GUIDELINE

Post-Operative Pain and Sedation Guideline

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

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Aim

This guideline aims to provide information on:

- Prevention, assessment and management of pain and sedation in neonates
- Analgesic and sedative agents
- Post-surgical pain management
- Weaning of analgesia and sedation

Risk

This guideline will help to improve post-operative pain management and reduce the risk of adverse physiological pain responses.

Background

Goals of pain management are to

- Make pain matter,
- Make pain understood,
- Make pain visible, and
- Make pain better.

Lancet Child Adolescent Health

Definition (IASP): pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Newborn babies experience multiple painful stimuli throughout their NICU stay. Each newborn may manifest pain with behavioural, physiological and neuroendocrine responses

Immature pain pathways in neonates may lead to:

- Exaggerated responses to both painful and non-painful stimuli
- Generalised responses to local pain

Classification of Pain

Pain may be classified by somatosensory mechanisms and by timing.

Mechanism

- Nociceptive: normal response to noxious insult or injury to tissues.
- Inflammatory: activation and sensitization of pain pathways from cytokines.
- Neuropathic: Injury/Inflammation of somatosensory nervous system.
- Psycho-emotional: Learnt pain responses that may exacerbate pain.

Timing

- Acute: occurs at the time of nociceptive insult (such as IV insertion/venepuncture).
- Acute Persistent: recurrent or persistent insult (such as inflammation post-surgery, neonatal infection, necrotizing enterocolitis) that lasts less than 3 months.
- Chronic pain: the persistent activation of inflammatory, neuropathic or emotional pathways that persist beyond the period of active inflammation or injury that continues for more than 3 months. This type of pain is not well understood in neonates.

Effects of Pain

Acute response to pain is dependent on multiple factors such as the cause and timing of pain as well as gestation. It may present as physiological, biochemical and behavioural changes. Persistent or repetitive pain leads to constant activation of pain pathways that may amplify the response to acute pain.

Repetitive, persistent and chronic pain may cause long-term problems with development of pain pathways leading to a permanent change in pain sensitization and psycho-emotional sequelae. This may then lead to exaggerated responses to non-painful stimuli or prolonged responses to painful stimuli.

Assessment of Pain

The PIPP and modified PAT scoring tools are used to assess pain (Appendix 1).

The following is a guide for when to assess pain in newborns:

- Identify Noxious Stimuli (actual or potential).
- Perform pain assessment with each “hands on” episode.
- Perform pain assessment during and after any painful clinical intervention.
- Perform pain assessment after analgesia has been given.
- Patients that are muscle relaxed cannot be effectively assessed, they should have regular review once muscle relaxant is discontinued.

Assessment of Sedation

The State Behavioral Scale (SBS) is used to assess sedation (Appendix 2).

Management Guidelines

A flow chart for acute pain management is provided in Appendix 4.

1. Avoid/prevent painful stimuli
   - Review the need for repetitive minor procedures, i.e. blood gas sampling.
   - Review the need for major painful procedures such as PICC insertions.
   - Administer appropriate and timely analgesia when pain is anticipated.
     - Understanding medications and time of onset, duration and offset.
     - Understanding differences between mode of delivery.
     - Consider non-pharmacological strategies.
2. Identify actual or potential causes for pain or noxious stimuli.
   - If no obvious cause for pain is identified, then use non-pharmacological interventions first.
   - Parental involvement has been demonstrated to be effective.
   - Before performing any procedure consider which of the 5 goals need to be satisfied:
     - Sedation
     - Anxiolysis
     - Analgesia
     - Amnesia
     - Motion control (for example an echocardiogram requires motion control but not analgesia).
3. Control pain early

- If an infant is experiencing pain aim to control the pain as quick as possible.
- This may limit the chronic activation of pain pathways and reduce the total analgesia required.
    - Persistent or repetitive painful stimuli.
    - Commence a constant background analgesic (regular simple analgesia or opiate infusion).
- Aim for baseline pain scores </= 5.
- Acute painful stimuli:
    - Minor procedures: consider non-pharmacological interventions +/- sucrose.
    - Major procedures: consider pharmacological interventions prior to procedure.

4. Sedation
    - Consider sedation if requiring high doses of opiates as an adjunct.
    - Useful in infants that are intubated or have persistent/repetitive pain.
    - Infants not requiring respiratory support:
        - Consider regular clonidine or diazepam as an adjunct to analgesia.
    - Infant intubated or ventilated:
        - If irritability is secondary to intubation, then consider extubation.
        - Regular diazepam, midazolam infusion or clonidine/dexmedetomidine infusion.
5. Difficult to Control or Chronic Pain or Withdrawal
    - Consider the possibility of withdrawal with the “agitated neonate”.
    - Chronic pain can be considered as chronic painful response shown by the infant after the painful/noxious stimuli has ceased.
    - Early referral and discussion with the pain service at PCH should be considered.

Non-Pharmacological Interventions

These are described in the Neonatal Pain Guideline

Pharmacological Interventions

These should be complimentary to non-pharmacological interventions/sucrose.

These can be divided pharmacological subsets:

- Opioids: Morphine, Fentanyl, Hydromorphone

- NMDA antagonists: Ketamine
- Atypical opioids: Tramadol
- Adjuncts: Clonidine, Dexmedetomidine, Gabapentinoids
- Benzodiazepines: Diazepam, Midazolam, Clonazepam
- Barbiturates: Chloral Hydrate

Table 1 & 2 describes the properties of different agents – Non-Opioid and Opioid.

Table 1. Properties of Analgesic Agents – Non-Opioid

Drug	Drug class and indication	Mode of action	Route of administration	Onset of effect and duration of effects	Elimination half-life
Sucrose	Procedural pain	Activation of the endogenous opioid system through taste receptors on the tip of the tongue[1]	Oral	Onset: 10 seconds Peak effect 2 minutes Duration: 5 to 10 min[2]	Not applicable
Paracetamol	Analgesia with antipyretic activity	Not fully determined. Activation of descending serotonergic inhibitory pathways in the CNS and inhibition of central prostaglandin synthesis through the cyclooxygenase(COX) pathway[1, 2]	Oral/ IV	Onset: IV: 15 minutes Oral: 30-60 minutes Duration: IV/Oral 4 to 6 hours	28-32 weeks GA= 11 hours 32-36 weeks GA= 5 hours Term = 3 to 3.5 hours[1, 3]
Clonidine	Alpha-2 agonist Analgesia	Produce analgesia at presynaptic and post junctional alpha- 2 adrenoceptors in the spinal cord by preventing pain signal transmission to the brain[2].	Oral/IV	Onset: Oral: 30-60 minutes	44- 72 hours [1]
Dexmedetomidine	Alpha- 2 agonist; Sedative, anxiolytic, analgesic and hemodynamic-stabilizing effects	Relatively selective, centrally acting alpha-2 adrenergic agonist with sympatholytic, sedative. Analgesic properties but without significantly ventilator effects.	IV	Onset: 5 to 10 minutes[3]	Preterm: 7.6 hours Term: 3.2 hours[3]
Chloral hydrate	Sedative/ hypnotic; Procedural sedation	Central nervous system depressant effects due to its active metabolite trichloroethanol	oral	Onset: 10 to 15 minutes Duration: 1 to 2 hours	Preterm: 1 hours Term: 3 hours Active metabolite trichloroethanol has longer half-life (1-2 days)

Diazepam	Long acting benzodiazepine; Benzodiazepine withdrawal	Potentiate the inhibitory effects of GABA throughout the CNS, resulting in anxiolytic, sedative, hypnotic, muscle relaxant and antiepileptic effects	Oral	Onset: 15 to 2.5 hours Duration: 60 to 120 min (paed; require neonate data)	Preterm: 54 hours Term: 30 hours[1]
Clonazepam	Long acting benzodiazepine	Potentiate the inhibitory effects of GABA throughout the CNS, resulting in anxiolytic, sedative, hypnotic, muscle relaxant and antiepileptic effects	Oral	Onset: 20 to 60 min Duration: 6 to 8 hours	22 to 81 hours
Ketamine	Sedative hypnotic; Procedural sedation and analgesia	Antagonizes N- methyl-D_aspartate (NMDA) receptors; also interacts with muscarinic receptors, descending monoaminergic pain pathways, voltage-sensitive calcium channels and opioid receptors in brain and spinal cord	IV/oral	IV Onset: Within 30 seconds Oral Onset: 30 min	Alpha: 10 to 15 minutes Beta 2.5 hours[2]
Midazolam	Very short acting benzodiazepine; sedation	Potentiate the inhibitory effects of GABA throughout the CNS, resulting in anxiolytic, sedative, hypnotic, muscle relaxant and antiepileptic effects	IV/oral	IV Onset: 3 to 5 minutes Oral Onset: 10 to 30 minutes[1]	4 to 12 hours

Table 2. Properties of Analgesic Agents – Opioid

Drug	Mode of action and pharmacokinetic properties	Route Of administration	Onset of effect	Elimination half-life
Fentanyl	• Strong agonist at μ and k receptors • 100-300 times more potent than morphine[4] • Faster onset of action as extremely lipid soluble; penetrates the CNS rapidly. • Metabolized in the liver by CYP 3A4 • Eliminated mainly by kidney	IV	Onset: 1.5 min[4] Time to peak effect: 4.5 to to 8 min[4]	Preterm and term: 7 to 12 hours[4]
Morphine	• An agonist of both the μ and the k receptors resulting in analgesia. • Slower onset of action as limited lipid solubility; slower rate of penetration through blood brain barrier. Vd is higher in preterm than in term • Metabolized in liver to M3G or to M6G (active metabolite) via conjugation with glucuronic acid • Clearance is decreased in infants HIE receiving therapeutic hypothermia[5]	IV Oral	IV Onset: 6 to 30 min[6] Oral: 1 hour	Preterm: 6 to 11 hours Term: 4 to 8 hours[6, 7]
Hydromorphone	A semi-synthetic opioid agonist and is a hydrogenated ketone of morphine[8]. Five times more potent than morphine[8] A potent μ receptor agonist[8]	IV Oral	IV Onset: 5 minutes[2]* Time to peak effect: 10 to 20 min[2]*	3- 4 hours*

NB: Information is based on adult data due to lack of data in children and neonates.

Post - Operative Pain Management – Refer to Appendix 3

- Prior to surgery attempt to discuss with anaesthetic team management plan:
  - Will the baby return intubated?
  - Pre-operative analgesia.
  - Expected post-operative analgesia.
  - If opiate analgesia expected, then complete an order for CIVAS.
  - Morphine is the preferred first line form of opioid analgesia.
- Receive handover from surgical and anaesthetic teams for post-operative plan.
  - Some babies require muscle relaxant such as tracheo-oesophageal fistula.
  - Anaesthetics will provide intraoperative information regarding analgesia.
  - Identify when the last dose of analgesia and muscle relaxant was given.
- Post-handover perform post-operative assessment and stabilise infant.
- If no surgical or medical contraindication for extubation then aim to extubate after commencing non-opiate analgesia (e.g. paracetamol).
  - For minor surgery with minimal anticipated pain (e.g. hernia repair, cystoscopy, pull through for Hirschsprung).
  - Baby should be on minimal ventilatory support and FiO2 < 25%.
- If extubation is not appropriate then assess pain and manage as per post-operative pain guideline (e.g. post major upper airway surgery, CDH repair, TOF repair).
  - What surgery did the baby have and what are the surgical instructions?
  - Does the baby require intubation and ventilation post-operatively?
  - Has the baby been on opiate medications pre-operatively?

Plateau Phase of Pain Management – Refer to Appendix 5

Aim: safely find the minimum analgesia and sedation for the infant plan for extubation.

- Titrate analgesia and sedation based on mPAT and SBS score.
- Aim for mPAT score of 0-5 and SBS score of -1 to +1.
- Make small changes 8 hourly and change only one medication at a time.
- For babies on opiates or benzodiazepines for < 5 days consider changes 4 hours.
- For babies on opiates or benzodiazepines for > 5 days consider changes 8 hourly.

- Use Fentanyl and Morphine alternate weeks.

Weaning from Analgesia and Sedation – Refer to Appendix 6

Aim: safely and efficiently reduce the amount of analgesia/sedation without developing withdrawal syndrome. Prolonged administration of opioids and/or benzodiazepines may induce drug tolerance and physiological dependency leading to Iatrogenically Acquired Narcotic Dependence. Refer to Narcotic Dependence Treatment of Iatrogenically Acquired Narcotic Dependence guideline

- Babies on < 5 days of opiates or benzodiazepines:
  - Commence adjunctive analgesia.
  - Consider ceasing or use low dose opiate and cease benzodiazepines.
- Babies on > 5 days of opiates or benzodiazepines:
  - Commence NAS score
  - Commence Adjunct Analgesia eg paracetamol, dexmedetomidine, clonidine, benzodiazepines.
  - If appropriate gut integrity, then consider conversion to enteral analgesia and sedation (conversion tables in Appendix 7).
  - Suggested weaning protocol:
    - Start weaning as early as possible and aim to reduce doses by 10-20% per day.
    - Alternate between analgesia and sedative medications (ie Day 1: wean morphine dose by 10%; Day 2: wean midazolam dose by 10%).
    - If NAS scores are > 8 then maintain current doses of medications
- Ventilated patients:
  - Aim to extubate safely and as early as possible.
  - Infants may develop tolerance to medications and have minimal respiratory depression and be extubated on opiates and benzodiazepines.
  - Perform a trial of ventilator CPAP with PS to test for safety of extubation each day.

Related CAHS internal policies, procedures and guidelines

Neonatology Clinical Guideline

- Pain Assessment and Management
- Neonatology Medication Monographs
- Narcotic Dependence: Treatment of Iatrogenically Acquired Narcotic Dependence

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Appendix 1: Modified PAT

TABLE A1. The Modified Pain Assessment Tool and Covers Scale

Parameters	0	1	2
The modified Pain Assessment Tool (PAT)			
Posture/tone	Relaxed Normal Some flexion	Extended Digits widespread Trunk rigid Limbs abducted Shoulders raised off bed	Flexed and/or tense Fists clenched Trunk guarded Limbs drawn to midline Head/shoulders resist posturing
Cry	No	Yes Consolable Can be settled	Yes When disturbed Does not settle after handling Loud Whimpering Whining
Sleep pattern	Relaxed	Easily woken	Agitated or withdrawn Wakes with startle Restless Squirming No clear sleep/wake pattern Eye aversion or "shut out"
Expression	Relaxed Normal	Frown Shallow furrows Eyes lightly closed	Grimace Deep furrows Eyes tightly closed Pupils dilated
Color	Pink, well perfused	Occasionally mottled or pale	Pale/dusky/flushed Palmar sweating
Respirations	Normal baseline rate	Tachypnea At rest	Apnea At rest/with handling
Heart rate	Normal baseline rate	Tachycardia At rest	Fluctuating Spontaneous/at rest
Oxygen saturation	Normal	Fleeting desaturation	Desaturation with/without handling
Blood pressure	Normal	Fluctuates with handling	Hypo-/hypertension at rest
Nurse perception	No pain perceived by me	I think the baby has pain only with handling	I think the baby is in pain

Adapted from O'Sullivan et al. (2016)

Scoring of the mPAT

- Observe neonate and score the following items: behavioral state, colour and facial expression.
- Then gently touch the neonate's limb to assess muscle tone.
- Score the neonate for each of the physiological and behavioral parameters, and for the nurse's perception of pain.
- Each item is scored from 0 to 2 and added to generate a total score out of 20 (the higher the score, the higher the level of pain).
- If a baby is muscle-relaxed the total score is out of 10, since a muscle-relaxed neonate can only be scored on the physiological indicators of pain, not the behavioral indicators of pain.
- A score of 2 for the 'nurse's perception of pain' should be given if the neonate is currently perceived to be in pain as a result of those other factors.

Intervention based on Score

mPAT Score	Intervention
< 5	Non-pharmacological measures
6-10	Non-opioid adjunct analgesia (e.g. Paracetamol/clonidine)
> 10	Opioid analgesia

Appendix 2: Sedation Score (State Behavioural Scale)

State Behavioral Scale (SBS)[1] **Score as patient's response to voice then touch then noxious stimuli** (Planned ETT suctioning or <5 seconds of nail bed pressure)		
Score	Description	Definition
-3	**Unresponsive**	No spontaneous respiratory effort No cough or coughs only with suctioning No response to noxious stimuli Unable to pay attention to care provider Does not distress with any procedure (including noxious) Does not move
-2	**Responsive to noxious stimuli**	Spontaneous yet supported breathing Coughs with suctioning/repositioning Responds to noxious stimuli Unable to pay attention to care provider Will distress with a noxious procedure Does not move/occasional movement of extremities or shifting of position
-1	**Responsive to gentle touch or voice**	Spontaneous but ineffective non-supported breaths Coughs with suctioning/repositioning Responds to touch/voice Able to pay attention but drifts off after stimulation Distresses with procedures Able to calm with comforting touch or voice when stimulus removed Occasional movement of extremities or shifting of position
0	**Awake and Able to calm**	Spontaneous and effective breathing Coughs when repositioned/Occasional spontaneous cough Responds to voice/No external stimulus is required to elicit response Spontaneously pays attention to care provider Distresses with procedures Able to calm with comforting touch or voice when stimulus removed Occasional movement of extremities or shifting of position/increased movement (restless, squirming)
+1	**Restless and difficult to calm**	Spontaneous effective breathing/Having difficulty breathing with ventilator Occasional spontaneous cough Responds to voice/ No external stimulus is required to elicit response Drifts off/ Spontaneously pays attention to care provider Intermittently unsafe Does not consistently calm despite 5 minute attempt/unable to console Increased movement (restless, squirming)
+2	**Agitated**	May have difficulty breathing with ventilator Coughing spontaneously No external stimulus required to elicit response Spontaneously pays attention to care provider Unsafe (biting ETT, pulling at lines, cannot be left alone) Unable to console Increased movement (restless, squirming or thrashing side-to-side, kicking legs)

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Scoring using SBS

- Scoring should be done with each pain score every 4 hours.
- Score first to noise such as response to voices, then to gentle touch of a limb.
- If no responses to voice or gentle touch then observe with a noxious stimuli (planned ETT suctioning, intravenous line insertion, or < 5 seconds of nail bed pressure).

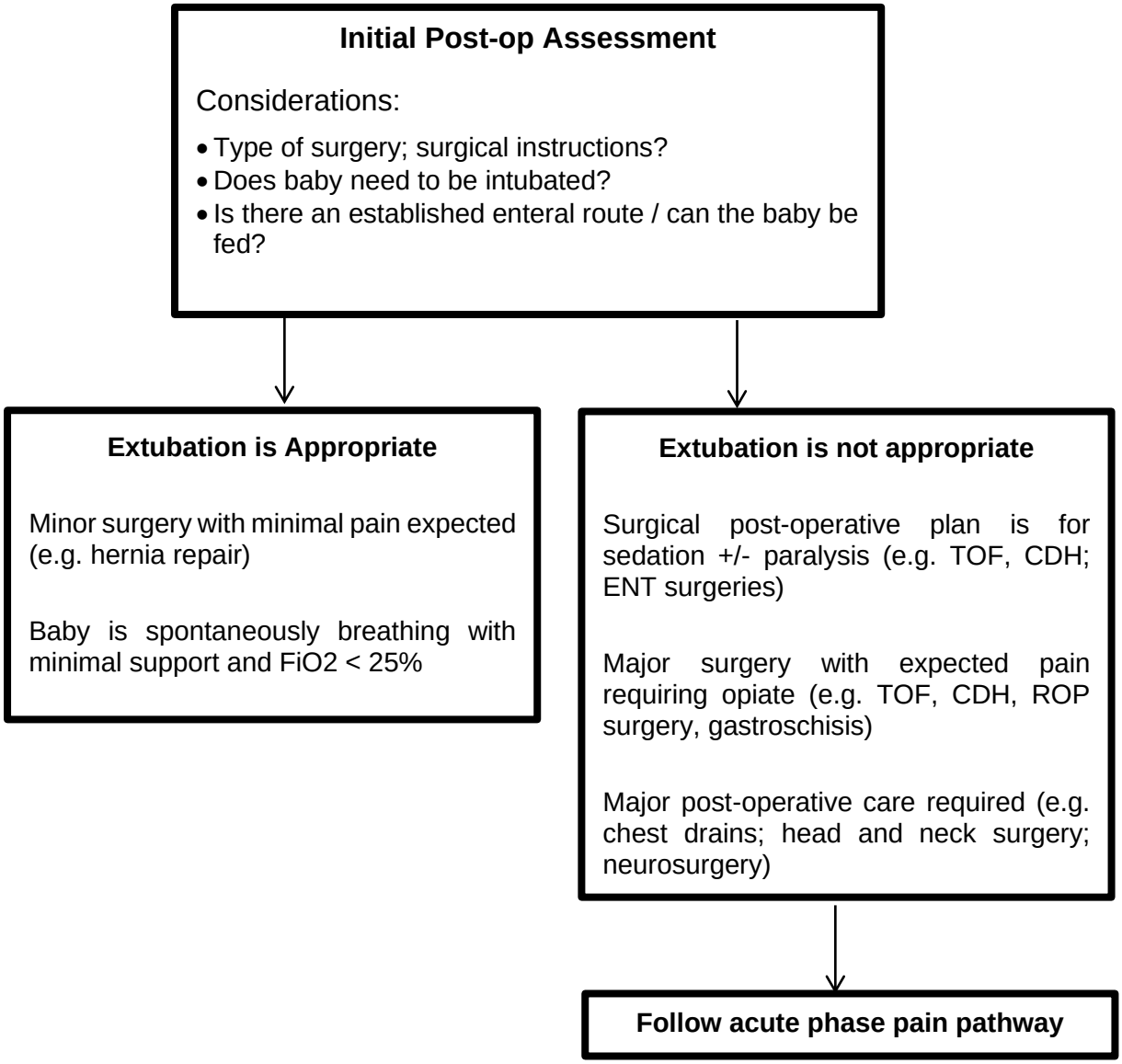
Intervention based on Score

SBS Score	Intervention
-3	Consider reducing sedative medication by 10%
-2	Consider reducing sedative medication by 5%
-1 to +1	Continue with current sedation
+2	Give a bolus of sedative medication and increase sedative medication by 10% or adjunct medication

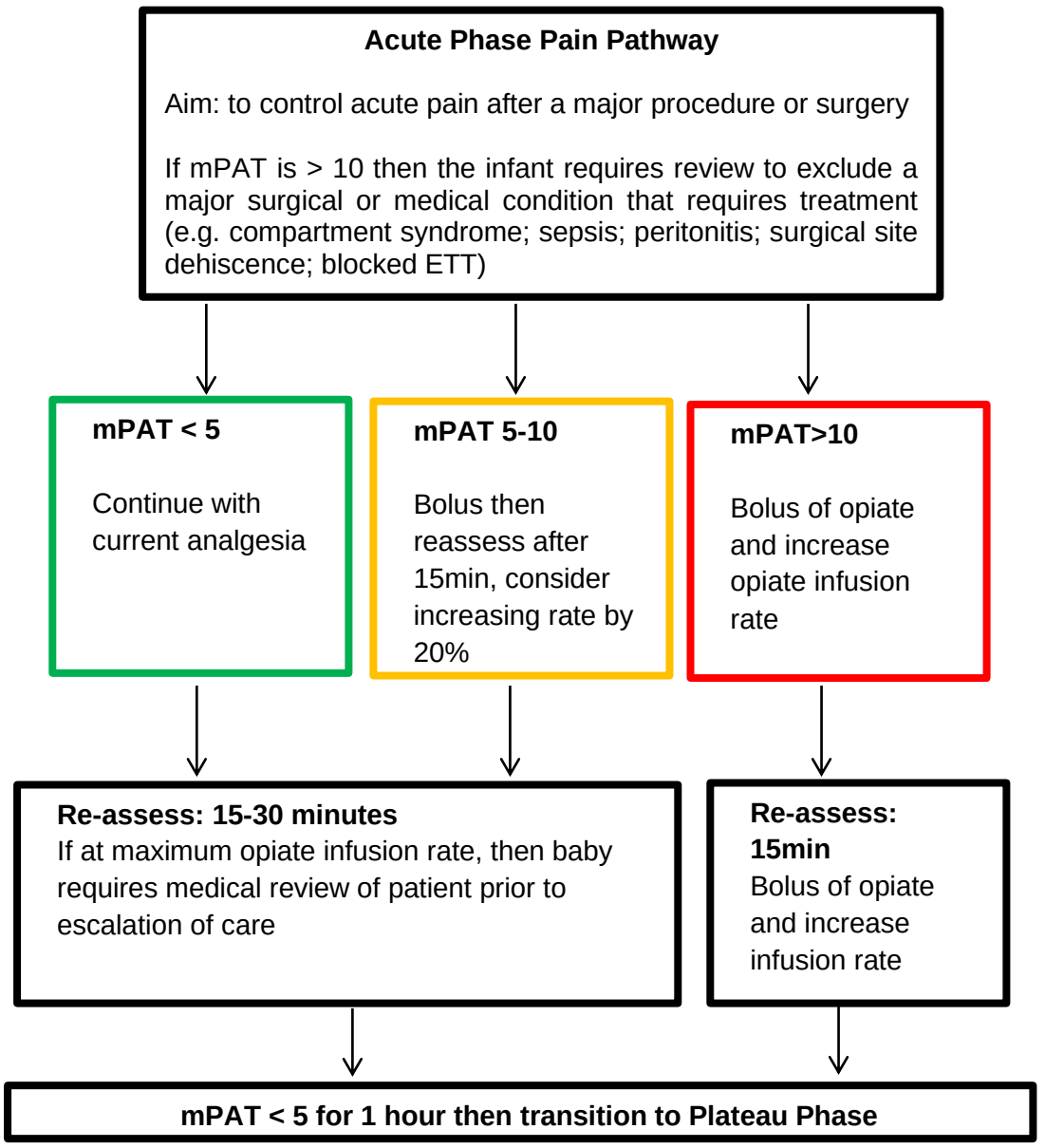
Notes

- The table above is a guide for management.
- The amount of sedation required differs based on underlying disease process (e.g. sedation for tracheoesophageal fistula, persistent pulmonary hypertension).
- Medical team to discuss individual plans for sedation and weaning on ward round.

Appendix 3: Surgical Pain Guideline – Initial Post-Op Assessment



Appendix 4: Surgical Pain Guideline – Acute Phase Pain Pathway



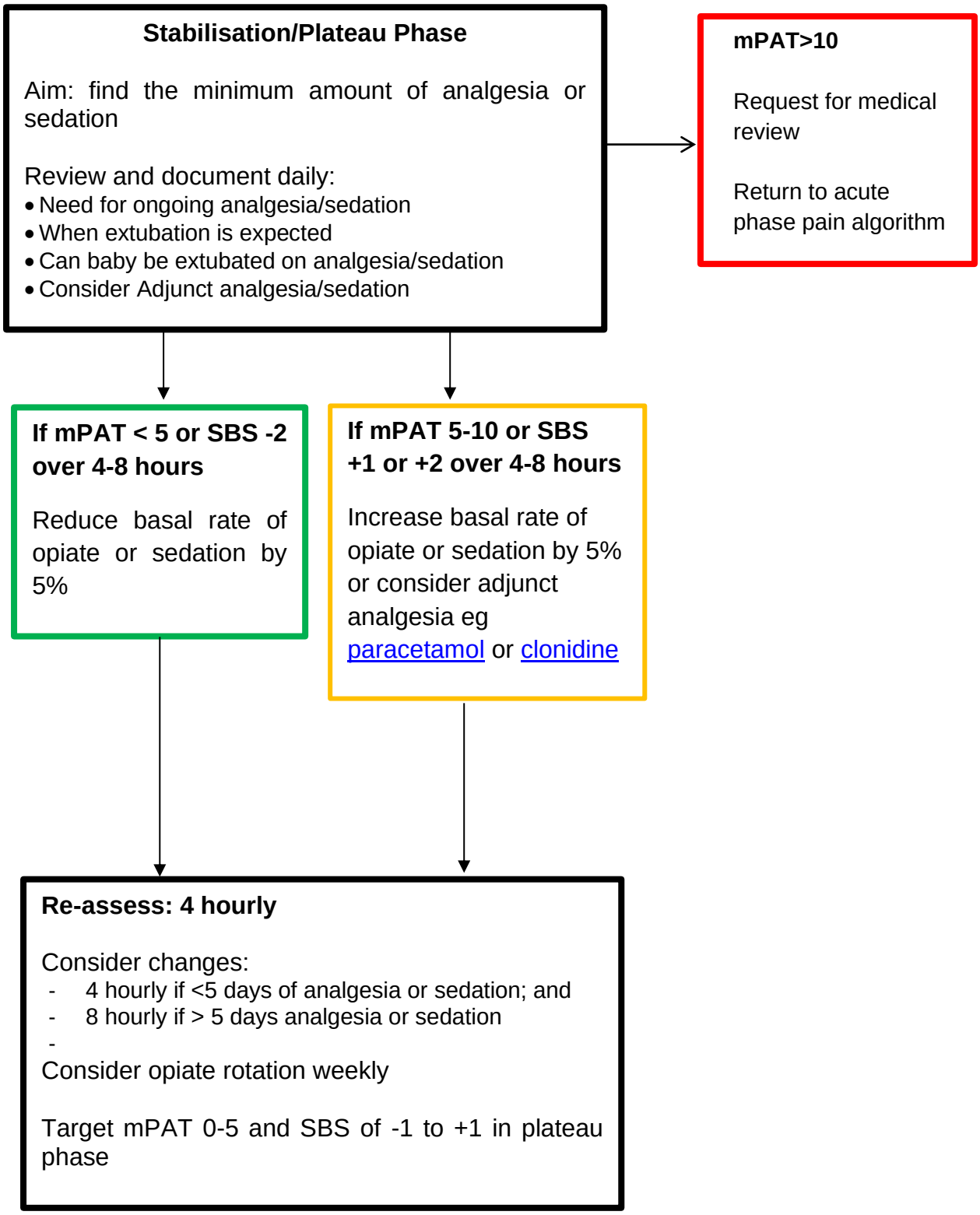
Maximum infusion rate and Bolus

Maximum infusion rates:	Morphine (30mcg/kg/hr) Fentanyl (2mcg/kg/hr)
Bolus:	Morphine (10-50mcg/kg/dose) Fentanyl (0.2-0.5mcg/kg/dose)

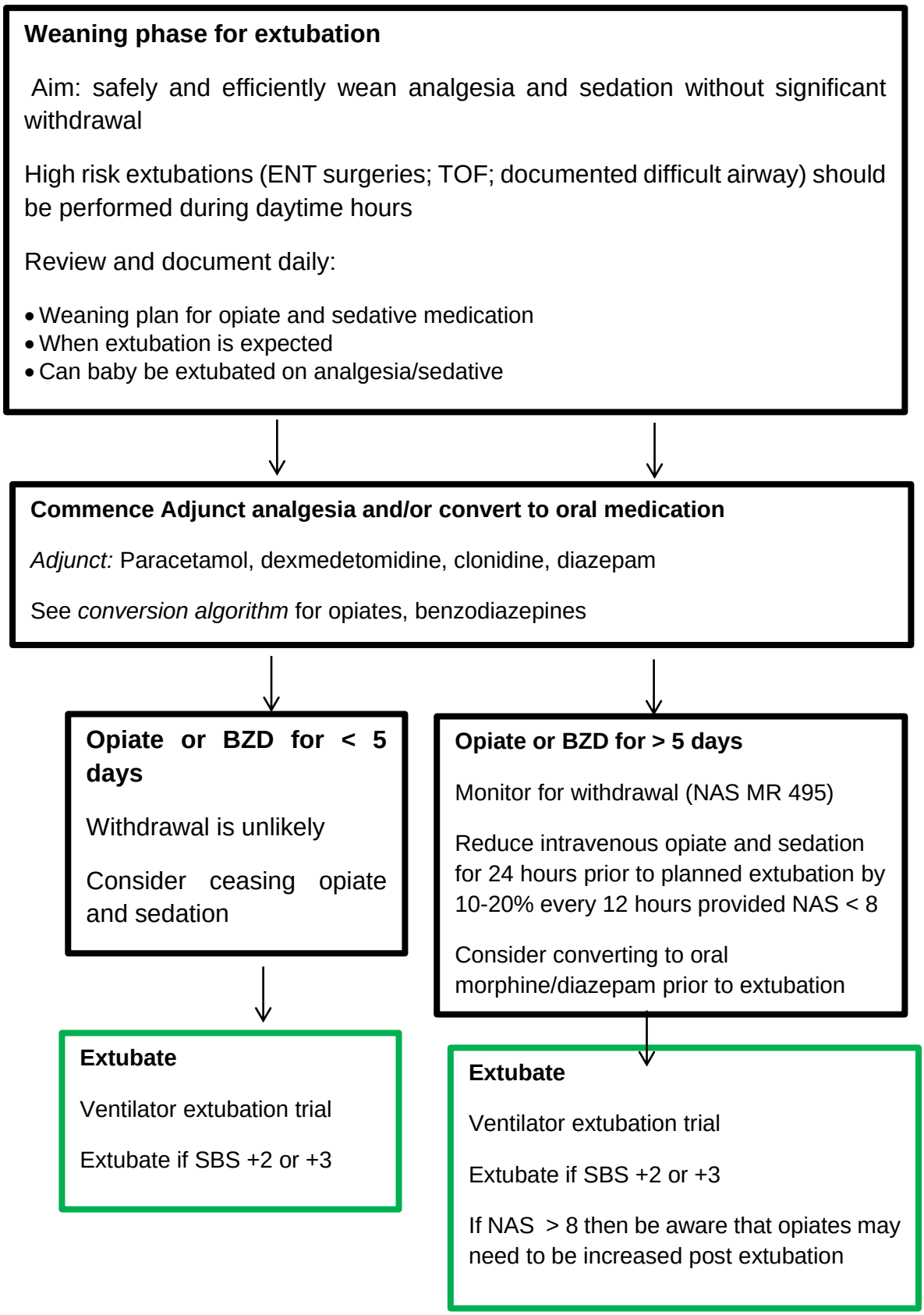
If at maximum opiate infusion rate reached and/or 3 opiate or sedative bolus then requires **medical review of patient** prior to escalation of care

- Discuss with SR or consultant
- Discuss with pain team

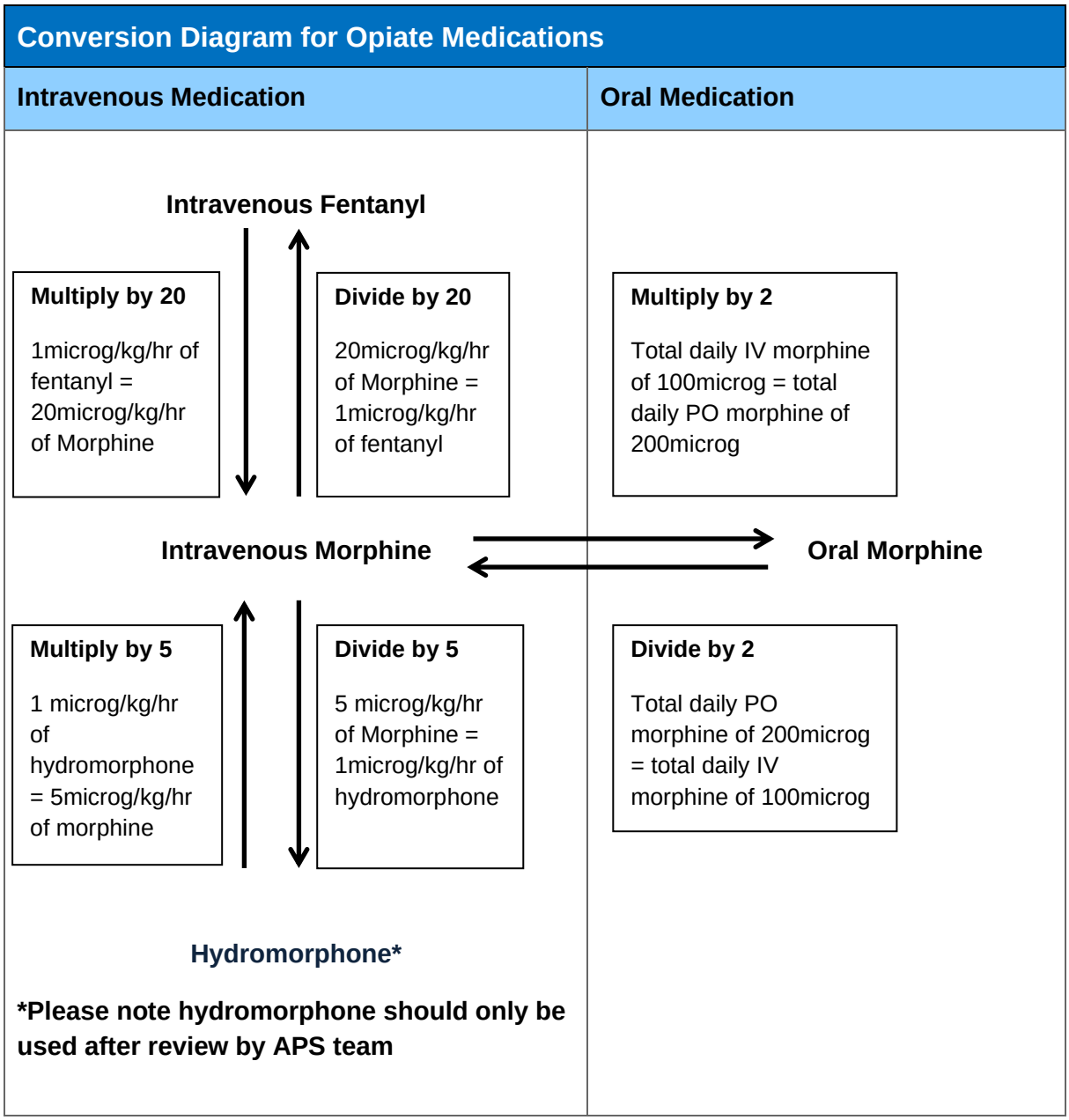
Appendix 5: Surgical Pain Guideline – Stabilisation/Plateau Phase



Appendix 6: Surgical Pain Guideline – Weaning Phase for Extubation



Appendix 7 : Conversion Diagram for Opiate Medications



Example:

A 24-hour total dose of IV morphine equals 1mg, oral morphine equivalent will be 2mg. (daily oral dose is twice the daily IV dose)

IV fentanyl continuous infusion at 1microgram/kg/hr in a 3kg patient

= 24microgram/kg/day = 72microgram in 24 hours.

1 microgram of fentanyl is equivalent to 20 microgram of IV morphine

Equivalent IV morphine 24-hour dose = 1440 microgram of IV morphine

Convert to oral morphine (Oral dose is twice the dose of IV morphine)

= 2880 microgram of oral morphine in 24 hours

= 720 microgram PO q6hourly, oral morphine.