ANALGESIA IN A NUTSHELL

INTRODUCTION

The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is influenced by attitudes, beliefs, personality and social factors, and can affect emotional and mental wellbeing.

There are three main categories of pain: acute, chronic and cancer pain.

Acute pain lasts for a short time and occurs following surgery or trauma or other condition. It acts as a warning to the body to seek help. Although it usually improves as the body heals, in some cases, it may not.

Chronic pain lasts beyond the time expected for healing following surgery, trauma or other condition. It can also exist without a clear reason at all. Although chronic pain can be a symptom of other disease, it can also be a disease in its own right, characterised by changes within the central nervous system.

Cancer pain can occur in patients with early stage and advanced disease, and in cancer survivors as a severe and debilitating side-effect of treatment. (3.)

The physiological and pathological pathways involved with pain transmission are complex, and not in the scope of this brief. Many different receptors and messengers are involved, from peripheral nociceptors via the spinal cord, to the brain. It makes sense to target specific mechanisms where they are obvious (e.g. anti-inflammatories for inflammatory pain), and the role of multimodal analgesia plays a large role in peri-operative pain management.

Multimodal analgesia employs the theory that agents with different mechanisms of analgesia may have synergistic effects in preventing or treating acute pain when used in combination. Using individual agents in optimal dosages maximizes efficacy and minimizes side effects from large doses of one single analgesic (mainly opioids). (1.)

Effective, timely management of acute pain is the most important factor in preventing the progression to chronic post-operative pain which is a debilitating condition, and difficult to treat.

ASSESSING PAIN

1.) Taking a history
   - Onset and duration of pain
   - Precipitating factors
   - Nature of pain (sharp/stabbing/ crushing/ throbbing/aching/burning/tingling?)
   - Intensity (see below)
   - What makes it worse?
   - What helps it?
   - Any associated factors (nausea/ sweating/ weakness etc.)
   - What medications do you take for pain? For how long? What dose?
   - Any co-morbidities?
   - What other medications?
   - Any allergies?
2.) Pain score:

- Numeric rating scale (NRS) Most commonly used:

![Pain Score 0-10 Numerical Rating](image)

- Wong-Baker faces – used in paediatrics, or if communication barrier:

![Wong-Baker Faces Pain Rating Scale](image)

- Visual analogue Scale (VAS) – pick a point on the continuum:

![Visual Analog Scale](image)

- Word descriptor scale:
  
  No pain – mild pain – moderate pain – severe pain – excruciating pain

MANAGING PAIN:

Once making an assessment of the nature and severity of the pain, you can decide how to manage it.

Generally, start simple, with oral non-opioid medications and escalate as needed. (See WHO analgesic ladder below) However, if someone is in extreme pain, a dose of oral paracetamol and ibuprofen isn’t going to touch it! Use some clinical acumen and common sense, it may be appropriate to start with an intravenous dose of opioid (with suitable monitoring and medical staff presence), and scale back down once the pain is under control.

In addition, specific types of pain, e.g. neuropathic pain, respond to specific treatments, and input from the acute pain service may be needed.

Below, please find some simple guidelines from the World Health Organisation, some essential pharmacology of commonly used analgesic drugs, and advice regarding pitfalls, side effects and contra-indications of analgesics. You will also find when to refer to the Pain Service, “Do’s and Don’ts” for the patient on a PCA, and considerations when discharging your patient on pain medications.
We have devised a flowchart to guide you when confronted with a patient in pain on the ward, and please also refer to the MNHHS Prescribing Guidelines which can be found on the Lib Guide.

**WORLD HEALTH ORGANISATION ANALGESIC LADDER (4)**

![World Health Organization Analgesic Ladder for Treating Cancer Pain](image)

The World Health Organisation (WHO) proposed this guideline in 1986 specifically for the management of cancer pain. The ladder proposes starting with simple non-opioid medication. If the pain is not properly controlled with a non-opioid, one should then introduce a weak opioid. If still insufficient to treat the pain, one can begin a more powerful opioid. One should never use 2 products belonging to the same category simultaneously. The analgesic ladder also includes the possibility of adding adjuvant treatments for neuropathic pain or for symptoms associated with cancer. Over the last three decades this model has attracted criticism, but the five simple recommendations that form its cornerstone are still relevant:

1.) Oral analgesics are preferred wherever possible

2.) Analgesics should be prescribed at regular intervals depending on the drug’s duration of efficacy, not simply on a “when needed” basis. Dose should be adjusted to make the patient comfortable.

3.) Analgesics should be prescribed according to pain intensity as measured by a validated Pain Score.

4.) Dosing of analgesia should be adapted to the individual.

5.) Analgesics should be prescribed with a constant concern for detail. The daily analgesic regimen should be explained to the patient and his/her family, as well as medical staff who will administer the drugs.

The original ladder has been adapted for acute pain and chronic non-cancer pain. The new ladder realizes that simple analgesics may be inadequate for intense pain, and allows a fast-track regime starting at step three and working down. This revision integrates a fourth step and includes consideration of invasive techniques, such as nerve blocks and neurolysis and brain stimulators. It has also been proposed and applied in the treatment of pediatric pain, can be used for acute pain in emergency departments and in postoperative situations.
ESSENTIAL PHARMACOLOGY:

One way of classifying analgesic drugs is as follows:

- Simple, non-opioid anagesics, such as paracetamol and NSAIDS
- Opioids
  - Secondary analgesics (these are drugs developed for other uses e.g. anti-epileptics, that happen to have anagesic properties too.)
  - Other drugs, e.g. Ketamine, Tramadol, Tapentadol
  - Adjuvants, such as muscle relaxants, antispasmodics, topical preparations.

SIMPLE/NON-OPIOID ANALGESICS:

PARACETAMOL

The regular use of paracetamol may reduce opioid requirements by 20-30% (i.e. it is opioid-sparing)

Prescribe: PARACETAMOL 1g orally or rectally every 6 hours. Max daily dose 4g daily.

IV paracetamol is restricted to anaesthetists for post-operative patients who are nil by mouth for a maximum duration of 48 hours

Dosing precautions:

- cachectic, frail, elderly patients, or weight < 50kg – maximum daily dose 60mg/kg
- Check that paracetamol has not been given / prescribed elsewhere –“one off” doses, PRN medications, in theatre during anaesthesia etc. Beware trade names and combination medications that include paracetamol.

Contra-indications:

- chronic liver disease, or extensive liver surgery

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

- Used as part of a multi-modal technique; regular use decreases opioid usage by 30-50% (Opioid sparing)
- May play a role in preventing the progression from acute to chronic post-operative pain
- Useful in dynamic pain (e.g. during coughing)
- Useful for treating pain with an inflammatory component
- Inadequate as a sole agent for severe pain.
Prescribe: **IBUPROFEN** 400mg orally 8hourly after food for 3 days then review

**Alternatives:**

**DICLOFENAC** suppositories 100mg once or twice daily

**KETOROLAC** IM 10-30mg 6hrly (Only on specialist advice, and monitor renal function closely. Maximum 5 days)

**PARECOXIB** injection – restricted for use as a single peri-operative dose for post-op pain. Often given during anaesthesia; no other NSAID to be given within 24 hours of PARECOXIB

**Dosing precautions:** - Risk of NSAID induced renal failure is increased in elderly patients, pre-existing renal dysfunction, hypotension, dehydration, and with other nephrotoxic agents such as ACE inhibitors, frusemide, gentamycin.
- Risk of cardiovascular thrombotic events
- Risk of gastric ulceration and GI haemorrhage
- Caution in asthmatics whose disease may be exacerbated by aspirin and non-selective NSAIDS
- Disrupt platelet function; increased risk of peri-operative bleeding
  
  Use the lowest effective dose for the shortest amount of time!

**Caution in elderly >65**

**Contra-indications:** - Known hypersensitivity to aspirin or other NSAIDS
  - Severe asthmatics
  - Patients at risk of bleeding, or on concurrent anticoagulants
- Known renal failure
- Known IHD, previous CABG, vascular surgery or heart disease.

**OPIOIDS**

- Used for the treatment of **moderate to severe pain** as part of a multimodal regime.
- Due to inter-patient differences, **no single opioid suits all**: some opioids are better tolerated in some patients than others. Rotate opioids if efficacy or side effects are unsatisfactory
- It make take **3 or more doses** to establish adequate opioid concentrations
- Beware the **opioid naïve patient** – start low and increase dose to desired effect
- Higher doses may be appropriate in the **opioid tolerant patient**, as long as side effects are minimal. Lower the dose equivalent by 25% if rotating opioids in these patients as cross-tolerance between different opioids is not complete.
- Severe pain requires **regular** dosing, not just PRN. PRN doses are prescribed concurrently for breakthrough pain. Review analgesic requirements daily.
- As soon as PRN usage decreases (<4 or 5 doses), wean dose of regular opioid by 20%.
- **Aim to wean patient off strong opioids as soon as practical.**
- **Transdermal patches** have no role in managing acute pain. If a patient is already on transdermal patches for chronic pain, continue patches and add additional analgesia as appropriate.
- For patients in whom **morphine is contra-indicated** – contact the APS.

**OXYCODONE** (immediate release IR) **ENDONE®**

Prescribe: **OXYCODONE** 5-10mg orally every 4 hours PRN

Good oral bioavailability (60-70%)

Onset of analgesia 15 minutes, peak effect 60 minutes.

**Dosing precautions:** decrease dose in elderly – 2.5-5.mg

- Metabolised in liver (caution in liver dysfunction)
- Do not prescribe IR oxycodone while a PCA is running.
**OXYCODONE (controlled release CR) OXYCONTIN®**

Prescribe: **OXYCODONE CR 10mg orally 12 hourly**

Review every 2 days, reduce dose in elderly / liver dysfunction.

CR form can run concurrently with PCA

**OXYCODONE / NALOXONE (TARGIN®)**

Partial agonist/antagonist – results in less side effects, in particular less bowel dysfunction compared with Oxycontin®

Prescribe: **OXYCODONE / NALOXONE 10/5mg orally 12 hourly**

Review every 2 days, reduce dose in elderly / liver dysfunction.

Can run concurrently with PCA

See all opioid side effects and contra-indications below.

**TRAMADOL**

- Opioid effects as well as serotonin and noradrenaline reuptake inhibition
- For moderate pain, or as part of a multi-modal analgesic regime. As a sole agent, probably not adequate for severe pain.
- Causes less respiratory depression and constipation than pure opioids
- Can be helpful in the treatment of neuropathic pain.

Prescribe: **TRAMADOL 50mg orally every 6 hours**

Or **TRAMADOL SR 100-200mg every 12 hours**

Prescribing precautions:

- Decrease does in renal dysfunction CrCl < 30ml/min
- Avoid if CrCl < 10ml/min
- Can cause nausea, vomiting, dry mouth, dizziness and drowsiness
- It can have reduced effect in 10% of Caucasians with reduced CYP2D6 activity, and excess effects in ultra-rapid metabolisers.

Contra-indications of Tramadol:

- Epilepsy, head injury or other medication that lowers seizure threshold.
- Concomitant use with SSRIs, TCAs, MAOIs – risk of serotonin syndrome
- Inhibits metabolism of warfarin.

**FENTANYL**

- Metabolised in the liver to mostly inactive metabolites, opioid of choice in renal impairment
- Due to short duration of action, often given IV, or by PCA
- Fentanyl Transdermal patches are not helpful in acute pain management
- It is unlikely that you will prescribe IV fentanyl on the ward. It is not advisable to give IV opioids in the ward unless administered or supervised by a doctor, and closely monitored.

**MORPHINE**

- Most commonly used opioid
- Metabolised in the liver to active metabolites which are excreted renally
- Some patients may be on controlled release morphine e.g. Kapanol. We do not prescribe it regularly in Caboolture Hospital for acute pain.
- Sometimes subcutaneous morphine is prescribed until oral analgesics can be initiated. The sub-cut dose is age dependent, see below for starting doses:
<table>
<thead>
<tr>
<th>Patient Age (years)</th>
<th>Subcutaneous dose range (mg) every 3 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-39</td>
<td>7.5-12.5</td>
</tr>
<tr>
<td>40-59</td>
<td>5-10</td>
</tr>
<tr>
<td>60-69</td>
<td>2.5-7.5</td>
</tr>
<tr>
<td>70-85</td>
<td>2.5-5</td>
</tr>
<tr>
<td>&gt;85</td>
<td>2-3</td>
</tr>
</tbody>
</table>

**BUPRENORPHINE**
- Partial agonist
- Only to be commenced by APS
- You may encounter this in patients who have had bowel surgery, and who are nil by mouth
- You may encounter chronic pain patients who have a buprenorphine patch (NORSPAN®) or patients on a drug rehabilitation program taking sublingual SUBUTEX® or SUBOXONE®

**PETHIDINE**
- LAM restriction – for use by anaesthetists and obstetricians only.
- Commonly used in obstetric epidurals (though not often in Caboolture Hospital).

**ADJUVANTS AND CO-ANALGESICS YOU MAY ENCOUNTER**

**KETAMINE**
- NMDA receptor antagonist which may reduce opioid requirements, opioid tolerance
- May be used as part of a multi-modal analgesic regime, especially in patients who are opioid tolerant
- Prescribed by APS, usually as a low dose infusion
- Commonly causes hallucinations, vivid dreams, tachycardia, hypertension, nausea

**CLONIDINE**
- $\alpha_2$ adrenoreceptor agonist, initially developed as an antihypertensive, but found to have analgesic and sedative properties too.
- May be prescribed by APS as part of a multimodal analgesic regime

**AMITRIPTYLINE**
- Tricyclic antidepressant with analgesic properties
- Useful first line drug for neuropathic pain
- Prescribe: AMITRIPTYLINE 10-25mg PO nocte

**GAPAPENTIN/PREGABALIN**
- Anti-epileptic medications which are useful in the treatment of neuropathic pain
- Prescribe: PREGABALIN 75mg PO twice daily, increasing as tolerated every 3-7days to a maximum daily dose of 600mg
- Renally excreted, reduce dose if CrCl, 30ml/min
- Patients with neuropathic pain probably require input from APS
OTHER CONSIDERATIONS IN PAIN MANAGEMENT

- **Exclude surgical or medical complications** if pain is unexpected or out of proportion to the insult, e.g. ischaemia, haemorrhage, compartment syndrome
- **Wind pain** with return of bowel function. Discourage patients from using opioids for wind pain. NSAIDs may be helpful, or peppermint water 10-20ml orally PRN
- **Intercostal drains** can be extremely painful and uncomfortable in situ. Consider paracetamol, NSAIDs, Ketamine, or injection of local anaesthetic down chest drain

CAUTIONS AND CONTRA-INDICATIONS PERTAINING TO OPIOIDS

All opioids have the potential to cause side effects. Attempt to use the lowest possible dose that provides adequate pain relief with the help of multimodal analgesia and adjuncts, and wean off opioids as soon as possible. Excessive side effects should prompt cessation or rotation of the opioid.

- **Constipation** – 100% incidence! Always consider prescribing aperients
  - Softener such as: Coloxyl® 120mg; 2 tablets with evening meal
  - Stimulant such as: bisacodyl 5 mg; 1-2 tablets in the evening OR Coloxyl and Senna® 2 tablets orally twice daily
  - Check with surgeons if prescribing a gut stimulant after bowel resection / anastomosis.

- **Nausea and vomiting** – very common. Always prescribe anti-emetics with opioids
  - Ondansetron 4mg wafer PO up to 3 times a day
  - Metoclopramide(Maxalon®) 10mg PO 8hrly is commonly prescribed but not very effective
  - Other options include prochlorperazine 5mg orally, or droperidol 0.25 – 0.5mg (discuss with APS)

- **Itching** – often due to histamine release, not an allergy. Prescribe:
  - Loratidine 10mg PO daily
  - Avoid sedating antihistamines such as promethazine (Phenergan®)
  - Severe itching may require naloxone 40mcg IV or subcutaneously (discuss with APS)
  - Itching after intrathecal (spinal route) opioids is not histamine-related and does not respond to anti-histamines such as loratidine. Naloxone is the best option if the itch is bothersome, but discuss with APS

- **Respiratory depression** is a common and serious side effect of opioid medication. This can occur up to 24 hours after a dose of morphine (including spinal morphine).
  - Beware cumulative dosing!
  - Avoid prescribing sedating medication with or after opioids, e.g. antihistamines and benzodiazepines!
  - Sedation is the most important modality to monitor as a predictor of respiratory depression. A drop in oxygen saturation is a late sign, and may give a false assurance if the patient is receiving supplemental oxygen. See table below:
**SEDATION SCORE:**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Awake and alert</td>
</tr>
<tr>
<td>1</td>
<td>Slightly drowsy, easily rousable</td>
</tr>
<tr>
<td>2</td>
<td>Frequently drowsy, rousable, drifts off to sleep during conversation</td>
</tr>
<tr>
<td>3</td>
<td>Somnolent, little or no response to physical stimulation</td>
</tr>
<tr>
<td>S</td>
<td>Normal sleep. If respiratory rate $\leq 10$, and irregular breathing pattern – wake to assess level of consciousness</td>
</tr>
</tbody>
</table>

**AIM TO KEEP SEDATION SCORE < 2**

- **Urinary retention** can occur. Rarely necessary to use naloxone.

- **Cognitive dysfunction and confusion** can occur, especially in the elderly. Reduce dose or try rotating opioids.

- **Tolerance and hyperalgesia**: as the body grows accustomed to opioid therapy, increasing doses are required to achieve the same analgesic effect. At very high doses, paradoxically, opioids can induce a hypersensitivity to pain. This is one reason why one should limit the dose and duration of opioids as much as possible, and use other modalities of analgesia. Opioids are rarely a solution for chronic pain (certainly not as sole agents), although many chronic pain patients are prescribed opioids and reliant on them.

- **Addiction and dependence**: physical dependence can occur after 7-10 days depending on dose used. Addiction to opioids is rare when they are used to treat acute pain. Wean the opioid dose by 20% every couple of days as tolerated until able to discontinue.

**MONITORING THE PATIENT ON OPIOID ANALGESIA/PCA/ PCEA**

**WHAT TO MONITOR:**

Any patient on analgesia should at the very least have observations 4 times daily, including Sedation score, pain score and functional activity score. Consider requesting increased frequency of obs for patients who are possibly sedated or requiring large amounts of opioids. Follow QADDS interventions for increasing sedation and pain scores. Be aware of QLD Health & Caboolture Standing Order for Naloxone (follow the links below):

Statewide Standing Order Naloxone Hydrochloride, January 2015 DOC (271k)

Procedure- Medication: Intravenous (IV) Naloxone

All monitoring requirements for PCA/Epidurals and Regional Analgesia are outlined on the pain management monitoring forms. Sedation score and pain scores will not be recorded on the QADDS form if a pain management monitoring form is in use.
For intravenous, epidural and regional analgesia, and intrathecal/epidural morphine:
- Sedation score; pain score, Functional activity score (FAS), PONV score, pruritic, cumulative total of drugs used, continuous infusion rate, demands delivered.

WHEN / HOW OFTEN?

For PCA and other IV opioids:
- Hourly for 8 hours
- 2 hourly for 16 hours
- Then 4 hourly
This also occurs every time you adjust the dose

For intrathecal / epidural morphine:
- Hourly for 12 hours
- 2 hourly for 12 hours
- Then 4 hourly

In addition, for epidural or regional analgesia, assess:
- Motor weakness, block height, catheter sites, signs of local anaesthetic toxicity, or new onset of back pain.
- Every 4 hours for duration of infusion, and continue monitoring for motor weakness / new back pain for 24 hours after cessation.

WHEN SHOULD I CALL THE ACUTE PAIN SERVICE? (8209 or after hours: 8212)

- If there is any issue with a PCA
- If a patient has any issue related to a spinal, or epidural, or has a PCEA (epidural PCA)
- Please always contact APS if you wish to change any PCA or epidural settings, or wish to prescribe any sedating medications or short-acting immediate release opioids while a patient is on a PCA
- Any patient with regional block catheters in situ
- Chronic pain patients who are complex and whose pain is difficult to manage.
- Any patient who has unresolved pain, and you have exhausted your resources. (See flowchart for pain management on the ward)
WHAT DO I NEED TO KNOW ABOUT PCAs / EPIDURALS / REGIONAL BLOCK CATHETERS?

These are always under the care of Anaesthetics and the Acute Pain Service (APS), if in doubt, call them!

- **PCAs** - patient controlled analgesia
  - Usually used for post-operative pain, rib fractures, or acute exacerbations of chronic pain.
  - Requires a patient with normal cognitive function who understands how to use it.
  - May have fentanyl, morphine or oxycodone prescribed, usually a 1ml patient bolus (with appropriate concentration of opioid) with a 5 minute lock-out. i.e. the next dose will only be delivered 5 minutes after the previous, no matter how often the patient presses the button.
  - We generally don’t run background continuous infusions.
  - Should have a dedicated line with an anti-reflux valve. Do not inject anything else through the PCA line in case you push in a bolus of opioid!
  - Observations as described above.
  - **Do not prescribe short-acting opioids such as Endone** while a PCA is running (without anaesthetic approval)
  - **Do not prescribe sedative medications** such as benzodiazepines and antihistamines (without anaesthetic approval)

- **Epidurals**
  - Frequently used in obstetrics to manage labour pain, also used in general surgery for post-operative pain relief.
  - Recommended as part of ERAS protocol to allow early mobilization and minimization of opioids and their side effects
  - Usually has a background infusion running with patient controlled boluses as required.
  - The more dilute the local anaesthetic, the less motor weakness, while retaining sensory loss / analgesia. We commonly use 0.2% ropivacaine (with or without fentanyl 2-4mg/ml). Ideally the patient should still have leg movement, or even be able to walk, with assistance. It is not uncommon though to get some motor loss, or even a unilateral block. Response should be to reduce or stop the background infusion, and call APS.

- **Spinals**
  - More common in obstetric practice, but some general surgical procedures may be done under spinal anaesthesia.
  - Spinal is a one-shot technique involving injection of local anaesthetic into the CSF in the intrathecal space, often with the addition of a small dose of opioid.
  - Expect a patient to have motor weakness for up to 3 or 4 hours after a spinal anaesthetic.
  - Intrathecal morphine is extremely effective; a small dose of 100micrograms offering up to 16 hours of analgesia, long after the local anaesthetic has worn off. Risks include delayed respiratory depression, pruritis (>90%), nausea and vomiting.
  - Due to the risk of delayed respiratory depression, the anaesthetist should place a neon sticker in the medication chart advising against administration of any IV opioids for 24 hrs after injection. Oral opioids may be given if required, but beware of any drugs with sedative effects.
  - The itch produced by intrathecal morphine is not due to histamine release, and, contrary to popular belief, does not respond to loratidine. Untreated, it should resolve within 24 hours, but if the patient requires some relief, a small dose of naloxone 40 mcg is the best antidote.
Patients are often discharged with unnecessarily large quantities of opioid analgesia. This results in surplus opioids lying around in people’s homes after a hospital discharge. With the high incidence of side effects, including tolerance and addiction, this is not advisable.

- Aim to send a post-operative patient home with a tapering dose of oral opioids for a maximum of 3-5 days depending on the nature of their pain, or extent of their surgery.
- Discussion with the patient and/or their family is crucial, so they understand how to taper their analgesia. Discuss other methods of analgesia, such as paracetamol, NSAIDs, if not contra-indicated, warm packs, or physiotherapy if appropriate. Advise them to follow up with their GP if further pain relief is required.
- Communication with the GP is equally important – make sure the GP is aware of the discharge medication plan.

e.g. a typical discharge script for a patient discharged day 5 after a laparoscopically assisted anterior resection may be as follows: (Assume a middle-aged patient with no allergies or contra-indications to meds)

- Paracetamol 1G orally 6 hourly x 7 days
- Oxycodone/naloxone (Targin®) 10/5mg orally 12 hourly x 2 days
- Oxycodone IR 5mg orally 4hourly PRN x10 tablets
- Ondansetron wafers 4mg orally up to 3 times daily x 6 wafers
- Coloxyl/Senna 1 sachet at bedtime x5

For complex patients, or if in doubt, discuss this with the Acute Pain Service.

References:


