the spinal cord, the first relay center. These impulses are then relayed to the opposite side of the spinal cord and travel cephalad to the thalamus, the second relay center. From the thalamus, signals are transmitted to numerous areas of the brain (including the limbic system) where the "perception of pain" occurs. At the same time, descending pathways modulate ongoing pain signals as a negative feedback loop.



Nociception vs. Pain. From "Essential Pain Management" https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management Used with permission.

One point which is often ignored is the fact that nociception and perception of pain are not identical. Nociception is the pathway by which signals travel from the site of injury to the brain. Pain is what is perceived by the patient and is influenced by many factors including cultural, social, psychological, and religious factors (see the figure above.) This again highlights the importance of asking patients to describe their pain, rather than assuming the patient is or is not having pain based on what injury or surgery they have undergone.

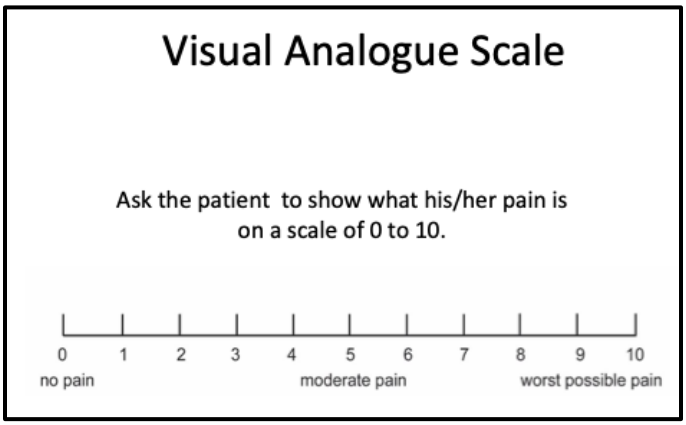
What we will emphasize in the final section of this chapter ("**Treatment of Pain**") is that this pain pathway can be interrupted at each level by both pharmacological and non-pharmacological interventions. Combining these therapies will allow us to create a "multi-modal analgesic plan" to optimize the pain control of our patients thus reducing their risk of complications linked to uncontrolled pain and reduce their suffering.

Recognition and Assessment of Pain

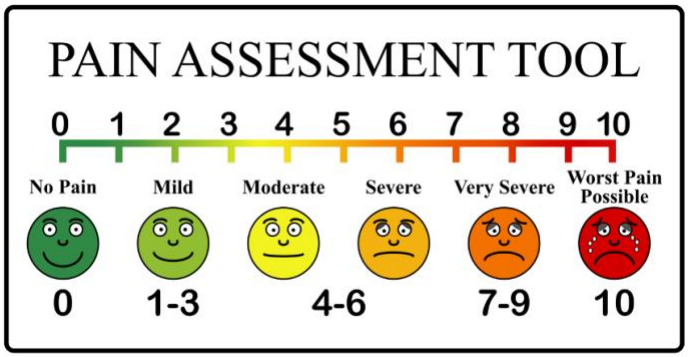
Pain is what the patient says it is. You cannot predict with any accuracy the amount of pain a patient is experiencing by the appearance on their face or by any other external factor. The only way to recognize pain is to ask the patient, "Are you having pain?" This simple question and your response to the answer, will ultimately determine their level of

suffering and will also greatly impact your relationship with that patient. It is natural to pay attention to pain when it is our own, or even that of our loved one. However, we often forget that every patient we are treating is someone's mother/father/sister/brother/son/daughter. And so, we should care about their pain, as we would care about the pain of someone we love.

In many parts of the world pain is considered the fifth vital sign and is assessed every time a patient's heart rate, blood pressure and respiratory rate are recorded. While this may be difficult to achieve in certain settings, especially those with very low nurse-to-patient ratios, it is reasonable and attainable to assess and record a patient's pain level at least daily during their hospitalization.



The Visual Analogue Scale. From "Essential Pain Management" https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management Used with permission



The Wong-Baker FACES Pain Rating Scale. From "Essential Pain Management" https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management Used with permission

There are many tools which can be used to assess the severity of pain but the two most widely used are the visual analogue scale) and the Wong-Baker FACES Pain Rating Scale. Most adult and even adolescent patients who are verbal can report a pain score between zero to ten with one or both of these scales. The utility of these scales is that their results will both direct treatment, as we will see in the following section of this chapter, and allow you to assess the effectiveness of an intervention when this score is re-evaluated post-treatment. A reported score of 0-3 is considered mild pain, a score of 4-6 moderate pain, and a score of 7-10 severe pain.

While these tools are useful for verbal patients, they are obviously of little value in assessing the pain of infants and young children. Other tools have been developed for these populations including the Neonatal Infant Pain Scale (NIPS) and the Faces, Legs, Activity, Cry, Consolability (FLACC) scale. These tools can easily be found on the internet.

Most patients during the perioperative period will be suffering from acute nociceptive pain. However, it is important to assess whether there is a neuropathic component (that caused by damage to the sensory nervous system) or whether acute pain is occurring in the setting of chronic pain (that which lasts longer than 3 months). Treatment for these will vary.

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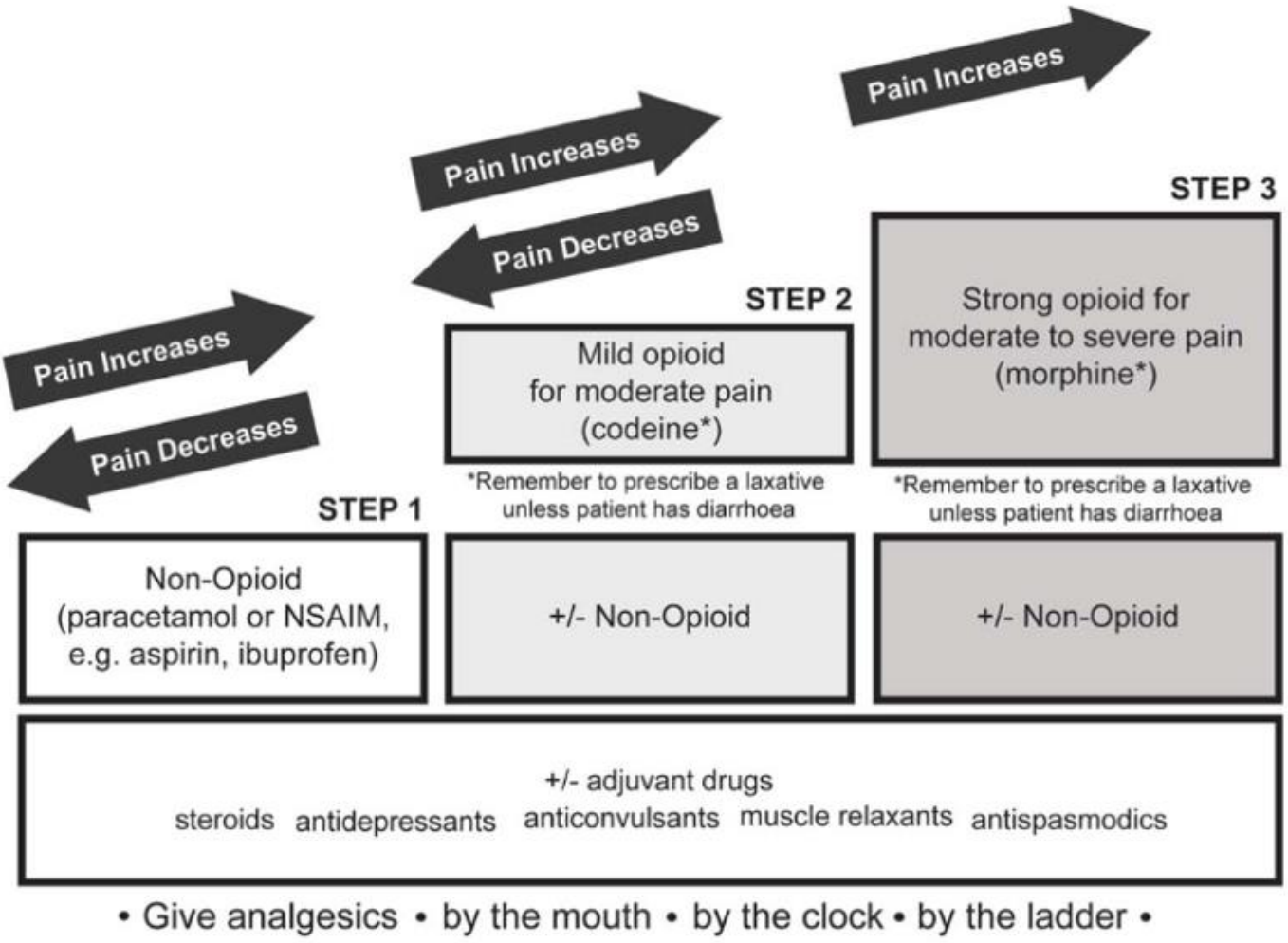

The World Health Organization Analgesic Ladder: World Health Organization and "Essential Pain Management" https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management Used with permission

Treatment of Pain

As stated in the previous section, an appropriate treatment of pain depends on an assessment to guide that treatment. The most useful and widely used tool for guiding treatment of perioperative pain is the World Health Organization Analgesic Ladder (Above) According to this ladder most patients with mild pain (pain score of 3 or less) can have their pain adequately controlled with simple analgesics (e.g., paracetamol and/or non-steroidal anti-inflammatories.) A patient with moderate pain (pain score of 4-6) will likely need a mild opioid (e.g., codeine or tramadol) in addition to simple analgesics. For these patients it is strongly recommended to continue the simple analgesics in conjunction with the mild opioid, as these medications will have a synergistic effect and provide better pain control than with the mild opioid alone.

Finally, patients with severe pain (pain score of 7 or higher) will very likely need a strong opioid such as morphine. Again, it is recommended that these patients continue to receive simple analgesics in conjunction with morphine to control their pain. Although there is much concern over the use of morphine in many parts of Sub-Saharan Africa, morphine can be used safely and effectively when the side effects and contraindications are understood and when appropriate dosing and frequency are used (see below.)

Morphine

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Morphine is on the World Health Organization's list of essential medications, both in oral and intravenous form. It is widely available in both high and low-resource settings. However, in many hospitals it is rarely used. There is a great deal of fear surrounding the use of morphine, especially with regards to its risk of addiction and side effects. Regarding addiction, there is more than sufficient evidence available that giving morphine to a patient in pain does not lead to addiction. Addiction occurs when patients take morphine for purposes that it is not indicated for, either to manage pain chronically or for recreational use. For patients with acute severe pain, however, morphine is most certainly indicated and it can be given safely if one is aware of the appropriate dosing and understands how to monitor for side effects.

For most patients with severe pain, a starting dose of intravenous morphine between 0.05 mg/kg and 0.2 mg/kg is appropriate, depending on their level of pain. This dose should be given every 3 to 4 hours for patients who continue to be in severe pain. If patients can take oral medications, oral morphine (syrup or tabs) may be more appropriate and has certain advantages, including slower onset and offset, lower cost, and the elimination of the need for an intravenous line to administer. The dose of oral morphine needs to be doubled or tripled compared to intravenous dosing due to its first-pass hepatic metabolism which rapidly reduces the active amount in the bloodstream. For example, a patient requiring 5 mg of intravenous morphine every 4 hours, may need 15 mg of oral morphine every 4 hours.

We discourage the use of intramuscular morphine for a variety of reasons. Although there is a popular idea that the effect will last longer if the medication is given intramuscular, this is not true. In addition, the absorption of intramuscular injections is variable with some patients receiving much less than the total amount absorbed into the bloodstream. Finally, intramuscular injections are painful for the patient. Therefore, our preference would be to administer oral morphine if possible. For patient who cannot tolerate orals, intravenous morphine should be given. Intramuscular morphine should only be used as a last resort for patients in severe pain who cannot take orals and for whom an IV is not possible.

Anesthetists around the world commonly add intrathecal morphine to their spinal anesthetic which can provide analgesia for up to 24 hours after the surgery. For most adult patients a dose of 0.15 mg administered intrathecally will provide potent analgesia with minimal risk of respiratory depression. Doses of 0.15 to 0.3 mg are associated with a slightly higher risk of this complication, whereas a dose greater than 0.3 mg poses a high risk of respiratory depression and should be avoided.

Morphine in any form should be used with caution in certain patients. Those patients include:

- Infants less than 6 months old
- Patients with renal failure
- Elderly patients
- Patients who are hemodynamically unstable
- Patients with known or suspected obstructive sleep apnea

Patients who receive morphine should ideally be monitored for signs of respiratory depression such as respiratory rate less than 8/minute, hypoxia (SpO_2 < 90%) or decreased level of consciousness. For intravenous morphine, patients should be monitored every 5 minutes for 20 minutes, then every hour. For patients receiving oral or intrathecal morphine, monitoring the patient every hour is sufficient. If signs of respiratory depression, arrest or inability to arouse the patient occur, naloxone can be given as the antidote. The dose of naloxone is 0.08 – 0.12 mg intravenously every 3 minutes until the patient's condition improves. For patients in respiratory arrest, a full dose of 0.4 mg can be given.

Other analgesics

There are numerous other analgesics which can be found in the appendix to this chapter. Intravenous fentanyl is often used intraoperatively during a standard anesthetic. A dose of 1 – 3 mcg/kg IV is a good starting point, but larger doses may be required for patients expected to experience severe postoperative pain. Ketamine is also a potent analgesic in addition to its anesthetic properties. Recent studies have shown that small doses (0.5

mg/kg) given intravenously toward the start of the procedure can significantly reduce post-operative pain scores. Dexamethasone in doses of 0.1 mg/kg IV or greater may also confer some analgesic effect. Additional analgesics including gabapentin, intravenous lidocaine, dexmedetomidine, clonidine and others may be useful when used pre or intra-operatively but are outside the scope of this chapter.

One point that should be emphasized is that the use of local anesthetics, either as a spinal anesthetic, peripheral nerve block, or local infiltration at the site of incision, can have a significant beneficial impact on postoperative pain scores. The authors would like to encourage all surgeons to consider the use of local anesthetics for each intervention, whenever possible. However, these too can lead to complications, the most deadly being local anesthetic systemic toxicity (LAST). This can usually be avoided by careful aspiration before each injection as well as by remembering the toxic dose of each local anesthetic. For lidocaine, a dose of up to 4.5 mg/kg plain lidocaine and a dose of up to 7 mg/kg lidocaine mixed with adrenaline is within the acceptable range and poses little risk of LAST. For bupivacaine a dose of 2.5 mg/kg is acceptable. Recall that a 1% solution will have a concentration of 10mg/mL.

Conclusions

As stated in the introduction, pain control is an important part of perioperative care and adequately controlling pain is possible even in low-resource settings. The most effective strategy is to create an analgesic plan BEFORE incision for every patient that incorporates one or more analgesics according to the expected severity and duration of pain. Using these strategies will improve the physical and emotional well-being of patients experiencing perioperative pain.

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Note: All Tables in following Appendix are from "Essential Pain Management" https://www.anzca.edu.au/safety-advocacy/global-health/essential-pain-management Used with permission

APPENDICES

Appendix 1: Medicine Formulary for Adults

Note: Exact formulations (e.g. tablet strength) may vary.
Exact morphine doses will depend on the individual patient.

Abbreviations:

- IM = intramuscular, IV = intravenous, PO = oral, PR = rectal, SC = subcutaneous
- OD = once daily, BD = twice daily, TDS = three times daily, QDS = four times daily

1. Simple Analgesics

Medication	Uses	Problems	Adult dose
Paracetamol / acetaminophen (Pamol, Panadol, Tylenol)	Generally very safe. Good for mild pain but can be useful for most nociceptive pain. Usually need to add other medications for moderate to severe pain. Also used to lower body temperature in fever.	Not all patients are able to take oral liquids or tablets. Can cause liver damage in overdose.	Usually given PO but can be given PR. PO or PR: 1G (two 500 mg tablets) QDS Maximum dose: 4G per 24 hours
Aspirin	Can be used with paracetamol. Good for nociceptive pain.	Not all patients are able to take oral tablets. Side effects: Gastro-intestinal problems, e.g. gastritis Kidney damage Fluid retention Increased risk of bleeding	PO: 600 mg (two 300 mg tablets) 4-6 hourly Maximum dose: 3.6 G per 24 hours

Diclofenac (Voltaren, Voltarol)	As above for aspirin.	As above for aspirin, but can be given IM or PR.	PO: 25-50 mg TDS PR: 100 mg OD IM: 75 mg BD Maximum dose: 150 mg per 24 hours
Ibuprofen (Brufen, Nurofen)	As above for aspirin.	As above for aspirin.	PO: 400 mg QDS
Naproxen (Naprosyn)	As above for aspirin.	As above for aspirin.	PO: 500 mg BD

2. Opioids

Medication	**Uses**	**Problems**	**Adult dose**
Codeine	Generally very safe. Often added to paracetamol and/or NSAIM for moderate pain.	Not all patients are able to take oral liquids or tablets. Similar side effects to other opioids: - Constipation - Respiratory depression in high dose Misunderstandings about addiction. Different patients require different doses (variable dose requirement).	Usually given PO but sometimes given IM. PO or IM: 30-60 mg 4-hourly
Tramadol (Tramal)	Can be used with paracetamol and/or opioids for nociceptive pain. Sometimes helpful for neuropathic pain. Less respiratory depression and constipation than morphine.	Not widely available. Nausea and vomiting Confusion	PO or IV: 50-100 mg QDS

Morphine	Very safe if used appropriately. Often added to paracetamol and/or NSAIM for moderate to severe pain. Oral morphine very useful for cancer pain. In general, should be avoided in chronic non-cancer pain. Available as either fast release tablets or syrup, or slow release tablets.	Similar problems to other opioids: Constipation Respiratory depression in high dose Nausea and vomiting Myths about addiction Oral dose is not the same as the injected dose.	Can be given PO, IV, IM or SC. Different patients require different doses. Oral dose is 2-3 times the injected dose. PO (fast): 10-30 mg 4-hourly (e.g. for controlling cancer pain) PO (slow): BD dosing (may need high doses for cancer pain) IV: 2.5-10 mg (e.g. during or after surgery) IM or SC: 5-10 mg 4-hourly
Pethidine (Demerol)	As above for morphine. Often added to paracetamol and/or NSAIM for moderate to severe pain.	As above for morphine. Seizures caused by metabolite (norpethidine) if high dose given for more than 48 hours.	PO: 50-100 mg 4-hourly IV or IM dose about 10 times morphine dose. IV: 25-50 mg (e.g. during or after surgery.) IM or SC: 50-100 mg 4-hourly
Oxycodone (Oxynorm, Oxycontin)	As above for morphine Can be used for cancer pain. Available as fast release (Oxynorm) or slow release (Oxycontin).	As above for morphine. Not widely available.	PO (fast): 5-10 mg 4-hourly PO (slow): 10 mg BD, increased as needed.

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3. Other Analgesics (in alphabetical order)

Medication	Uses	Problems	Adult dose
Amitriptyline	Useful in neuropathic pain. Also used to treat depression and improve sleep.	Sedation Postural hypotension (low blood pressure) Cholinergic side effects: Dry mouth Urinary retention Constipation	PO: Usually 25 mg at night "Start low, go slow", especially in elderly patients (e.g. start at 10 mg, increase every 2-3 days as tolerated)
Carbamazepine (Tegretol)	Anticonvulsant ("membrane stabiliser") Useful in neuropathic pain.	Sedation Unsteadiness Confusion in high dose	PO: 100-200 mg BD, increased to 200-400 mg QDS as tolerated "Start low, go slow", especially in elderly patients
Clonidine	May be useful if pain is difficult to treat.	Not widely available. Sedation Hypotension	IV: 15-30 mcg 15-minutely up to 1-2 mcg/kg PO: 2 mcg/kg
Gabapentin	Anticonvulsant ("membrane stabiliser") Useful in neuropathic pain.	Sedation	PO: 100 mg TDS, increased to 300 mg TDS as tolerated
Ketamine	May be useful in severe pain (nociceptive or neuropathic). Also used as a general anaesthetic	Sedation (only need small dose for pain relief) Dreams, delirium, hallucinations	IV: 5-10 mg for severe acute pain SC infusion: 100 mg over 24 hours for 3 days, can be increased to 300 mg, then 500 mg per 24 hours
Sodium valproate (Epilim)	Anticonvulsant ("membrane stabiliser") Useful in neuropathic pain.	Gastro-intestinal side effects, sedation	PO: 200 mg 8-12-hourly

Appendix 2: Paediatric Medicine Doses

Note: Exact formulations (e.g. tablet strength) may vary.
Exact morphine doses will depend on the individual patient.

Abbreviations:

- IM = intramuscular, IV = intravenous, PO = oral, PR = rectal, SC = subcutaneous
- OD = once daily, BD = twice daily, TDS = three times daily, QDS = four times daily

1. Simple Analgesics

Paracetamol / acetaminophen	PO or PR: 15 mg/kg 4-hourly Maximum dose: 90 mg/kg per 24 hours
Aspirin	PO: 15 mg/kg 4-6 hourly Not for children under 10 years old
Diclofenac Ibuprofen	PO or PR: 1 mg/kg BD or TDS PO: 5 mg/kg QDS
Indomethacin	PO: 0.5-1 mg/kg TDS
Naproxen	PO: 5-10 mg/kg BD or TDS Not for children under 2 years old

2. Opioids

Codeine (**see below**)	PO: 0.5-1 mg/kg 4-hourly
Tramadol	PO or IV: 1-2 mg/kg QDS
Morphine – fast	IV: 0.02 mg/kg 10-minutely (e.g. after surgery) IM or SC: 0.1-0.2 mg/kg 3-4-hourly PO (fast release): 0.2-0.4 mg/kg 3-4-hourly (e.g. for controlling cancer pain)
Morphine – slow	PO (slow release): Start with 0.6 mg/kg BD, increase every 48 hours as required
Pethidine / meperidine	IV: 0.5 mg/kg 10-minutely (e.g. after surgery) IM: 1mg/kg 3-4-hourly
Oxycodone	IV, SC or PO (fast): 0.1 mg/kg 4-hourly PO (slow): 0.2-0.5 mg/kg BD

3. Other Analgesics

Amitriptyline	PO: 0.5 mg/kg at night
Carbamazepine	PO: 2 mg/kg BD to TDS
Clonidine	PO: 2.5 mcg/kg as a pre-med for painful procedures
Sodium valproate	PO: 5 mg/kg BD to TDS Can be increased to 10 mg/kg/dose

Note:
In the United Kingdom and many other countries, **codeine is not recommended for** children aged less than or equal to 12 years.

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Appendix 5: WHO Essential Medicines List

The following table is based on the WHO Model List, 16th edition (updated). Medicines useful for managing pain can be found in a variety of sections of the list (e.g. anticonvulsants, medicines used in mood disorders).

For the full list, see:
http://www.who.int/medicines/publications/essentialmedicines/en/

Analgesics, Antipyretics, Non-Steroidal Anti-Inflammatory Medicines (NSAIMs) (section 2)	
Non-opioids and NSAIMs (section 2.1)	
Acetylsalicylic acid (aspirin)	**Suppository:** 50 mg to 150 mg **Tablet:** 100 mg to 500 mg
Ibuprofen (>3 months)	**Tablet:** 200 mg; 400 mg
Paracetamol	**Oral liquid:** 125 mg per 5ml **Suppository:** 100 mg **Tablet:** 100 mg to 500 mg
Opioid Analgesics (section 2.2)	
Codeine	**Tablet:** 15 mg (phosphate); 30 mg (phosphate)
Morphine	**Injection:** 10 mg (morphine hydrochloride or morphine sulfate) in 1 ml ampoule **Oral liquid:** 10 mg (morphine hydrochloride or morphine sulfate) per 5 ml **Tablet:** 10 mg (morphine sulfate) **Tablet (prolonged release):** 10 mg; 30 mg; 60 mg (morphine sulfate)
Anticonvulsants, Antiepileptics (section 5)	
Carbamazepine	**Oral liquid:** 100 mg per 5 ml **Tablet (chewable):** 100 mg; 200 mg **Tablet (scored):** 100 mg; 200 mg

Valproic acid (sodium valproate)	**Oral liquid:** 200 mg/5 ml **Tablet (crushable):** 100 mg **Tablet (enteric-coated):** 200 mg; 500 mg
Medicines Used in Mood Disorders (section 24)	
Amitriptyline	**Tablet:** 25 mg (hydrochloride)
Other Medicines	
General Anaesthetics (section 1.1)	
Ketamine	**Injection:** 50 mg (as hydrochloride) per ml in 10 ml vial
Nitrous oxide	**Inhalation**
Local Anaesthetics (section 1.2)	
Bupivacaine	**Injection:** 0.25%; 0.5% (hydrochloride) in vial
Lidocaine (lignocaine)	**Injection:** 1%; 2% (hydrochloride) in vial
Lidocaine + epinephrine (lignocaine + adrenaline)	**Injection:** 1%; 2% (hydrochloride) + epinephrine 1:200 000 in vial
Antiemetic Medicines (section 17.2)	
Dexamethasone	**Injection:** 4 mg/ml in 1-ml ampoule **Oral liquid:** 0.5 mg/5 ml; 2 mg per ml **Solid oral dosage form:** 0.5 mg; 0.75 mg; 1.5 mg; 4 mg
Metoclopramide (not in neonates)	**Injection:** 5 mg (hydrochloride)/ml in 2-ml ampoule **Tablet:** 10 mg (hydrochloride)
Ondansetron (>1 month)	**Injection:** 2 mg base/ml in 2-ml ampoule (as hydrochloride) **Oral liquid:** 4 mg base/5 ml **Solid oral dosage form:** Eq 4 mg base; Eq 8 mg base; Eq 24 mg base.