

SUMMARY OF GUIDELINES OF PAIN MANAGEMENT

Pain can be due to

1. **chronic diseases** such as arthritis, sickle cell disease and rheumatologic disorders constitute important causes of musculoskeletal pain and chronic conditions such as inflammatory bowel disease can cause recurrent abdominal pain.

2. **trauma – physical, thermal, electrical and chemical injuries** (e.g. burns) and lead to, for instance, phantom limb pain or lower back pain.

3. **life threatening diseases** and their treatment such as simultaneous acute and chronic pain in cancer and HIV/AIDS.

Idiopathic pain has no identifiable etiology. Examples are most headaches and recurrent abdominal pain.¹

Types of pain according to duration:

Acute pain is of sudden onset, is felt immediately following injury, is severe in intensity, but is usually short-lasting

Chronic pain is continuous or recurrent pain that persists beyond the expected normal time of Healing

Episodic or recurrent pain occurs intermittently over a long period of time and the child can be pain free in between each painful episode.

Breakthrough pain is characterized as a temporary increase in the severity of pain over and above there-existing baseline pain level, e.g. if a child is taking pain medicines and has good pain control with a stable analgesic regimen and suddenly develops acute exacerbation of pain. It is usually of sudden onset, severe, and of short duration.

End of dose pain results when the blood level of the medicine falls below the minimum effective analgesic level towards the end of dosing interval.

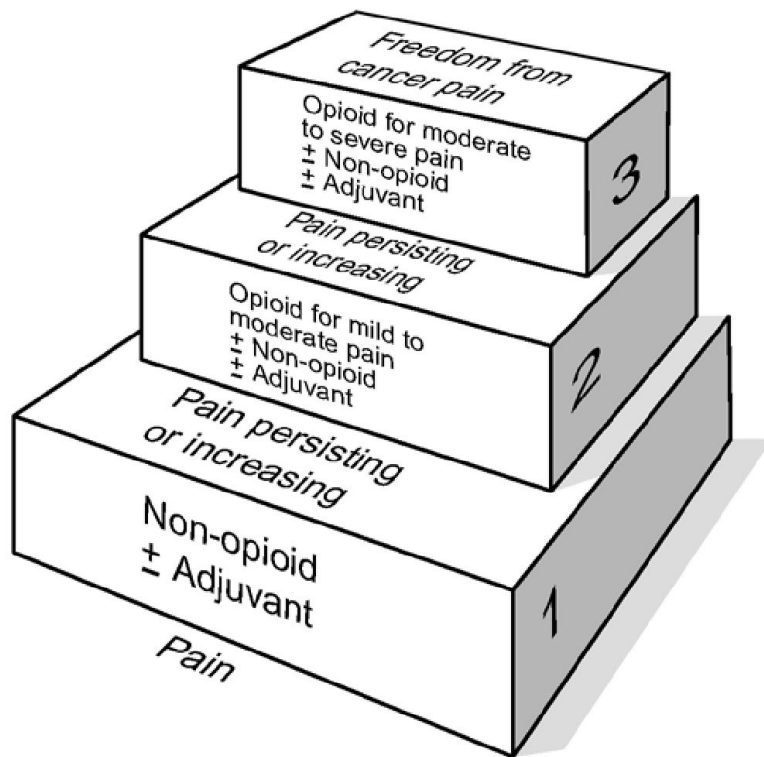
The main **behavioural indicators of acute pain** are:

- facial expression
- body movement and body posture
- inability to be consoled
- crying
- groaning.

These behavioural responses may be reduced in persisting pain, except during acute exacerbation.

Behaviour in children with chronic pain can include (32):

- abnormal posturing
- fear of being moved
- lack of facial expression
- lack of interest in surroundings
- undue quietness
- increased irritability
- low mood
- sleep disruption
- anger
- changes in appetite
- poor school performance



This is no longer used

Now the second step is omitted and it is only a 2 step approach

The three-step analgesic ladder recommended the use of codeine as a weak opioid for the treatment of moderate pain, while the two-step approach considers the use of low doses of strong opioidanalgesics for the treatment of moderate pain.

Drugs

The World Health Organization (WHO) has produced new guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. They include several clinical recommendations, including a new two-step approach of pharmacological treatment. These guidelines exclude acute traumas, and perioperative and procedural pain.^[5]

The guidelines have replaced the previous three-step guidelines which recommended the use of codeine as a weak opioid for the treatment of moderate pain. The two-step approach advises the use of low doses of strong opioid, which is considered safer than using codeine or tramadol which are weak opioids.

The correct use of analgesic medicines will relieve pain in most children with persisting pain due to medical illness, and relies on the following key concepts:

- Using a two-step strategy.
- Dosing at regular intervals.
- Using the appropriate route of administration.
- Adapting treatment to the individual child.

The first step: mild pain

Paracetamol and ibuprofen are the medicines of choice in the first step (mild pain).

Above 3 month ORAL para and ibu

Below 3 month PARACETAMOL ONLY

Table 3.1 Non-opioid analgesics for the relief of pain in neonates, infants and children

Medicine	Dose (oral route)			Maximum daily dose
	Neonates from 0 to 29 days	Infants from 30 days to 3 months	Infants from 3 to 12 months or child from 1 to 12 years	
Paracetamol	5–10 mg/kg every 6–8 hrs ^a	10 mg/kg every 4–6 hrs ^a	10–15 mg/kg every 4–6 hrs ^{a,b}	Neonates, infants and children: 4 doses/day
Ibuprofen			5–10 mg/kg every 6–8 hrs	Child: 40 mg/kg/day

^a Children who are malnourished or in a poor nutritional state are more likely to be susceptible to toxicity at standard dose regimens due to reduced natural detoxifying glutathione enzyme.

^b Maximum of 1 gram at a time.

The second step: moderate to severe pain

If pain severity associated with a medical illness is assessed as moderate or severe, the administration of a strong opioid is necessary. Morphine is the medicine of choice for the second step, although other strong opioids should be considered and made available to ensure an alternative to morphine in case of intolerable side-effects.

To obtain a dose that provides adequate relief of pain with an acceptable degree of side-effects the doses of morphine or other strong opioids need to be gradually increased until effective. Unlike paracetamol and NSAIDs, there is no upper dosage limit for opioid analgesics because there is no “ceiling” analgesic effect. The appropriate dose is the dose that produces pain relief for the individual child. The goal of titration to pain relief is to select a dose that prevents the child from experiencing pain between two doses using the lowest effective dose. This is best achieved by frequent assessment of the child’s pain relief response and adjusting the analgesic doses as necessary.

Long-term opioid use is usually associated with constipation and patients should also receive a combination of a stimulant laxative and a stool softener prophylactically.

Pethidine (also called: mepiridine) should no longer be used, because it is considered inferior to morphine due to its toxicity on the central nervous system (74).

Oral tablet morphine formulations are commercially available both as immediate-release and prolonged-release. Immediate-release tablets are used for titrating morphine dosage for the individual child and defining the adequate dose for pain control. They are also indispensable for the management of episodic or breakthrough pain.

Prolonged-release oral formulations allow for longer dose intervals, therefore, improving the patient's compliance by reducing dose frequency. Prolonged-release oral formulations of morphine are administered every 8 to 12 hours (compared with every 4 hours for immediate-release tablets) but are unsuitable for the treatment of breakthrough pain. Therefore, availability of immediate-release formulations has priority over prolonged-release formulations of morphine.

Oral morphine solution is used when a child is not able to swallow tablets. Prolonged-release tablets cannot be crushed, chewed or cut, but prolonged-release granules can replace prolonged-release tablets in such a case.

Box 3.2 Formulations of morphine listed in the WHO model list of essential medicines for children, 2010

- *Injection*: 10 mg in 1 ml ampoule (morphine hydrochloride or morphine sulfate).
- *Granules (prolonged-release) (to mix with water)*: 20 mg, 30 mg, 60 mg, 100 mg, 200 mg (morphine sulfate).
- *Oral liquid*: 10 mg/5 ml (morphine hydrochloride or morphine sulfate).
- *Tablet (immediate-release)*: 10 mg (morphine sulfate).
- *Tablet (prolonged-release)*: 10 mg, 30 mg, 60 mg, 100 mg, 200 mg (morphine sulfate).

There is inadequate evidence to support a preference for alternative routes of administration other than the oral route. The available studies dealt with the management of acute or post-operative pain and did not provide conclusive evidence to guide recommendations. Trials are needed for future guidance on the use of alternative routes. The subcutaneous route (via continuous infusion or intermittent bolus through an indwelling catheter) is widely used and could be a valuable alternative.

IMMEDIATE RELEASE MORPHINE OR IV MORPHINE ARE THE MOST SUITABLE TTT FOR BREAKTHROUGH PAIN IT SHOULD BE about 5-10% of the daily dose

Tolerance to opioids occurs when the body becomes accustomed to a certain dose of the medicine and therefore an increased dose is required to obtain the same effect. This physiological phenomenon is not to be confused with **dependence syndrome**, which involves behavioural and cognitive phenomena, including a strong desire to take the psychoactive drug, persisting in its use despite harmful consequences, and giving a higher priority to drug use than to other activities and obligations (75).

Table 3.2 Starting dosages for opioid analgesics for opioid-naive neonates

Medicine	Route of administration	Starting dose
Morphine	IV injection ^a	25–50 mcg/kg every 6 hrs
	SC injection	
	IV infusion	Initial IV dose ^a 25–50 mcg/kg, then 5–10 mcg/kg/hr 100 mcg/kg every 6 or 4 hrs
Fentanyl	IV injection ^b	1–2 mcg/kg every 2–4 hrs ^c
	IV infusion ^b	Initial IV dose ^c 1–2 mcg/kg, then 0.5–1 mcg/kg/hr

^a Administer IV morphine slowly over at least 5 minutes.

^b The intravenous doses for neonates are based on acute pain management and sedation dosing information. Lower doses are required for non-ventilated neonates.

^c Administer IV fentanyl slowly over 3–5 minutes.

Table 3.3 Starting dosages for opioid analgesics in opioid-naive infants (1 month – 1 year)

Medicine	Route of administration	Starting dose
Morphine	Oral (immediate release)	80–200 mcg/kg every 4 hrs
	IV injection ^a	1–6 months: 100 mcg/kg every 6 hrs 6–12 months: 100 mcg/kg every 4 hrs (max 2.5 mg /dose)
	SC injection	
	IV infusion ^a	1–6 months: Initial IV dose: 50 mcg/kg, then: 10–30 mcg/kg/hr 6–12 months: Initial IV dose: 100–200 mcg/kg, then: 20–30 mcg/kg/hr
	SC infusion	1–3 months: 10 mcg/kg/hr 3–12 months: 20 mcg/kg/hr
Fentanyl ^b	IV injection	1–2 mcg/kg every 2–4 hrs ^c
	IV infusion	Initial IV dose 1–2 mcg/kg ^c , then 0.5–1 mcg/kg/hr
Oxycodone	Oral (immediate release)	50–125 mcg/kg every 4 hours

^a Administer IV morphine slowly over at least 5 minutes.

^b The intravenous doses of fentanyl for infants are based on acute pain management and sedation dosing information.

^c Administer IV fentanyl slowly over 3–5 minutes.

Table 3.4 Starting dosages for opioid analgesics in opioid-naïve children (1–12 years)

Medicine	Route of administration	Starting dose
Morphine	Oral (immediate release)	1–2 years: 200–400 mcg/kg every 4 hrs 2–12 years: 200–500 mcg/kg every 4 hrs (max 5 mg)
	Oral (prolonged release)	200–800 mcg/kg every 12 hrs
	IV injection ^a	1–2 years: 100 mcg/kg every 4 hrs 2–12 years: 100–200 mcg/kg every 4 hrs (max 2.5 mg)
	SC injection	
	IV Infusion	Initial IV dose : 100–200mcg/kg ^e , then 20–30 mcg/kg/hr
	SC infusion	20 mcg/kg/hr
Fentanyl	IV injection	1–2 mcg/kg ^b , repeated every 30–60 minutes
	IV infusion	Initial IV dose 1–2 mcg/kg ^b , then 1 mcg/kg/hr
Hydromorphone ^c	Oral (immediate release)	30–80 mcg/kg every 3–4 hrs (max 2 mg/dose)
	IV injection ^d or SC injection	15 mcg/kg every 3–6 hrs
Methadone ^e	Oral (immediate release)	100–200 mcg/kg every 4 hrs for the first 2–3 doses, then every 6–12 hrs (max 5 mg/dose initially) ^f
	IV injection ^g and SC injection	
Oxycodone	Oral (immediate release)	125–200 mcg/kg every 4 hours (max 5 mg/dose)
	Oral (prolonged release)	5 mg every 12 hours

^a Administer IV morphine slowly over at least 5 minutes.

^b Administer IV fentanyl slowly over 3–5 minutes.

^c Hydromorphone is a potent opioid and significant differences exist between oral and intravenous dosing. Use extreme caution when converting from one route to another. In converting from parenteral hydromorphone to oral hydromorphone, doses may need to be titrated up to 5 times the IV dose.

^d Administer IV hydromorphone slowly over 2–3 minutes.

^e Due to the complex nature and wide inter-individual variation in the pharmacokinetics of methadone, methadone should only be commenced by practitioners experienced with its use.

^f Methadone should initially be titrated like other strong opioids. The dosage may need to be reduced by 50% 2–3 days after the effective dose has been found to prevent adverse effects due to methadone accumulation. From then on dosage increases should be performed at intervals of one week or over and with a maximum increase of 50%.

^g Administer IV methadone slowly over 3–5 minutes.

Table 3.5 Approximate dose ratios for switching between parenteral and oral dosage forms

Medicine	Dose ratio (parenteral : oral)
Morphine	1:2 – 1:3
Hydromorphone	1:2 – 1:5 ^a
Methadone	1:1 – 1:2

^a Hydromorphone is a potent opioid and significant differences exist between oral and intravenous dosing. Use extreme caution when converting from one route to another. In converting from parenteral hydromorphone to oral hydromorphone, doses may need to be titrated up to 5 times the IV dose.

- The use of corticosteroids as adjuvant medicines is **not** recommended in the treatment of persisting pain in children with medical illnesses.
- The use of bisphosphonates as adjuvant medicines is **not** recommended in the treatment of bone pain in children.

At present, it is not possible to make a recommendation for any anticonvulsant as an adjuvant in the management of neuropathic pain in children.

At present, it is not possible to make a recommendation for or against the use of tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) as adjuvant medicines in the treatment of neuropathic pain in children.

- Codeine should not be used in any children (under 18 years of age) who undergo removal of tonsils or adenoids due to sleep apnoea.
- Codeine should only be used in children over 12 years of age.

