CHAPTER 12 ANAESTHESIOLOGY AND INTENSIVE CARE

Anaesthetic and sedative medication may only be administered by medical practitioners trained and experienced in their use.

Sound theoretical and practical training followed by several years of supervised experience in the administration of anaesthetics is essential to develop the skills of the anaesthetist. Even within the recommended dosage range, anaesthetic agents can cause death when inappropriately used and only as a last resort should they be administered by non-specialised personnel.

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Medicines and equipment for resuscitation should be functional and immediately available whenever general anaesthesia, regional anaesthesia or sedation is administered.

The following is a list of medicines required for anaesthesia that should be available at district and regional hospitals.

The doses of the medicines given are those recommended for healthy adults. Patients who are acutely or chronically sick, and or elderly, may require substantial reductions in the doses given otherwise lifethreatening adverse effects may ensue.

12.1 PREMEDICATION

- Lorazepam, 1–2 mg, oral, the night before surgery and 1–2 hours preoperatively
 - Use half the dose in the elderly.
 - Duration of action (10–20 hours).
 - o Unsuitable for day case surgery.

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- Midazolam, 5–7.5 mg, oral, one hour preoperatively.
 - Use only in healthy adults <65 years of age.
 - Duration of action 1–4 hours.
 - Suitable for day case surgery.

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12.2 ANAESTHESIA, GENERAL

12.2.1 INTRAVENOUS INDUCTION (AND/OR MAINTENANCE) AGENTS

Inject intravenous induction agents over 30 seconds (>60 seconds in the elderly).

Titrate the dose to effect.

Respiratory depression occurs following induction of anaesthesia and ventilation should be supported as required.

Administer at appropriate doses, after consideration of patient factors, surgical factors and contraindications:

- » Propofol is the most widely used IV induction agent but can produce hypotension.
- » Etomidate or ketamine is preferred in haemodynamically unstable patients.
- » Thiopental has a rapid onset, is contraindicated in porphyria and may be preferred for Caesarean deliveries.
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- Propofol, IV, 1.5–2.5 mg/kg.
 - 6–12 mg/kg/hour IV infusion for maintenance, if volatile agent use contraindicated.
- Etomidate, IV, 0.3 mg/kg (0.2–0.6 mg/kg)
- Ketamine, IV, 1–2 mg/kg.
- Thiopental, IV, 3-5 mg/kg.

12.2.2 INHALATION AGENTS

12.2.2.1 INDUCTION

In adults, intravenous induction is preferable.

Inhalational induction is reserved for patients with difficult airways or severe needle phobia.

Use only halothane or sevoflurane (isoflurane is too irritant). Halothane can cause hepatitis after repeated exposure within 3 months. Halothane sensitises the heart to catecholamines and may cause cardiac dysrhythmias, particularly if anaesthesia is too light or the patient hypercarbic.

Sevoflurane is not associated with these problems, has a faster onset and emergence time.

Halothane, titrated to effect.

OR

Sevoflurane, titrated to effect.

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12.2.2.2 MAINTENANCE

In spontaneously breathing patients, the dose of a volatile agent is titrated to clinical effect. If a neuromuscular blocking agent has been used, the dose of the volatile agents must be adequate to prevent awareness. This is about 1 minimum alveolar concentration (MAC), but must be titrated according to clinical signs of awareness (e.g. tachycardia, hypertension, sweating, lacrimation).

Isoflurane (MAC = 1.2%).

12.3 MUSCLE RELAXANTS

Used to facilitate intubation and to provide intraoperative muscle relaxation for surgery. It must not be used if difficult intubation anticipated.

12.3.1 DEPOLARISING MUSCLE RELAXANTS

- Suxamethonium, IV, 1–1.5 mg/kg.
 - o Onset 30-60 seconds.
 - Duration 5 minutes.
 - Repeated doses associated with bradycardia and prolonged neuromuscular block.
 - Contraindicated in patients at risk for developing suxamethoniuminduced hyperkalaemia, e.g. upper or lower motor neuron defect, prolonged chemical denervation (ICU >3 days), direct muscle trauma, tumour or inflammation, burns, disuse atrophy, severe infection, preexisting hyperkalaemia.

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12.3.2 NON-DEPOLARISING MUSCLE RELAXANTS (NDMR)

Use a nerve stimulator to monitor effect and determine when subsequent doses (about a fifth of the intubating dose) are required.

Higher doses result in shorter onset times but longer duration of action.

Intermediate-acting neuromuscular blocking agents, e.g.:

Cisatracurium (shorter-acting)

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- o Intubation dose 0.1–0.15 mg/kg.
- Onset 3–5 minutes.
- Duration of action 45–55 minutes.
- Eliminated by Hoffman degradation, therefore can be used in renal or liver impairment.
- Vecuronium
 - Intubation dose 0.08–0.1 mg/kg.
 - o Intubate after 2 minutes.

LoE:III^{viii}

- Duration 20–30 minutes.
- Eliminated by liver and kidney: avoid in renal and liver impairment.

12.3.3 MUSCLE RELAXATION FOR RAPID SEQUENCE INTUBATION

Patients at risk of aspiration (e.g. emergency surgery, incomplete gastric emptying) require a rapid sequence intubation.

An IV induction agent is given through an IV line with fast running fluids, immediately followed by a rapidly acting muscle relaxant.

Cricoid pressure is applied and then intubation proceeds.

The rapid onset of action enables the time to intubation to be short enough to avoid mask ventilation, as this can result in gastric insufflation and aspiration of gastric contents.

- Suxamethonium, 1–1.5 mg/kg, IV. (See section 12.3.1: Depolarising muscle relaxants).
 - Preferred agent as, in the event of a failed intubation, it wears off quickly enabling spontaneous respiration to resume.
 - Contraindications to suxamethonium
 - Congenital and acquired medical conditions associated with severe, potentially lethal suxamethonium-induced <u>hyperkalaemia</u>.
 - Malignant hyperthermia.

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If suxamethonium is contra-indicated, consider:

- Rocuronium, 0.9 mg/kg, IV.
 - Duration +/- 60 minutes.

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Sub-optimal conditions for intubating and prolonged effect can be problematic in the event of a difficult or failed intubation and if the procedure is short.

12.3.4 MEDICINES TO REVERSE MUSCLE RELAXATION

Only administer when the clinical signs of NDMR are wearing off or at least 2 twitches occur using train-of-four on nerve stimulator.

Neostigmine has profound cholinergic effects and, to counteract resultant profound bradycardia, is administered mixed with an anticholinergic agent, atropine or glycopyrrolate.

Whilst atropine is effective and can be used for this purpose in otherwise healthy patients, the onset of neostigmine and duration of action more closely matches that of glycopyrrolate, so this is the preferred combination agent for patients who poorly tolerate tachycardia or bradycardia.

Neostigmine, IV, 50 mcg/kg.

WITH EITHER:

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• Atropine, IV, 20 mcg/kg (maximum 1.2 mg).

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OR

Glycopyrrolate, IV, 10 mcg/kg.

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12.4 PERIOPERATIVE ANALGESIA

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- » The perioperative period includes the preoperative, intraoperative and post-operative stages of surgery.
- » Perioperative analgesia should be multi-modal, i.e. use analgesics, where possible, from different classes to reduce side effects from high doses of a single agent (e.g. paracetamol, NSAID and a weak/strong opioid) with either a regional block or wound infiltration with local anaesthetic.
- » Patients with pain before surgery should be given analgesia preoperatively.
- » Paracetamol may be given orally with premedication to prophylactically reduce perioperative pain.
- » Intraoperatively, analgesics are given intravenously and/or a central neuraxial or regional local anaesthetic block may be used. The analgesic effect of these may extend into the early postoperative period.
- » Postoperatively analgesics are given IV, IM and/or rectally, until the patient is able to take oral medication. Patients with a functioning block may not require analgesia until the block wears off but analgesics should be prescribed in anticipation of this.
- » Pain severity should be assessed frequently post-operatively (see Section 12.5.3: Postoperative analgesia ward prescriptions).

12.4.1 PERIOPERATIVE ANALGESICS

12.4.1.1 ORAL ANALGESICS

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
 - Maximum dose: 15 mg/kg/dose.

AND

LoE:I^{xiv}

- Tramadol, oral, 50 to 100 mg, 6 hourly as a starting dose. (Doctor prescribed.)
 - $\circ\quad$ May be increased to a maximum daily dose of 400 mg.
 - Avoid in head injury and epilepsy.
 - Improved effect when given with paracetamol.

AND

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- NSAID, e.a.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

Note: Do not administer NSAIDs to patients at risk of hypovolaemia, renal impairment or gastrointestinal bleeding. Avoid in patients with asthma who

experience bronchospasm with NSAIDs.

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12.4.1.2 INTRAVENOUS ANALGESICS

- Fentanyl, IV, 1–2 mcg/kg
 - Onset ± 3 minutes, duration of action 30–60 minutes. Higher doses last longer.
- Morphine, IV/IM, 3–5 mg as a single dose then further boluses at intervals
 of 5–10 minutes and monitor all vitals closely.

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 - o Dilute 10 mg up to 10 mL with sodium chloride 0.9%.
 - Total maximum dose: 10 mg.
 - o Repeat after 4 hours if necessary.
 - Monitor response to pain and effects on respiration and BP.
 - o Onset 5-10 minutes. Duration of action ± 3 hours.
 - o Histamine release may cause intraoperative hypotension.
- Ketamine, IV, 0.1–0.3 mg/kg a subanaesthetic dose given pre-incision may reduce persistent post-surgical pain.

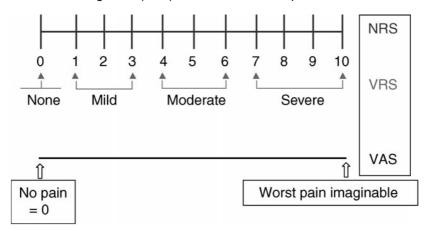
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12.4.2 POSTOPERATIVE PAIN IN THE RECOVERY ROOM

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Pain should be assessed on arrival in the recovery room and at regular intervals postoperatively. Pain Scores should be recorded with other routine postoperative observations.

A Numeric Rating Scale (NRS) can be used to score pain:



Source: Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, Kvarstein G, Stubhaug A. Assessment of pain. *Br J Anaesth*. 2008 Jul;101(1):17-24.

The patient is asked to indicate on the scale the numeric value that best indicates their pain intensity or verbally if they cannot visualise the scale.

Severe pain (use lower doses if pain less):

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).
 - Monitor conscious level and pulse oximetry continuously. Also monitor respiration, heart rate and BP at 5 minute intervals and for at least 20 minutes after the last IV morphine bolus.

In patients at high risk for respiratory depression, tramadol may be used instead of morphine as it causes less respiratory depression (although respiratory depression may still occur with tramadol).

<u>Tramadol is a weak opioid agonist and increases spinal cord levels of serotonin and noradrenaline.</u>

- Tramadol, IV, 50–100 mg over 3 minutes to reduce side-effects of nausea and vomiting (Specialist prescribed).
 - Ceiling effect i.e. higher doses do not improve pain LoE:III^{px} relief.

<u>In addition to morphine or tramadol, diclofenac may also be given to supplement analgesia and reduce opioid requirements:</u>

- Diclofenac, deep IM, 75 mg 12 hourly.
 - Administer for a maximum of 2 days.
 - Avoid the same injection site.
 - Counsel patient prior to injection of adverse events (scarring) at inject site, if applicable.

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12.4.3 POSTOPERATIVE ANALGESIA WARD PRESCRIPTIONS

Analgesia should be prescribed according to the severity of pain anticipated from the surgery and the anticipated, appropriate, postoperative route of administration.

Pain should be assessed at regular intervals on the ward postoperatively. Pain scores should be recorded with other routine postoperative observations.

Respiratory rate should be monitored for opioid-induced respiratory depression.

12.4.3.1 EXAMPLES OF WARD PRESCRIPTIONS FOR POSTOPERATIVE ANALGESIA ACCORDING TO ANTICIPATED PAIN SEVERITY

R52.9

MILD PAIN:

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
 - o Maximum dose: 15 mg/kg/dose.

AND

- NSAID, oral, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly after meals.

CAUTION

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).

NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.

Do not use NSAID in pregnancy or while breastfeeding.

AND

- Tramadol, oral, 50 to 100 mg, 6 hourly as a starting dose. (Doctor prescribed.)
 - May be increased to a maximum daily dose of 400 mg.
 - o Avoid in head injury and epilepsy.
 - o Improved effect when given with paracetamol.

MODERATE PAIN:

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
 - o Maximum dose: 15 mg/kg/dose.

AND

- NSAID, oral, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

CAUTION

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).

NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.

Do not use NSAID in pregnancy or while breastfeeding.

AND

- Tramadol, oral, 50 to 100 mg, 6 hourly as a starting dose. (Doctor prescribed.)
 - May be increased to a maximum daily dose of 400 mg.
 - o Avoid in head injury and epilepsy.
 - o Improved effect when given with paracetamol.

OR

Morphine, IM, 0.1–0.2 mg/kg 4 hourly or IV via a patientcontrolled analgesia device (see below).

SEVERE PAIN:

Morphine, IM, 0.1–0.2 mg/kg 4 hourly or IV via a PCA device.

AND

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
 - Maximum dose: 15 mg/kg/dose.

AND

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

Note:

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Patient controlled analgesia

If a device is available that will administer patient controlled analgesia:

- Morphine, IV, in boluses of 1 mg every 6-10 minutes, with a maximum dose of 0.1–0.2 mg/kg 4 hourly.
 - In the elderly and frail, the dose of morphine should be reduced and the dosage interval increased.

LoE:Ixxiii

If unable to take oral medication, stop oral ibuprofen and use:

- Diclofenac, **deep IM**, 75 mg 12 hourly, to upper, outer quadrant of buttock.
 - Administer for a maximum of 2 days.
 - Avoid the same injection site.

 Counsel patient prior to injection of adverse events (scarring) at injection site if applicable.

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12.5 INTRAVENOUS FLUIDS

The following IV fluids should be available for perioperative fluid replacement and maintenance therapy.

12.5.1 CRYSTALLOIDS

Most commonly used crystalloid for perioperative fluid maintenance:

Sodium chloride 0.9%. IV.

Higher sodium content than indicated if there is a perioperative risk of hyponatraemia e.g. transurethral resection of prostate.

Balanced solutions may be appropriate in some patients (i.e. presentation with hyponatraemia, previous renal placement therapy):

- Balanced solution, e.g.:
- · Ringer Lactate, IV.

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12.6 MEDICINES TO TREAT COMPLICATIONS OF ANAESTHESIA

12.6.1 MALIGNANT HYPERTHERMIA

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- Dantrolene IV, 2.5 mg/kg as a single dose (preferably through large bore cannula).
 - Reconstitute with 60 mL water for injection. For a 70 kg patient, 175 mg (9 vials) is required.
 - Administer subsequent doses to clinical effect (cardiac and respiratory symptoms stabilise, muscle tone and body temperature reduced).
 - Doses higher than 10 mg/kg is uncommon and the clinician should question the diagnosis.
 - o Although, high doses of 10 mg/kg may be required in muscular males.

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12.6.2 LOCAL ANAESTHETIC TOXICITY

T413

Airway management:

· Ventilate with 100% oxygen.

Seizure suppression:

Diazepam, IV, 10 mg.

Cardiopulmonary resuscitation may be required:

• Reduce individual adrenaline (epinephrine) doses to <1 mcg/kg.

LoE:III^{xxvii}

- Lipid emulsion (20%), IV, 1.5 mL/kg over 1 minute, then continuous infusion 0.25 mL/kg/minute.
 - Repeat bolus 1–2 times for persistent cardiovascular collapse.
 - o Double infusion rate to 0.5 mL/kg/minute if BP remains low.
 - Continue infusion for at least 10 minutes after cardiovascular stability attained.
 - Recommended upper limit: approximately 10 mL/kg lipid emulsion over the first 30 minutes.

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12.6.3 ANAESTHETIC-RELATED ACUTE HYPOTENSION

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Treat the cause of hypotension.

Ensure appropriate fluids are given to correct hypovolaemia.

The medicines given below all require significant dilution before administration.

- Adrenergic and dopaminergic agents, e.g.:
- Ephedrine IV, 3–5 mg as a single dose and then further boluses as required to a maximum of 30 mg.
 - Increases heart rate and contractility, and vasoconstrictor.
 - o Repeated administration can result in tolerance and tachyphylaxis.
 - Alternative vasopressor infusion (e.g. adrenaline (epinephrine)) may be needed to mitigate unresponsiveness to treatment.

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OR

Phenylephrine IV, 50–100 mcg as a single dose and then infuse at 60–180 mcg/minute.

Vasoconstrictor.

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High doses may cause significant reflex.
 bradycardia: treat this by discontinuing the phenylephrine only.

12.6.4 ANAESTHETIC-RELATED ACUTE HYPERTENSION 197.3

To obtund the hypertensive response to intubation e.g. pre-eclampsia:

Alfentanil, IV, 7.5 mcg/kg (with magnesium sulfate, IV 30 mg/kg).

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During anaesthesia or post-operatively, establish the cause (e.g. light anaesthesia or inadequate pain relief) and treat as appropriate.

- Labetalol IV, 5–10mg IV over 2 minutes.
 - o Repeated at intervals of at least 5 minutes to maximum 200 mg.

- Duration of action 50 minutes.
- Vasodilates and slows heart rate.

LoE:IIIxxxi

12.6.5 POSTOPERATIVE NAUSEA AND VOMITING (PONV)

12.6.5.1 PREVENTION OF PONV

R11.2

Patients identified preoperatively as medium or high risk for PONV should be considered for prophylactic antiemetics.

Prophylactic antiemetics also required if postoperative vomiting is potentially dangerous, e.g. after jaws wired, open eye surgery, oesophageal surgery. High risk patients should receive anti-emetics from ≥ 1 class.

Adequate IV hydration associated with less PONV.

Risk factors for PONV		Points	
Female Gender		1	
Non-Smoker		1	
History of PONV and/or mo	tion	1	
sickness			
Postoperative opioids		1	
Sum	Sum		
Points	Risk for PO	ONV (%)	Risk category
0	10		Low
1	20		Low
2	40		Medium
3	60		High
4	80		High

Class	Anti-emetic	Prophylactic Dose and timing	Notes
Corticosteroid (glucorticoids)	e.g.: Dexamethasone	4-8 mg, IV, on induction.	Increases blood glucose in diabetics.
		=====	Only used for prophylaxis, not established PONV.
5-HT ₃ receptor antagonist	e.g.: Ondansetron	4–8 mg, slow IV/IM, on induction.	Prolongs QTc interval
Phenothiazine	Promethazine	6.25–12.5 mg, IV (large bore cannula) diluted to 20 mL over 10-20 minutes, or	Intra-arterial injection causes gangrene. Extravasation or subcutaneous injection

12.6.5.2 TREATMENT OF PONV

R11.2

Ensure adequate hydration and correct hypotension if present. Give an emetic from a different class than the prophylactic agent given (except dexamethasone, which is only used for prophylaxis).

- Metoclopramide, IM/IV
 - o If <60 kg: 5 mg IM or IV (over 2 minutes).
 - o If ≥60 kg: 10 mg IM or IV (over 2 minutes).
 - Repeat 8 hourly if required.

Note: Metoclopramide can cause extrapyramidal side effects.

Treat acute dystonic reactions with:

- Anticholinergic agent, e.g.:
- Biperiden, IM/IV, 2 mg.
 - Repeat as necessary.

If an anticholinergic agent is not available:

- Promethazine, deep IM, 25–50 mg.
 - o In the elderly 25 mg.

If an anticholinergic agent or promethazine is not available:

Diazepam, IV, 5–10 mg for symptom relief.

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12.6.6 ACID ASPIRATION PROPHYLAXIS

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The use of a non-particulate, non-effervescent antacid reduces the risk of pneumonitis if gastric fluid is aspirated. Give to patients at risk of aspiration, e.g. pregnant women before Caesarean delivery.

- Sodium citrate, 0.3M, oral, 30 mL.
 - Not more than 30 minutes pre-induction of anaesthesia.

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12.7 ANAESTHESIA, SPINAL (INTRATHECAL)

Only preservative free medicines may be used. Larger doses cause block to spread higher, with risks of respiratory depression, hypotension and loss of consciousness.

- Bupivacaine 0.5% (Spinal use)
 - Give up to 3 mL according to desired level of block.

- Becomes hypobaric (light) within CSF so block may spread higher than anticipated.
- Bupivacaine 0.5% with dextrose (Spinal use)
 - o Give up to 3 mL according to desired level of block.
 - o Hyperbaric (heavy) so block spreads according to patient position.

To increase duration of analgesia:

ADD

• Fentanyl, 10–25 mcg (i.e. small amounts).

Caesarean deliveries

Lower doses are required due to physiologic changes of pregnancy:

Bupivacaine 0,5% with dextrose, 1.8 mL (9 mg).

AND

Fentanyl, 10 mcg (0.2 mL).

12.7.1 ANTICOAGULANTS AND SPINAL OR EPIDURAL BLOCKS

Patients on anticoagulants are at risk of developing a spinal haematoma with subsequent paralysis after a spinal or epidural block. These anticoagulants should be stopped before the spinal or epidural is performed according to the guidelines given below. In order to encourage safe and quality care of patients, please consult a specialist prior to attempting blocks on patients on anticoagulants. There are a range of oral anticoagulation, with each having specific recommendations with regard to neuraxial blocks.

Timing of anticoagulants in patients receiving neuraxial anaesthesia:

Anticoagulant	Before Neuraxial Block	After Neuraxial block	
Warfarin, oral	Consult with specialist to stop warfarin.	Restart after neuraxial block performed (do not delay) and epidural catheter removed. Monitor INR daily with indwelling catheter.	
Unfractionated Heparin, SC	Neuraxial techniques may be performed if total daily dose is <10 000U. Check PTT if higher doses are used.		
Unfractionated Heparin, IV	and check PTT<40 bolus/infusion restarted		
Prophylactic LMWH, SC	12 hours after last dose	4 hours after neuraxial block performed and epidural catheter removed	

Therapeutic LMWH, SC	24 hours after last dose	>24 hours and consult a specialist (bleeding risk of surgery should be assessed).
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Note. After neuraxial block or epidural catheter removal, patients should be observed closely for new or progressive neurological symptoms. A spinal haematoma can result in permanent paralysis unless decompressive surgery is performed within 8 hours of paralysis onset.

Clopidogrel and platelet GPIIb/IIIa inhibitors have variable durations of effects on clotting after stopping these medications. Specialist advice should be sought before performing neuraxial blocks on patients receiving these medications.

For patients on warfarin the use of bridging anticoagulation (giving heparin after warfarin is stopped in preparation for surgery or invasive procedures) remains unsettled. Practitioners should exercise careful judgment of competing risks in individual patients. Heparin may increase the risk of bleeding. Whatever practice is adopted the most important consideration is to ensure that adequate anticoagulation with warfarin is re-instituted once the risk of bleeding is past.

12.8 ANAESTHESIA, EPIDURAL

Only preservative free medicines may be used.

Local anaesthetics are administered through a catheter inserted into the epidural space at a spinal level appropriate for the surgery.

Aspiration and a test dose (2–3 mL) of local anaesthetic should be given to confirm catheter not intravascular or intrathecal. Subsequent doses should be fractionated (3–5 mL boluses).

- Bupivacaine 0.5%.
 - Onset ±10 minutes.

LoE:III^{xxxvi}

- Duration +4 hours.
- Motor block is less with lower concentrations.
- Maximum dose 2 mg/kg.

12.9 PERIPHERAL NERVE BLOCK OR WOUND INFILTRATION

Only preservative free medicines may be used for nerve blocks. Lidocaine has a faster onset of action than bupivacaine, but a shorter duration of action.

Lidocaine 1% or 2%.

- Higher concentrations cause more pain on injection.
- Maximum dose: 3 mg/kg.
- Lidocaine 2% plus adrenaline.
 - Not to be used in areas supplied by an end-artery e.g. finger, ear, penis.
 - Maximum dose: 7 mg/kg.
- Bupivacaine 0.5%
 - Not be used in mucosal areas as risk of systemic toxicity.
 - Maximum dose: 2 mg/kg.

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12.10 ANAESTHESIA, TOPICAL

- Lidocaine jelly, topical, 2 g/100mL.
 - o For urethral catheterisation: female 5-7 mL, male 10-15 mL.

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- Lidocaine topical spray, 4%.

 Maximum does 160 mg.
 - o Maximum dose 160 mg.
 - To assist with awake intubation or reduce haemodynamic response to intubation.

For venepuncture analgesia in adults or oncology patients requiring repeated invasive procedures (e.g. lumbar punctures, venepuncture):

- Lidocaine/prilocaine, topical cream, 2.5/2.5%.
 - Apply at least 1 hour before and cover with occlusive dressing.

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12.11 SEDATION

See chapter 23: Sedation.

12.12 PAIN, CHRONIC

See chapter 26: Pain.

12.13 INTENSIVE CARE

12.13.1 NUTRITIONAL SUPPORT

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Establish a multidisciplinary nutrition support team to assess and address the nutritional requirements of patients. This team should include a dietician.

Nutrition support should be considered in patients at risk, defined as those who have a poor absorptive capacity and/or high nutrient losses and/or increased nutritional needs from causes such as catabolism.

Oral feeding, if feasible, is preferred. Enteral tube feeding is the next best option.

Total parenteral nutrition (TPN) is indicated in exceptional circumstances. For short-term care (≤ two weeks), the current standard formulas in multichamber bags that have a long shelf-life are considered to provide adequate nutritional support. Clinicians should be aware of the possibility of clinically important hypovitaminosis in individual patients, and replace selected vitamins where appropriate.

Refer to the most current version of the National Department of Health Parenteral Nutrition Practice Guidelines for Adults, available at: www.health.gov.za

In selecting the treatment modality, the team should consider:

- » The likely duration of nutrition support.
- » Patient activity levels and the underlying clinical condition, e.g. catabolism.
- » Gastrointestinal tolerance, potential metabolic instability and risks of refeeding.

Potential complications harms of nutritional support include:

- » Re-feeding syndrome: Hypophosphataemia occurs when patients are refed too quickly with high carbohydrate feeds. The syndrome usually begins within 4 days of re-feeding. A multitude of life-threatening complications involving multiple organs may occur, causing: respiratory failure, cardiac failure, cardiac dyshythmias, rhabdomyolysis, seizures, coma, red cell and leukocyte dysfunction. The most effective way to prevent re-feeding syndrome is that feeds should be started slowly with aggressive supplementation of magnesium, phosphate and potassium.
- » Diarrhoea.
- » Lactose intolerance.

Regularly review the need for ongoing therapeutic nutritional support.

Vitamin and mineral supplementation should be considered on a case-bycase basis.

Enteral tube feeding

Enteral tube feeding should be used in patients who cannot swallow or who are at risk of aspiration.

Patients should be fed via a nasogastric tube unless this is contra-indicated. Patients with upper gastro-intestinal dysfunction (or an inaccessible upper gastro-intestinal tract) should receive post-pyloric (duodenal or jejunal) feeding.

Percutaneous endoscopic gastrostomy feeding should be used in patients likely to need long-term (≥4 weeks) enteral tube feeding.

Parenteral feeding

The team should consider parenteral nutrition in patients who are malnourished or at risk of malnutrition and fit the following criteria:

- » inadequate or unsafe oral and enteral tube nutritional intake, or
- » a non-functional, inaccessible or perforated (leaking) gastrointestinal tract.

Note: For short-term care, the current standard formulas in multi-chamber bags that have a long shelf-life are considered to provide adequate nutritional support.

The addition of glutamine does not confer any clear clinical benefits and is thus not recommended.

Parenteral nutrition can be withdrawn once adequate oral or enteral nutrition is tolerated and nutritional status is stable. Withdrawal should be planned and done in a stepwise way with a daily review of the patient's progress.

References:

- Anaesthetics and sedatives: World Health Organisation, WHO model prescribing information; Drugs used in anaesthesia, 1994. https://apps.who.int/medicinedocs/en/d/Jh2929e/2.html
- Lorazepam, oral: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Midazolam, IV: Walker KJ, Smith AF, Premedication for anxiety in adult day surgery, Cochrane Database Syst Rev. 2009 Oct 7;(4):CD002192. https://www.ncbi.nlm.nih.gov/pubmed/19821294
- Midazloma, IV: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Thiopental, IV (contraindication-porphyria): South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Sevoflurane: National Department of Health, Essential Drugs Programme, Medicine review: Sevoflurane, 5 March 2015. http://health.gov.za/
- Sevoflurane: National Department of Health, Essential Drugs Programme. Cost analysis report for halothane versus sevoflurane for induction of anaesthesia in adults at hospital level, 10 September 2015. http://health.gov.za/ Suxamethonium: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Intermediate-acting neuromuscular blocking agents: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Intermediate-acting neuromuscular blocking agents: Joint Formulary Committee, British National Formulary. London: BMJ Group and Pharmaceutical Press: 2019.
- Vecuronium: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016
- Suxamethonium: Perry JJ, Lee JS, Sillberg VA, Wells GA. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD002788. http://www.ncbi.nlm.nih.gov/pubmed/18425883
- Rocuronium: Perry JJ, Lee JS, Sillberg VA, Wells GA. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD002788. http://www.ncbi.nlm.nih.gov/pubmed/18425883

Rocuronium: Contract circular price: HP06-2014SVP. http://health.gov.za/

- Rocuronium: National Department of Health, Essential Drugs Programme. Medicine review: Rocuronium for muscle relaxation for rapid sequence induction, 31 March 2015. http://health.gov.za/
- Neostigmine: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Atropine: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Glycopyrrolate: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- Paracetamol, oral: The South African Society of Anaesthesiologists. South African Acute Pain Guidelines. SAJAA 2009;15(6):1-120. http://www.sasaweb.com/content/images/SASA Pain Guidelines.pdf

Paracetamol: Bandolier. Oxford league table of analgesics in acute pain. Available at:

- http://www.medicine.ox.ac.uk/bandolier/booth/painpag/acutrev/analgesics/leagtab.html

 *** Tramadol, oral: The South African Society of Anaesthesiologists. South African Acute Pain Guidelines. SAJAA 2009;15(6):1-120. http://www.sasaweb.com/content/images/SASA Pain Guidelines.pdf
- Ibuprofen, oral: The South African Society of Anaesthesiologists. South African Acute Pain Guidelines. SAJAA 2009:15(6):1-120, http://www.sasaweb.com/content/images/SASA Pain Guidelines.pdf
- xvii Fentanyl, IV: The South African Society of Anaesthesiologists. South African Acute Pain Guidelines. SAJAA 2009;15(6):1-120. http://www.sasaweb.com/content/images/SASA Pain Guidelines.pdf
- Fentanyl, IV: Scholz J, Steinfath M, Schulz M. Clinical pharmacokinetics of alfentanil, fentanyl and sufentanil. An update, Clin Pharmacokinet, 1996 Oct;31(4):275-92, http://www.ncbi.nlm.nih.gov/pubmed/8896944
- kviii Morphine, IV (dosing): South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.
- xix Ketamine, IV: McNicol ED, Schumann R, Haroutounian S. A systematic review and meta-analysis of ketamine for the prevention of persistent post-surgical pain, Acta Anaesthesiol Scand, 2014 Nov:58(10):1199-213. http://www.ncbi.nlm.nih.gov/pubmed/25060512
- Ketamine, IV: Brinck EC, Tiippana E, Heesen M, Bell RF, Straube S, Moore RA, Kontinen V. Perioperative intravenous ketamine for acute postoperative pain in adults. Cochrane Database Syst Rev. 2018 Dec 20;12:CD012033. https://www.ncbi.nlm.nih.gov/pubmed/30570761
- xx Tramadol, IV: Houmes RJ, Voets MA, Verkaaik A, Erdmann W, Lachmann B. Efficacy and safety of tramadol versus morphine for moderate and severe postoperative pain with special regard to respiratory depression. Anesth Analg. 1992 Apr;74(4):510-4. http://www.ncbi.nlm.nih.gov/pubmed/1554117
- Tramadol, IV: National Department of Health, Essential Drugs Programme. Medicine review: Tramadolol, IV July 2015. http://health.gov.za/
- xxi Diclofenac, IM (potential for scarring): Tarloff D, Lamacraft G, Joubert G. The prevalence of skin scars in patients previously given intramuscular diclofenac injections attending the Pain Clinic at Universitas Academic Hospital, Bloemfontein, South Africa. S Afr Med J. 2017 Jan 30;107(2):101-105. https://www.ncbi.nlm.nih.gov/pubmed/28220730

xxii Ward prescriptions for postoperative analgesia according to anticipated pain severity: The South African Society of Anaesthesiologists. South African Acute Pain Guidelines. SAJAA 2009;15(6):1-120. http://www.sasaweb.com/content/images/SASA Pain Guidelines.pdf

Patient controlled analgesia: Hudcova J, McNicol E, Quah C, Lau J, Carr DB. Patient controlled opioid analgesia versus conventional opioid analgesia for postoperative pain. Cochrane Database Syst Rev. 2006 Oct 18:(4):CD003348. Review. Update in: Cochrane Database Syst Rev. 2015;6:CD003348... http://www.ncbi.nlm.nih.gov/pubmed/17054167

Diclofenac, IM (potential for scarring): Tarloff D, Lamacraft G, Joubert G. The prevalence of skin scars in patients previously given intramuscular diclofenac injections attending the Pain Clinic at Universitas Academic Hospital, Bloemfontein, South Africa. S Afr Med J. 2017 Jan 30;107(2):101-105. https://www.ncbi.nlm.nih.gov/pubmed/28220730

xxv Ringer Lactate, IV: National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Ringer Lactate for resuscitation in adults, updated review, August 2019. http://www.health.gov.za/

Ringer Lactate, IV: Antequera Martin AM. Barea Mendoza JA. Muriel A. Saez I. Chico-Fernandez M. Estrada-Lorenzo JM, et al. Buffered solutions versus 0.9% saline for resuscitation in critically ill adults and children. Cochrane Database Syst Rev. 2019 Jul 19;7:CD012247. https://www.ncbi.nlm.nih.gov/pubmed/31334842

Ringer Lactate, IV: Liu C, Lu G, Wang D, Lei Y, Mao Z, Hu P, Hu J, Liu R, Han D, Zhou F. Balanced crystalloids versus normal saline for fluid resuscitation in critically ill patients: A systematic review and meta-analysis with trial sequential analysis. Am J Emerg Med. 2019 Mar 1. pii: S0735-6757(19)30149-4. https://www.ncbi.nlm.nih.gov/pubmed/3085204

Ringer Lactate, IV: Brown RM, Wang L, Coston TD, Krishnan NI, Casey JD, Wanderer JP, et al. Balanced Crystalloids Versus Saline in Sepsis: A Secondary Analysis of the SMART Trial, Am J Respir Crit Care Med. 2019 Aug 27. doi: 10.1164/rccm.201903-0557OC. [Epub ahead of print]

Ringer Lactate, IV: Rochwerg B, Alhazzani W, Sindi A, Heels-Ansdell D, Thabane L, Fox-Robichaud A, et al. Fluid resuscitation in sepsis: A systematic review and network meta-analysis. Ann Intern Med. 2014;161(5):347-55. https://www.ncbi.nlm.nih.gov/pubmed/250474

xxvi Dantrolene, IV: Kolb ME, Horne ML, Martz R. Dantrolene in human malignant hyperthermia.

Anesthesiology. 1982 Apr;56(4):254-62. https://www.ncbi.nlm.nih.gov/pubmed/7039419

Dantrolene, IV: Flewellen EH, Nelson TE, Jones WP, Arens JF, Wagner DL. Dantrolene dose response in awake man: implications for management of malignant hyperthermia. Anesthesiology. 1983 Oct;59(4):275-80. https://www.ncbi.nlm.nih.gov/pubmed/6614536

Dantrolene, IV: Larach MG. Brandom BW. Allen GC. Gronert GA. Lehman EB. Cardiac arrests and deaths associated with malignant hyperthermia in north america from 1987 to 2006: a report from the north American malignant hyperthermia registry of the malignant hyperthermia association of the United States. Anesthesiology. 2008 Apr;108(4):603-11. https://www.ncbi.nlm.nih.gov/pubmed/18362591

Dantrolene, IV: Chapin et al. Medscape: Malignant Hyperthermia Treatment & Management, 28 November 2018. [Internet][Accessed 2 December 2019] https://emedicine.medscape.com/article/2231150-treatment#d11 Dantrolene, IV: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxviii Oxygen: Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. Reg Anesth Pain Med. 2012 Jan-Feb;37(1):16-8. http://www.ncbi.nlm.nih.gov/pubmed/22189574

Diazepam, IV: Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. Reg Anesth Pain Med. 2012 Jan-Feb;37(1):16-8. http://www.ncbi.nlm.nih.gov/pubmed/22189574

Adrenaline (epinephrine): Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. Reg Anesth Pain Med. 2012 Jan-Feb;37(1):16-8. http://www.ncbi.nlm.nih.gov/pubmed/22189574

xxviii Lipid emulsion (20%), IV: Jamaty C, Bailey B, Larocque A, Notebaert E, Sanogo K, Chauny JM. Lipid emulsions in the treatment of acute poisoning: a systematic review of human and animal studies. Clin Toxicol (Phila). 2010 Jan;48(1):1-27. http://www.ncbi.nlm.nih.gov/pubmed/20095812

Lipid emulsion (20%), IV: Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. Reg Anesth Pain Med. 2012 Jan-Feb;37(1):16-8. http://www.ncbi.nlm.nih.gov/pubmed/22189574

Lipid emulsion (20%), IV: National Department of Health, Essential Drugs Programme. Cost analysis report for intralipid 20% emulsion for local anesthetic systemic toxicity, 8 October 2015. http://health.gov.za/

xxix Ephedrine, IV: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxx Phenylephrine, IV: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxxi Labetalol, Scott DB. The use of labetalol in anaesthesia. Br J Clin Pharmacol. 1982 Jun;13(1 Suppl):133S-135S. http://www.ncbi.nlm.nih.gov/pubmed/7093097

Labetalol, IV: Varon J, Marik PE. Perioperative hypertension management. Vascular Health and Risk Management. 2008;4(3):615-627. http://www.ncbi.nlm.nih.gov/pubmed/18827911

xxxxiii Dexamethasone, IV: Carlisle JB, Stevenson CA. Drugs for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD004125. http://www.ncbi.nlm.nih.gov/pubmed/16856030
Ondansetron, IV: Carlisle JB, Stevenson CA. Drugs for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD004125. http://www.ncbi.nlm.nih.gov/pubmed/16856030
Promethazine, IV: Carlisle JB, Stevenson CA. Drugs for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD004125. http://www.ncbi.nlm.nih.gov/pubmed/16856030
xxxiiii Ondansetron, IV/IM (PONV): Zhang D, Shen Z, You J, Zhu X, Tang QF. Effect of ondansetron in preventing postoperative nausea and vomiting under different conditions of general anesthesia: a preliminary, randomized.

controlled study. Ups J Med Sci. 2013 May;118(2):87-90. https://www.ncbi.nlm.nih.gov/pubmed/23441598 Ondansetron, IV/IM (PONV): South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxxiiv Sodium citrate, solution: Paranjothy S, Griffiths JD, Broughton HK, Gyte GM, Brown HC, Thomas J. Interventions at caesarean section for reducing the risk of aspiration pneumonitis. Cochrane Database Syst Rev. 2014 Feb 5;2:CD004943. http://www.ncbi.nlm.nih.gov/pubmed/24497372

Sodium citrate solution: National Department of Health, Essential Drugs Programme. Medicine review: Sodium citrate solution to reduce the risk of aspiration pneumonitis in patients undergoing Caeserean section. September 2015. http://health.gov.za/

xxxx Timing of anticoagulants: The BRIDGE Study Investigators .Bridging Anticoagulation: Is it Needed When Warfarin Is Interrupted Around the Time of Surgery or a Procedure? Circulation 2012;125:e496-e498. http://www.nobi.nlm.nih.gov/pubmed/22451610

Timing of anticoagulants: Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). Reg Anesth Pain Med. 2018 Apr;43(3):263-309. https://www.ncbi.nlm.nih.gov/pubmed/29561531

xxxivi Bupivicaine, 0.5%: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxxxiii Lidocaine 1% or 2%: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

Lidocaine 2% plus adrenaline: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

Bupivicaine 0.5%: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxxviii Lidocaine topical jelly: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

xxxix Lidocaine topical spray: South African Medicines Formulary. 12th Edition. Division of Clinical Pharmacology. University of Cape Town, 2016.

^{xl} Lidocaine/prilocaine, topical cream, 2.5/2.5%.: Sharma SK, Gajraj NM, Sidawi JE, Lowe K. EMLA cream efficively reduces the pain of spinal needle insertion. Regional anesthesia. 1996 Nov-Dec;21(6):561-4. http://www.ncbi.nlm.nih.gov/pubmed/8956393





SOUTH AFRICAN ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST CHAPTER 12: ANAESTHESIOLOGY AND INTENSIVE CARE NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2017 -2019)

Medicine amendment recommendations, with supporting evidence and rationale are listed below. Kindly review the medicine amendments in the context of the chapter for anaesthesiology and intensive care.

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED
12.1 Premedication	Midazolam, IV	Dose amended
12.2.1 Intravenous induction	Thiopental, IV	Contraindication added
(and/or maintenance) agents		
12.2.2.1 Induction (inhalation	Halothane, inhalation	Directions for use amended
agents)	Sevoflurane, inhalation	Directions for use not amended
12.2.2.3 Maintenance	Isoflurane, inhalation	Retained
(inhalation agents)	Sevoflurane, inhalation	Not added
	Desflurane, inhalation	Not added
12.3.1 Depolarising muscle	Suxamethonium, IV	Directions for use amended
relaxants		
12.3.2 Non-depolarising muscle re	laxants (NDMR)	
	Intermediate-acting neuromuscular-	Added as a therapeutic class
	blocking agents	
	Cisatracurium	Retained as an example of class
	Vecuronium	Retained as an example of class
	Rocuronium	Added as a therapeutic alternative;
		Intubation dose amended from "0.601
		mg/kg" to "0.6-1.2 mg/kg"
	Atracarium	Added as a therapeutic alternative;
		Intubation dose amended from "01-0.2
		mg/kg" to "0.3-0.6mg/kg"
12.3.4 Medicines to reverse	Suggamadex, IV	Not added
muscle relaxation		
12.4.1.2 Intravenous	Morphine, IV	Directions for use amended
analgesics		
	Ketamine, IV	Dose amended
	Paracetamol, IV	Not added
12.4.2 Postoperative pain in	Fentanyl, IV	Retained
the recovery room	Sufentanil, IV	Not added
	Diclofenac, IM	Directions for use amended
	Parecoxib, IV	Not added
	Lornoxicam, IV	Not added
12.4.3.1 Examples of ward	NSAIDs	Caution box added
prescriptions for postoperative		
analgesia according to		
anticipated pain severity	21.16	
	Diclofenac, IM	Directions for use amended
12.5.1 Crystalloids	Balanced solutions, IV	Added as a therapeutic class
	Ringer Lactate, IV	Listed as example of therapeutic class in
	B 1 1 0/	STG
	Balsol, IV	Listed as an example of therapeutic class
	Discoverinte D. IV	in therapeutic interchange database
	Plasmalyte B, IV	Listed as an example of therapeutic class
42.54	Dantalana IV	in therapeutic interchange database
12.6.1 Malignant	Dantrolene, IV	Dose and directions for use amended
hyperthermia	Fahadrina IV	Directions for use one and ad
12.6.3 Anaesthetic-related	Ephedrine, IV	Directions for use amended

acute hypotension				
12.6.5.1 Prevention of PONV	Combination therapy	not added		
	Droperidol, IM/IV	not added		
	Ondansetron, IV/IM	Dose and directions for use amended		
12.6.5.2 Treatment of PONV	Droperidol, IV	Not added		
	Ondansetron, IV	Not added		
- If an anticholinergic agent or promethazine is not available:	Diazepam, IV	Dose amended from "10 mg" to "5-10 mg".		
12.7.1 Anticoagulants and spinal or epidural blocks	Table on timing of anticoagulants for neuraxial anaesthesia	Not amended		
12.8 Epidural anaesthesia	Lidocaine 2% (preservative-free)	Deleted		
12.9 Peripheral nerve block or wound infiltration	Ropivacaine, IV	Not added		
12.13.1 Nutritional support	Multi-chamber bags	Guidance for short-term use at secondary level of care clarified		

Note:

- Limited capacity and limited support from external stakeholders received for the review of this
 chapter during the 2017-2019 review cycle. Furthermore, a number of comments were
 received to consider medicines for inclusion on the EML, without submission of supporting
 motivations or evidence.
- Therefore, extensive medicine reviews are required to be developed for this chapter in the next review cycle possibly in collaboration with external stakeholders.
- STGs relating to chronic pain management have been moved to the pain chapter.
- External comment received from a dietitian has been noted and a cross-reference to the NEMLC reviewed NDoH Parenteral Nutrition for Adults, 2017 Guidelines will be included in the text of the STG (the NDoH guideline provides guidance for secondary, tertiary and quaternary levels of care).

12.1 PREMEDICATION

Midazolam, IV: dose amended

Aligned with SAMF, 2016¹ and RCTs (low quality) in Cochrane review² that showed no difference in time to discharge from hospital, assessed by clinical criteria, in patients who received anxiolytic premedication versus placebo for day case surgery with significantly deeper sedation (preoperatively and postoperatively) shown for midazolam vs. placebo. Doses ranged from 0.05 to 0.2 mg/kg IV, PO, IM or SL.

Level of Evidence: II Systematic review of RCTs of low quality, Guidelines

12.2.1 INTRAVENOUS INDUCTION (AND/OR MAINTENANCE) AGENTS

<u>Thiopental, IV:</u> contraindication added Agent contraindicated in porphyria. **Level of Evidence: III Guidelines**³

12.2.2.1 INDUCTION (INHALATION AGENTS)

<u>Halothane, inhalation:</u> *directions for use amended* Sevoflurane, inhalation: *directions for use amended*

South African Society of Anaesthesiologists commented that dosing recommended are maximum vapouriser settings (4% and 8% for halothane and sevoflurane, respectively); and that agents should

¹ SAMF, 2016

² Walker, K.J. and A.F. Smith, *Premedication for anxiety in adult day surgery*. Cochrane Database Syst Rev, 2009(4): p. CD002192

³ SAMF, 2016

preferably be titrated to effect, using end-tidal concentrations (if available) which reflect agent uptake to the brain.

Level of Evidence: III Expert opinion

12.2.2.3 MAINTENENACE (INHALATION AGENTS)

<u>Isoflurane, inhalation</u>: retained <u>Sevoflurane, inhalation</u>: not added <u>Desflurane, inhalation</u>: not added

South African Society of Anaesthesiologists commented that sevoflurane and desflurane be included in the secondary level EML for maintenance of anaesthesia. However, NEMLC had previously considered sevoflurane cost-prohibitive for the local secondary level setting^{4 5}. Desoflurane is also cost-prohibitive but may possibly be considered for teaching purposes. Desoflurane and sevoflurane has been shown to have a quicker recover time compared to isoflurane and sevoflurane is comparable to desflurane in day surgery discharge time⁶, though desflurane is the most expensive⁷.

Recommendation: Evidence review and costing analysis to determine affordability would be required to inform decision-making for consideration of using desflurane at academic institutions.

Level of Evidence: Expert opinion

12.3.1 DEPOLARISING MUSCLE RELAXANTS

Suxamethonium, IV: directions for use amended

Text of the STG was updated as follows for clarity purposes:

- Suxamethonium, IV, 1-1.5 mg/kg.
 - Onset 30-60 seconds.
 - o Duration 5 minutes.
 - Repeated doses associated with bradycardia and prolonged neuromuscular block.
 - Contraindicated in patients at risk for developing suxamethonium-induced hyperkalaemia, e.g. upper or lower motor neuron defect, prolonged chemical denervation (ICU > 3 days), direct muscle trauma, tumour or inflammation, thermal trauma burns, disuse atrophy, severe infection, pre-existing hyperkalaemia.

Level of Evidence: III Standard of care

12.3.2 NON-DEPOLARISING MUSCLE RELAXANTS (NDMR)

Intermediate-acting neuromuscular-blocking agents: added as a therapeutic class

<u>Cisatracurium:</u> retained as an example of class <u>Vecuronium</u>: retained as an example of class <u>Rocuronium:</u> added as a therapeutic alternative Atracurium: added as a therapeutic alternative

Availability of NMDRs are inconsistent due to supply shortages. However, the choice of NDMRs is largely dependent on the following parameters: **onset, duration of action, adverse reactions, metabolism and elimination and price**⁸.

Contract price (RT300-2017): Sevoflurane 250ml= R792.48; Isoflurane 100ml= R162.47; 250ml= R234.60

⁴ National Department of Health, Essential Drugs Programme. Medicine review: Sevoflurane, 5 March 2015. http://health.gov.za/

⁵ National Department of Health, Essential Drugs Programme. Cost analysis report for halothane versus sevoflurane for induction of anaesthesia in adults at hospital level, 10 September 2015. http://health.gov.za/

⁶ Jindal R, Kumra VP, Narani KK, Sood J. Comparison of maintenance and emergence characteristics after desflurane or sevoflurane in outpatient anaesthesia. Indian J Anaesth. 2011 Jan;55(1):36-42. https://www.ncbi.nlm.nih.gov/pubmed/21431051

⁷ SEP price of desflurane 250ml = R1980. 63 [Internet] [Accessed 1 December 2019] https://mpr.code4sa.org/

⁸ SAMF, 2016

A circular was previously disseminated, when there were supply challenges with cisatracurium and atracurium. The circular advised of the rational use of NMDRs; and where there is no clinical indication for the use of cisatracurium or atracurium, (e.g.: no renal or liver impairment) rocuronium or vecuronium (if available) is preferred⁹.

The recommended therapeutic alternative for cisatracurium is atracurium. Atracurium is eliminated by Hoffman degradation and ester hydrolysis¹⁰ and can therefore be safely used in renal or liver impairment; but significant histamine release is associated with cardiovascular effects. Cisatracurium provides greater cardiovascular stability as it lacks histamine-releasing effects. Although, the increased adverse events with atracurium was noted to be not clinically significant (p <0.05) with significant lower cost per patient total dose (p<0.01)¹¹. Atracurium and vecuronium are listed on the WHO EML list, 2017 edition.

Comparison of the intermediate-acting NDMRs¹²:

Medicine	Intubation dose (mg/kg)	Time to intubation (onset)	Elimination	Duration	Price
Atracurium	0.3–0.6 (70kg:42mg)#	3-5 min	Eliminated by Hoffman degradation; can be used in renal or liver impairment.	15-35 mins	25mg/2.5ml: R57.84** (70kg:2 amps = R115.68)#
Cisatracurium	0.1–0.15 (70kg:10.5mg)#	4-6 min	Eliminated by Hoffman degradation; can be used in renal or liver impairment.	45-55 mins	5mg/2.5ml: R33.51** (70kg:R167.55)#
Vecuronium	0.08–0.1 (70kg:7mg)#	3-4 min	Eliminated by liver and kidney; avoid in renal and liver impairment.	20-30 mins	4mg/2ml: R802.93** (70kg:R1605.86)#
Rocuronium	0.6-1.2 (70kg:84mg)#	1-2 min	Eliminated by liver and kidney; avoid in renal and liver impairment.	45-60 mins	50/5ml: R52.93*; R182.15** (70kg: 2 amps = R105.86*; R364.30**)#

^{*} Contract circular: Hp06-2017SVP; ** SEP database, 12 December 2018; # Estimated dose and price for a 70 kg adult

Recommendation: The Adult Hospital Level Committee recommends that atracurium, cistracurium, vecuronium and rocuronium be included in the therapeutic class of intermediate-acting non-depolarising muscle relaxants.

Rationale: Availability of intermediate-acting NMDRs are inconsistent due to continuous supply shortages.

Level or Evidence: III Guidelines

12.3.4 MEDICINES TO REVERSE MUSCLE RELAXATION

Suggamadex, IV: not added

South African Society of Anaesthesiologists commented that suggamadex should be considered for addition (no evidence or motivation submitted).

Suggamadex is anticipated for consideration in unanticipated difficult airway as provides immediate reversal and prolonged repeated doses with post tetanic count prolonged.

Recommendation: Medicine review is required for suggamadex to be used at the respective level of care to inform decision-making for consideration for inclusion on the EML.

⁹ NDoH: Affordable Medicines Directorate. Circular: Non-depolarising muscle relaxants, December 2016.

¹⁰Craig RG, Hunter JM. Neuromuscular blocking drugs and their antagonists in patients with organ disease. Anaesthesia 2009;64 Supp 1:55.

¹¹ Movafegh, A.et al. Cost analysis and safety comparison of Cisatracurium and Atracurium in patients undergoing general anesthesia .Eur Rev Med Pharmacol Sci .2013;17(N. 4):447-450

¹² SAMF, 2016; BNF, 2019

12.4.1.2 INTRAVENOUS ANALGESICS

<u>Sufentanil, IV</u>: not added Fentanyl, IV: retained

The recommendation from the previous review cycle of the Adult Hospital Level STGS and EML was upheld - See below, the extract from the minutes of the Adult Hospital Level Committee meeting of 29 October 2015:

Sufentanil: The option of sufentanil was discussed. However, this agent has a longer duration of action than fentanyl, and most anaesthesiologists are more comfortable with the shorter acting agent. Sufentanil is also more expensive than fentanyl¹³.

Morphine, IV: directions for use amended

Guidance provided to administer bolus doses of morphine at intervals of 5-10 minutes, aligned with SAMF 2016¹⁴.

Level of Evidence: III Guidelines

Ketamine, IV: dose amended

Dosing was aligned with RCTs reviewed in two systematic reviews¹⁵ ¹⁶, where dosing is dependent on surgery procedure. Cochrane review provides review provides evidence of efficacy of perioperative ketamine in providing effective analgesia, but does not conclude on optimal dosing.

Level of Evidence: III

Paracetamol, IV: not added

The South African Society of Anaesthesiology commented that IV paracetamol should be considered as it is the safest analgesic and avoids first pass metabolism, thus attaining far higher blood levels than oral (no evidence submitted).

In the previous review cycle, NEMLC considered the price of paracetamol, IV to be cost prohibitive (willingness to pay price was provided as R5.00). The IV formulation was considered to be comparable to oral paracetamol in terms of safety and efficacy.

Current medicine prices of paracetamol, IV and tablets are listed below (note that the price of the administration set has not been included):

Medicine	Contract circular price	SEP ¹⁷
Paracetamol 500 mg tablets, 20's	R 2.863 ¹⁸	
Paracetamol, IV 1g (Fresenius Kabi)	R 10.83 ¹⁹	R163.19
Cetafuse, IV 1g®		R17.90
INtramol, IV 1g®		R23.25
Perfalgan, IV 1g®		R321.66
Paracetamol Biotech, IV 1g®		R17.82
Paraspen, IV 1g®		R163.19

Recommendation: Paracetmol, IV not be added to the hospital EML.

Review indicator: Price

¹³ Prices from Contract circular HP06-2017SVP

⁻ Fentanyl, 10 mcg (0.2ml) IV: R0.30 (using weighted average price for 0.05mg/ml 2ml amp = R2.982

⁻ Sufentanil, 0.5 mcg (IV): R4.60 (0.5 mcg/2ml amp = R9.20)

¹⁴ SAMF, 2016

¹⁵ Brinck EC, Tiippana E, Heesen M, Bell RF, Straube S, Moore RA, Kontinen V. Perioperative intravenous ketamine for acute postoperative pain in adults. Cochrane Database Syst Rev. 2018 Dec 20;12:CD012033. https://www.ncbi.nlm.nih.gov/pubmed/30570761

¹⁶ McNicol ED, Schumann R, Haroutounian S. A systematic review and meta-analysis of ketamine for the prevention of persistent post-surgical pain. Acta Anaesthesiol Scand. 2014 Nov;58(10):1199-213. http://www.ncbi.nlm.nih.gov/pubmed/25060512

¹⁷ SEP Price [Internet] [Accessed 2 December 2019] https://mpr.code4sa.org/

¹⁸ Contract circular RT289-2019

¹⁹ Contract circular RT297-2019

12.4.2 POSTOPERATIVE PAIN IN THE RECOVERY ROOM

Diclofenac, IM: directions for use amended

External comment advising of Nicolau's syndrome associated with IM diclofenac. However, this is rare; but commentator's motivation for providing guidance to counsel patients of the potential for scarring, as amended, was considered and the following STG text was updated:

- Diclofenac, deep IM, 75 mg 12 hourly.
 - O Administer for a maximum of 2 days.
 - O Avoid the same injection site.
 - o Counsel patient prior to injection of adverse events (scarring) at inject site, if applicable.

Level of Evidence: III Observational study²⁰

NEMLC MEETING OF 5 DECEMBER 2019:

NEMLC recommended that the general description of the site of IM injection, in the "upper outer quadrant of the buttocks" not be included as random IM injection into the buttock risks damaging the sciatic nerve which may result in medicolegal implications. Thus, safe injection practice for IM injection to the upper outer quadrant of the buttock is required, appropriately identifying the safer injection site in the deltoid muscle for each patient (ventrogluteal or dorsogluteal sites) which is not in the scope of the STGs and EML.

Parecoxib, IV: not added

External comment received to consider parecoxib IV as an alternative to diclofenac IM as it has greater efficacy (no evidence submitted).

Lornoxicam, IV: not added

External comment received to consider lornoxicam, IV rather than parecoxib, IV as the latter contains sulphur, is more expensive and cannot be administered IM.

Recommendation: HTA be done/commissioned for parenteral NSAIDs for postoperative pain in the recovery room.

12.4.3.1 EXAMPLES OF WARD PRESCRIPTIONS FOR POSTOPERATIVE ANALGESIA ACCORDING TO ANTICIPATED PAIN SEVERITY

NSAIDs: caution box added

Aligned with chapter 13: Musculoskeletal conditions.

Diclofenac, IM: directions for use amended

Aligned with section 12.4.2 Postoperative pain in the recovery room.

12.5.1 CRYSTALLOIDS

Balanced solutions, IV: added as a therapeutic class

Ringer Lactate, IV: listed as example of therapeutic class in STG

Balsol, IV: listed as an example of therapeutic class in therapeutic interchange database

<u>Plasmalyte B, IV:</u> listed as an example of therapeutic class in therapeutic interchange database

Aligned to chapter 20: Emergencies and injuries²¹, informed by the updated Ringer lactate review, September 2019²².

²⁰ Tarloff D, Lamacraft G, Joubert G. The prevalence of skin scars in patients previously given intramuscular diclofenac injections attending the Pain Clinic at Universitas Academic Hospital, Bloemfontein, South Africa. S Afr Med J. 2017 Jan 30;107(2):101-105. https://www.ncbi.nlm.nih.gov/pubmed/28220730

 $^{^{\}rm 21}$ Minutes of the NEMLC meeting of 26 September 2019.

²² National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Ringer Lactate for resuscitation in adults, updated review, August 2019. http://www.health.gov.za/

And, STG text updated to:

Balanced solutions may be appropriate in some patients (i.e. presentation with hyponatraemia, previous renal placement therapy):

- Balanced solution, e.g.:
- Ringers lactate, IV.

12.6.1 MALIGNANT HYPERTHERMIA

<u>Dantrolene</u>, IV: dose and directions for use amended

Amended, as dantrolene should be titrated to effect (reduction in muscle tone, cardiac and respiratory symptoms stabilise). Dose amended to dose used in standard clinical practice, based on old RCT evidence^{23 24} and 2010 observational study²⁵. Use of higher doses is uncommon, and clinical experience warrants the diagnosis to be queried if a rapid response is not seen, though muscular males may require doses >10 mg/kg²⁶.

Level of Evidence: II RCTs of low quality, Observational study, Expert opinion

STG text amended from:

- Dantrolene IV, 2 mg/kg as a single dose.
 - O Repeat doses until cardiac and respiratory symptoms stabilise.
 - O Up to 10 mg/kg may be required.

To

- Dantrolene IV, 2.5 mg/kg as a single dose (preferably through large bore cannula).
 - O Reconstitute with 60 mL water for injection. For a 70 kg patient, 175 mg (9 vials) is required.
 - Administer subsequent doses to clinical effect (cardiac and respiratory symptoms stabilise, muscle tone and body temperature reduced).
 - O Doses higher than 10 mg/kg is uncommon and the clinician should question the diagnosis.
 - O Although, high doses of 10 mg/kg may be required in muscular males.

12.6.3 ANAESTHETIC-RELATED ACUTE HYPOTENSION

Ephedrine, IV: directions for use amended

STG text amended as flows based on standard clinical practice and expert opinion:

- Ephedrine IV, 3-5 mg as a single dose and then further boluses as required to a maximum of 30 mg.
 - O Increases heart rate and contractility, and vasoconstrictor.
 - O Repeated administration can result in tolerance and tachyphylaxis.
- O Alternative vasopressor infusion (e.g. adrenaline (epinephrine)) may be needed to mitigate unresponsiveness to treatment.

Level of Evidence: III Expert opinion

12.6.5.1 PREVENTION OF PONV

Combination therapy: not added

External comment from stakeholder received that recommendations should include a combination of prophylactic antiemetics ie: dexamenthasone with ondansetron.

Recommendation: Combination anti-emetic therapy for prevention of PONV to be reviewed in the

²³ Kolb ME, Horne ML, Martz R. Dantrolene in human malignant hyperthermia. Anesthesiology. 1982 Apr;56(4):254-62. https://www.ncbi.nlm.nih.gov/pubmed/7039419

²⁴ Flewellen EH, Nelson TE, Jones WP, Arens JF, Wagner DL. Dantrolene dose response in awake man: implications for management of malignant hyperthermia. Anesthesiology. 1983 Oct;59(4):275-80. https://www.ncbi.nlm.nih.gov/pubmed/6614536

²⁵ Larach MG, Brandom BW, Allen GC, Gronert GA, Lehman EB. Cardiac arrests and deaths associated with malignant hyperthermia in north america from 1987 to 2006: a report from the north American malignant hyperthermia registry of the malignant hyperthermia association of the United States. Anesthesiology. 2008 Apr;108(4):603-11. https://www.ncbi.nlm.nih.gov/pubmed/18362591

²⁶ Chapin et al. Medscape: Malignant Hyperthermia Treatment & Management, 28 November 2018. [Internet][Accessed 2 December 2019] https://emedicine.medscape.com/article/2231150-treatment#d11

next review cycle.

Droperidol, IM/IV: not added

External comment received to consider droperidol as it is a very effective anti-emetic (no evidence

submitted).

Recommendation: For review in the next review cycle.

Ondansetron, IV/IM: dose and directions for use amended

Low quality RCT²⁷ suggests that ondansetron 8 mg is more effective than 4 mg in preventing vomiting (though comparable in reducing nausea) in patients undergoing general anaesthesia. Registered indication of PONV with dosing as a single dose of 4 mg given by intramuscular or slow intravenous injection at induction of anaesthesia²⁸ - intramuscular route of administration added.

Level of Evidence: III Disease oriented RCT, Guidelines

Guidance in STG updated to, "4-8 mg slow IV/IM".

12.6.5.2 TREATMENT OF PONV

Droperidol, IV: not added

External comment received to consider droperidol as it is a very effective anti-emetic (no evidence submitted).

Recommendation: For review in the next review cycle.

Ondansetron, IV: not added

External comment received to consider ondansetron, IV as it is a very effective anti-emetic (no evidence submitted).

Recommendation: For review in the next review cycle.

If an anticholinergic agent or promethazine is not available:

Diazepam, IV: dose amended from "10 mg" to "5-10 mg".

Standard of care.

Level of Evidence: III Expert opinion

12.7.1 ANTICOAGULANTS AND SPINAL OR EPIDURAL BLOCKS

The table on timing of anticoagulants in patients receiving neuraxial anaesthesia was amended in accordance with more recent American Society for Regional Anaesthesia, 2018 Guidelines²⁹.

However, due to the complex nature of management of patients on anticoagulants, the Committee recommended that specialists should be consulted for management.

And, the following STG text was added:

In order to encourage safe and quality care of patients, please consult a specialist prior to attempting blocks on patients on anticoagulants.

There are a range of oral anticoagulation, with each having specific recommendations with regard to neuraxial blocks.

²⁷ Zhang D, Shen Z, You J, Zhu X, Tang QF. Effect of ondansetron in preventing postoperative nausea and vomiting under different conditions of general anesthesia: a preliminary, randomized, controlled study. Ups J Med Sci. 2013 May;118(2):87-90. https://www.ncbi.nlm.nih.gov/pubmed/23441598

²⁸ SAMF, 2016

²⁹ Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). Reg Anesth Pain Med. 2018 Apr;43(3):263-309. https://www.ncbi.nlm.nih.gov/pubmed/29561531

12.8 EPIDURAL ANAESTHESIA

Lidocaine 2% (preservative-free): deleted

Reported to not be commonly used in practice, as a test dose is required.

Level of Evidence: III Expert opinion

12.9 PERIPHERAL NERVE BLOCK OR WOUND INFILTRATION

Ropivacaine, IV: not added

External comment received to consider ropivacaine as an alternative to bupivacaine, as there is some suggestion of greater safety at equivalent doses, no evidence submitted.

Recommendation: For review in the next review cycle.

12.13.1 NUTRITIONAL SUPPORT

<u>Multi-chamber bags:</u> Guidance for short-term use at secondary level of care clarified, as per NEMLC's recommendation, below.

Level of Evidence: III Expert opinion

AT THE NEMLC MEETING OF 11 APRIL 2019, NEMLC RECOMMENDED THE FOLLOWING:

As the Adult Hospital Level STGs provides guidance for **short-term** nutritional care, the following statement was added to the STG: "For short-term care, the current standard formulas in multichamber bags that have a long shelf-life are considered to provide adequate nutritional support. Clinicians should be aware of the possibility of clinically important hypovitaminosis in individual patients, and replace selected vitamins where appropriate".

Report prepared by TD Leong: Secretariat to the Adult Hospital Level Committee (2017-2020)

- Note: Information was sourced from NEMLC ratified minutes and NEMLC-approved documents.