South African Acute Pain Guidelines

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DRUGS AT A GLANCE

(Bold=paediatric)

LOCAL ANAESTHETIC DOSES AND INFUSION RATES FOR PERIPHERAL NERVE BLOCKS IN ADULTS (From Table II, page 61)

Technique	Drugs	Adult dose	Considerations
Plexus block	Bupivacaine	*LD: 0,25–0,5%, 20–40 ml *CI: 0,125–0,25%, 5–10 ml/h	Maximum 2 mg/kg or 6 mg/kg/24h; maximum 150 mg or 1 ml/kg bolus
	Levobupivacaine	As for bupivacaine	As for bupivacaine
	Ropivacaine	*LD: 0,5–,75%, 10–40 ml *CI: 0,2%, 0,1 ml/kg/h	Maximum 800 mg/24 h or 28 mg/h. Maximum 1 ml/kg bolus
Minor nerve blocks or infiltration	Bupivacaine	0,25–0,5% 5–10 ml/nerve	Maximum 2,5 mg/kg or 150 mg
	Levobupivacaine	0,25–0,5% 1–60 ml	Maximum 2,5 mg/kg or 150 mg
	Ropivacaine	0,2% 1–100 ml	Maximum dose 200 mg

LD = Loading dose *CI = Continuous infusion

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Acknowledgements

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and

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1. Acute pain management – Foreword

Acute pain management is not a luxury, it is a human right!

We as the South African consensus group tasked with making recommendations for the management of acute pain agree with every other international body that the management of acute pain is still less than optimal. Under ideal circumstances patient rights should include; the right to be believed; to be properly assessed; to access appropriate effective pain management strategies; to have education about effective pain management options; and to be cared for by health professionals with training and experience in the management of pain.

In order to provide better acute pain therapy an understanding of pain physiology, analgesic drugs, and the techniques of drug delivery are essential. All clinical staff dealing with the management of acute pain should understand the principles of pain management and the methods and techniques of providing analgesia so that they can make informed therapeutic decisions.

The development of this guideline reflects the current emphasis on delivering care that is patient-centred, cost-effective, and fair. This will endeavour to facilitate comparable standards of acute pain therapy for patients regardless of where they access services.

Key principles of best practice statements

A best practice statement describes best and achievable practice in a specific area of care. Such statements are based on a number of universally acceptable principles:

- Best practice statements are intended to guide practice and promote a consistent and cohesive approach to care.
- Best practice statements are primarily intended for use by medical practitioners, registered nurses, midwives and support staff.
- Statements are derived from the best available current evidence.
- Language use must be accessible and meaningful.
- Consultation with relevant role-players must take place.
- Statements will be regularly reviewed and updated.

The aim of this publication is to combine all of the above principles, summarise all the data and present it in a concise and easily readable form. The recommendations contained in this document have resulted from a multidisciplinary committee evaluating the information available and considering the scientific merit and evidence of this information.

How can these guidelines be used?

This information on acute pain management can be used in a variety of ways. It is primarily intended to serve as a guide to good practice and to promote a consistent and cohesive approach to care. The document is intended to be realistic and practical.

It is a basis for

- Developing and improving acute pain management.
- Stimulating learning among medical teams.
- Promoting effective interdisciplinary team working.
- Measuring quality in acute pain management.

This document must be considered as an aid to any health care professional managing acute pain, rather than a "recommended' regimen. It remains the prerogative of the practitioner to evaluate the patient and to adapt any of the suggestions to the circumstances surrounding that particular patient.

It is hoped that by using the information provided in this publication that there will be meaningful benefit for both the medical professional and the patient. The use of the principles provided will ensure that the right of all patients to adequate and effective pain management will be fulfilled.

Dr Milton Raff
President
SA Society of Anaesthesiologists, 2010

2. Introduction

This is the first edition of the South African Acute Pain Guidelines. It has been compiled in response to recognition of the need for guidelines to assist practitioners in acute pain management at ALL levels of medical care and in all types of practices. The guidelines are being published in two versions – this hard copy bedside reference, as well as a more comprehensive web-based version. The latter will also contain the references for these guidelines.

Both of these versions need to be seen as "works in progress", and the guidelines committee of the South African Society of Anaesthesiologists would appreciate inputs from colleagues from all sectors of medical practice over the next few years. Address your contributions and opinions to the SASA Councillor responsible for Practice Guidelines, currently Dr Hyla Kluyts through email: sasa@uiplay.com. A formal review of these guidelines is due in 2015, at the discretion of the South African Society of Anaesthesiologists.

The South African Society of Anaesthesiologists appointed a consensus group of practitioners from varying specialities, with varying areas of expertise and interest, to write these guidelines, which cover a wide range of clinical topics. It is by no means comprehensive, and will be expanded in the next edition, as needs dictate.

Acknowledgements

The authors acknowledge the very generous and constructive input of Prof Stephan Schug, who has shared his extensive knowledge with us, and given generously of his time, during two recent visits to South Africa.

The authors also acknowledge the following document as one of the primary references for these guidelines: *Acute Pain Management: Scientific Evidence 2nd Edition,* as published by the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine.

And finally, the publication would not have been possible without the very generous sponsorship by Bristol Myers Squibb and Pfizer Pharmaceuticals.

Christina Lundgren (editor) and Werner Mohr (SASA Council)

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3. Physiology of acute pain

Pain is a complex interaction of sensory, emotional and behavioural factors. There are no pain pathways only nociception pathways. Nociception is modulated at the level of the spinal cord and interpreted by the cortex, resulting in varying degrees of discomfort and pain.

- Pain is defined by the International Association for the Study of Pain (IASP) as an "unpleasant sensory and emotional experience, associated with actual or potential tissue damage or described in terms of such damage." (Mersky 1979).
- Acute pain is defined as pain of short and limited duration. The pain is related to an identifiable cause (trauma, surgery, inflammation etc).

Acute and chronic pain, represent a continuum of a process where inflammatory neuropathic visceral and somatic pain play a role. The CNS is not a hard-wired system, it allows for peripheral, central, intra-cellular and synaptic modifications. Acute pain can result in long-term changes and a subsequently modified response to sensory input (neuroplasticity).

Pain is divided into physiological pain and pathophysiological or clinical pain.

- Physiological pain is the activation of nociceptors in response to a noxious stimulus whereas the clinical pain includes tissue and/or nerve injury and the inflammatory response. Physiological pain serves as a protective mechanism, is well localised, is transient and is well differentiated from touch.
- Clinical pain outlasts the stimulus and spreads to non damaged areas leading to primary hyperalgesia. Peripheral sensitisation occurs as part of the inflammatory response and results in activation of the high threshold A beta fibres. This leads to the sensation of touch not being differentiated from pain. Antidromic impulses result in the release of neurotransmitters from nerve endings of a primary afferent in response to noxious stimulation.

Understanding nociceptive pathways

Primary afferent fibres and the dorsal horn

Peripheral nociceptors are organs that respond to pressure, temperature and chemical stimuli. The nociceptor cells are located in the Dorsa Root Ganglia except for the fibres innervating the head and

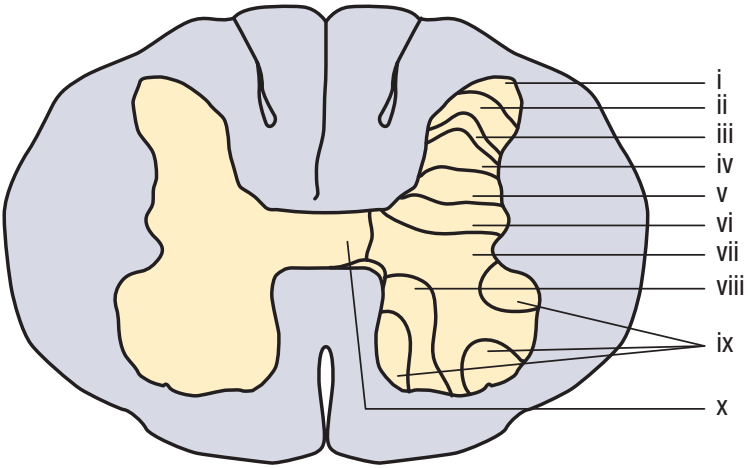
the oral cavity whose cell bodies are located at the trigeminal ganglion. There are 2 main categories of nociceptors:

- Aδ fibres (10-20%) are thinly myelinated and transmit mechanothermal stimuli.
- C fibres (80-90%) are non myelinated and are poly modal.

The Aδ and C fibres are high threshold fibres. Inflammatory soup chemicals sensitise high threshold nociceptors. (common after surgery and trauma).

*Silent nociceptors*_become active in the presence of inflammation and play part in peripheral sensitisation

Figure 1: Laminae in dorsal horn



The dorsal horn is made out of Lamina I to X

- Lamina I- consists of mainly Aδ fibres.
- Lamina II is called the substantia gelatinosa and contains mainly C fibres and inter neurons. There are no ascending tracts originating from lamina II.
- Laminas III & IV contain interneurons.
- Lamina V contains the WDR neurons (high threshold interneurons.)
- Lamina IX represents mainly motor neurons and lamina X is made of visceral interneurons.

Primary afferents interact extensively with other afferents as well as with interneurons (second order neurons) and endings of descending fibres. Second order neurons are divided into high threshold neurons (nociceptive specific) and "wide dynamic range (WDR)" neurons. The WDR neurons when sensitised respond to, and discharge in response to tactile non noxious stimuli (allodynia).

Central sensitisation results from activation of the N-methyl-D-aspartic acid (NMDA) receptors and leads to secondary hyperalgesia, "wind up" and LTP (long term potentiation) that represents increased activity in the dorsal horn following repetitive stimulation. Repetitive low threshold stimulation results in

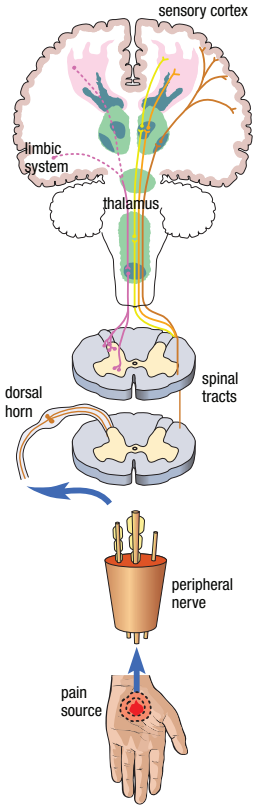
the phenomenon of "wind up" and temporal summation. These phenomena represent the decreased threshold and increased intensity that occurs in the spinal cord neurons as a result of repetitive stimulation from the primary nociceptors.

A stimulus occurring at a low threshold now results in an increased magnitude and longer duration of depolarisation at the post synaptic neuron.

Ten per cent of the primary afferents terminate in the anterior horn. (Explaining the possible failure of rhisotomy.)

Collateral branches of the small fibres Aδ and C may travel in the lateral part of the entry zone for several segments before synapsing in the dorsal horn (Lissauer's tract).

Figure 2: Basic afferent pain pathway



Neurotransmitters

At the periphery

Peripheral sensitisation occurs due to substances released by the damaged tissues, blood vessels and sympathetic terminals. This is termed the inflammatory soup and contains hydrogen and potassium ions, bradykinine, histamine, noradrenaline, 5-HT, PG, substance P, leukotrienes, nerve growth factor and others.

Dorsal horn

Excitatory

Substance P, neurokinine 1, glutamate: These in turn activate the low threshold AMPA and NK-1 receptors which in turn sensitise and activate the high threshold NMDA receptor.

Inhibitory

Predominantly at the descending pathways._Noradrenaline , dopamine, serotonine, histamine, oxytocin and vasopressin, acetyl choline, GABA, glycin and opioids

Intra cellular events

NMDA activation in the CNS (removal of the Mg plug) leads to Ca influx to the cell, Production of NO and secondary messengers, and PG production. C-fos gene expression – occurs within minutes of a painful stimulus and serves as a marker for noxious stimulation. C fos is thought to be the link between acute and chronic pain.

Receptors and ligands

Ligands transducer the specific stimulus into an action potential which is sodium channel (Na) dependant. Tetrodotoxin which is present in all sensory neurons rapidly deactivates the sodium current. Local anaesthetics act at this level, but as sodium channels are present in all nerve fibres, blocking of autonomic motor and the sensory fibres can occur. Agent blocking subtypes of sodium channels (specific to sensory fibres) are not yet available.

Pain modulation can be achieved by decreasing excitation (opioids receptor, Na channel blockers, ketamine) and/or increasing inhibition (Increased alpha-2 agonism (clonidine), glycine (GABA-agonists) at the level of the spinal cord.)

The most common receptors and ligands are outlined in Table 1:

Table 1: Receptors and ligands

RECEPTOR	SUBTYPES	LIGANDS
Transient receptor potential receptors (TRPs)	TRPV1 TRPV2 TRPA	Heat > 42 Celsius, H+, Capsaicin Heat over 54 Celsius Cold < 17 Celsius
Acid sensing	ASIC DRASIC	Protons
Purine	P2X3	ATP
Serotonin	5HT3	5HT
N-methyl-D-aspartic acid (NMDA) receptor	NRI	Glutamate
AMPA	iGlutR1	Glutamate
Kainate	iGlutR5	Glutamate
Prostanoids	EP1-4 IP	PGE2 PGI2
Histamine	HI	HA
Serotonine	5HT1A;5HT2A;5HT4	5HT
Bradykinine	BK1; BK2	BK
Cannabinoids	CB1-2	Anandamide
Opioids	Mu; Delta; Kappa;	Enkepalin; dynorphin; Beta-endorphin
Thacykinine	NeuroKinine1(NK!)	Substance P; neurokinine A

Ascending pathways

Spinothalamic tract originates in lamina I, II and V and ascends to the thalamus and then the somatosensory cortex, providing information about the type and the site of the painful stimulus. Spinomesencephlic tract originates mainly in lamina I and mediates the affective and emotional component of the nociceptive stimulus. Autonomic and sensory coordination is provided by this pathway. The cingulate cortex, insula, PAG, reticular formation and prefrontal cortex receive multiple inputs and help to coordinate autonomic and emotional responses.

Descending inhibition

These pathways modulate the nociception by action on the primary afferents and inter neurons at the level of the dorsal horn. They inhibit transmission towards the cortex and other higher centres. Tracts originate in the cortex, PAG (Periaqeductal grey) and brain stem nuclei. These fibres terminate in the dorsal horn facilitating inhibition and modulating the nociceptive input. Tricyclic antidepressants, opioids and Alpha 2 agonist are important agents for modulating nociception via the descending pathways. Inhibitory neurotransmitters include opioid, 5HT, NE and GABA.

Neuropathic pain

By definition, it is pain originating in the nervous system. There is no clear distinction between neuropathic and nociceptive pain as they often co-exist. Trauma and surgery cause nociceptive as well as neuropathic pain (cutting nerve endings) while pure nerve destraction results in an inflammatory process.

Receptors

Activation of nociceptors produces depolarisation and eventually triggers an action potential and release of ligands from the nerve endings.

Opiate receptors

Were first identified in 1973. Are synthesised by the cell body in the dorsal horn and respond to endogenous and exogenous opiates. Note that opiate receptors are also transmitted peripherally along the nerve fibre. This explains the opioid's effect when administered intra-articularly or into the subcutaneous tissue. Located mainly (75%) presynaptically, the activation of opioid receptors reduces the release of neurotransmitters from the primary afferent neuron. Inflammation and nerve injury result in loss of opioid receptors presynaptically, and formation of the metabolite morphine 3 glucoronide which antagonises opioid analgesia.

GABA and the glycine receptors (CNS)

Have an inhibitory function. GABA-A is largely post synaptic and responds to endogenous GABA ligand and benzodiazepines. GABA B is a presynaptic receptor that responds to endogenous GABA and baclofen. Barbiturate, anaesthetic drugs and corticosteroids are also thought to activate the GABA receptor.

Adrenoreceptors

Activation of alpha adrenoreceptors at the dorsal horn has an analgesic effect (endogenous NE, exogenous clonidin). The effect is synergistic with opioid agonists.

N-methyl-D-aspartic acid (NMDA) receptor

Release of glutamate and substance P from the nociceptive primary afferents, activates the low threshold AMPA and NK1 receptors which in turn activate the NMDA receptor. Removal of the Mg plug is followed by influx of Ca into the cell and subsequent depolarisation. Ketamine is an NMDA antagonist with the potential to provide analgesia and modulate development of chronic pain. The NMDA receptor is involved in development of tolerance to opioids

Transient receptor potential receptors (TRPs)

TRPV-1 (previously called VR1) is a non selective ion channel, activated by capsaicin (a vanilloid compound), heat above 43 degrees Celsius, lipoxygenase, products of arachidonic acid and N-archidonoyl-dopamine.

Other members of the TRP family of ion channels have been described and found to be important in nociceptor activation. TRPV2-4 as well as TRPM8 and TRPA1 are all activated by temperature in the noxious and non-noxious range and together encode the entire temperature spectrum.

The autonomic nervous system

The autonomic nervous system is closely linked to the nociceptive pathways.

Remember: The sympathetic system is an **EFFERENT** system**.**

A biofeedback is maintained at the levels of:

- Extensive synapses between the afferent and sympathetic fibres take place at the dorsal horn level.
- DRG level: sympathetic fibres form a "basket" around the DRG influencing afferent transmission.
- Peripheral: somatic and visceral nociception causes vasodilatation, tissue damage and subsequent release of neurotransmitters. Circulating cathecolamines as well as NE released from the sympathetic fibres, perpetuate the noxious stimulus.

The gate control theory

In 1965 Melsack and Wall first published the gate control theory. The modulating role of the dorsal horn was conceptualised. In the initial theory Melsack and Wall postulated that the large fibres are "closing the gate" to nociception transmission into the higher centers. In 1982 they modified the theory to include the inhibitory descending mechanisms. This theory is still valid today but the role of the small fibres in modulating nociception is now being looked at more closely.

Psychological aspects of acute pain

Pain is an individual Bio-Psycho-Social phenomenon (Turk 1995) and is largely influenced by culture, previous pain experience and ability to cope. It is a personal and subjective experience. Psychological factors that influence the pain experience are: catastrophising and focusing on the pain, secondary gain and environmental factors, fear avoidance and anxiety. Preoperative anxiety has been shown to contribute to increased postoperative pain while preoperative depression is a predictor of postoperative pain.

Clinical practice points

1. Identifying and attending to fear avoidance, catastrophising and the presence of possible gain factors, can lessen the impact of pain.
2. Anxiety and depression are associated with higher pain intensity.
3. Cognitive behavioural modification, by patient education.
4. Multidisciplinary approach is the key.

Progression of acute to chronic pain

Chronic pain can develop following an acute pain episode. Postoperative pain, post zoster pain and low back pain are often associated with chronic pain. 1.5% of all surgical procedures result in chronic pain development.

Risk factors for the development of chronic pain are:

- Intense and prolonged preoperative and/or postoperative pain
- Repeated surgery
- Chemo and/or radiotherapy perioperatively
- Postoperative complications (i.e. infection)

There is some evidence to suggest that epidural analgesia initiated before thoracotomy and carried into the postoperative period reduces development of chronic pain compared with patients who received IV PCA.

Some surgical procedures result in an increased incidence of chronic pain:

Procedure	Incidence
Dental surgery	5-13%
Vasectomy	0-37%
Cholecystectomy	3-56%
Mastectomy	11-57%
Inguinal hernia repair	0-63%
Thoracotomy	5-67%
Amputations	30-85%

The pathophysiological mechanism postulated to be involved in chronic pain development is central sensitisation and wind up phenomena.

Clinical practice points

1. Attention to pain control throughout the pre-, intra- and postoperative period might reduce development of chronic pain.
2. Neuroaxial blockade and nerve blocks in the perioperative period might reduce chronic pain development by minimising central sensitisation.
3. NMDA receptor antagonist drugs show preventive analgesic effect.

Adverse effects of pain

Acute pain provokes physiological modification in multiple organ systems. The stress response involves neuro- humoral changes with multiple implications. Adequate pain management aims at providing pain relief as a humane measure as well as to minimise the multi-system deleterious effects caused by the stress response.

A catabolic state, sympathetic stimulation and immunosuppresion are the hallmark of the stress response. The psychological effects can create a vicious cycle maintaining the negative effects. The endocrine system changes result in a catabolic state, increased ACTH, cortisol ADH, cathecolamines, angiotensin II, IL-1, IL-6, TNF.

Table II: Adverse effects of pain

Endocrine
Increased catabolism
↓ ACTH, ADH,GH, Cathecolamines, angiotensin II, IL-1,IL-6, TNF
Decreased anabolism
↓ Insulin, testosterone
Metabolic
Carbohydrates
Hyperglycaemia, glucose intolerance, insulin resistance
Protein
Increase acute phase protein catabolism
Lipid
↓ lypolysis
Water and electrolyte
Water retention
Potassium loss

Sympathetic stimulation results in increased heart rate and blood pressure, increasing risk of myocardial ischaemia. Pain limits coughing and decreases FRC which in turn increases the risk of atelectasis and pulmonary infection. Decreased mobility results in increased risk of DVT. Anxiety, helplessness, loss of control, inability to interact and sleep deprivation all contribute to psychological disturbances, which can increase the risk for development of persistent pain.

4. Measurement and assessment of acute pain

The key issues to be discussed in this section are:

4.1 Tools for pain measurement

4.2 Regular assessment and monitoring of pain as the 5th vital sign

4.3 Adjust treatment according to intensity of pain

4.4 The need for a pain services team documentation and evaluation of service

4.1 Pain assessment tools

Patient's **personal report** is essential as pain is subjective. Assessment and rating of pain provide an objective tool that provides a guideline for management. Always believe the patient. Validated scales for children and adults with impaired cognition are available but are beyond the scope of this chapter.

It is vital to record the patient's level of consciousness in order to avoid complications and opiate overdose.

Acute pain requires only a **unidimentional** assessment and measurement.

We need to measure pain intensity and it is not practical nor is it efficient to employ questionnaires and assess qualitative aspects of pain. The qualitative aspects are relevant for assessment of chronic pain and are employed at its management.

Simple to administer scales, that are easily understood by the patient need to be employed. There are a large number of validated scales presented in the literature; each one of them has got its own strengths and weaknesses. The most widely used scales are:

VAS (Visual analogue scale)

It is a sensitive tool consisting of a 0-100 mm straight line. The one end is marked with "no pain" while the other end is marked as "worst possible pain".

The patient is requested to mark on the scale the point that best describes their pain. The result as presented as a ratio.

VAS measurement is accurate but it requires the assessing nurse/doctor to carry the required "instrument", some patients do not understand the tool.

Figure 1: Visual analogue scale (VAS)

VNRS (Verbal numeric rating scale)

This scale is simple, quick and correlates well with VAS.

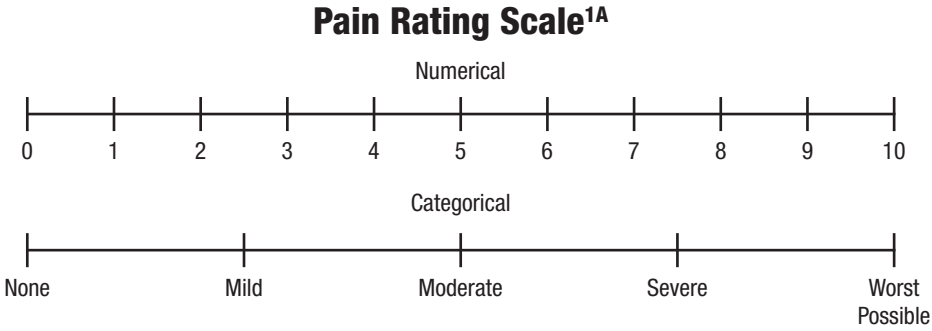
This tool consists of a simple 0-10 verbal scale. The patient is asked to rate their pain verbally on the scale of 1 to 10 with 1 being a very slight discomfort and 10 being the most severe pain ever imagined or experienced.

This scale is operator friendly as it does not require specific "tools" to be carried around.

It is patient friendly as it requires short explanation and is easily understood.

And it is also research-friendly (Using a numeric scale provides a simple documentation, reporting and comparison tool).

Figure 2: Pain rating scale



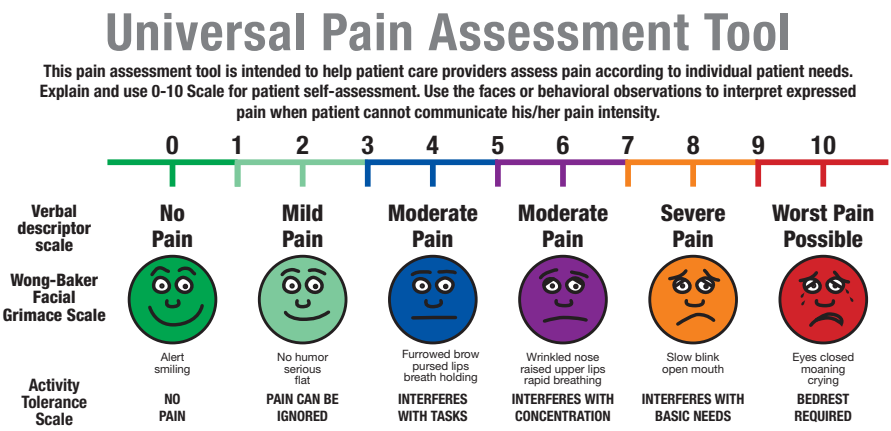
VRS (Verbal rating scale) or VDS (Verbal descriptor scale)

This scale requires the patient to report their pain as: none, mild, moderate severe or very severe. This tool's effectiveness is limited in a multilingual society.

Faces (Facial expressions) (Wong Baker)

This scale has been validated for children over the age of 5 Years. It can also be used for adults with cognitive impairment.

Figure 3: Universal pain assessment tool



NO PAIN **EXCRUCIATING PAIN**

VAS, NRS, and faces scales are available from various pharmaceutical companies and can be easily acquired for the ward nursing staff as well as other health professionals involved in treatment of the postoperative patient.

PAINAD Scale

Assessing pain of patients with advanced dementia presents a unique challenge.

A common example for this group are the elderly patients presenting to theatre with femur fractures. The scale most often used internationally for this group is the

PAINAD Scale (Pain Assessment in Advanced Dementia). This is a five item observational tool that requires observation of the patient for a period of time and can be time consuming. The higher score indicates increased level of pain.

ITEMS	0	1	2	SCORE
BREATHING INDEPENDENT OF VOCALISATION	NORMAL	Occasional laboured breathing. Short period of hyperventilation	Noisy laboured breathing. Long period of hyperventilation.	
NEGATIVE VOCALISATION	NONE	Occasional moan or groan. Low level speech with a negative or disapproving quality.	Repeated troubled calling out. Loud moaning or groaning. Crying.	
FACIAL EXPRESSION	SMILING/ INEXPRESSIVE	Sad. Frightened. Frown	Facial grimacing.	

ITEMS	0	1	2	SCORE
BODY LANGUAGE	RELAXED	Relaxed tense. Distressed pacing. Fidgeting.	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out.	
CONSOLABILITY	NO NEED TO CONSOLE	Distracted or reassured by voice or touch.	Unable to console, distract or reassure	

Breathing

1. Normal breathing is characterised by effortless, quiet, rhythmic (smooth) respirations.
2. Occasional laboured breathing is characterised by episodic bursts of harsh, difficult or wearing respirations.
3. Short period of hyperventilation is characterised by intervals of rapid, deep breaths lasting a short period of time.
4. Noisy laboured breathing is characterised by negative-sounding respirations on inspiration or expiration. They may be loud, gurgling, or wheezing. They appear strenuous or wearing.
5. Long period of hyperventilation is characterised by an excessive rate and depth of respirations lasting a considerable time.
6. Cheyne-Stokes respirations are characterised by rhythmic waxing and waning of breathing from very deep to shallow respirations with periods of apnoea (cessation of breathing).

Negative vocalisation

1. None is characterised by speech or vocalisation that has a neutral or pleasant quality.
2. Occasional moan or groan is characterised by mournful or murmuring sounds, wails or laments. Groaning is characterised by louder than usual inarticulate involuntary sounds, often abruptly beginning and ending.
3. Low level speech with a negative or disapproving quality is characterised by muttering, mumbling, whining, grumbling, or swearing in a low volume with a complaining, sarcastic or caustic tone.
4. Repeated troubled calling out is characterised by phrases or words being used over and over in a tone that suggests anxiety, uneasiness, or distress.
5. Loud moaning or groaning is characterised by mournful or murmuring sounds, wails or laments much louder than usual volume. Loud groaning is characterised by louder than usual inarticulate involuntary sounds, often abruptly beginning and ending.
6. Crying is characterised by an utterance of emotion accompanied by tears. There may be sobbing or quiet weeping.

Facial expression

1. Smiling is characterised by upturned corners of the mouth, brightening of the eyes and a look of pleasure or contentment. Inexpressive refers to a neutral, at ease, relaxed, or blank look.
2. Sad is characterised by an unhappy, lonesome, sorrowful, or dejected look. There may be tears in the eyes.
3. Frightened is characterised by a look of fear, alarm or heightened anxiety. Eyes appear wide open.

Recommended tools

The assessment tool needs to be appropriate to the patient's developmental age, cognitive status and emotional status.

In the routine clinical setting we use the **VNRS** for adults and the "**faces" scale** for children or adults with impaired cognition, or when there is a language barrier.

In your institution/your practice choose a scale and be consistent, use the same scale for all your patients for pain assessment.

There should be coordination and collaboration between nurses and medical practitioners in order to avoid confusion and facilitate reliable documentation and management.

4.2 Regular assessment and the 5th vital sign

Regular pain evaluation is as important and as basic as monitoring BP, pulse rate, temperature and respiratory rate in the patient with acute pain, therefore pain is considered to be the 5th vital sign.

It is important to remember that: Pain is **subjective.**

While nociception is a universal concept, pain is **subjective** and is dependant on personality, culture, previous experiences and expectations. Pain is a Bio-Psycho-Social phenomenon and pain is **dynamic**. Pain intensity varies with activity and with time.

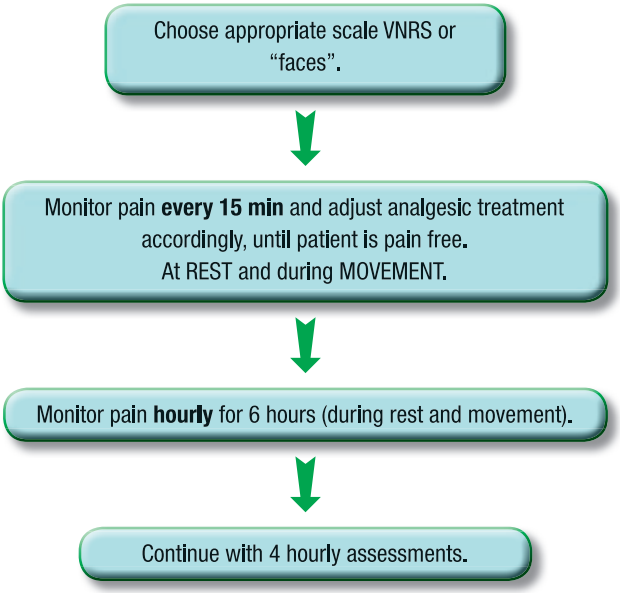
Pain needs to be measured during rest as well as with movement. (Moving legs, coughing, etc). It is in our scope of practice to provide safe and effective pain relief that is relevant to patient expectations as well as to the local South African conditions.

The vital signs monitoring chart should include a column dedicated to reporting pain intensity at regular intervals. All care providers who deal with surgical post operative patients need to be educated on an ongoing basis and awareness should be raised re the importance of monitoring pain intensity. It is vital that the nurse has a clear and immediate line of communication with the doctor responsible for pain control so that rapid adjustment of pain medication can take place.

Recommended strategy

1. Nursing chart to include 5th vital sign monitoring.
2. Assess pain at rest and during movement.
3. Respond and treat promptly and appropriately.

Figure 3: Designing a pain measuring and monitoring protocol



IF PAIN INTENSITY INCREASES TO > 5/10

1. CONTACT RELEVANT PHYSICIAN
2. ADJUST PAIN TREATMENT
3. GO BACK TO 15 MIN AND THEN AN HOURLY MONITORING SCHEDULE.

IN THE MEANTIME:

1. Look for complication that might cause pain (DVT, compartment syndrome, infection, etc)
2. Monitor the medication's side effects (excessive sedation, respiratory depression, nausea and vomiting)

4.3 How to adjust treatment according to intensity of pain

Employ a treatment ladder based on the severity of the pain, available drugs and patient condition. Recommended treatment according to pain scale is as follows:

Pain scale	Interpretation	Action
0-2/10	No pain	No treatment or NSAIDS or paracetamol
3-5/10	Mild pain	Paracetamol, and "weak opioids (codeine, D-propoxyphene)
6-8/10	Moderate	Codeine, paracetamol, NSAIDs, morphine
9-10/10	Severe	PCA or epidural or morphine and paracetamol and NSAIDs

4.4 The pain team and the need to document and evaluate the service

In order to control pain effectively a pain team is needed to perform the following functions:

1. Provide specialised, prompt, efficient, safe and multimodal pain management around the clock.
2. Develop protocols and guidelines to assist in the provision of safe and effective treatment, tailor made to the specific conditions at the institution.
3. Provide an up-to-date, evidence-based and appropriate understanding of postoperative pain management to all health workers involved in looking after postoperative patients, in the form of formal lectures, informal teaching and printed communications.
4. Provide the links to chronic and palliative care services.
5. Provide patient information and preoperative counselling.
6. Monitor patient outcomes and document the results in the institution, in order to compare and improve services.
7. Promote participation in a national audit of pain services.

In conclusion

While it might not be possible for all hospitals to have access to a pain unit, it is desirable that there is a consultant anaesthetist designated to acute pain management around the clock.

Clinical practice points

1. Assess patients regularly for pain.
2. A simple tool used consistently is more important than which tool you use.
3. Act on the score immediately.
4. Look for complications that can increase the level of pain.
5. Instituting pain teams at the hospital/clinic level is desirable.
6. The team's role would be to provide continuous pain relief and to educate staff and patients re benefits and techniques available for pain management.

5. Drug listings – Enteral and Parenteral

Porphyria guide:

- USE = Safe
- UWC = Use with caution
- UWECO = use with extreme caution, may be unsafe,
- AVOID

5.1 OPIOIDS – mainly for SEVERE pain

Group into:	Side effects:
1. Opioid agonists 2. Opioid dualists – both antagonism and agonism. Theoretically side effects should be cancelled out 3. Opioid antagonists 4. Atypical opioids	1. Respiratory depression 2. Sedation 3. Nausea and vomiting 4. Pruritis 5. Constipation 6. Tolerance

(5.2 OPIOIDS)

MORPHINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
SRM-RHOTARD MST Continus	***Oral*** 10–2 0 mg q 12 h	Morphine and cyclicine USE	Usually oral morphine preparations are used in the treatment of chronic pain. Dosage is dependent upon severity of pain and patient's previous analgesic history.
Merck Morphine sulphate Micro Morphine Injection Morphine Sulphate-Fresenius ***Combination*: Morphine + Cyclizine = Cyclimorph**	***Intramuscular*** 0,1–0,3 mg/kg q 4 h ***Intravenous*** *Bolus* 1–5 mg q 1 h* *Infusion** Give a loading dose, then titration depending pain and sedation scale = 3–5 mg/hr		*** Only in ICU.** • **Infusions may readily cause excessive accumulation of drug with respiratory *depression* and, if undetected, DEATH.** • **PCA is a safer option.** • IV opioid PCA provides better analgesia than conventional parenteral opioid regimens. • Patient preference for IV PCA is higher when compared with conventional regimens. • Extreme caution with neuraxial morphine is advised as the onset of respiratory depression only occurs 8–12 hrs post-administration. • Respiratory depression in the elderly is more prevalent and the neuraxial dose of opioids should be drastically decreased.
	PCA Bolus 1–2 mg with 5–10 min lockout time		Any opioid injected neuraxially should be "preservative-free" i.e. PF. ***Side effects of opioids:*** 1. Respiratory depression 2. Sedation (best indicator of incipient resp. depression) 3. Nausea and vomiting 4. Constipation Please note that these symptoms will occur with all opioid type drugs.

PETHIDINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Merck-Pethidine HCl Micro-Pethidine Pethidine HCl-Fresenius	***Intramuscular*** 1–1,5 mg/kg q 3–4 h ***PCA*** 10–2 mg bolus with 5–10 min lockout	USE	• No one opioid has ever been shown to be superior than another. • It depends on the preference and experience of the prescriber. • Pethidine commonly causes euphoria/dysphoria.

(5.2 OPIOIDS)

PAPAVERATUM			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Omnopon-Fresenius	***Intramuscular*** 0,15 mg q 4 h		**Not for children below 1 year old.**

DIHYDROCODEINE TARTRATE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
DF-118	***Oral*** 30 mg q 4–6 h ***Intramuscular*** 25–50 mg q 4–6 h	USE	**Not for children below 4 yrs.** 30 mg of DF-118 exhibits comparative analgesia to 10 mg morphine. May worsen asthma.

DIPIPANONE HCl (10 mg) + cyclizine (30 mg)			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Wellconal	***Oral*** 1 tab q 6 h. May increase by ½ tab increments to max of 3 tabs.		FOR MODERATE TO SEVERE PAIN

PROPOXYPHENE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Doloxene	65 mg (1 cap) q 4 h to a maximum of 390 mg/day		FOR MILD TO MODERATE PAIN Low affinity agonist.

Codeine			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Lennon-Codeine Phosphate	15–60 mg daily po	USE	MILD TO MODERATE PAIN • Low affinity agonist. • May not have any analgesic activity, but 10% demethylated to morphine and this is probably active.

5.2 OPIOID DUALISTS

PENTAZOCINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Pentazozine-Fresenius Sosenol	***Injection*** 30–40 mg q 3–4 h IM/IV/SC (If IV, only 30 mg/dose) Max 360 mg/24 hrs	AVOID	FOR MODERATE TO SEVERE PAIN • Not known as a potent analgesic, but proponents claim superior analgesia especially postop in females having varicose vein operations. • Also increases peripheral vascular resistance. This afterload increase may be detrimental in the elderly. • Watch out for respiratory depression in children.

BUPRENORPHINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Temgesic Subutex	***Oral*** 0,2–0,4 mg q 6–8 h SL. ***IM/slow IV infusion:*** 0,3–0,6 mg q 6–8 h	USE	FOR MODERATE TO SEVERE PAIN • May experience excitation/hallucinations • ***Contra-indications***:. ▪ Concomitant MAOI ▪ Acute asthma ▪ Not for children < 12 yrs ▪ IM injection must be “deep”

5.3 OPIOID ANTAGONISTS

NALOXONE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Narcan	IV = 0,006 mg/kg		• May cause pulmonary oedema if entire calculated dose is rapidly administrated. • Ampoule contains 0,4 mg. This should be diluted in 10 ml prior to administration. • Will reverse all effects of opioids. But half-live 15–60 min. Unwanted side effects of opioid may re-occur, warranting re-administration of naloxone.

5.4 ATYPICAL OPIOID

TRAMADOL			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Tramal **Dolotram** **Tramahexal**	***Oral*** • *Caps:* 50–150mg q4–6h to a max of 400mg/day **SR** tabs: 100-150mg q12h • *Drops:* 100mg = 1 ml = 40 drops Start with 20drops and titrate up if necessary. Do not exceed 400 mg/24 h ***Rectal*** 100 mg/suppository. Do not exceed > 400 mg/24 h ***IV/IM*** 100 mg im Intravenous administration must be slow		**Not for children < 12 yrs** • Avoid using $5HT_3$ antagonists (anti-emetics) with tramadol, as tramadol works on μ-receptors, noradrenaline and *serotonin* receptors. • Caution use with SSRI as serotonergic syndrome effects e.g. sweating and anxiey may occur. • Avoid rapid IV administration → increased incidence of nausea and vomiting. • Higher doses may cause nausea and vomiting. • Large dose variation due to reduced *active* metabolite production in 10% of Caucasian population. • ***Therapeutic range:*** moderate to severe pain.

5.5 PARACETAMOL

DRUG	ADULT	PORPHYRIA	RELEVANT INFORMATION
ENTERAL ***Oral* – 500 mg/tab** **Adco-Paracetamol, Antalgic, Fevamol** **Go-Pain P, Pacimol** **Painomol Be Tabs** **Panado, Prolief, Tylenol, Tylenol, Extended Release**	0,5–1 G q 4 h to a **maximum** of 4 G/day	USE	MILD TO MODERATE PAIN ONLY **Not recommended for children below 3 mths.**
Varipan	2 caplets q 8 h, max 6 caplets/24 h		**Do not crush, chew or dissolve the extended release caplets.**
Paediatric syrups **Adco-Paracetamol** **Antalgic, Calpol GSK, Go –Pain, Napamol, Panamol, Panado, Pyradol**			

(5.5 PARACETAMOL)

DRUG	ADULT	PORPHYRIA	RELEVANT INFORMATION
Rectal **Empaped**	N/A		• Rectal absorption is inconsistent. • Beware of renal and liver disease.
PARENTERAL			
Intravenous **Perfalgan**	***Adults*** (> 50 kg) 1 g q 6 h to max dose 4 g/24 hrs		• Administer as a 15minute infusion, else the efficacy of the drug may be reduced. • Registered for use for 24 hrs only. • An adjuvant to be used as a baseline analgesia unless contra-indicated • Do not administer any other oral paracetamol concomitantly; beware of combination analgesics that may contain paracetamol.

5.6 NSAIDs (for MILD to MODERATE Pain Relief)

Divide into:	Parenteral administration:	Side effects:
1. Salicylic acid 2. COX inhibitors 3. Selective COX-2-inhibitors 4. Specific COX-2-inhibitors	1. Ketorolac 2. Tenoxicam 3. Parecoxib	1. Renal damage, especially if prior renal impairment or if patient is hypovolaemic. 2. Platelet impairment. 3. Gastric erosions and haemorrhage. 4. Surgeons are concerned about possible poor wound healing. 5. Asthma may be exacerbated in some patients.

ASPIRIN			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Bayer Aspirin, Be Tabs Aspirin, Dispirin, Ecotrin, Myoprin	300–900 mg q 4–6 h to a max of 4 g daily	USE	• Associated with Reye's syndrome. • Beware elderly. • Beware renal function. • Beware gastric bleeds.

(5.6 NSAIDs)

DICLOFENAC			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
ACU-Diclofenac inj, Adco-Diclofenac, Austell-Diclofenac Sodium, BE-TABS, Diclofenac inj, Cataflam D, Dicloflam, Diclohexal Diclohexal-KDynak, Fortfen, Infla-Ban, K-Fenak, Merck Diclofenac, Micro Diclofenac, Panamor supposit. + tabs, Rolab-Diclofenac Sodium, Sandoz Diclofenac Sodium, Veltex, Voltaren, Voltaren Acti-Go	***Oral*** 25–50 mg q 8 h, to a maximum of 150 mg/day ***Drops: (only Voltaren)*** 15 mg = ml, 1drop = 0,5 mg, 1 ml = 30 drops 100 mg in 2–3 divided doses, Daily max =150 mg ***Intramuscular*** 75 mg q 12 h, maximum of 150 mg/day for 2 days only ***Suppositories*** 100 mg daily. The maximum by all routes is 150 mg/day	UWECO	MILD TO MODERATE PAIN • Available in drops. • **Not for children < 2 yrs via all routes.** • Good COX-1:COX-2 ratio. • Beware of asthma/GIT/renal disease • Renal damage may be especially prevalent in hypovolaemia, beware hypovolaemic postop patient. • ***Intramuscular injections:*** ▪ Must be deep intra-gluteal ▪ Beware of necrotising fasciitis – change to oral therapy ASAP ▪ Inadvertent injection into nerve may cause irreversible neural damage • Suppositories can cause proctitis, avoid use for longer than 5 days. • For moderate/severe pain. • Controversial for post-tonsillectomy use.
Arthrotec (diclofenac 75 mg + misoprostol 20 0µg)	tab q 12 h		• Swallow tablet whole with food. Do not chew. • Combination of NSAID and prostacyclin may decrease NSAID side effects.

IBUPROFEN			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Advil, Ibumax, Ibumed, Norflam T, Nurofen, Adco-Ibuprofen, Betaprofen, Brufen Iboflam, Inza, Ranfen, Sandoz Ibuprofen	200–400 mg q 4–6 h to a maximum of 1200 mg/day	USE	• Beware of GIT bleeds. • Beware of asthma. • For moderate pain.

(5.6 NSAIDs)

INDOMETHACIN			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Adco-Indomethacin, Aflamin, Arthrexin Betacin, Flamecid Indocid , suppositories, Methocaps, NISAID-25, Rolab-Indomethacin LA Sandoz Indomethacin	25–50 mg q 6–8 h to a maximum of 200 mg/day	USE	• Take with food/antacid/milk. • GIT bleeds/asthma/renal insufficiency. • CNS disturbances.

KETOPROFEN			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Ketoflam Oruvail	200 mg daily with food, do not exceed 300 mg/day		

KETOROLAC			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Toradol	10–30 mgIV/IM q 4–6 h Not for longer than 24 hrs Give IV injection slowly ***Oral*** 10 mg q 4–6 h	UWECO	• **Not for children < 16 yrs.** • Not for longer than 5 days.

MEFENAMIC ACID			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Adco-Mefenamic Acid, Fenamin, Ponac, Ponstan, Ponstel, Sandoz, Mefenamic Acid	500 mg q 8 h		• Not for children < 6 mths or weighing < 10 kgd. • Do not administer for longer than 5 days

(5.6 NSAIDs)

LORNOXICAM			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Xefo	8–16 mg/day, in 2–3divided doses		• Not for children < 18 yrs. • GIT, renal and platelet concerns are relevant.

NAPROXEN			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Adco-Naproxen Aleve, Aspen Naproxen, Merck-Naproxen, Nafasol Napflam, Rolab-Naproxen, Synflex	500 mg q 12 h		**Not for children < 5 yrs.** • Beware in patients with GIT bleeding diathesis. • Renal compromise. • Asthma. • Drug interactions with hydantoins/anticoagulants/ sulphonylureas. • For mild to moderate pain.

PIROXICAM			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Adco-Piroxicam, Brexecam, CPL Alliance Piroxicam, Pixicam, Pyrocaps, Rheugesic, Rolab-Piroxicam, Sandoz-Piroxicam, Xycam	20–30–40 mg daily		• Not recommended for children. • Usual concerns with NSAIDs • Beware hepatic insufficiency • Long half-life may be given as a single daily dose • For moderate pain.

SULINDAC			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Adco-Sulindac	100–200 mg q 12 h. Max 400 mg/day		• Caution in renal and hepatic insufficiency. • GIT bleeds. • Asthma.

(5.6 NSAIDs)

TENOXICAM			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Tilcotil	***Oral:*** 20 mg daily ***IV/IM:*** 20 mg daily for only 1–2 days		Parenteral use

SELECTIVE COX-2-inhibitors

MELOXICAM			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Coxflam, Flexocam, Loxiflam, Melflam Mobic, Sandoz Meloxicam, Zydus Meloxicam	7,5 mg q 12 h or15 mg daily Max dose 15 mg/day		Give with food. Selective COX-2 inhibitor – i.e. in very high doses may have COX-1 inhibition as well.

SPECIFIC CYCLO-OXYGENASE-2 INHIBITORS (COXIB)

CELECOXIB			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Celebrex	100–200 mg q 12 h to a max of 400 mg/day		• Not for children < 18 yrs. • Contra-indicated if sulphonamide allergy. • Specific cyclo-oxygenase-2 inhibitor COXIB i.e. only has COX-2 effects even at very large doses.

PARECOXIB			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Rayzon	40 mg q 6–12 h IV/IM, max 80 mg/day		Not for children < 18 yrs.

APPROACH TO COMBINATION ANALGESICS

- **Combinations of the ORAL drugs described above are used extensively in South Africa.**
- **It is not possible to include all combinations in this section.**
- **The rationale to combine drugs is to reduced the dose of each drug and hence the side effect profile should be improved.**
- **The list below tables some components in these combination preparations and highlights specific effects or side effects.**

1. **PARACETAMOL**	• Usually a lower dose is seen in combinations. • Beware of adding a combination preparation if the patient is receiving paracetamol via another route e.g. IV or rectally, as an overdose can occur.
2. **CAFFEINE HYDRATE**	• Has a vasodilatory effect and may be good for migraine.
3. **CODEINE PHOSPHATE**	• Has mild analgesic effect. Has to be metabolised to morphine. In a subset of patients excessive sedation is problematic.
4. **ASPIRIN**	• Beware if patient has prior history of dyspepsia and bleeding diathesis.
5. **PROPOXYPHENE NAPSYLATE**	• Weak analgesic effect, but some sedation.
6. **DEXTROPROPOXYPHENE HCl**	• Weak analgesic effect, sedation and ↓QT interval.
7. **NSAIDs**	• Beware if patient has prior history of dyspepsia or bleeding diathesis and renal impairment.
8. **MEPROBAMATE**	• Weak analgesic. Probable addiction after 10 days of use. This is a physical as well as emotional addiction. NB. This is one of the main constituents of STOPAYNE.
9. **DOXYLAMINE SUCCINATE**	• Don't know the rationale for inclusion into analgesic drugs.
10. **PROMETHAZINE**	• Phenothiazine with anti-emetic and sedatory effects. • "Blackbox" in US… ↓QT interval.
11. **ORPHENADRINE**	• Antimuscurinic effect.
12. **DIPHENHYDRAMINE**	• Antihistamine with sedatory effect (blackbox).

5.7 N-methyl-D-aspartic acid (NMDA) receptor antagonists

KETAMINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
	Oral: 0.25mg/kg ***PCA*** May be added to PCA in combination with morphine	USE	• Side effects such as hallucinations and excessive salivation. • Synergism with opioids and supposedly decreases tolerance to opioid. • No decrease in opioid side effects. • May give some pre-emptive analgesia. • May reduce opioid requirements in opioid-tolerant patients.

MAGNESIUM			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
	30 mg/kg at start of induction and then 25 mg/kg/hr	USE	• Concern regarding potentiation of muscle relaxation. • Decrease in blood pressure, easy to manage.

NITROUS OXIDE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Entonox	Nitrous xxide (N_2O) 50%/ oxygen (O_2) 50%	USE	• Do not store cylinders in temperatures below 7°C. • Used in labour for analgesia. • Used in dental chair. • Appropriate monitoring should always be applied. • Bone marrow depression occurs with PROLONGED use.

DEXTROMETORPHAN			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Benylin Original, Benylin Dry Cough, Benalin	45 mg po pre-operatively		• Use pre-emptively preoperatively. • Said to decrease use of other analgesics post-tonsillectomy in adults. • Usually only prescribed with the premedication.

5.8 α_2- AGONISTS

CLONIDINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
	Oral: 2,5µg/kg as a premed ***Intravenous:*** 2,5µg/kg slow injection ***Epidural/ caudal:*** 2–10 µg/kg epidurally in 10 ml saline	?	• Used as a premedicant for sedation and pre-emptive analgesia. • Partial agonist, so may give hyper/hypotension. • Bradycardia may be problematic.

DEXMEDETOMIDINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
	LD =1 µg/kg slowly over 30 min MD = 0.2 - 0.7 µg/kghr		FOR MODERATE TO SEVERE PAIN • Expensive, so initiate drug 1 hour before end of surgery. • Loading dose (LD) should be given slowly over 10–30 min. • Patients should always go to ICU for monitoring of level of sedation and hypotension. • Arterial line is essential for monitoring if drug is given as an infusion. • **Side effects:** ▪ Hypotension ▪ Sedation ▪ Bradycardia

5.9 LOCAL ANAESTHETICS

1. SHORT ACTING – Lignocaine 2. LONG ACTING – Bupivacaine, ropivacaine, L-bupivacaine	**Take note regarding side effects:** 1. Toxic doses 2. CardiotoxicityNeurotoxicity

LIGNOCAINE 2%			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Renucaine	**Toxic dose:** • *Without adrenaline:* 5 mg/kg • *With adrenaline*: 7 mg/kg • *For mucous membranes*: 9 mg/kg		• Neurotoxicity occurs before cardiotoxicity. • Should not be used intrathecally due to toxicity to spinal cord and nerves. • Continuous perineural infusions of lignocaine result in less effective analgesia and more motor block than long-acting local anaesthesia.

BUPIVACAINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Microbupivacaine **Macaine**	**Toxic dose:** 2 mg/kg		• Cardiotoxicity occurs before neurotoxicity. • Intralipid may be used for cardiotoxicity 1–1,5 ml/kg IV stat. • More potent than isomers as described below and so motor block and cardiotoxicity are more pronounced. • However there are no consistent differences between ropivacaine, levobupivacaine and bupivacaine when given in low doses for regional analgesia in terms of quality of analgesia or motor blockade.

L-BUPIVACAINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Chirocaine	**Toxic dose:** 2 mg/kg		

ROPIVACAINE			
DRUG	**ADULT**	**PORPHYRIA**	**RELEVANT INFORMATION**
Naropin	**Toxic dose** 2 mg/kg		

6. Paediatric guidelines

Key points
- Good pain control is a basic human right.
- Anxiety, fear, and pain in children are closely linked.
- Decide what is required: Analgesia, sedation, amnesia, and/or anxiolysis and make the drug choice accordingly.
- Drug administration should be the right drug for the right patient for the right reasons via the right route at the right time

Neurobiology of pain
- Even the most premature neonate responds to painful stimuli.
- In early development, in response to lower intensity painful stimuli, more generalised reflex responses occur.
- Pain and injury early in life may have adverse long-term consequences.

Pain measurement and assessment are pre-requisites to optimal pain management
- Pain assessment and measurement are important components of paediatric pain management.
- Pain measurement tools are available for children of all ages (refer web page).
- Pain measurement tools must be matched to the age and development of the child, be appropriate for the clinical context, be explained clearly, and used consistently.

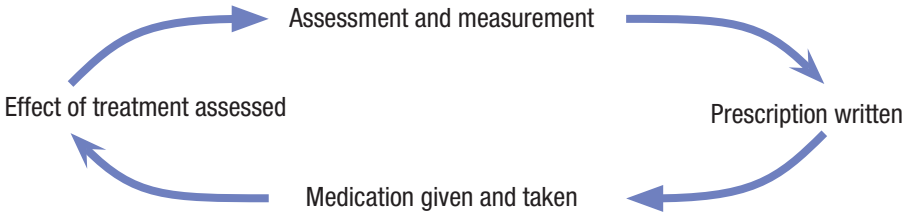
Consequences of poorly managed pain

Organ system	Possible clinical manifestations
Cardiovascular	Tachycardia, hypertension, ↑ systemic vascular, resistance, ↑ cardiac workload
Pulmonary	Tachypnoea, hypoxia, hypercarbia, ↓ cough, ↓ VC and FRC, atelectasis, pneumonia, V/Q mismatching
Gastrointestinal	Anorexia, nausea, vomiting, ileus
Renal	Oliguria, urinary retention
Neuro-endocrine	↑ adrenergic activity, catabolism and ↑ oxygen consumption, vagal inhibition
Central nervous system	Anxiety, fear sedation, fatigue, depression
Immunological	Impaired, especially cell-mediated immunity
Musculoskeletal	Reduced mobility, pressure sores, ↑ risk of DVTs

Types of acute pain

Post-operative pain

For effective pain control, the circle described below should not be broken.



The type of surgery is the greatest predictor of increased requirements for analgesia:

Thoracic and abdominal > neurosurgery, orthopaedics > lumps and bumps.

Procedural

The aim of procedural pain management is to minimise physical discomfort or pain, movement, and psychological disturbance without compromising patient safety.

Management:

- Pharmacological: analgesic agents, sedatives, or general anaesthesia.
- Non-pharmacological methods: bubble blowing, distraction techniques.

The use of hypnotics increases the risk of side effects.

Types of procedures

Analgesic and anxiolytic requirement may be **mild, moderate, or major.**

Venepuncture and intravenous cannulation

Topical local anaesthesia, inhaled nitrous oxide, distraction. Do not apply pressure above venous pressure to the arm. Hard pressure is painful, and will not help fill the vein. At the end of the procedure, do not press on the needle when withdrawing from skin: remove the needle and then press on the puncture site.

Arterial puncture

Is painful, and should only be used when absolutely essential. If repeated specimens are required, consider the use of an arterial line. After arterial puncture, to avoid the development of a haematoma, compress the puncture site for a timed 5 minutes.

Lumbar punctures

Inhaled nitrous oxide, local anaesthesia (topical then infiltrated), simple analgesics. Avoid hyper-flexion of the neck for the procedure as this adds to the discomfort.

Heel pricks

Avoid using the same site each time as bruising aggravates pain; warm the heel; avoid the apex of the heel where there is less subcutaneous tissue; 2 minutes prior to heel pricks, give oral sucrose, breastfeeding or breast milk.

Major procedures

The following may require the use of a number of analgesic techniques:

Chest drains

Insertion or removal: local analgesia/anaesthesia, oral or intravenous analgesics and anxiolytics, inhaled nitrous oxide. GA is often preferred.

Marrow punctures or trephines

Local anaesthetics (topical and infiltration), analgesia and anxiolysis with sedation are often required. Ketamine is often useful. GA is often preferred. In oncology patients prior to sedation and analgesic techniques, airway and mediastinal chest assessment is critical as lymphoid tissue hyperplasia may compromise the upper and/or lower airway.

Endotracheal intubation outside the operating theatre

Techniques chosen will depend on the experience of the operator, the condition of the child, and the drugs available. Options include propofol, ketamine, etomidate, midazolam, or fentanyl, with or without the use of muscle relaxation. Paralysis should never be used when the airway maintenance cannot be ensured.

Control of pain and anxiety

Non-pharmacological methods

- Psychological preparation: pre-operative explanation, discussion and education of child and parents.
- Teaching coping strategies, especially to children and their parents (breathing exercises, blowing bubbles).
- Relaxation therapies to calm and quieten the mind, and free from anxiety and muscle tension.
- Distraction techniques, guided imagery (virtual reality).
- Splinting and immobilisation of wounds.
- Hypnosis.

Pharmacological options

"Multimodal analgesia" describes the use of different types of drugs, not exceeding the recommended dose of any one, used in combination to increase efficacy but also to decrease the incidence of the side effects of any one. These include

Local anaesthetics

- Short-acting or long-acting, with or without adrenaline.
- Infiltration, nerve block, regional or central blockade; with or without catheters.
- Some of these techniques may require specialist expertise.

Simple analgesics

- Paracetamol (oral, rectal, intravenous).
- Non-selective non-steroidal anti-inflammatories (nsNSAIDs) (oral, rectal, intravenous, transdermal patches).
- Steroid anti-inflammatory drugs (hydrocortisone, methyl prednisolone, dexa-methazone) given orally, intravenously, and into joints.

Opioids and tramadol

- Short-acting: remifentanil, alfentanil, fentanyl, sufentanil.
- Intermediate: morphine, meperidine (pethidine), tramadol, tilidine HCl (valoron), codeine.
- Long-acting: methadone, duragesic (entanyl patches) in bigger children.

Inhalational agents

- Entonox: inhaled nitrous oxide (scavenging should be available).

Anxiolytics

- Benzodiazepines: midazolam, diazepam, lorazepam.
- Clonidine.

Others

- Ketamine: oral, intravenous (intramuscular when there is no alternative).
- Steroidal anti-inflammatories: dexamethasone (150 mcg/kg).
- Alpha-2 adrenoreceptor agonists.
  - Clonidine.
  - Dexmedetomidine: highly selective, intravenously administered $\alpha 2$ agonist.
- Combinations of drugs: numerous options.
- Sucrose (25%), breast milk: important for use in neonates and infants.

Clinical practice points

- Intermittent intramuscular injections are distressing for children and are less effective for pain control than intravenous infusions.
- Intravenous opioids can be used safely and effectively in children of all ages.
- Initial doses of opioid should be based on the age and weight of the child and then titrated against the individual's response.
- Unwanted side effects should be anticipated and treated.
- Effective PCA prescription in children incorporates a bolus that is adequate for control of movement-related pain, and may include a low-dose background infusion to improve efficacy and sleep.
- Caudal local anaesthesia provides prolonged analgesia after surgery for lower abdominal, perineal, and lower limb surgery and has a low incidence of complication.
- Clonidine prolongs analgesia when added to caudal local anaesthetic blocks, and prolongs analgesia when added to local anaesthetic epidural infusions.

- Continuous epidural infusions provide effective post-operative analgesia in children of all ages, and are safe if appropriate doses and equipment are used by experienced practitioners with adequate monitoring and management of complications.
- Epidural infusions of local anaesthetic compared with systemic opioids provide similar levels of analgesia.
- Topical local anaesthetic does not provide adequate pain control for circumcisions in awake neonates.
- Wound infiltration, peripheral nerve blocks, and caudal local anaesthetic provide effective analgesia after day-case inguinal surgery.
- nsNSAIDs do not increase the risk of re-operation for bleeding after tonsillectomies.
- Dexamethazone reduces post-tonsillectomy pain, nausea and vomiting, but high doses may increase the risk of bleeding.
- Paracetamol and nsNSAIDS are effective for moderate to severe pain and decrease opioid requirements after major surgery.
- The efficacy of oral codeine is variable, and individual differences in the ability to generate the active metabolite may reduce efficacy or increase side effects.
- Safe dosing of paracetamol requires consideration of the age and body weight of the child, and the duration of therapy.
- Aspirin should be avoided in children.
- Serious adverse events after nsNSAIDs are rare in children over 6 months of age.
- In infants under 3 months of age, nsNSAIDs may cause pulmonary hypertension and alterations in cerebral, gastro-intestinal, and renal blood flow.

Doses of commonly used drugs

Local anaesthetics

LIGNOCAINE	
Topical	Maximum Spray 5 mg/kg/dose • Gels: 2% • EMLA cream: eutectic mixture of local anaesthetic creams • 2.5% lignocaine + 2.5% prilocaine 1.5g/10cm^2 under occlusive dressing for 1–3 hrs
Infiltration or nerve block	With adrenaline: 7 mg/kg/dose
	Without adrenaline : 4 mg/kg/dose
Intravenous	1 mg/kg/dose
BUPIVICAINE	Maximum dose 2–3 mg/kg/dose (0.4–0.6 ml/kg of 0.5%)
ROPIVACAINE	Maximum dose 2–3 mg/kg/dose

Paracetamol

Oral	20 mg/kg stat, then 15 mg/kg/dose 4-hourly (max 90 mg/kg/day, or 4 g/day)
Rectal	40 mg/kg stat, then 30 mg/kg/dose 6-hourly (max 5 g/day)
	Neonates: 60 mg/kg/day in divided doses
	Other infants and children: 90 mg/kg/day
Intravenous	Neonates: 7.5 mg/kg/dose 6-hourly (max 30 mg/kg/day) (decrease the dose and increase the interval in jaundiced babies)
	Other infants and children: 15 mg/kg/dose 6-hourly (max 60 mg/kg/day)

Paracetamol antidote

N-ACETYLCYSTEINE	
	For paracetamol poisoning, regardless of the time delay Start with 150 mg/kg in 5% dextrose IVI over one hour Continue then at 10 mg/kg/hour for: • 20 hours (delay < 10 hrs) • 32 hrs (delay 10–16 hrs) • 72 hrs (delay > 16 hrs) Continue for longer if still encephalopathic. Monitor potassium
Oral	140 mg/kg stat, then70 mg/kg dose 4-hourly for 72 hours* Monitor potassium

Non-specific NSAIDs (nsNSAIDs)

IBUPROFEN	5–10 mg/kg/dose 4–8 hourly
DICLOFENAC	1 mg/kg/dose 8–12-hourly po, pr 1–3 mg/kg/day
KETOROLAC	Oral : 0.2 mg/kg/dose (max 10 mg) (max 0.8 mg/kg/day)
MEFANAMIC ACID	10 mg/kg/dose po 8-hourly

Opioids and tramadol

MORPHINE	
Intravenous	0.1 mg/kg/dose 4–6 hourly
Itramuscular	0.2 mg/kg/dose 4–6 hourly
Oral	0.3–0.4 mg/kg/dose 4–6 hourly
Infusion	5–40 mcg/kg/hour. Draw up 0.5 mg/kg of morphine sulphate in 50 ml normal saline. Run and 0.5–4 ml/hour, which will deliver 5–40 mcg/kg/hour. (One ml = 10 mcg/kg morphine)
PCA	20 mcg/kg bolus with 5 minute lockout time. If a background infusion is used, the dose for this is 5 mcg/kg/hour Slow-release morphine: 0.6 mg/kg/dose 12-hourly, increasing every 48 hrs if required

TILIDINE HCL (VALORON)	
Sublingual	1 mg/kg/dose sublingual drops (2.5 mg/drop) **Weight in kg divided by 2.5 = number of drops required** Obese older children: 1 drop per year of age
CODEINE PHOSPHATE	Analgesia: 0.5–1 mg/kg/dose 4-hourly po Antitussive: 0.25 - 0.5 mg/kg/dose 6-hourly
DIHYDROCODEINE	0.5–1 mg/kg/dose 4–6-hourly po
PETHIDINE	0.5–1 mg/kg/dose

FENTANYL	
Slow bolus	1–3 mcg/kg/dose stat IVI
Infusion	1–5 mcg/kg/hr in theatre or ICU
Intranasal	1.5–2 mcg/kg/dose
ALFENTANIL HCL	10 mcg/kg/dose. When ventilated, 10–50 mcg/kg/dose
REMIFENTANIL	1 mcg/kg slowly ivi. Infusion: 0.05–0.2 mcg/kg/min
TRAMADOL	1–2 mg/kg/dose 4–6-hourly po (max 400 mg/day)

Opioid antagonists

NALOXONE	For opioid overdose: 0.1 mg/kg/dose (max 2mg) IVI, IMI, sc, intratracheal. Infusion: 0.01 mg/kg/hour

Anaesthetic agents

PROPOFOL	Sole agent intubating dose 3–4 mg/kg/dose
KETAMINE	
Intravenous	Sedation + analgesia: 0.25–0.5 mg/kg/dose Anaesthesia: bolus: 1–2 mg/kg/dose Infusion: 10–20 mcg/kg/min 1–4 mg/kg/hour
Intramuscular	Sedation + analgesia: 2–4 mg/kg/dose Anaesthesia: 7–10 mg/kg/dose
Oral	Sedation + analgesia: 2–5 mg/kg/dose Anaesthesia: 10 mg/kg/dose

Alpha-2 agonists

CLONIDINE	• 1–6 mcg/kg/dose po 8–12-hourly • 2–3 mcg/kg/dose po for premed single dose one hour before procedure

Anxiolytics (Benzodiazepines provide NO analgesia)

DIAZEPAM	Dose: 0.2–0.4 mg/kg/dose IVI or rectal. Do not give as an infusion as it binds to PVC

LORAZEPAM	
Oral	0.02–0.06 mg/kg/dose 8–24-hourly po
Intravenous	0.05–0.2 mg/kg/dose slowly IVI
Infusion	0.01–0.1 mg/kg/hour
MIDAZOLAM	
Oral sedation	0.25–0.5 mg/kg/dose (max 7.5 mg)
Intravenous	0.05–0.1 mg/kg/dose
Intramuscular	0.1 mg/kg/dose
Intranasal	0.2–1 mg/kg/dose
Infusion	0.1–0.2 mg/kg/hr
Anticonvulsant	0.2 mg/kg/dose IVI

Antidote to benzodiazepines

FLUMAZENIL (ANEXATE)	5 mcg/g IVI every 60 secs to maximum total 40 mcg/kg (max 2 mg) Infusion: 2–10 mcg/kg/hr

In conclusion

Important principles of management include the following:

1. Allow sufficient time for local anaesthetics and oral drugs to work before starting a planned procedure.
2. Keep the environment safe and predictable.
3. Only do what is necessary when it is necessary.
4. Tell the truth – in good time, and do not exclude the parents.
5. Education and explanation prior to procedures or operations are invaluable, and will decrease the need for medications.
6. Use appropriate restraint. Restraint should not hurt the child, and should only be sufficient for the procedure to be performed efficiently and quickly.
7. Monitor according to condition of patient, drug choice made, procedure being performed, and experience and expertise of the medical carer/operator.
8. Drug choices should be rational, multimodal, and safe.

Pain is soul-destroying. No patient should have to endure intense pain unnecessarily. The quality of mercy is essential to the practice of medicine. Here of all places it should not be strained.

The Quality of Mercy

ACUTE PAIN CONTROL FOR SPECIFIC PROCEDURES IN PAEDIATRICS

MEDICAL PROCEDURES

Pain management for procedures should, whenever possible, include both pharmacological and non-pharmacological strategies.

Procedural pain in the neonate

General recommendations

If feasible, breastfeeding mothers should be encouraged to breastfeed during the procedure. Non-nutritive sucking and/or the use of sucrose or other sweet solutions should be used for brief procedures.

Specific recommendations

Blood sampling

Sucrose or other sweet solutions should be used. Topical local anaesthetics may be used for venepuncture pain.

Heel prick (lancing)

Avoid the same site each time as bruising aggravates pain; warm the heel; avoid the apex of the heel where there is less subcutaneous tissue; give oral sucrose; breastfeeding. Because it is less painful, venepuncture is preferred to a heel prick. Topical local anaesthetics alone are insufficient for heel lance pain.Morphine alone is insufficient for heel lance pain. Sensory stimulation including tactile stimulation, such as holding or stroking, can be used or combined with sucrose where feasible, as it may further reduce the pain response.

Percutaneous central venous catheter insertion (PICC)

Topical LA with tetracaine alone is insufficient to abolish pain of PICC line insertion; tetracaine plus morphine is superior (in ventilated infants). In difficult cases, general anaesthesia may be the preferred option.

Ocular examination for retinopathy of prematurity

Infants should receive local anaesthetic eye drops, and/or be offered a pacifier. Sucrose may contribute to a reduction in the response to pain.

Lumbar puncture

Topical local anaesthesia is effective in reducing LP pain. Topical LA and LA infiltration are effective for LP pain and do not decrease success rates. Inhaled Entonox (50% nitrous oxide in oxygen) should be offered to children willing and able to cooperate. Consider adding simple analgesics. Avoid hyperflexion of the neck for the procedure as this adds to discomfort.

Urine sampling

Transurethral catheterisation with LA gel is preferred as it is less painful than suprapubic aspiration using topical LA.

Procedural pain in older children

General comments

Children and their parents/carers may benefit from psychological preparation prior to painful procedures. Pain management for procedures should include both pharmacologic and non- pharmacologic strategies where possible. Entonox should be considered for painful procedures in children who are able to cooperate with self-administration. Sedation or general anaesthesia should be considered, particularly for invasive, multiple and repeated procedures.

ACUTE PAIN CONTROL FOR SPECIFIC PROCEDURES IN PAEDIATRICS

MEDICAL PROCEDURES

Specific recommendations

Blood sampling and intravenous cannulation

Topical local anaesthesia should be used for intravenous cannulation. Psychological strategies, e.g. distraction or hypnosis, to reduce pain and anxiety should be used. Nitrous oxide is effective for pain reduction in venous cannulation.

Lumbar puncture

Behavioural techniques of pain management should be used to reduce LP pain. Topical LA and LA infiltration are effective for LP pain and do not decrease success rates. Inhaled Entonox (50% nitrous oxide in oxygen) should be offered to children willing and able to cooperate.

Chest drain (tube) insertion and removal

For chest drain insertion, consider general anaesthesia or sedation combined with subcutaneous infiltration of buffered lidocaine. Selection of appropriate drain type may reduce pain by facilitating easy insertion. For chest drain removal, consider a combination of two or more strategies known to be effective for painful procedures such as psychological interventions, sucrose or pacifier (in neonates), opioids, nitrous oxide and NSAIDs.

Urine sampling

Lubricant, containing local anaesthesia, should be applied to the urethral mucosa prior to bladder catheterisation (e.g Cathigel). Recommendation: Psychological preparation and psychological and behavioural interventions should be used during bladder catheterisation and invasive investigations of the renal tract.

Insertion of nasogastric tubes

Topical local anaesthetics such as lidocaine-containing lubricant gel or atomised or nebulised 4–10% lidocaine applied prior to placement are likely to reduce the pain and discomfort of NGT insertion.

Repair of lacerations

For extensive wounds or children who are very anxious, consider sedation or general anaesthesia

Recommendations

For repair of simple low tension lacerations: tissue adhesives should be considered as they are less painful, quick to use and have a similar cosmetic outcome to sutures or adhesive skin closures (steristrips).

If sutures are needed: topical anaesthetic preparations, e.g. lidocaine-adrenaline-tetracaine (LAT) if available, can be used in preference to injected lidocaine, as they are less painful to apply and are equianalgesic; it is not necessary to use a preparation containing cocaine. Buffering of injected lidocaine with sodium bicarbonate should be considered.

'Hair apposition technique' (HAT): should be considered for scalp lacerations. It is less painful than suturing, does not require shaving and produces a similar outcome.

If injected lidocaine is used: pretreatment of the wound with a topical anaesthetic preparation, e.g. LAT gel reduces the pain of subsequent injection.

50% nitrous oxide reduces pain and anxiety during laceration repair.

ACUTE PAIN CONTROL FOR SPECIFIC PROCEDURES IN PAEDIATRICS

SURGICAL PROCEDURES

Circumcision

A dorsal penile nerve block provides similar analgesia to caudal block and is more effective than application of topical local anaesthetic cream (EMLA). Subcutaneous ring block of the penis is less effective than dorsal penile nerve block and has a higher failure rate than caudal analgesia, but potentially fewer complications. Topical local anaesthetic cream only partially attenuates the pain response to circumcision in awake neonates, so more effective analgesic techniques such as dorsal penile nerve block are recommended. Toxic effects with EMLA are seen with repeated doses in the postoperative period.

Inguinal hernia repair

Similar levels of efficacy for reducing pain following inguinal hernia repair have been found following wound infiltration, ilioinguinal/iliohypogastric nerve block or caudal analgesia. Supplementation with paracetamol is recommended.

ENT procedures

Myringotomy

Good practice point: As myringotomy is a brief procedure, oral paracetamol or NSAID should be administered preoperatively to ensure adequate analgesia at the end of the case.

Recommendations

Oral paracetamol, ibuprofen or diclofenac, in suitable doses, administered 30 min preoperatively can achieve adequate early postoperative analgesia.

Ketorolac can provide satisfactory analgesia.

Opioids are effective but not recommended for routine use because of increased side effects of nausea and vomiting compared with minor analgesics.

Tonsillectomy

Good practice point: As significant levels of pain, behavioural disturbance, sleep disruption and altered activity can persist for 5–8 days following tonsillectomy, regular administration of paracetamol and NSAID may be necessary during this period. Information for families about pain assessment and medication use following discharge is particularly important.

Recommendations

A combination of individually titrated intraoperative opioids and regularly administered perioperative mild analgesics (NSAID and/or paracetamol) is required for management of tonsillectomy pain.

Local anaesthesia injection in the tonsillar fossa may improve pain scores, reduce time to first oral intake, and reduce the incidence of referred ear pain following tonsillectomy.

Tramadol can produce similar analgesia to morphine or pethidine.

Intraoperative intravenous (IV) ketamine does not provide significant postoperative advantage compared with opioid.

Implementation of standardised protocols including intraoperative opioid ± anti-emetic, perioperative NSAID (diclofenac or ibuprofen) and paracetamol are associated with acceptable pain relief and low rates of post-operative nausea and vomiting (PONV).

ACUTE PAIN CONTROL FOR SPECIFIC PROCEDURES IN PAEDIATRICS

SURGICAL PROCEDURES

Mastoid and middle ear surgery

Great auricular nerve block can provide similar analgesia and reduced PONV compared with morphine. Especially if a vasoconstrictor agent is used, local anaesthetic infiltration is a valuable option. Pre-incision timing of the block confers no additional benefit. Compared with middle-ear surgery, mastoid surgery is associated with increased pain: patients are therefore more likely to require opioids, treatment for PONV, and hospital admission.

Ophthalmology

Strabismus surgery

Intraoperative LA blocks (subtenon or peribulbar) reduce PONV and may improve perioperative analgesia in comparison with IV opioid. Topical NSAIDs do not improve pain scores or postoperative analgesic requirements when compared with topical LA or placebo. Intraoperative opioid and NSAID provide similar postoperative analgesia but opioid use is associated with increased PONV.

Vitreo-retinal surgery

NSAID provides similar analgesia but lower rates of PONV compared with opioid. Peribulbar block improves analgesia and reduces PONV compared with opioid.

7. Routes of systemic drug administration

The commonest and cheapest route of administration for medications to treat acute pain is orally (enterally). In special circumstances, particularly in the perioperative management of patients, or during medical and/or surgical emergencies, alternative routes of administration may be required. Alternative routes allow for more rapid onset, as well as titration of the dose, and avoidance of the gastrointestinal tract, should it be inaccessible.

Therapeutic interventions for pain relief should be individualised on the basis of actual or expected pain severity, patient characteristics and available resources for monitoring (both for analgesia effectiveness and adverse effects).

Drugs for pain relief should be prescribed regularly, rather than on an "as needed" (prn) basis. Frequent monitoring of the degree of pain, as well as for the presence of drug side effects, is required, so that drug doses, dosing intervals, and routes of administration can be adjusted.

The routes of administration of drugs used in pain relief can be classified as follows:

7.1 **ENTERAL ADMINISTRATION**

- 7.1.1 **Oral**
- 7.1.2 **Rectal**
- 7.1.3 **Sublingual**
- 7.1.4 **Via feeding tube: Oro-/naso-gastric, post-pyloric, gastrostomy, enterostomy**

7.2 **PARENTERAL ADMINISTRATION**

- 7.2.1 **Systemic non-invasive**
  - ***Intranasal***
    Droplet
    Spray
  - ***Transdermal***
    Passive diffusion
    Iontophoretic

7.2.2 **Systemic invasive**

- ***Subcutaneous***
- ***Intramuscular***
- ***Intravenous***
- ***Intraosseous (short term until resuscitated)***

7.2.3 **Regional (plexus)**

- ***Single shot/catheters – local anaesthetics ± vasoconstrictor***

7.2.4 **Neuraxial**

- ***Intrathecal/epidural***
- ***Single shot/catheters***

7.1 Enteral administration

7.1.1 Oral route

The oral route is the cheapest and best accepted method of administering drugs for pain relief. Efficacy of oral drugs is determined by the following factors:

1. Gastrointestinal motility
   Delayed gastric emptying may result in inadequate analgesia, especially when vomiting occurs. Conversely, drugs can accumulate in the stomach with multiple doses that enter the proximal gastrointestinal tract as a bolus with return of gastric motility, resulting in high systemic levels (dumping).
2. Drug formulation
   a. Liquids are absorbed faster than capsules, while tablets are absorbed slowest.
   b. Enteric coating delays dissolution until entry into the proximal gastrointestinal tract. Enterically-coated tablets should never be split or broken.
   c. Slow-release preparations allow for delivery of a larger dose of medication with slower onset, longer duration and reduced peak levels (and hence reduced side effects). A number of pain medications in a slow release (SR) are marketed as having a 12-hour duration of action; however most require 8-hourly administration to maintain adequate pain relief. These drugs are most useful for provision of baseline analgesia for acute pain, and for long-term therapy of chronic and cancer pain.
3. Hepatic first pass metabolism
   It occurs when drugs are absorbed from the gastric, intestinal or rectal mucosa (NOT from the sublingual mucosa) and has two consequences:
   a. The amount of drug reaching the systemic circulation is reduced by 20–50%, thus reducing both peak levels and duration of action, when compared with parenteral administration.
   b. The liver is exposed to higher levels of administered drug than other organs.

Specific drug classes administered orally

1. *Anti-hyperalgesic drugs*
   a. Paracetamol: safe to administer preoperatively. Loading dose is 40 mg/kg. Maintenance dose is 20 mg/kg (max 1g) 6 hrly (max 4 g/day).
   b. Non-selective non-steroidal anti-inflammatory drugs (ns-NSAIDs): these drugs have potential renal, gastrointestinal and antiplatelet effects, which make them less suitable for preoperative administration (after a period of fasting), or in bleeding and/or hypovolaemic emergency patients. Parenteral administration should be considered after fluid repletion in patients, provided they have no contraindications to the administration of these drugs.
   c. Coxibs: Compared with the nsNSAIDs coxibs have a lower propensity to cause gastrointestinal side effects, no antiplatelet effects but similar renal effects. Coxibs may thus also precipitate renal dysfunction in hypovolaemic patients. Administration may thus need to be parenteral initially after adequate fluid repletion
2. *Primary analgesics*
   a. Codeine: may be given orally in doses of 0.5–1mg/kg. A number of genetic variants of the cytochrome that metabolises codeine to morphine to provide analgesia exist:
      - Ultra-rapid metabolisers – achieve rapid high morphine levels with the potential for respiratory depression, coma and death.
      - Slow metabolisers – have slow or absent metabolism of codeine to morphine and thus have inadequate analgesia but still develop constipation, a codeine-mediated side effect.

      Codeine can thus not be recommended for preoperative administration. If a patient has not taken codeine before, the patient should receive 0.5 mg/kg and be observed at 10–15 minute intervals for the first 90 minutes after administration. In the acute pain setting, codeine is most effective when combined with paracetamol and/or an NSAID (coxib or non-selective).
   b. Dextro-propoxyphene: is given orally in a similar dose to codeine. The drug is addictive and has been implicated in a significant number of successful suicides, leading to withdrawal of the drug from markets in the USA and European Union. This drug is not suitable for preoperative administration but may be useful as a postoperative analgesic in patients who achieve inadequate analgesia with codeine. As with codeine, dextro-propoxyphene is most effective when combined with paracetamol and/or an NSAID (coxib or non-selective).
   c. Tramadol: is rapidly absorbed with a minimal risk of respiratory depression making it a useful drug for premedication. The slow-release preparation not only provides a longer duration of action but limits the peak level. High peak levels are responsible for the main side effects of nausea and dysphoria.
   d. Morphine: Oral morphine is available as liquid (most commonly formulated as 20 mg/5ml), immediate-release tablets and slow-release formulations. Oral morphine is effective in acute pain relief at a dose of 20 mg every 30 minutes. The main concern with this therapy, particularly with poorly staffed wards, is diversion of the oral morphine to visitors for illicit use.

With longer-term use, daily oral morphine use should be quantified and 60% of the requirement administered as an 8-hourly slow-release formulation, with 40% used as needed for breakthrough pain.

e. Procedural sedation: The IV formulations of ketamine 5 mg/kg and midazolam 0.2 mg/kg may be combined and added to 20–40 mg/kg paracetamol syrup as a useful oral preparation for procedural sedation in children (in other words, the child drinks fluid from ampoules usually intended for IV use). Onset is within 20–30 minutes, and duration is 30–45 minutes.

3. *Secondary analgesics*

   a. Amitryptiline / Dothiepin: These drugs are well absorbed orally and provide analgesia, light sedation superior to the benzodiazepines, and relief of muscle spasm.

   b. Clonidine: The available oral formulation (Dixarit™) contains 25mcg clonidine. Effective dosing is 1.5-3mcg/kg BD – hence the number of tablets required may be as many as 12 per dose.

7.1.2 Rectal route

Rectal administration of medication, particularly NSAIDs and paracetamol, is commonly practised in South Africa.

Rectal administration allows drugs to be given where the upper GI tract is inaccessible or inactive (gastropareisis). Absorption from the rectum is slow and may be erratic, especially if the patient is hypovolaemic, and splanchnic blood flow is reduced. Hepatic first pass metabolism also occurs with rectally administered medications absorbed through the superior rectal veins. Absorption from the inferior veins is directly into the systemic circulation. Local irritation and diarrhoea have been reported after suppository use, and this route is contraindicated if significant lesions (inflammatory and/or neoplastic) of the anorectal area are present.

Division of suppositories to titrate dose cannot be recommended as active drug may be unevenly distributed within the suppository.

Consent to administration of rectal medication cannot be presumed – it should be obtained prior to administration, especially if administration is to be done while a patient is anaesthetised, and/or the surgical procedure does not require exposure of the perineum.

Paracetamol can usually be given orally prior to surgery; however suppositories are substantially cheaper than the IV formulation for use in acute painful emergency scenarios. Rectal paracetamol still undergoes hepatic first pass metabolism, hence absorption may be slow in hypovolaemic patients with reduced splanchnic blood flow.

NSAIDs were originally recommended in suppository formulation to avoid direct exposure of the gastric mucosa to the nsNSAIDs. Gastric side effects are, however, dependent on the systemic level of the NSAID, rather than the level in the gastric lumen. Similarly, the renal and antiplatelet effects are independent of route of administration.

Rectal administration of NSAIDs allows administration after adequate hydration, which is preferable to preoperative oral administration, due to the inevitable dehydration that occurs with preoperative fasting.

The only opioid available for rectal administration is tramadol. No dosage adjustment is necessary.

7.1.3 Sublingual route

Sublingual drug administration is different from oral administration, as drug is absorbed directly into the systemic circulation. This results in a faster onset and higher peak levels, as there is direct absorption into the systemic circulation, with no hepatic first pass metabolism.

Drugs in an intravenous formulation may be given sublingually prior to establishment of IV access. In the case of a drug which requires a loading dose over a period of 20–30 minutes such as dexmedetomidine, sublingual administration appears to provide equivalent onset of action, without the need for an infusion pump.

In the prehospital setting or emergency department, sublingual administration of drugs, such as morphine or fentanyl, will provide more reliable onset of analgesia than intramuscular (IM) or subcutaneous (sc) administration, as peripheral blood flow is reduced in situations of sympathetic activation and/or hypovolaemia. Once IV access is established, further titration of pain relief can occur via the IV route.

Oral transmucosal systems for analgesic administration include fentanyl, formulated as a lollipop and as a rapidly dispersible wafer. Both are associated with intense facial pruritis, and the lollipop has raised concerns with dependence and addiction issues. Neither is available in South Africa.

7.1.4 Feeding tubes; nasogastric, post-pyloric, gastrostomy, enterostomy

All drugs given orally, except those in a slow-release formulation, may be given via a feeding tube.

Liquids or suspensions should be used for administration via feeding tubes, if possible.

Contents of capsules may be removed from the capsule and directly administered down the tube.

Should a particular medication only be available in a tablet, crushing is required.

The powdered medication should be well flushed through the tube, to prevent tube occlusion.

Slow release preparations cannot be crushed and are unsuitable for administration via a feeding tube.

7.2 Parenteral administration

7.2.1 Non-invasive systemic drug administration

Intranasal droplets

The intravenous formulation of analgesics, such as morphine and fentanyl, as well as sedatives, such as midazolam, dexmedetomidine and ketamine, may be given via the nose. This route remains accessible in uncooperative patients, who refuse to open their mouths.

The aim is for systemic absorption of the nasally administered drug via the nasal mucosa, with fast onset and high peak levels of drug, providing efficacy similar to intravenous administration.

In reality, more than 70% of the medication administered by this route passes through the nasal passage and into the nasopharynx, to be swallowed. The swallowed medication is then absorbed via the GI tract, with a slow onset and low peak due to hepatic first pass metabolism, as with any orally administered drug.

Another disadvantage of nasal droplet administration is that most IV formulations are bitter. Medication passing from the nasopharynx to the oropharynx comes into contact with the posterior tongue, the site of the bitter taste receptors, making the experience extremely unpleasant for the patient.

Administration of opioids via the nasal route is associated with intense pruritis, due to large numbers of histamine-releasing immune cells in the nasal mucosa that are degranulated after exposure to opioids, particularly the synthetic fentanyl derivatives.

Nasal transmucosal administration

A device known as the mucosal atomizer device (MAD, Wolf-Torey Medical, USA) produces a fine mist (droplet size < 0.2 micron) when medication is injected from a standard syringe via the MAD. More than 90% of the medication in the droplets from the MAD is absorbed by the nasal mucosa. Less than 10% is swallowed. The result is that MAD-administered drugs, such as morphine, midazolam and dexmedetomidine, achieve fast onset and high peak levels equivalent to IV administration. There is extensive experience with this method of drug administration in the prehospital environment and for paediatric premedication. Efficacy is equivalent to that of intravenous administration.

Less than 10% of drug administered by MAD reaches the oropharynx, so bitter receptors on the posterior tongue are minimally activated. Nasal pruritis remains a significant side effect.

Passive transdermal drug delivery

Fat soluble drugs may be delivered from a matrix reservoir into the stratum corneum of the skin and from there into subcutaneous veins. Onset of action of transdermally-delivered drugs is slow, with maximum plasma levels achieved 6–8 hours after application of the transdermal patch. The effect of the drug will persist for 6–8 hours after patch removal, as a reservoir of drug remains in the stratum corneum. Compliance is improved by using transdermal patches, as the patch only needs to be changed (with application at a new site) every 3 days.

The technology of transdermal drug delivery has been widely used for delivery of hormone replacement and nicotine.

Fentanyl is available in a transdermal delivery system in South Africa (Durogesic™, Janssen-Cilag). Transdermal delivery systems are available in Europe for delivery of buprenorphine and capsaicin.

Transdermal is not suitable for acute pain management, particularly in opioid-naïve patients. Not only is the onset of action too slow for acute pain relief, but the sustained blood level may induce respiratory depression, coma and death in particularly opioid-sensitive patients.

There have been reports of clinicians cutting transdermal fentanyl patches to reduce the rate of drug delivery in the acute pain setting. This is negligent practice that is impossible to justify, and will carry significant medico-legal consequences in the event of an adverse outcome.

Transdermal fentanyl is best suited for maintenance of opioid analgesia in patients with chronic pain or cancer pain. There is no role for transdermal fentanyl in acute pain management. The role of transdermal buprenorphine will have to be assessed if/when the drug is released in South Africa.

7.2.2 Invasive systemic drug delivery

Subcutaneous drug delivery

Drugs that are formulated for intravenous use may also be safely administered subcutaneously.

Conversely, drugs that are formulated for intramuscular (IM) administration are not suitable for subcutaneous administration, as the volume is excessive, and the solution is irritant (e.g. diclofenac).

The rate of administration of subcutaneous drugs should not exceed 1 ml in a single bolus, or 3 ml/hr total dose. At least 30 minutes should be allowed to elapse between 1 ml boluses, to allow for drug dispersion and absorption. Smaller boluses may be given more frequently (e.g. every 5–6 minutes in disposable Patient Controlled Analgesia (PCA) systems).

A subcutaneous butterfly, or 22G IV cannula, under a clear, breathable dressing (e.g. Op-Site™, Tegaderm™, etc.) is the route of choice for administration of subcutaneous drugs. The subcutaneous device should be capped with a needle free injection port. The most comfortable sites for butterfly/cannula insertion, with best consistency in drug absorption, are the subclavian or anterior upper arm areas. For patients having surgery where systemic opioids and/or NSAIDs are likely to be required for postoperative pain relief, the cannula/butterfly is best inserted in the operating theatre, during or after the operation. The butterfly/cannula simplifies administration of analgesic drugs in wards. Staff has less exposure to needles, and thus reduced risk of needlestick injury. Patients are spared the pain and inconvenience of multiple injections. Sites need to be changed every 48–72 hours.

PCA may also be delivered subcutaneously. The subcutaneous route may be less comfortable, with minor localised burning on injection (which is sometimes interpreted by African and Asian patients as an indicator of efficacy) and localised swelling and redness after 24–48 hours that resolves rapidly on butterfly/cannula removal and replacement, at an alternative site. There are a number of advantages to sc PCA administration:

a. PCA may be continued when IV access is no longer required.
b. Misconnection of the PCA device to the IV line is not possible.
c. Efficacy of PCA is independent of presence of a flowing IV infusion.
d. The danger of dead-space in IV infusion tubing (that may become filled with PCA solution if the IV infusion is stopped) is obviated.

Intramuscular drug delivery

The intramuscular route of drug delivery remains the commonest route of delivery for opioid delivery in postoperative patients.

This popularity persists despite well recognised complications that include:

1. Drug toxicity from intra-/perivascular injection.
2. Inadequate analgesia:
    a. Inappropriate dosing.
    b. Morphine is commonly dosed at 10–15 mg, and pethidine at 50–100 mg, both 4–6 hrly. With optimal IM injection these prescriptions will provide adequate post-surgical analgesia in < 50% of post-surgical patients but will cause significant respiratory depression in up to 2%.
    c. Reduced blood muscle and skin flow – particularly after surgery/in emergency situations
    d. Injection into fat/subcutaneously.
3. Nerve damage.
4. Injection abscesses: that are increased with the following risk factors:
    a. High injection volume
    b. Increasingly irritant injectate
    c. Immunocompromised patients

For appropriate management of postoperative pain by intramuscular injection, the following principles should apply:

1. Intramuscular injections should be given at 2-hourly, rather than 4-hourly, intervals
2. Medications for adult patients over 50 kg in weight should be:
    a. Morphine 5–10 mg
    b. Tramadol 50–100 mg
    c. Pethidine should be avoided, but prescribed at 50 mg if used.
3. After 3 IM injections, with persistent pain, consideration should be given to:
    a. Hourly subcutaneous bolus analgesic injections
    b. Subcutaneous PCA

There is no place for IM drug administration in the emergency management of acute pain.

Intravenous drug delivery

Intravenous drug delivery provides the most rapid onset of action, through direct access to the systemic circulation. However, side effects, as well as overdose, are also more common.
Intravenous administration of drugs for pain relief often requires monitoring:

a. Paracetamol and NSAIDs do not cause acute, life-threatening complications, but monitoring (every 4–6 hours) for longer-term complications, particularly for reduced urine output and gastric bleeding in the case of the NSAIDs, is required.

b. Opioids given intravenously have the potential to cause fatal respiratory depression. Patients should be constantly monitored, with clinical assessment of respiratory rate and level of consciousness, preferably using pulse oximetry.

The limitations and dangers of IV PCA have been discussed above, as well as in the relevant section on PCA elsewhere in these guidelines.

Intraosseous drug delivery

There are rare situations, particularly in paediatric burns, where the only access for administration of drugs for pain relief may be an intraosseous line. Morphine, in weight-appropriate doses, may be administered via an intraosseous line, until establishment of IV access.

The sections below are discussed in detail in the relevant sections of the guidelines.

7.2.3 Regional (plexus)

1. Single shot/catheters – local anaesthetics ± vasoconstrictor

7.2.4 Neuraxial

1. Intrathecal /epidural
2. Single shot/catheters

8. Locally and regionally administered analgesic drugs

The key issues to be discussed in this section are:

8.1 Local anaesthetics

Local anaesthetics exert their effect as analgesics by the blockade of sodium channels and hence impeding neuronal excitation and/or conduction.

8.1.1 Short-duration local anaesthetics

Lignocaine is the most widely used short-duration local anaesthetic in acute pain management. Although the plasma half-life is approximately 90 minutes, the duration of local anaesthetic effect depends on the site of administration, dose administered and the presence or absence of vasoconstrictors. Although lignocaine is hydrophilic, it is delivered in high concentrations and therefore usually diffuses well into nerve bundles, resulting in little separation of sensory and motor blocking actions.

8.1.2 Long-duration local anaesthetics

The three commonly used long-duration local anaesthetic agents, bupivacaine, levobupivacaine and ropivacaine, are structurally related. Whereas bupivacaine is a racemic mixture of S- and R-enantiomers, levobupivacaine is the S- (or levo) enantiomer of bupivacaine; ropivacaine is an S-enantiomer formulation as well.

Clinical practice points

1. Continuous perineural infusion of lignocaine provides less effective analgesia and results in denser motor block than ropivacaine, levobupivacaine and bupivacaine.
2. There are no differences in terms of quality of analgesia or motor blockade between ropivacaine, levobupivacaine and bupivacaine when given in low doses for regional analgesia.
3. Ropivacaine and levobupivacaine cause less severe cardiovascular and central nervous system toxic effects than racemic bupivacaine.
4. Lipid emulsion may be effective in resuscitation of circulatory collapse due to local anaesthetic toxicity but must be used in conjunction with advanced cardiac life support.
5. Resuscitation following accidental overdose with ropivacaine is more likely to be successful than with bupivacaine overdose.

8.2 Opioids

Clinical practice points

1. When compared with placebo, intra-articular morphine following knee arthroscopy does not improve analgesia.
2. There is no conclusive evidence that opioids have a peripheral effect at perineural level.

8.3 Adjuvant drugs

Clinical practice points

1. Clonidine prolongs duration of analgesia and anaesthesia when added to local anaesthetics for axillary and peribulbar blocks, but evidence is inconclusive when clonidine is added to supraclavicular brachial plexus blocks or continuous catheter techniques.
2. Adding clonidine to lignocaine intravenous regional anaesthesia delays tourniquet pain.
3. Long-term effects of perineural magnesium are unclear.
4. Magnesium sulphate improves intra- and postoperative analgesia and tourniquet tolerance when added to lignocaine intravenous regional analgesia
5. Ketamine reduces pain when applied topically in oral mucositis.

8.4 Anti-inflammatory drugs

8.4.1 Corticosteroids

Clinical practice points

1. Subacromial injections of corticosteroids are more effective than oral NSAIDs when treating rotator cuff tendonitis.
2. Intra-articular steroids in combination with either local anaesthetic or opioids reduce pain, analgesic consumption and duration of immobilisation after knee arthroscopy.
3. Combining dexamethasone with lignocaine for intravenous regional anaesthesia improves analgesia for up to 24 hours *(Bigat, 2006).*
4. Intra-articular steroids increase the risk of septic arthritis.

8.4.2 Non-steroidal anti-inflammatory drugs

Clinical practice points

5. Topical NSAIDs cause fewer gastrointestinal side effects compared with oral NSAIDs and are of limited efficacy in lateral elbow pain, providing short-term functional improvement.
6. Adding a non-selective NSAID to local anaesthetic solutions for intravenous regional anaesthesia improves postoperative analgesia.
7. Topical diclofenac and ketoprofen are comparable to oral naproxen in reducing pain and inflammation associated with musculoskeletal injuries and other inflammatory conditions. Indomethacin is ineffective when applied topically.
8. Topical NSAIDs provide effective analgesia for traumatic corneal abrasion.

8.5 Regional and local analgesic techniques

Various techniques exist for administering analgesic drugs at peripheral sites. Peripheral nerve blocks may be performed either as a single shot or via indwelling perineural catheter. Wound infusions, intraperitoneal and intra-articular administration of analgesics are well documented, and transdermal analgesics are used in various formulations.

Peripheral nerve blocks and infusion of local anaesthetics

Table I: Advantages and disadvantages of peripheral nerve blocks

Advantages	*Disadvantages*
• Excellent analgesia • Avoids complications of systemic analgesics • Promotes early mobilisation/physiotherapy	• Small risk of bleeding with anticoagulation • Continual monitoring of analgesia with adjustment of dose/infusion rate • Potential local anaesthetic toxicity with prolonged infusion (RARE) • Catheter migration with resulting ineffective analgesia • Infection risk with indwelling catheter

Table II: Local anaesthetic doses and infusion rates for peripheral nerve blocks in adults

Technique	Drugs	Adult dose	Considerations
Plexus block	Bupivacaine	*LD: 0,25–0,5%, 20–40 ml *CI: 0,125–0,25%, 5–10 ml/h	Maximum 2 mg/kg or 6 mg/kg/24h; maximum 150 mg or 1 ml/kg bolus
	Levobupivacaine	As for bupivacaine	As for bupivacaine
	Ropivacaine	*LD: 0,5–,75%, 10–40 ml *CI: 0,2%, 0,1 ml/kg/h	Maximum 800 mg/24 h or 28 mg/h. Maximum 1 ml/kg bolus
Minor nerve blocks or infiltration	Bupivacaine	0,25–0,5% 5–10 ml/nerve	Maximum 2,5 mg/kg or 150 mg
	Levobupivacaine	0,25–0,5% 1–60 ml	Maximum 2,5 mg/kg or 150 mg
	Ropivacaine	0,2% 1–100 ml	Maximum dose 200 mg

LD = Loading dose *CI = Continuous infusion

Table III: Intravenous regional analgesia

Drug	Dose	Comments
Lignocaine	Maximum dose 200 mg or 2 mg/kg	Dilute to 40 ml total volume, adding dexamethasone prolongs analgesia

Table IV: Intra-articular analgesia

Drug	Dose	Comments
Bupi-/ropi-/chirocaine	10–20 ml, 0,5 %–1 % solution	Limited postoperative analgesia only

Table V: Topical analgesia

Drug	Application	Comments
EMLA↑↑[R]	Venous ulcer debridement	
Amethocaine	IV cannulation in children	Superior to EMLA

Drug	Application	Comments
Local anaesthetic on swab	Direct application to tonsil bed with tonsillectomy	Similar analgesia to local anaesthetic infiltration
Ketamine	Mouthwash	Reduced pain from oral mucositis
NSAID eye drops	Traumatic corneal abrasions	

Clinical practice points for regional and local analgesic techniques

Topical techniques

1. Topical EMLA cream (eutectic mixture of lignocaine and prilocaine) reduces the pain associated with venous ulcer debridement.

Intra-articular techniques

1. When compared with placebo, intra-articular morphine following knee arthroscopy does not improve analgesia.
2. Postoperative pain is reduced to a limited degree by intra-articular local anaesthetics.

Continuous wound infusions

1. Continuous local anaesthetic wound infusions lead to reductions in pain at rest and on movement. Decreased opioid consumption, postoperative nausea and vomiting, and length of hospital stay are reported, while there is no difference in the incidence of wound infections.
2. Following laparoscopic cholecystectomy, intraperitoneal local anaesthetics reduce early postoperative pain scores.

Peripheral nerve blocks

1. Continuous peripheral nerve blockade (regardless of catheter location) provides better postoperative analgesia than systemic opioids and leads to reductions in opioid use and side effects (nausea, vomiting, pruritus and sedation).
2. When compared with nerve localisation using a peripheral nerve stimulator, ultrasound guided blocks are faster to perform, have a faster onset and longer duration of action, and are more often successful.
3. Continuous thoracic paravertebral catheters results in comparable analgesia to thoracic epidurals with less urinary retention, hypotension, nausea, and vomiting and a lower incidence of postoperative pulmonary complications.
4. Following open shoulder surgery, continuous interscalene analgesia provides better analgesia and improved patient satisfaction with reduced opioid-related side effects compared with opioid-based intravenous patient-controlled analgesia.
5. After total knee arthroplasty femoral nerve block provides better analgesia than parenteral opioid-based techniques.

6. Continuous femoral nerve blockade is equi-analgesic to epidural analgesia but with fewer side effects following total knee arthroplasty.
7. Continuous posterior lumbar plexus analgesia and continuous femoral analgesia are equally effective following total knee arthroplasty.

Safety considerations for regional and local analgesic techniques

Anticoagulation

In patients with impaired coagulation, caution is advised when performing blocks where direct pressure in the event of a traumatised blood vessel is not possible (e.g. lumbar plexus, psoas compartment, infraclavicular), as a plexopathy may follow haematoma-induced pressure. Guidelines for removal of peripheral catheters from non-compressible sites are similar to those for removal of epidural catheters.

Nerve injury

Most nerve injuries following nerve blocks present as a transient neuropathy with paraesthesia and rarely as permanent neurological injury (persisting for more than 6 to 12 months). The incidence of transient neuropathy (radiculopathy) varies for different block sites: 2, 84% for interscalene brachial plexus block, 1, 48% for axillary brachial plexus block and 0, 34% for femoral nerve block.

Permanent neurological injury was reported following injection of local anaesthetic directly into the cervical spinal cord when an interscalene block was performed under general anaesthesia.

While ultrasound guidance has been shown to reduce the incidence of intravascular injection, the effect on neurological injury has not been elucidated.

Toxicity

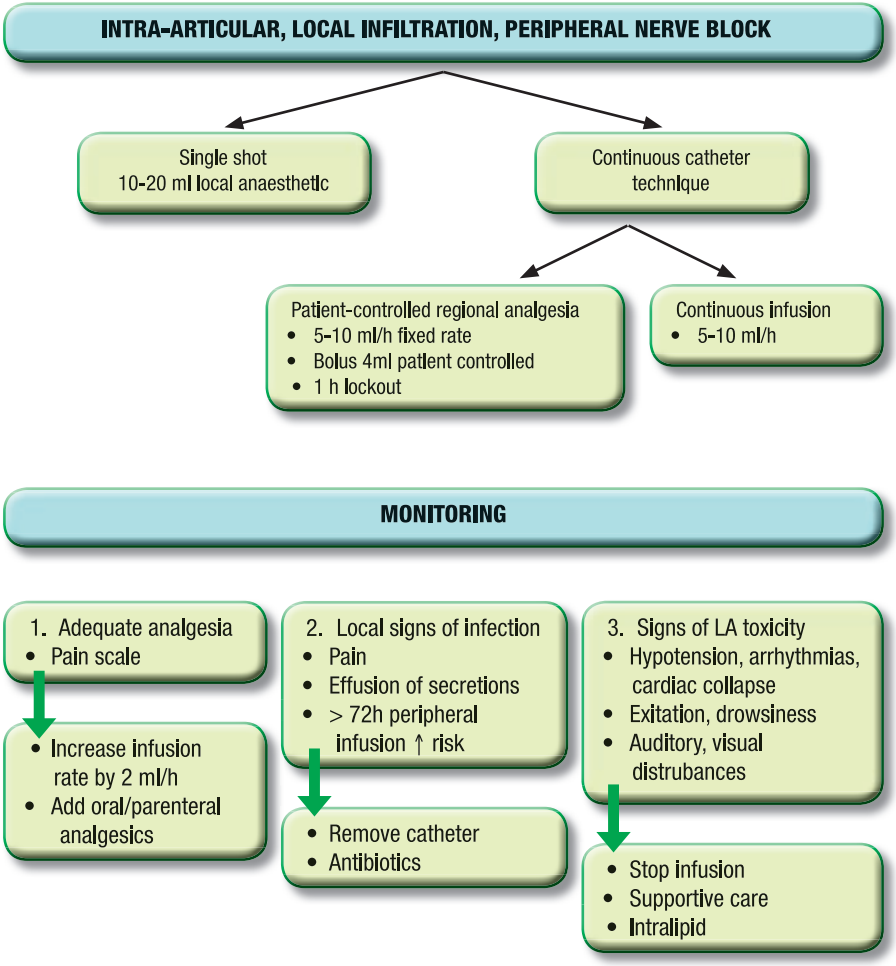
Accidental intravascular injection or rapid absorption of local anaesthetic can lead to toxicity. In a prospective study involving more than 21 000 cases, the incidence of cardiac arrest was 1.4 per 10 000, while that for seizures was 7.5 per 10 000. Surveys specifically investigating brachial plexus blocks have reported a higher rate of seizures (0.2%).

Infection

Although bacterial colonisation of indwelling continuous peripheral nerve catheters is high (16-57*%)*, serious infections and abscess formation are rare. Risk factors for colonisation are catheter placement in the groin and repeated dressing changes. Catheter tunnelling significantly reduces bacterial colonisation.

The strongest recommendations for preventing infection are hand hygiene and effective skin preparation, preferably with alcohol-based chlorhexidine solutions.

Figure 1: Clinical approach to peripheral regional analgesia



9. Techniques of drug administration

9.1 Clinical guidelines on the use of patient-controlled analgesia (PCA)

PCA is a conceptual framework that refers to a method of pain control whereby a patient self-administers small doses of an analgesic agent, and usually implies the use of a programmable pump.

The following key aspect will be discussed:

8.1.1 **Rationale for use**

8.1.2 **Standards of care**
- **Chart 1:** Prescription chart
- **Figure 1:** Proposed treatment algorithm for PCA management

8.1.3 **Equipment**

8.1.4 **Medication**

8.1.5 **Method**
- **Table I:** Proposed PCA management regimens

9.1.1 Rationale for use

Key points

1. The proposed *benefits* of patient-controlled or self-administered analgesia compared to nurse administered analgesia include the following:
   - Improved pain control
   - Patient preference for IV PCA is higher
   - Decreased risk of overdose (but risk remains)
   - Less labour intensive from nursing perspective
2. The decision to provide PCA is taken after *discussion with the patient*, where possible. Ongoing communication regarding, for example, adjustment of demand dosing may influence the success of PCA management.
3. Pain control with PCA is only effective after initial *rapid pain control* under supervision of the prescribing physician, for example in the theatre recovery room postoperatively.

4. These guidelines do not apply for patients that are opioid tolerant or with chronic pain.
5. *PCA in children*
   The concept of PCA continues to be developed in children, with patient-controlled epidural analgesia, subcutaneous PCA and intranasal PCA being recent extensions of the method. There may also be a role for patient-controlled sedation. PCA, when used with adequate monitoring, is a well-tolerated technique with high patient and staff acceptance. It can now be regarded as a standard for the delivery of postoperative analgesia in children aged > 5 years.

9.1.2 Standards of care

Key points

1. Appropriate routine monitoring of patients should detect changing pain scores and detect the presence of side effects to prevent *complications* such as inadvertent overdose (for example nurse administration of intended PCA bolus) and the masking of pain from new problems such as compartment syndrome of limbs, urinary retention, pulmonary embolism or myocardial infarction.
2. Monitoring not only addresses prevention of complications but assures repeated assessment for *adequacy* of pain management.
3. Intensive and frequent monitoring is essential in patients at risk for the development of respiratory depression and other side effects. If peripheral oxygen saturation cannot be continuously monitored, it may be indicated to administer oxygen by nasal cannula or face mask for the duration of IV opioid administration.
4. *Standardised prescriptions* within institutions also prevent complications from supplemental medication such as opioids by other routes, or sedatives.
   a. Proposed prescription chart *(see next page)*

Chart 1: Proposed prescription chart

INSTRUCTIONS

- Nursing staff are not allowed to change settings on the pump
- PCA boluses must only be administered by the patient not the nursing staff

	Treatment changes			Bag change YES/NO (repetition of bag)
	1	2	3	
Date/time				
Drug 1				**Drug 1**
• Concentration mg/ml				• Amount mg
Drug 2				• Solution
• Concentration mg/ml				• Bag size ml
Drug 3				**Drug 2**
• Concentration mg/ml				• Amount mg
Continuous infusion ml/hr				**Drug 3**
Loading dose Drug 1 mg				• Amount mg
PCA Bolus Drug 1 mg				
Lockout time min				
4 hour maximum Drug 1 mg				
Total amount Drug 1 mg				

PRESCRIPTION

Doctor: _____ **Signature:** _____ **Contact no:** _____

MONITORING (Hourly)	FINDINGS	ACTION
Pain (use Visual Analogue Scale)	Moderate to severe	Contact doctor
Sedation	Difficult to wake	Administer Narcan 0,2 mg stat IV. Contact doctor
Respiratory rate	< 10/min	Administer Narcan 0,2 mg stat IV. Contact doctor
Pupil size	< 2 mm	Contact doctor
Blood pressure	Systolic BP < 90 mmHg	Contact doctor
Heart rate	< 50/min or > 100/min	Contact doctor

Attending nurse: _____ **Additional instructions:**

_____

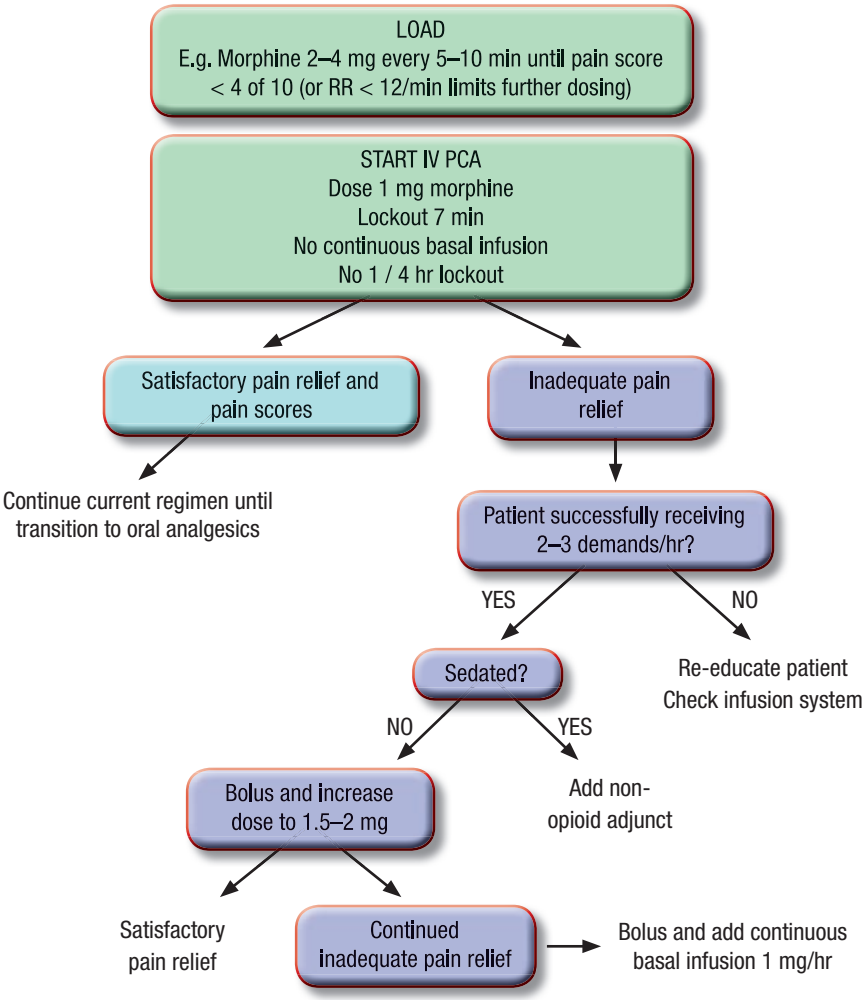
Day 1 Shift 1 _____ Day 1 Shift 2 _____ _____

Day 2 Shift 1 _____ Day 2 Shift 2 _____ _____

Day 3 Shift1 _____ Day 3 Shift 2 _____ _____

1. A standardised *treatment algorithm* may improve pain management by integrating pain assessment and side effects for the establishment of a clear reaction pathway.

Figure 1: Proposed treatment algorithm for PCA management



9.1.3 Equipment

There are several PCA equipment variations available in SA. It can be broadly categorised into 2 groups: systems that use durable (often bulky) pumps with disposable cartridges that usually have

multiple programmable options, or systems that utilise completely disposable components with built-in mechanisms for bolus administration, but do not allow background infusion administration or provide programmable options. The effectiveness of these latter systems may be compromised by the fact that no dose adjustments can be made, but it may provide a cost benefit. All PCA infusion systems must incorporate antisyphon valves and in non-dedicated lines, antireflux valves.

9.1.4 Medication

Opioid analgesics

The most commonly used opioid analgesics for PCA in South Africa include the following:

1. Morphine sulphate (IV)
2. Pethidine (IV)

The following should only be used for short duration and carefully monitored in patients with demonstrated intolerance to all other μ agonists:

1. Remifentanyl (IV)
2. Sufentanil (IV)
3. Fentanyl (IV)

In contrast to the longer-acting opioids, it may be necessary to use a small background infusion to sustain analgesia with use of one of the following short-acting opioids:

1. Tramadol (IV)
2. Dihydrocodeine tartrate (SC)

Generally, there does not appear to be major differences in the efficacy of various opioid drugs for PCA. On an individual basis, one opioid may be better tolerated than another and it may be beneficial to change to an alternative agent if a patient is experiencing intolerable side effects.

Local anaesthetics

The most commonly used local anaesthetics used for regional (PCRA) or epidural (PCEA) PCA in South Africa are bupivacain, ropivacain and levo-bupivacain. Opioid analgesics are sometimes added to the local anaesthetic with the use of PCEA.

Additives

Commonly used drugs that are used as additives to PCA in South Africa, either to improve efficiency by synergistic or additive action with the opioid, or to decrease side effects of the opioid, include the following:

Dexmedetomidine

There is some evidence that the use of dexmedetomidine when added to IV morphine PCA may improve analgesia and reduce morphine-related side effects without increasing sedation or haemodynamic side effects.

Ketamine
The addition of ketamine may not improve pain control or reduce the incidence of side effects of opiod analgesics.

Droperidol
Droperidol is an effective anti-emetic but may cause unacceptable sedation at the dose necessary to prevent nausea and vomiting

Hydroxyzine
There is no evidence to support the use of hydroxizine in PCA.

Naloxone
The incidence of nausea and pruritis may be decreased with the addition of naloxone to IV morphine PCA

5 HT_3 antagonists
The routine addition of anti-emetics to PCA infusions is not advocated, as it provides no benefit over selective administration on indication.

Magnesium sulphate

9.1.5 Method

Route

Intravenous

Subcutaneous
Can be as effective as IV PCA

Intranasal
Can be as effective as IV PCA

Transdermal
New non-invasive systems for transdermal delivery of ionisable drugs such as fentanyl HCl by application of an external electrical field, has been developed.

Regional/peripheral nerve catheter

Wound infiltration
Patient-controlled infusion of regional local anaesthetic agents, including wound infiltrations, may be effective.

Epidural
PCEA results in lower cumulative doses of the drugs used without differences in pain relief or side effects

Pump settings

Dose

The optimal bolus dose should provide adequate pain relief with minimal side effects. Age and a history of prior opioid use can influence the efficacy of the bolus dose. The initial dose should be adjusted according to response. The optimal initial dose of IV morphine is 1 mg.

Lockout time

The lockout interval should be long enough for the analgesic to have its full effect. The optimal lockout for morphine is 7 to 11 minutes.

4 hour limit

Overdose with PCA is usually due to the effect of large doses accumulating after hours or days. Limiting the maximum dose over several hours may be the most effective way of preventing overdose.

Background

The risk of respiratory depression is higher when a background infusion is used, and it does not improve pain control. It may be useful in opioid-tolerant patients.

Total amount, concentration

Drug concentrations should be standardised within institutions to reduce the occurrence of programming errors.

Table I: Proposed PCA management regimens (this is based on opinion, limited evidence for proposed regimens exists):

Opioid	Opioid dilution	Additive	Additive dilution	Pump settings
Morphine IV	1 mg/ml	Dexmedetomidine or Ketamine	2–5 µg/ml	Bolus 1 mg (1 ml) Lockout 7 min
			2 mg/ml	
		Droperidol or Ondansetron	15–100 µg/1 mg morphine or 5 mg/100 ml	
			16 mg/100 ml	
Tramadol IV	5 mg/ml	Dexmedetomidine	1–2 µg/ml	Bolus 10–20 mg Lockout 5–10 min
Remifentanil IV	50 µg/ml			Bolus 50 µg over 5 min (Background 0.075–0.15 µg/kg/min) Lockout 5 min
Sufentanil IV	1 µg/ml			Bolus 4–6 µg (Background 1.15 µg/hr) Lockout 1 min
Fentanyl IV	1 µg/ml			Bolus 2–30 µg Lockout 6–8 min

9.2 Epidural and spinal drug administration for acute pain

The following key points will be discussed in this section:

9.2.1 Epidural analgesia

Clinical practice points

- ***Local anaesthetics***
- ***Epidural opioids***
- ***Insertion of epidural catheter***
- ***The level of the epidural***
- ***Test doses***
- ***Patient-controlled epidural analgesia (PCEA***
- ***Systemic analgesia in combination with epidural analgesia***
- ***Complications, side effects and treatment***
- ***Respiratory depression***
- ***Duration of epidural analgesia***
- **Table IV:** Drugs and doses used in epidural analgesia

9.2.2 Spinal (intrathecal) analgesia

- ***Drugs used for intrathecal analgesia***
- ***Clinical-practice points***

9.2.3 Regional analgesia and concurrent anticoagulant medications

- **Table VI:** Clinical approach to neuraxial analgesia in the patient on medication with anticoagulation effects

9.2.1 Epidural analgesia

Epidural analgesia (i.e. the provision of pain relief by continuous administration of pharmacological agents into the epidural space via an indwelling catheter) has become a widely used technique for the management of acute pain in adults and children, particularly after surgery, trauma and in the parturient.

Clinical practice points

1. The decision to do an epidural and the technique that you choose should be appropriate to the intensity of pain anticipated and congruent to the level of the tissue damage.
2. All techniques of epidural analgesia (except for epidural using a lipophylic opioid only) for all types of surgery provide better postoperative pain relief compared with parenteral opioids (including PCA) administration.
3. Complete absence of pain is seldom achievable and not realistic even with neuraxis techniques. The objective should be a balance between analgesia, patient satisfaction, safety and available resources.

4. Combinations of low concentrations of local anaesthetics and opioids provide better analgesia than either component alone and reduce the dose requirements of both drugs.
5. Epidural analgesia at the correct level for an appropriate duration may decrease pulmonary complications, ventilatory requirements or myocardial infarction and may improve bowel recovery. The data on improved outcomes is, however, controversial and the focus should be on pain relief and patient satisfaction.
6. Permanent neurological damage with epidural techniques is rare but devastating and efforts should be made to prevent, diagnose and treat these in time. Immediate decompression of a haematoma or abscess increases the likelihood of neurological recovery. Because of these complications, the advantages and risks should be discussed with the patient and informed consent obtained.
7. Insertion of the epidural catheter on the spinal level matching the dermatome of the surgery (i.e. catheter-incision congruent analgesia) results in optimal postoperative epidural analgesia by infusing analgesic agents to the appropriate incisional level providing superior analgesia and minimising side effects.
8. Infusions of epidural local anaesthetic plus opioid combinations in a general ward have been advocated to be safe, but the precondition is supervision by an anaesthesia-based pain or similar service with 24-hour medical staff cover and monitoring by well-trained nursing staff. This may not be available in many hospital wards.

Local anaesthetics

Table 1: Local anaesthetics available in South Africa for epidural use

Duration of action	Formulations	Dosage
Short acting	Lignocaine in various formulations	
Long acting	Bupivacaine	Macaine® 5 mg/ml with or without adrenalin
	Levobupivacaine	Chirocaine® 5/7.5 mg/ml
	Ropivacaine	Naropin® 2/7.5/10 mg/ml and 2 mg/ml as the 100/200 ml polybag

There are no consistent differences between ropivacaine, levobupivacaine and bupivacaine when given in low doses for regional analgesia in terms of quality of analgesia or motor blockade.

Epidural opioids

The behaviour of epidural opioids is governed largely by their lipid solubility. Morphine is the least lipid soluble of the opioids administered epidurally. As it has a prolonged analgesic effect it can be given by intermittent bolus dose or infusion; the risk of respiratory depression may be higher and analgesia less effective with bolus dose regimens. Lipophilic opioids (e.g. fentanyl, sufentanyl and alfentanyl) have a faster onset but shorter duration of action compared with hydrophilic drugs.

Insertion of epidural catheter

Epidural catheters are inserted under sterile conditions for obvious reasons. Theatre gowns, masks and hats are to be worn for this procedure. It does seem prudent to use a chlorhexidine solution to prepare the skin, maximise sterility at insertion, maintain sterility at the puncture and infusion ports and to remove the catheter before or on day five. Chlorhexidine impregnated dressings of epidural catheters reduce the incidence of catheter bacterial colonisation.

The level of the epidural

The benefits of post-operative epidural analgesia are optimised when the epidural catheter is inserted in a location corresponding to the dermatomes covered by the surgical incision (i.e. catheter-incision congruent analgesia), resulting in a lower dose of drug administered and decreased incidence of drug-induced side effects, such as pruritus, nausea, vomiting, urinary retention, motor block and hypotension.

Table II: Level of epidural

Surgery	Level of epidural
Thoracotomy	T 4–8
Upper abdominal	T 6–8
Middle abdomen	T 8–10
Lower abdominal	T 8–12
Lower extremity	L 1–L4

Test doses

This procedure is standard when the epidural is commenced but should be repeated before top-up doses for analgesic purposes. Although the migration of the catheter to the intravascular or intrathecal from the epidural space is uncommon, aspiration and the administration of a test dose of adrenalin and local anaesthetic before bolus dosing for pain may prevent complications (e.g. high or total spinal, seizures, neurotoxicity) associated with accidental administration of local anaesthetics into these spaces. After negative aspiration, 3 ml of a short acting local anaesthetic or the highest concentration of the local anaesthetic to be used (e.g. 0.75% levobupivacaine) plus 15 µg of epinephrine can be administered as a test dose. If, after 2 min, there is no evidence of intravascular or subarachnoid injection (tachycardia ≥ 100 bpm or hypotension [systolic blood pressure < 90 mm Hg]) it can be considered safe to proceed.

Patient-controlled epidural analgesia (PCEA)

The use of PCEA is based on individualisation of therapy similar to other patient-controlled techniques but data regarding reduced epidural analgesic requirements, superior analgesia and greater patient satisfaction is not consistent.

Systemic analgesia in combination with epidural analgesia

The use of epidural analgesia does not preclude the use of systemic analgesia. Patients with epidural analgesia should have concomitant paracetamol prescribed to treat other aches and pains and facilitate withdrawal of epidural analgesia.

Complications, side effects and treatment

The concentrations at the lower end of the effective dose ranges are used for continuous infusion epidural techniques in order to:

- Limit side effects and motor block and
- Facilitate clinical evaluation for neurological complications

In the event of complications or side effects, the first reaction *should not be to stop the epidural and switch to IM injections.* This may leave the patient with rebound pain and actually be detrimental in the risk benefit analysis.

Table III: Complications

Complication	Incidence	Treatment	Remarks
Nausea and vomiting	Common	Odansetron or class equivalent, droperidol or prochlorperazine	Dose dependant
Pruritis	Common	Antihistamine, naloxone or droperidol	Dose dependant
Urinary retention	Common	Catheterise	
Post-dural puncture headache	Uncommon unless dura is perforated	Wait, bed rest and analgesics	Blood patch controversial
Hypotension	Uncommon	IV volume Decrease dose/rate of epidural	Prevent hypovolaemia
Motor block	Common with higher concentrations	Decrease dose if significant	May be more frequent with bupivacaine
Treatment failure	Variable	Rectify cause or treat side effects	Consider another technique
Respiratory depression	Uncommon	See below	Sedation is the early warning sign
Toxicity	Uncommon	Prevent CPR	Bupivacaine > Levobupivacaine [3] Ropivacaine
Epidural haematoma or abscess	Rare	Surgical decompression within 8 hours	Early scan if suspected
Permanent neurological damage	Rare	Prevent	

Respiratory depression

A strategy to detect and treat this complication should be in place. The incidence is between 1% (decreased respiratory rate) – 15% (desaturation) depending on the criteria used, but clinically significant in less than 1% of patients. High risk patients for this should be identified preoperatively, e.g. sleep apnoea and obesity. All patients receiving neuraxial opioids should be monitored clinically for adequacy of ventilation, oxygenation and level of consciousness 1–2 hourly for the first 24 hours after the injection with morphine or during the entire time an infusion is in use. The absence of a decreased respiratory rate is not a reliable warning sign of respiratory depression, but it is almost

always preceded by sedation. The treatment of this complication is a graded response appropriate to the level of hypoventilation:

1. Supplemental oxygen should be available for patients receiving neuraxial opioids and administered to those with an altered level of consciousness, respiratory depression or hypoxaemia.
2. The reason for the respiratory depression should be assessed and the dose of the neuraxial infusion should be decreased if this is the cause. If an infusion of epidural drugs is stopped, alternative pain treatment should be prescribed. Indiscriminately stopping the epidural may lead to severe pain and concurrent medications, e.g. parenteral opioids may precipitate severe respiratory depression.
3. Intravenous access should be maintained if respiratory depression is suspected or when it occurs. Ensure that naloxone is readily available.
4. It should be considered to transfer the patient to a higher level of nursing care and monitoring if the existing one is not appropriate to the risk. When available, pulse oximetry and end-tidal CO2 can be considered, but is not proven to be better than clinical monitoring.
5. Naloxone should be administered if preliminary measures fail to rectify the problem. It is administered IV in small increments sufficient to improve ventilation but without reversing the analgesic effect.
6. Non-invasive positive-pressure ventilation may be considered for improving ventilatory status. In the infrequent event of life-threatening apnoea the airway should be maintained and the patient ventilated with a bag and mask pending naloxone administration.

Duration of epidural analgesia

The catheter is commonly left in place for 2–4 days, but it is impossible to determine scientifically what the maximum safe time would be to persist with a percutaneous catheter due to the rarity of epidural infections.

In summary:

Consider the risk vs benefit for every patient, but remember that:

- Epidural analgesia is probably the best we can offer for acute severe pain.
- Use combinations of local anaesthetic and opioids through an indwelling catheter.
- Target the administration to the appropriate dermatome.
- The smallest dose and concentration required to produce the desired result should be administered.
- The rapid injection of a large volume of local anaesthetic solution should be avoided and incremental doses should always be used.
- Dilutions of local anaesthetic solutions should be made with preservative free 0.9% saline according to standard hospital procedures for sterility.

Table IV: Drugs and doses used in epidural analgesia

Recommendations only, scientific evidence as such not available

Drug	Dose	Onset	Duration	Remarks
Lipophilic opioids:				
Fentanyl Sufentanil	Dilute single dose in 10 ml normal saline 50–100 µg 25–100 µg/hr 10–50 µg 10–20 µg/hr	5–10 min	2–4 h	Limited spread in CSF. Early respiratory depression most likely. Opioids alone via the epidural route seem to be of limited benefit.
Hydrophilic				
Morphine	1–5 mg 0.1–1 mg/hr	30–60 min	6–24 h	Extensive spread in CSF. Early and delayed respiratory depression possible.
Local anaesthetics				
Bupivacaine Not commonly used alone in analgesic infusion	5–8 ml/h 1.2 mg/ml or Incremental doses of 3–5 ml of 1.25–2.50 mg/ml	10–20 min, 30 min for optimal	3–4 h	Establish the block with 0.5% bolus 15– 30 ml. Recommendation: limit to 2 mg /kg in 4 h and 400 mg/24 h
L-bupivacaine	10–15 ml/h of 1.25 mg/ml Or 5–7.5 ml/h of 2.5 mg/ml		150 (–240) min	Minimal to moderate motor block, dilution stable for up to 7 days at 20°C. Maximum dose over 24 h of 400 mg.
Ropivacaine	2 mg/ml Bolus:10–20 ml 6–14 ml/h	15–20 min	140 (–200) min	Establish the block for surgery with 15–25 ml of 7.5 mg/ml for lumbar or 5–15 ml for thoracic epidural.
Combinations				
Ropivacaine 2 mg/mL + fentanyl 4 µg/ml	6–14 ml/ h			This combination is marketed as a polybag in some countries.
Bupivacaine 1 mg/ml + fentanyl 4 µg/ml	Bolus 1(–2) µg/kg fentanyl + infuse 0.5 (–2) µg/kg/h			Prepare by adding 5 x 10 ml 5 mg/ml bupivacaine + 2 x 10 ml fentanyl to 180 ml normal saline.
Patient (PCEA)- controlled epidural analgesia	**Continuous infusion in ml/h**	**Demand dose in ml**	**Lockout in minutes**	
Levobupivacaine 1,25 mg/ml + fentanyl 4 µg/ml	Initial rate of 4 ml/h	2	10	Stability proven for up to 40 hours at 20°C.
1 mg/ml bupivacaine + 5 µg/ml fentanyl	6 (3–4 ml/h for thoracic)	2	10–15	
1–2 mg/ml ropivacaine + 2–5 µg/ml fentanyl	3–5	2	10–20	

9.2.2 Spinal (intrathecal) analgesia

A single injection of intrathecal local anaesthetic plus an opioid is an acknowledged part of a postoperative analgesia strategy. It is effective or even better than other established techniques although the duration of the relief is limited to the first 24 hours and side effects are common.

Drugs used for intrathecal analgesia

Local anaesthetics are often combined with opioids to provide a smooth transition from the anaesthetic technique into the analgesic plan.

Table V: Drugs for intrathecal analgesia

Drug (preservative free)	Intrathecal single dose	Onset	Duration
Fentanyl	5–25 µg	5–10 min	1–4 h
Sufentanil	2–10 µg	5–10 min	2–6 h
Morphine	0.1–0.3–0.5 mg	45–75min	18–24 h

The longer duration of morphine has established it as the drug of choice but this advantage is gained at the increased risk of respiratory depression. At doses of 100–800 micrograms intrathecal morphine for pain relief following a range of surgical procedures produces a high degree of patient satisfaction and effective analgesia in the first 24 hours after the procedure. Particularly the lower doses of 100–200 micrograms offers effective analgesia with a low risk of adverse effects e.g. for hip replacement in the elderly, but higher doses are required for thoracotomy and abdominal surgery. The significant side effects are:

- Respiratory depression 3% ($PaCO2 > 50$ mmHg and/or respiratory rate < 8/min)
- Pruritus (itching up to 30%)
- Nausea and vomiting (25%) and
- Urinary retention (35% with morphine)

When intrathecal morphine has been administered, the patient should be nursed in a high care equivalent situation due to the risk of undetected respiratory depression on an ordinary surgical ward. The monitoring and treatment of these complications are similar to when they occur with epidural opioids. The analgesic effect rivals that of PCA, but does not last for longer than a day. A multimodal plan of alternatives should be in place to prevent (preferably) or treat rebound pain. Lipophilic opioids may be suitable for outpatient surgery but morphine is not.

Clinical practice points

1. Intrathecal morphine offers improved analgesia and opioid sparing for up to 24 h.
2. Intrathecal morphine doses of 300 mcg or more increase the risk of respiratory depression.
3. After major surgery, the incidence of respiratory depression and pruritus is higher with intrathecal morphine compared with IV PCA opioids, but there is no difference in the incidence of nausea and vomiting.
4. The lowest effective dose should be used in all circumstances.
5. Indwelling spinal catheters are not established as a routine technique for treatment of short term pain.

9.2.3 Regional analgesia and concurrent anticoagulant medications

Neurological compromise due to haemorrhagic complications is rare but devastating and it can be difficult to decide whether it is worth the risk to do the spinal or epidural. The risk of haematoma is almost impossible to determine but has been calculated at 1:150 000 for epidurals and 1:220 000 for spinals. Due to the paucity of scientific evidence, the clinician has to rely on clinical judgement, consensus expert opinion and knowledge of pharmacology to decide if it is worth the risk to do the spinal or epidural for anaesthesia per se or as an analgesia technique. This risk is increased by:

- Anticoagulation: the most important risk factor.
- Any other coagulopathy.
- Increase in age.
- Indwelling catheter techniques.
- Difficulty in needle placement.
- Abnormalities of the vertebral canal or spinal cord.

1. No absolute recommendations can be made in many clinical situations. The opinions of experts in the field should be considered, for example the Consensus Conference of the American Society of Regional Anesthesia and Pain Medicine can be found at http://www.asra.com/consensus-statements/2.html.
2. The medications, indications and information continue to evolve – keep your knowledge current.
3. Individualise every case according to risk vs benefit in that situation. What may be feasible to the expert in a specialised environment may not be a worthwhile risk to the regular anaesthetist in routine practice. Err on the side of safety.
4. It does seem prudent to raise the level of vigilance as the haemostatic compromise increases and evaluate the patient every 2 hours if the risk is deemed to be high. The implication of this is that the anaesthetist cannot perform the neuraxis technique and consider that to be the end of the commitment to that patient's care.
5. Be careful of a combination of anticoagulation effects.
6. Low molecular weight heparin has a longer duration of action compared to unfractionated heparin, cannot be monitored and is not completely reversed by protamine.
7. It can be foreseen that inadvertent or unavoidable anticoagulation is instituted in a patient with a neuraxis catheter in situ. In this case the treating physicians should consider the safest compromise and optimal timing to remove the catheter.
8. The following table is a summary of a reasonable approach to practical management of neuraxis anaesthesia and analgesia in the patient on anticoagulation medication. The recommendations are not absolute and the risk vs benefit must be considered in every clinical scenario.

Table VI: Clinical approach to neuraxial analgesia in the patient on medication with anticoagulation effects

Medication	Indication	Epidural or spinal reasonable	Monitor	Timing to insert	Timing to remove	Remarks
Herbal (ginko, garlic, ginseng)	Random non medical	Yes	None	Any time	Any time	Combinations with others may be unsafe
NSAIDs COX-2 inhibitors preferred	Anti-inflammatory and pain	Yes	No wholly accepted test	Any time	Any time	Combinations with others may be unsafe
Aspirin	Cardiovasc indications 60–325 mg/d	Yes	Bleeding time not proven	Any time	Any time	Combinations with others may be unsafe
Unfractionated heparin SC	DVT prophylaxis q 12 h	Yes	aPTT high limit normal	> 6 h after dose > 2 h before next	> 6 h after dose > 2 h before next	Consider HITT if > 4 days on heparin and do platelet count
Heparin IVI during surgery	5 000– 10 000 U for vasc surgery	Yes	aPTT ACT	Do ³ 1 h before heparin	2–4 h after dosing or reversal	"Bloody tap" not absolute indication to cancel surgery
LMWH	DVT prophylaxis	Yes	None	> 12 h after last dose ³ 2 h before next dose	> 12 h after last dose, ³ 2 h before next dose	E.g. enoxaparin 40 mg/ day SC or 30 mg q 12 h or dalteparin 5 000 U q 12 h SC
Warfarin prophylaxis	DVT prophylaxis	Yes if < 24 h of 1st dose	INR < 1.5 useful if > 24 h	Do within 24 h of 1st dose	INR < 1.5 If > 3 cut warfarin	Warfarin usually started evening before surgery
Heparin IVI cardiac surgery	Full IVI for card pulm bypass	Not known	aPTT ACT	Do ³ 1 h before heparin	4 h after dosing or reversal	Certainly not routine practice, some place epidural 12 h preop
Thrombin inhibitors: hirudin group	HITT	Not known	aPTT	Not known	Not known	Given IVI with effect for up to 3 h No antagonist
Fondaparinux	DVT prophylaxis	Not known		Not known	Avoid catheter	Anti FXa effect for days

Medication	Indication	Epidural or spinal reasonable	Monitor	Timing to insert	Timing to remove	Remarks
Heparin IVI maintenance	Full therapeutic	No	aPTT	NA	NA	Often replaced with LMWH
Warfarin	Established therapeutic	No	INR	NA	NA	Can do if feasible to stop for 5 days
LMWH for DVT, PE or acute MI	Therapeutic eg enoxaparin 1 mg/kg BD	No	None	If feasible stop +wait ³ 24 h	Unknown	Usually also on others: aspirin and clopidogrel
Antiplatelet clopidogrel* ticlopidine#	Acute MI, vascular disease	(most likely) No	Platelet ADP	If feasible wait ³ 7* to 14# days	Remove before! starting Rx	Given PO and inhibits ADP platelet aggregation
Antiplatelet GPIIb/IIIa antagonists	Acute MI	No		Feasible? waiting time 4–48 h	NA	Usually also on others: aspirin and LMWH
Fybrinolysis and thrombolysis	Acute MI + thrombo embolism	No	? Fibrinogen level	NA within 10 days	Not known	Effect may last 27 h also effect on platelets

10. Non-pharmacological techniques

Most psychological interventions used in acute pain management are seen as adjuncts to the pharmacological and physical therapeutic modalities.

The role of the traditional healers must not be underestimated as tribal beliefs play a major role in pain management. Tribal custom may also view pain expression as a form of weakness leading to symptom denial by believers. A slight cautionary is necessary as these practitioners may, in addition to psychological counselling, prescribe remedies for ailments that are devoid of therapeutic value but many of these mixtures contain active substances including anticoagulants and cardio-active agents such as digitalis and bella donna alkaloids.

Table 1: Examples of non-pharmacological interventions

Cognitive-behavioural
• Reassurance • Education and information • Relaxation • Imagery • Distraction • Biofeedback • Hypnosis
Physical
• Heat and cold application • Massage, exercise and immobilisation • Transcutaneous nerve stimulation (TENS) • Acupuncture

Reassurance and provision of information

This reduces pain and distress after minor procedures and may improve pain relief after more major surgery. There is no significant benefit after non-surgical procedures. As too much information may provoke anxiety it is useful to assess the normal approach of that patient to managing stress.

Relaxation training

This form of therapy usually implies teaching patients to calm themselves by either breathing control, altering muscle tension, or use of music. These methods are similar to meditation and self hypnosis. This is not effective in the perioperative setting but can be of use in cancer related pain.

Attentional techniques

Such techniques include distraction, imagery and music therapy. Distraction may reduce analgesic consumption in the perioperative phase but music therapy is ineffective.

Hypnosis

As techniques differ, this form of therapy is difficult to assess. There is evidence that acute procedural pain for minor procedures, burn wound care, obstetrics, and bone biopsy can effectively be managed by hypnosis.

Transcutaneous electrical nerve stimulation (TENS)

TENS is not thought to be effective in postoperative pain. Opinions differ in this regard as, to be effective, one must use maximal tolerable stimulation. These parameters are a current amplitude greater than 15 mA, a strong or sub-noxious stimulus, and/or a maximal non-painful stimulus. High frequency TENS is effective for dysmennorrhoea but ineffective for labour analgesia.

Acupuncture

Acupuncture may be effective for pain in childbirth, idiopathic cluster headache, and dental pain. In postoperative pain it has reduced analgesic requirements.

Massage and manual therapy

This form of therapy usually involves physiotherapy and chiropractic intervention and has no use in postoperative pain. They may aid recovery from acute back pain.

Heat and cold therapy

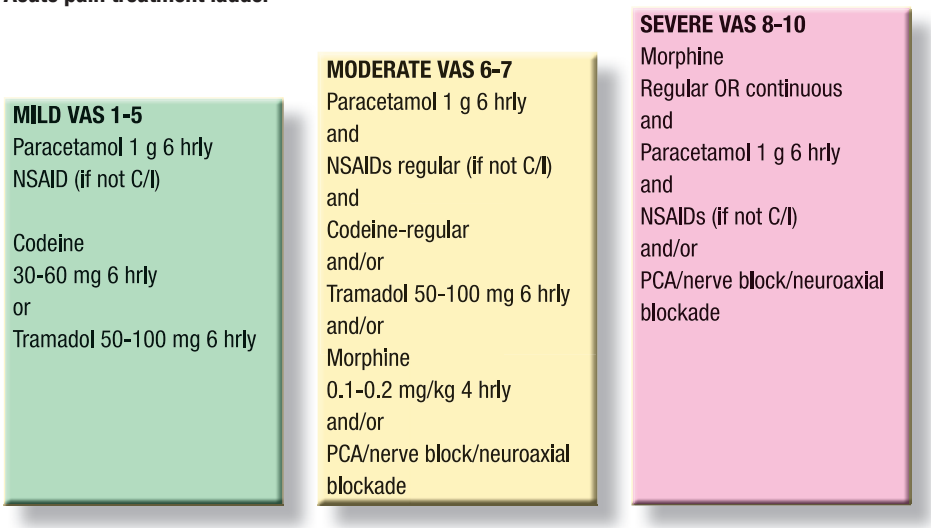
Application of heat or cold may reduce opioid consumption after orthopaedic trauma but are of no help after other major surgeries.

Clinical practice points

1. Combined sensory-procedural information can be effective in reducing pain and distress.
2. Hypnosis reduces procedure related pain
3. Training in coping methods or behavioural modification must be done prior to surgery to be effective. It may not be of any use in other acute pain scenarios.
4. Certain stimulation patterns of TENS may be effective in some acute pain settings.
5. Acupuncture has some efficacy in acute pain.

11. Management of acute pain in specific scenarios

Acute pain treatment ladder



Please note:

- VAS= Visual analogue scale
- The terms 'opioid analgesics', 'opiate agonists' and 'narcotic analgesics' are used interchangeably.
- 'Meperidine' and 'pethidine' are used interchangeably in the literature.
- The terms 'cyclo-oxygenase type-2 inhibitors', 'selective COX-2 NSAIDs' and 'coxibs' are used interchangeably in the literature and in this guideline.
- Drugs prescribed on a PRN basis are given Preferably Never!!!!

11.1 Acute pain as an outpatient

1. Management of minor and moderate acute pain as an out-patient is usually easily achieved with routine oral agents.
2. Severe, recurring, unrelenting or intractable acute pain usually mandates admission and specialist investigation.

3. Most commonly prescribed agents are paracetamol, aspirin, other NSAIDs, coxibs and opioid derivatives. Generally these agents are safe for routine usage as short courses of therapy for acute pain.
4. Following an acute episode of acute pain, only a short course of pain medication should be prescribed. It is seldom necessary for therapy in medical conditions for longer than 5 days and in many acute medical conditions, 24 hours therapy is more than adequate.
5. Acute pain medication should never be prescribed for longer than 10 days without review.
6. Remember that analgesics can mask the progression of many clinical scenarios and patients should be warned to return for review should their pain not settle completely within an appropriate time for the specific condition.
7. Patients should be warned regarding common side effects and special precautions relating to their prescribed analgesics, as well as serious drug interactions.
8. Topical analgesic agents are useful tools in treating out-patient conditions, especially trauma. This can decrease the reliance on oral drug therapy.
9. Generally modes of analgesic administration other than oral or topical are not appropriate for routine out-patient therapies. Rectal suppositories should only be considered in infants and patients unable to tolerate oral medications, this is usually due to nausea and vomiting. Rectal therapy is generally to be avoided in young children and teenagers.
10. There is no role for ongoing routine parenteral analgesic therapy as an out-patient, unless under the supervision of an appropriate medical specialist.

11.2 The casualty department

1. Pain is the single most common presenting symptom to emergency rooms throughout the world.
2. The management of pain in the majority of routine non-critical and non-severe cases is as it is for any out-patient scenario. Similarly severe pain and serious disease entities will usually entail admission into the facility, as above.
3. Unique however in this setting, are those patients and conditions which are associated with severe pain but are in fact non-serious conditions not requiring admission (e.g. extensive abrasions requiring cleansing and dressings); serious conditions which may be adequately settled in the casualty department allowing discharge home (e.g. joint dislocation) and several minor conditions which may necessitate a single dose of a potent analgesic to relieve the associated severe pain (e.g. migraine headache). Clearly these patients require significant and potent analgesia, but their discharge home thereafter affects their management.
4. Intravenous titrated opioid therapy remains the therapy of choice for severe acute pain in the emergency department. Usually intravenous access is routine and appropriate monitoring equipment, resuscitation equipment and medical and nursing expertise is available.

5. The reversal agent naloxone (Narcan®) should always be available in any situation where intravenous narcotics are used. In cases of opioid over-dosage reversal, repeated doses of naloxone may be required due to the relatively short half life of this agent.
6. Morphine is still the most widely available and utilised agent and is safe and reliable when used correctly.
7. Other potent opioids such as pentazocine (Sosenol®), meperidine (Pethidine®), dihydro-codeine (DF 118®) and morphine/papaveretum combination (Omnopon®) are also available and can be used instead, but offer no significant advantages over morphine sulphate itself.
8. The only clinical scenario where meperidine (Pethidine®) has been shown to possibly be more effective is renal colic. In this scenario, NSAID analgesics have been shown equally effective as opioids. Meperidine superiority in biliary colic remains controversial and unsubstantiated.
9. When opioids are used in the emergency department, one needs to keep the patient for observation before discharge home for a sufficient length of time, bearing in mind the half-life of the narcotic selected, concomitant medications which may affect respiration or haemodynamics and the age and mass of the individual patient.
10. Nalbuphine (Nubain®) is an effective and safer opioid which has intermittently been available in South Africa. It is less potent than morphine and has likewise a lower side-effect profile, making it a reasonable choice for usage in the emergency department scenario when available.
11. Tramadol (Tramal®) has emerged as a very useful drug in the emergency department scenario and this trend is to be encouraged. Tramadol has a far lower serious side-effect profile than the other narcotics, enabling safer discharge from the hospital. Potency of analgesia is usually adequate for the vast majority of conditions and in the majority of patients.
12. Standard adult dosage of tramadol is intravenous bolussing of 50–200 mg per dose.
13. Tramadol is also a very useful agent in the emergency department in cases where the severity of the condition will mandate admission. In these serious cases, the significantly lower risk of respiratory depression, hypotensive collapse and over sedation are major advantages.
14. Usage of tramadol in the trauma scenario is increasing and is appropriate.
15. Where opioids cannot safely be administered intravenously, they may be given by intra-muscular injection. This is however not ideal in the emergency department due to the longer onset of action and the less predictable and titratable response. This usually necessitates a far longer observation period thereafter. Occasionally sublingual, oral or rectal routes may be indicated.
16. Intravenous bolus doses of NSAIDs and coxibs are also extremely useful for the treatment of severe pain in the emergency department.
17. Lack of sedation, respiratory depression or haemodynamic instability are the major advantages of intravenous NSAIDs in patients that can subsequently be sent home.
18. The intravenous COX-2 selective anti-inflammatory available in South Africa is parecoxib (Rayzon®) and evidence suggests that it is as effective for acute pain therapy as are non-selective intravenous NSAIDs.

19. Parecoxib is safer than the non-selective NSAID's in patients likely to undergo surgical procedures.
20. The intravenous NSAID ketorolac (Tora-Dol®) has been shown to be efficacious and opioid-sparing in the emergency setting.
21. An advantage of intravenous NSAIDs in patients to subsequently be admitted is that there is no sedative effect which is of major importance when one requires the patient to be able to sign consent for procedures or surgery.
22. NSAIDs are contra-indicated in anyone at risk for renal failure (including pre-renal insults such as shock and dehydration), cardiac patients, peptic ulcer patients, those at risk for haemorrhage (including those on any anti-coagulant agents) and those at risk for allergic reactions.
23. Intravenous paracetamol (Perfalgan®) is similarly as safe as NSAIDs in these patients, but in addition can be used safely in almost every clinical scenario, including those mentioned above (care needed only not to exceed the maximal daily dose and in elderly and hepatically-impaired patients).
24. Although usually not adequate for analgesia alone, the opioid-sparing effect of intravenous paracetamol is extremely attractive in those patients that can be discharged and the lack of side effects or sedation is of benefit in those patients being admitted.
25. For completeness sake, it is necessary to mention that ketamine is an option for analgesia in pain relief and anaesthesia for certain casualty-based procedures. This has largely been discarded as a modality due to side effects and newer agents, but may be appropriate in selected scenarios and in peripheral places, providing the practitioner is experienced in its usage. Adequate analgesia can usually be achieved with intravenous doses of up to 0,5 mg/kg and the well-known psychological side effects usually only occur with doses exceeding 1 mg/kg. For anaesthesia, an initial dose of 2-4 mg/kg intravenously usually produces anaesthesia within 30 seconds and lasts up to 10 minutes. Thereafter repeated increments of half the induction dose can be usually given every 5 to 10 minutes without significant accumulation. An alternative is the administration of 10 mg/kg intramuscularly, which induces anaesthesia in 3 to 4 minutes and which lasts approximately 15-20 minutes.
26. One must caution appropriate monitoring during casualty-based procedures in general. Oxygen, monitoring equipment and resuscitation equipment in good working order are mandatory.
27. It is often routine in casualty-based sedation to combine opioids with a benzodiazepine. This increases the risk for respiratory depression and over-sedation and dramatically lengthens the post-procedure observation time prior to safe discharge.
28. When performed, only short-acting benzodiazepines such as midazolam should be used for emergency room and out-patient sedation and these should be titrated.
29. Caution is also required in reversing the benzodiazepine sedation with flumazenil (Anexate®), as this agent's half-life is also short and re-sedation may occur after its effect wears off.

30. Anaesthetic induction agents such as propofol, thiopentone (Pentothal®) and etomidate (Hypnomidate®) should never be used in the emergency department, unless there has been a decision taken that the patient requires intubation and ventilation and thus hospital admission.
31. The risk of aspiration must always be considered whenever any sedative agent is administered to a patient, especially in the case of agents which exacerbate nausea and in patients who are not starved.
32. Inhaled nitrous oxide may be a useful adjunct for pain control in the emergency room scenario and in the pre-hospital scenario. It may also be useful as analgesia for minor procedures.

11.3 The Intensive Care Unit (ICU)

1. The availability of well trained support staff, excellent monitoring facilities and resuscitation equipment in intensive care units allows safer usage of more potent agents.
2. In conscious and orientated patients, intravenous titration of opioid narcotics remains the method of choice.
3. Morphine is effective, the cheapest agent readily available and the agent with which most practitioners have the most experience. Its length of action is well suited to this environment.
4. Fentanyl is emerging as a useful agent in this scenario, but remains more costly than morphine.
5. There is a definite role for the usage in experienced hands of the potent short-acting narcotics alfentanil (Rapifen®) and sufentanil (Sufenta®) for acute, severe pain. These are similarly titrated intravenously and are of use especially in patients immediately post major surgery.
6. Ventilated patients are unable to vocalise when they are in pain. As such, regular potent analgesia must be administered regularly in all patients likely to have pain.
7. It is a wise policy to administer the analgesia before the sedation routinely, which should reduce the risk of sedated patients having inadequate pain control.
8. Even in patients unlikely to have pain, it is routine to include an opioid analgesic in the sedation regimen of ventilated patients as this augments the sedation and alleviates the discomfort associated with interventions and procedures.
9. Non-pharmocological issues are extremely important in the ICU setting and affect both pain level and pain perception. These include nursing care, pressure care, devices, masks, oxygen gas flow, humidification, physiotherapy, secretion formation, noise levels, day-night routines, visitation and sleep.
10. Morphine is the usually preferred analgesic sedative in mechanically ventilated patients and in combination with the short acting benzodiazepine, midazolam (Dormicum®, Midacum®) remains the gold standard.
11. Other narcotic potent analgesics can be substituted for morphine, but are more expensive, have no additional benefits and staff are less *au fait* with their usage.
12. Morphine should be used with care in renal failure due to accumulation of the drug.

13. Fentanyl (Sublimaze®) is the best alternative opioid for usage in the ICU, should an alternative to morphine be required. Fentanyl has the advantage of being associated with lesser haemodynamic instability, but may accumulate with prolonged use due to its half-life.
14. Partial opioid agonists should be avoided in ICU due to their risk for producing dependency in prolonged usage, without additional benefits in efficacy.
15. Similarly, other benzodiazepines, such as diazepam (Valium®, Pax®) or lorazepam (Ativan®) can be used in place of midazolam, but these are all longer-acting, and hence are prone to accumulate more, hence negatively affecting the weaning process.
16. Usual precautions are required in monitoring ventilated patients during sedation and analgesia with morphine. Although respiratory depression and over-sedation are less of a concern in ventilated patients, these become extremely important during weaning from mechanical ventilation. Other negative effects of narcotics, especially hypotension, remain a concern.
17. A newer agent, remifentanil (Ultiva®) is emerging as a very useful agent for use in the critical care environment. It is an ultra-short-acting, very potent fentanyl derivative which is easily titratable as an adjustable intravenous infusion.
18. Remifentanil is currently the superior agent for analgesia in ventilated patients undergoing invasive, uncomfortable or painful procedures. It is easily titrated for the duration of the procedure, irrespective of its duration (useful in short procedures e.g. placement of invasive monitoring lines and catheters, chest drainage tubes, etc as well as longer procedures such as major burns dressings).
19. The recommended dosage of remifentanil in this setting is 0,1–0,5 µg/kg/min infusion for adults. Children may require higher dosages of up to 1 µg/kg/min.
20. Remifentanil infusion is effective for ongoing analgesia in the immediate post-operative phase following major surgery associated with significant pain. When used intra-operatively in these cases, it is advantageous to continue this through into the early postoperative period.
21. Remifentanil can be used effectively in combination with propofol (Diprivan®) for the sedation and analgesia of ventilated patients, as an alternative to morphine and midazolam. This combination is even more short acting and titratable than the 'gold standard' but cannot be advocated for routine usage due to the significantly higher cost of both agents. In addition, propofol should not be used for more than 3 days.
22. The major indication for using the remifentanil plus propofol regimen is in cases of major surgery requiring post-operative ventilation which are suitable for rapid weaning from ventilation within 48 hours.
23. Remifentanil is useful for ICU sedation in patients with renal failure, as its clearance is independent of renal function.
24. The dosage of remifentanil required for ICU sedation is usually 0,025–0,2 µg/kg/min.
25. The recommended dosage for propofol for ICU sedation is 5–50 µg/kg/min.

26. Dexmedetomidine (Precedex®) is another useful agent for use during ICU procedures and combines analgesia with anxiolysis as well.
27. The recommended is dosage of dexmedetomidine in ICU is 0,5–3 µg/kg per single dose as a slow intravenous bolus (usually 1 µg/kg for procedures) and 0,2–1 µg/kg/hour (usually 0,6–0,7 µg/kg/hour) for continuous infusion.
28. Dexmedetomidine should not be used for longer than 24 hours continuously.
29. IV paracetamol (Perfalgan®) may be used for pain and fever if not contra-indicated.

11.4 Postoperative pain

1. The management of postoperative pain in hospital is generally the scenario in which medical, pharmacy and nursing staff have the most experience. Experience gleaned in this scenario has been extrapolated to guide pain control in most other medical scenarios.
2. Failure to treat the pain may result in a physiological stress-response, which may lead to myocardial ischaemia.
3. Immediate postoperative pain control in the recovery room (and subsequently if the patient is transferred to a high dependency or critical care environment) is best achieved by titrating an intravenous opioid agent.
4. Alfentanil and sufentanil are the commonest agents used immediately postoperatively by anaesthesiologists.
5. It is common practice to administer a longer-acting intravenous opioid such as morphine or fentanyl towards the end of the surgical procedure, to ensure sustained and adequate analgesia on waking. Appropriate monitoring again needs to be stressed.
6. It is also generally routine to administer an intravenous non-steroidal analgesic at the end of anaesthesia, providing there are no contra-indications. This practice is to be encouraged.
7. Intravenous NSAID administration is preferable to rectal suppository NSAID administration when intravenous access is available.
8. Initially NSAIDs should preferably be given intravenously and thereafter an oral course of on average 5 days would be appropriate for most routine post-surgical scenarios.
9. NSAIDs give effective and sustained analgesia, enhance multimodal analgesic efficacy and decrease opioid requirements. They should be given routinely after all major, invasive and severely painful operations; except where a specific contra-indication exists.
10. Inherent contra-indications to the administration of an NSAID include allergy to these agents, asthma, ischaemic heart disease, hypertensive cardiac disease, peptic ulcer disease, vascular disease, renal disease, significant hepatic disease, coagulopathies and concomitant anti-coagulation therapy.
11. Routine postoperative prophylactic anti-coagulation is not a contra-indication to NSAID therapy.
12. Intraoperative complications which would be contra-indications to NSAID therapy include significant blood or fluid loss, hypotensive insult, the use of significant dosages of anti-

coagulation and procedures which enhance the risk for postoperative complications (e.g. aortic cross-clamping would increase the risk for developing renal failure).

13. In the vast majority of cases, it would be appropriate to preferably use the newer coxib NSAIDs as opposed to the older non-selective cyclo-oxygenase inhibiting NSAIDs for most scenarios of postoperative pain control.
14. The use of COX-2 selective NSAIDs preferentially definitely reduces postoperative complications, especially the risks of gastro-intestinal haemorrhage due to peptic ulceration and all complications related to over anti-coagulation. The exceptions would be cardiac cases and cardiovascular surgery (see below).
15. Intravenous paracetamol is a useful adjunct in postoperative pain control and should be used routinely postoperatively for its multimodal effects and to decrease the amount of narcotics needed.
16. Failure to achieve appropriate pain control postoperatively has been shown to be the major risk factor for the development of neuropathic pain and the conversion of acute pain into chronic pain syndromes. Early and effective pain relief reduces this risk dramatically. Various agents have been used with variable success in an attempt to diminish this incidence and/or to treat the condition. Agents with some benefit include calcitonin, ketamine, morphine, gabapentin, lignocaine, carbamazepine and amitriptyline.
17. Day case surgery also warrants specific mention. The severe pain incidence in these procedures is usually only about 5 %. However inadequate pain control is common due to concerns in administering powerful agents to patients being discharged, and reluctance on the part of staff to delay the discharge process. Common scenarios where pain control is often inadequate are orthopaedic procedures, plastic surgical procedures, laparoscopic procedures and hernia repairs. Risk factors for developing severe pain are patients with an increased Body Mass Index (BMI) and procedures requiring longer general anaesthesia.
18. The use of local anaesthesia and regional anaesthesia where possible in the day case scenario is strongly advocated.

11.4.1 General surgery

1. Of particular importance in gastro-intestinal and other intra-abdominal procedures, is the fact that these patients will be kept *nil per os* for varying lengths of time.
2. Prolonged periods *nil per os* increases the risk for peptic or stress ulceration and as such non-selective NSAIDs should be used with caution or avoided where possible. When NSAIDs are utilised in this scenario, the risk of gastric or duodenal erosions and ulceration can be decreased by the simultaneous administration of intravenous proton pump inhibitors (PPIs) or H_2-receptor blockers or alternatively sucralfate via the nasogastric or orogastric tube. Despite evidence existing however that these regimens may increase septic complications, especially pneumonia in ventilated patients, these practices are common and accepted as routine.

3. With non-selective NSAIDs often contra-indicated in post-laparotomy patients, this means that opioid analgesics are the most commonly utilised agents in these scenarios.
4. Opioids too should be used with caution and sparingly if possible (ensuring adequate pain control though). This relates to the unwanted side-effects of nausea and vomiting, which is common in these patients in any event, and also delaying gastro-intestinal motility recovery, which further prolongs postoperative ileus and exacerbates post-surgical constipation.
5. Paracetamol and coxibs are generally safe for use post gastro-intestinal surgery, but are seldom adequate without opioids initially.
6. All classes of analgesics are generally used safely and routinely in all other general surgical procedures not involving laparotomy.
7. Local anaesthesia and regional anaesthesia, especially lumbar epidural analgesia post-laparotomy, are supported wherever possible too, depending on local expertise and monitoring.

11.4.2 Vascular surgery

1. Vascular patients are often cardiac and/or renal patients too. Hence the use of NSAIDs (including coxibs) should be judicious in all vascular patients and is actively discouraged in patients with hypertensive or ischaemic heart disease and those with renal dysfunction.
2. In addition, these patients may be at added risk for haemorrhage or may require concomitant anti-coagulation therapy, which also contra-indicates NSAID usage, although coxibs may be used cautiously in these cases.
3. Prostaglandin inhibition may be completely contra-indicated in certain cases (especially peripheral vascular disease), as this may exacerbate ischaemia by vasoconstriction.
4. Opioid narcotics and paracetamol are generally safe in the majority of these patients.
5. Regional and spinal blockade and epidural anaesthesia are also encouraged in vascular patients, in that the concomitant sympathectomy effect will generally cause vasodilatation and improve blood perfusion.
6. Contra-indications to blockade and neuraxial analgesia include concomitant anti-coagulation, patients with fixed cardiac output states and those in whom hypotensive events could be a disaster and those requiring peripheral limb monitoring (those requiring peripheral neurological function monitoring and those at risk for developing compartment syndromes).

11.4.3 Cardiothoracic surgery

1. Postoperative cardiac surgery patients are usually nursed in intensive care and powerful, titratable narcotics (fentanyl derivatives or morphine) are routinely used initially.
2. NSAIDs are effective analgesics for sternotomy and thoracotomy wounds, but usually cannot be utilised due to anti-coagulation therapy or concomitant cardiac or renal disease.
3. Neuraxial blockade is often contra-indicated due to anti-coagulation therapy.
4. In thoracic procedures, non-selective NSAIDs and coxibs are useful adjuncts to opioid therapy. Multimodal therapy with coxibs and paracetamol may be beneficial in terms of opioid-sparing and

decreasing respiratory depressant concerns. Thoracic epidurals, pleural blocks and intercostal blocks are all extremely useful adjuncts to pain management.

11.4.4 Neurosurgery

1. Pain control in most post-neurosurgical operations is managed similarly to most other scenarios, that is with a multimodal approach, usually combining opioids and NSAIDs or coxibs.
2. Issues warranting special mention are that accurate neurological assessments and level of consciousness monitoring may be severely impaired by the sedative side effects of opioid narcotics, limiting their use in certain scenarios. Careful titration and experienced dosing is required to overcome these issues. In other circumstances, actual over-sedation may be desirable, e.g. when wanting to limit stimuli which would raise intra-cranial pressure. Here, monitoring for over-dosage, hypotension and respiratory depression is required.
3. Other side effects of opioids may also be problematic. Patients with intra-cerebral tumours and/or raised intra-cranial pressure tend to suffer from severe nausea in any event and vomiting may be exacerbated.
4. Spinal patients are prone to constipation (spinal cord injury, autonomic dysfunction and prolonged bedrest the culprits) and this is exacerbated by opioids.
5. NSAIDs also need to be used cautiously in certain neurosurgical patients, due to the fact that any post-surgical haemorrhage in a neurosurgical patient may be disastrous; and due to the high incidence of peptic ulceration in these patients, as a consequence of chronic NSAID usage (spinal patients), stress ulceration (head injury patients), irregular enteral feeding and concomitant steroid therapy (raised intra-cranial pressure patients).
6. Coxibs are preferable to older non-selective NSAIDs in these patients and evidence exists that COX-2 inhibitors are the drugs of choice following spinal cord injury.
7. All NSAIDs should be used cautiously in patients at risk for developing renal failure. These are mainly patients at risk for dehydration and pre-renal insult. This includes patients on diuretic therapy for raised intra-cranial pressure and those who develop diabetes insipidus.
8. The use of local, regional and neuraxial blockade in these patients needs to be carefully considered. These offer excellent pain control in spinal and peripheral nerve surgeries and injuries, but will impair motor and sensory neurological monitoring. They may also be contra-indicated due to sepsis and haemorrhage risks.

11.4.5 Orthopaedic surgery

1. Orthopaedic procedures are particularly painful procedures and pain control is vital to allow early mobilisation, prevent complications (deep vein thrombosis, pulmonary embolism, contractures, pressure sores, etc) and decrease chronic pain syndromes.
2. Initial postoperative parenteral opioid usage is routine, followed by substitution with oral agents.
3. NSAID therapy is extremely efficacious in these patients, but needs to be used judiciously.

4. Orthopaedic patients often have utilised NSAIDs chronically preoperatively and thus having a high incidence of known or occult peptic ulceration.
5. Routine upper gastro-intestinal endoscopy at the time of major spinal, pelvic and lower limb surgery, especially joint arthroplasties, is encouraged to exclude a lesion at risk for haemorrhage. These patients are at particular risk for deep vein thrombosis and postsurgical prolonged anti-coagulation is mandatory. Routine postsurgical usage of PPI therapy is advisable.
6. NSAIDs have been shown to delay bone healing times post-surgery and after fractures. This is not generally a clinically relevant problem in most cases and is not a problem with selective COX-2-inhibitors.
7. Intra-articular instillation of analgesics, local anaesthetics and corticosteroids in joint surgery, day case arthroscopy and joint injury has been controversial and the evidence in the literature is conflicting. Currently there is evidence to support instillation of local anaesthetic in the acute situation and cortisone in the chronic situation. There is no evidence to support intra-articular opioid instillation in any circumstance.
8. Regional and neuraxial blocks are particularly useful in the early postoperative period. Routine post-surgical prophylactic anticoagulation does not contra-indicate the use of epidural usage postoperatively, but experience is required in managing the dosaging of such therapy to allow safe catheter removal without intra-spinal haemorrhage risk.

11.5 Acute spinal cord injury

Pain can develop in weeks, months or years following spinal cord injury.

Pain resulting from spinal cord injury is termed central. Pain can be neuropathic, above at level or above the level of injury. Nociceptive pain, CRPS and phantom pain can also develop. Treatment of the condition is extrapolated from studies of chronic neuropathic pain.

Primary and secondary analgesics can be used (opioids, ketamine, local anaesthetics, anti-depressants and anti-convulsants).

11.6 Acute burns injury

1. Post-burn injury pain is both nociceptive and neuropathic in origin.
2. Management requires therapy for the constant baseline pain, as well as acute intermittent exacerbations and exacerbations associated with procedures, such as line or dressing changes.
3. Cooling is a major factor in the early management of these patients and is vital for limiting burn tissue extension and pain alleviation.
4. Evidence suggests that intravenous opioid titration is best at adequate pain control in these patients.
5. PCA may be a useful tool in managing the opioid administration in burns patients.
6. For pain exacerbations associated with quick procedures in these patients, single dose bolussing of a short acting powerful opioid such as alfentanil is appropriate.

7. For longer procedures, especially major dressing changes, titrated remifentanil infusion is definitely the technique of choice currently. Where this is not available, fentanyl or morphine may be used.
8. Other agents used for burn pain control include nitrous oxide, intravenous lignocaine and ketamine. These are predominantly used in peripheral areas and situations where intensive monitoring may be limited.
9. Topical adjunctive analgesics are available in the form of lignocaine-soaked dressings and morphine-infused creams, such as silver sulphadiazine (Flamazine®).
10. Concomitant sedation is useful and humane. Numerous agents are available and have been successfully used according to local experience and expertise. These include benzodiazepines and antihistamines such as lorazepam, midazolam and hydroxyzine (Aterax®), propofol and occasionally phenothiazine-type drugs such as chlorpromazine (Largactil®), haloperidol (Serenace®) or clotiapine (Etomine®).

11.7 Acute back pain

1. Acute spinal pain, cervical, thoracic, lumbar or sacral, affects the majority of the population at some stage of their life.
2. Once “red flags” (fracture, infection, tumour and metastasis) are excluded, one can expect a self-limiting and benign course.
3. Range of movement and focused neurological examination is indicated.
4. Psychosocial and occupational factors (yellow flags) need to be identified early.
5. Management of the condition needs to focus on education and maintaining activity. Multi-disciplinary approach is indicated aiming at prevention of chronic pain development.
6. Treatment consists of short term rest, hot/cold packs, NSAIDs and muscle relaxants. Physiotherapy is recommended.

11.8 Acute musculoskeletal pain

1. NSAIDs are generally the drugs of choice in this scenario.
2. Coxibs are preferable in the elderly and in patients where prolonged therapy is envisaged.
3. Oral opioids are usually also required in the acute phase, followed by oral NSAIDs and paracetamol.
4. Topical NSAIDs and cortisone injections are effective in selected cases.
5. Adjuvant therapy with physiotherapy, exercise, ultrasound, infra-red therapy and laser is beneficial.
6. No evidence exists for the routine usage of muscle relaxants, anti-depressants or anti-convulsants.

11.9 Post-trauma pain

1. The management of acute pain due to trauma is similar to that of postoperative pain.

2. Initial therapy of significant trauma pain is best achieved by titration of intravenous opioids.
3. Morphine remains the most widely used agent and is cheap and effective. However hypotension, respiratory depression and over-sedation are real concerns.
4. Tramadol is advocated as an effective and safer alternative to morphine.
5. Intravenous COX-2-inhibitors are also effective and useful agents which should be administered early in the therapy of trauma. These are safer alternatives to the older non-specific NSAIDs but may be less efficacious.
6. Non-selective NSAIDs are extremely effective analgesics in the trauma setting and are advocated initially for trauma by intravenous or intramuscular injection.
7. NSAIDs are generally safe and their use supported, but these agents should obviously not be used in patients at risk for haemorrhage or in patients at risk for renal failure (shocked patients).
8. Care should be taken when using NSAIDs in the elderly. Intravenous paracetamol or coxibs are preferable in these patients.
9. NSAIDs are usually continued post-hospital discharge in oral formulation, alone or in combination with an opioid derivative such as codeine.
10. Topical NSAIDs are useful in gel or patch form and decrease the systemic analgesic requirement.

11.10 Acute pain management in sports medicine

The health benefits associated with increased physical activity have been established. However, with increased participation in physical activity comes a subsequent increase in sports and exercise-related injury. This chapter will review the agents that are used for pain management in acute sports injury and suggest a rational approach to the use of these agents.

When tissue is injured, phospholipids are released from the cell membrane and are converted into arachidonic acid by the enzyme phospholipase A2. Arachidonic acid in turn is a substrate for the enzyme cyclo-oxygenase resulting in the production of various prostaglandins. This pathway and the substances that are produced are responsible for the pain and inflammation of sports injury but it also initiates the healing process.

It is this process that we attempt to change with our medications. It is believed that use or abuse of analgesic medications and non-steroidal anti-inflammatory agents (NSAIDs) is widespread in sports medicine amongst professional and amateur athletes. The pressure is on the medical professional to relieve pain and to return the athlete to training and competition as soon as possible *without compromising tissue healing*. However, acute and long-term use of some of these agents can be problematic and not without significant side effects.

Analgesics are commonly used in the acute management of acute sports injury to reduce pain. Further use of the analgesics will depend on the intensity and duration of pain. Agents in this group, used either as single agents or in combination, include:

- Paracetamol up to 3-4 g/day
- Codeine (reserved for more severe pain) and

- Tramadol (reserved for more severe injury)

It is important to note that these medications do not inhibit the inflammatory response.

NSAIDs including the Cyclo-oxygenase-2 inhibitors (COXIBs)

These are widely used and are effective to decrease pain and swelling and have an earlier return to sport, but this comes with a cautionary: Whilst there are a number of studies that prove benefit in acute sports injuries, the majority of the efficacy and safety studies have been widely tested in chronic arthritis models and the side-effect profile has been extensively discussed. These agents may have adverse effects on the healing process if used too early in acute sports injuries. A review of the literature of both animal studies and clinical research,suggests that the anti-inflammatory agents and indeed both the non-selective NSAIDs and the COXIBs can have a significant negative effect on musculoskeletal tissue healing (bone, tendon, muscle and ligaments). Although this finding remains a subject of much debate and more clinical trials are required, it appears that the athlete that does receive these agents in the first 48 h after injury may in fact be disadvantaged.

Topical analgesics

The majority of these agents are skin counterirritants and contain a combination of substances including methyl salicylate, eucalyptus, menthol, capsicum and camphor. The active ingredients cause erythrema and blood-vessel dilatation and stimulate the pain and temperature receptors. These agents can be used in addition to a warm-up and can be of some benefit for minor sprains and strains. Topical NSAIDs are effective in relieving the pain associated with soft tissue injuries without causing serious adverse effects.

Clinical practice points

1. As is evident from the above discussion, the inflammatory process seems to be an important part of the healing process in the musculoskeletal tissue in humans. Use only analgesics in the first 48 hours following injury to allow the first part of the physiological healing process to occur. Examples of agents that are used for pain management in this phase are paracetamol or paracetamol plus codeine.
2. **R**est
Ice
Compression
Elevation } are the important elements of the patient management in the first 48 hours following injury.
3. After 48 hours post-injury, if repeat assessment of the injury reveals clinical signs and symptoms of excessive inflammation (swelling and pain) we use an NSAID or COXIB for up to a limited period (five days) as these agents have shown to reduce pain and promote function following injury.
4. If the athlete has a history of gastro-intestinal side effects or other side effect following non-selective NSAID use, paracetamol should be continued or a COXIB or COXIB plus proton pump inhibitor should be considered.
5. Physiotherapy, including therapeutic ultrasound, followed by rehabilitation form an essential part of treatment from 24 hours after injury.

6. Generally, if the use of an NSAID, COXIB or analgesic is required for longer than a five day period, the patient should be reassessed and the diagnosis revisited.
7. NSAIDs and COXIBs should not be used prophylactically to prevent muscle soreness after exercise or to prevent pain during sport.
8. There is evidence of efficacy of use of the NSAIDs and COXIBs in the following injuries: ligament sprains of the ankle, knee and shoulder joints; conditions where the pathological disorder is tissue entrapment or impingement of nerves and other structures due to soft-tissue swelling, for example in the following conditions: carpal tunnel syndrome, Morton's neuroma, intervertebral disc prolapse, thoracic outlet syndrome, bursitis in rotator cuff disease, trochanteric bursitis and iliotibial band friction syndrome.
9. There is no role for NSAIDs and COXIBs in the management of the chronic degenerative tendon conditions including Achilles tendinosis, as the pathology has been shown not to be inflammatory in origin. Furthermore, there is no evidence to support use of NSAIDs for long-term pain from sports injury without impingement.
10. Take sufficient time off training to allow for complete tissue healing. Athletes may in fact ingest these agents to facilitate early return to sport which can put them at risk of further injury. Adequate time for recovery, physiotherapy and rehabilitation should be allowed before returning to sport.

11.11 Acute abdominal pain

1. Acute abdominal pain usually begins as visceral pain and as the pathology progresses, the pain develops into somatic pain.
2. Visceral pain can be acute or chronic and is classically colicky in nature.
3. Local inflammation results in the progression to classical acute somatic pain, with localisation of the affected area and progression to the clinical picture of peritonism.
4. Adequate analgesia should be administered without fear of masking clinical signs, as appropriate dosing will not interfere with the progression of clinical signs and symptoms.
5. Opioids are the drugs of choice for treating severe acute abdominal pain with peritonism.
6. Be aware of the side effects of decreasing gastro-intestinal motility and the exacerbation of nausea and vomiting.
7. Parenteral opioid preparations on the market are available in combination with an anti-cholinergic anti-histaminic-type of anti-emetic drug (cyclizine) and certain opioid parenterals can safely be mixed with a phenothiazine-type anti-emetic (prochlorperazine) for intramuscular injection.
8. Alternatively, an anti-emetic can be administered separately as required.
9. Anti-emetics of the serotonin antagonist type such as ondansetron (Zofran®) or granisetron (Kytril®) are currently the most efficacious agents available for the suppression of nausea in this scenario.

10. Other anti-emetics of the dopamine antagonist type may be preferable, as these are prokinetic as well, and as such improve gastric emptying and enhance intestinal motility. This diminishes the negative effects of the opioid and decreases the risk for aspiration. Metoclopramide (Maxalon®, Clopamon®) is the drug of choice in this group and is available in parenteral and oral formulation. Alternatives are droperidol (Inapsin®) – parenteral only and domperidone (Motilium®) – oral only.
11. For relief of gastro-intestinal origin colic visceral pain, anti-spasmodic analgesics may be utilised with varying response.
12. In acute exacerbations of chronic cramping pain, such as the irritable bowel syndrome, smooth muscle relaxants and peppermint oil have been shown to be the most effective agents.
13. In the treatment of renal colic, the debate as to whether pethidine or morphine is superior has persisted, but in clinical practice the agents are equivocal and effective.
14. NSAIDs have been shown to be as effective analgesics as opioids in renal colic, and actually superior in one study.
15. NSAIDs are most effective in renal colic and the onset of action most rapid when administered intravenously.
16. There is no evidence-based medical evidence in renal colic for adding anti-cholinergic or anti-spasmodic agents (e.g. hyoscine), as these agents are less efficacious than opioids or NSAIDs and combination therapy is equivalent to the usage of opioids or NSAIDs alone.
17. In acute abdominal pain of biliary or pancreatic origin, the debate as to pethidine being superior to morphine (alleged lesser effect on the sphincter of Oddi) has also raged on. There would appear to be no evidence that pethidine paradoxically relaxes sphincter of Oddi spasm. All opioids in fact increase sphincter spasm and hence bile duct pressures, however pethidine would appear to have the least effect. This is unlikely to have any clinical relevance.
18. Opioids are in effect excellent analgesics in biliary colic.
19. The parenteral NSAIDs ketorolac (Tora-Dol®), tenoxicam (Tilcotil®) and diclofenac (Voltaren®, Veltex®) have been shown to be equally efficacious as opioids in biliary colic.
20. Anti-spasmodics have been shown to be inferior to opioids and NSAIDs in biliary colic.
21. In the management of pain due to dysmenorrhoea, non-selective COX inhibitory NSAIDs have been shown to be the drugs of choice.
22. In dysmenorrhoea, ibuprofen (Brufen®, Nurofen®, Inza®, Advil®, Ibumax®, Ranfen®), naproxen (Naprosyn®, Nafasol®, Napflam®, Aleve®) and mefanamic acid (Ponstan®, Ponac®, Fenamin®) have all been shown to be efficacious. They are all more efficacious than aspirin or paracetamol alone.
23. Combination products of ibuprofen together with paracetamol and/or codeine (Myprodol®, Mybulen®, Mypaid®, Lotem®, Betagesic®) are widely used and popular for the treatment of dysmenorrhoea in South Africa, but no studies exist comparing these to ibuprofen alone.
24. The supplementation of vitamin B1 has been shown to be beneficial in treating dysmenorrhoea.

25. Application of heat to the lower abdomen (by hot water bottle or heating pads, etc) has also scientifically been shown to be effective at easing dysmenorrhoea cramping.

11.12 Acute cardiac pain

1. Acute cardiac pain results from acute coronary ischaemic states and includes acute myocardial infarction and unstable angina.
2. The mainstay of treating acute cardiac pain is the restoration of adequate coronary blood flow, which will limit cardiac muscle damage and reverse ischaemic pain. Optimising myocardial oxygen delivery is the prime goal, which in turn will settle ischaemic pain. However, early pain control is important in decreasing myocardial oxygen demand by decreasing the stress response.
3. Supplemental oxygen is the simplest and quickest method to improve myocardial oxygenation and is the first therapy that should be initiated whenever possible.
4. Nitroglycerine administration decreases acute myocardial ischaemic pain, irrespective of the presence of coronary artery disease.
5. Intravenous morphine has been shown to be very effective at suppressing acute cardiac ischaemic pain, usually within 20 minutes and utilising relatively low doses (on average a total of only 7 mg).
6. Alfentanil is equally efficacious as morphine in treating ischaemic cardiac pain and its onset of action is more rapid.
7. Buprenorphine and pethidine are equivalent in efficacy and side-effect profile to morphine in treating cardiac ischaemic pain.
8. Intravenous tramadol has been demonstrated to provide adequate analgesia in this scenario.
9. Inhaled nitrous oxide has been shown to be effective at relieving acute cardiac ischaemic pain.
10. Acute cardiac pain due to pericarditis is a somatic pain opposed to ischaemic pain and is best treated with NSAIDs.

11.13 Acute headache

1. Headaches are a very common cause of acute pain.
2. Although the vast majority are not due to a serious underlying pathology, it is important to adequately investigate severe, unrelenting or repeated headaches as the cause can be due to a serious intra-cranial pathology such as infection, tumour, stroke, aneurysm, glaucoma or temporal arteritis.
3. Most commonly acute headache is due to migraine, episodic tension headaches, cluster headaches, post-trauma, post-drug usage or withdrawal, or due to various less common primary headache causes.
4. Headache is also frequently due to non-cranial origin, usually cervical pathology or cervicogenic due to neck muscle spasm, or may be due to other non-CNS causes such as sinusitis.

11.13.1 Migraine

1. Migraine is usually a severe unilateral headache, often retro-orbital and associated with nausea, vomiting, photophobia, phonophobia and worsened by movement.
2. Migraine may be preceded by an aura, usually of visual disturbances, but also may include other sensory, motor or speech disturbances.
3. It is vascular in origin, usually characterised by initial cerebral arterial vasoconstriction, followed by the release of inflammatory mediators and excessive compensatory vasodilatation with painful pulsation.
4. Migraine occurs significantly more frequently in females and attacks have been linked to fluctuations in serum levels of oestrogen and secondarily related to the menstrual cycle, pregnancy, menopause, hormone therapy and the oral contraceptive.
5. Numerous other trigger factors have been identified (see full guideline for a more detailed list).
6. Migraine is often debilitating in severity.
7. Most attacks occur in repeated sufferers and as such are treated by the patients themselves without presenting to hospital.
8. Due to its common prevalence, migraine is commonly seen at emergency departments. Eighty per cent of these patients will have attempted self medication at home before presentation.
9. Minor migraine attacks can be treated successfully with resolution of symptoms by 2 hours utilising common analgesics often combined with an anti-emetic.
10. In minor cases, regimens such as aspirin or paracetamol combined with metoclopramide have been shown to be as effective as the newer triptan agents.
11. Severe attacks, unrelenting attacks, attacks with significant disability and recurrent attacks are most effectively treated with triptans, which have revolutionised the treatment of acute migraine attacks.
12. Several triptan agents are available on the market. Oral agents are the best tolerated by patients, but intra-nasal sprays and subcutaneous injections give the most rapid onset of action and are more efficacious. This is probably due to impaired absorption and gastric stasis. Oral wafers for sublingual absorption and suppositories are also available and are better absorbed.
13. Side effects with triptan therapy are common but are generally non-serious. These include nausea, fatigue, dizziness, paraesthesias and sensory sensitivity to touch and temperature.
14. Triptan therapy is contra-indicated in active ischaemic heart disease, uncontrolled hypertension and should not be used in combination with ergot preparations.
15. Ergot derivatives (ergotamine and dihydro-ergotamine) have been widely used in the past for the treatment of acute migraine attacks.
16. Caffeine has also been used in combination with ergot derivatives.
17. Ergotamines are effective medications, but are less efficacious than triptans with a higher side-effect profile and as such are being superseded by triptan therapy.

18. Opioids are not effective analgesics for the treatment of migraine headaches and are not recommended, except as a last resort for acute, severe migraine in patients in whom triptans, ergot derivatives and other agents are contra-indicated.
19. Intravenous anti-emetic therapy is effective in treating acute migraine. Prochlorperazine, metoclopramide, chlorpromazine and droperidol have all been utilised successfully.
20. The danger of akinesias and athetosis (extra-pyramidal side effects) with anti-emetics, especially in young female patients, should be remembered. Should this occur, it can rapidly be reversed with biperiden (Akineton) 5-10mg slow bolus intravenously.
21. There is no evidence that anti-epileptic medications (e.g. sodium valproate) or anti-arrhythmic agents (e.g. intravenous lignocaine) are effective in treating migraine and the use of these medications in this scenario is discouraged.
22. Research is currently underway to assess intravenous magnesium sulphate as therapy for acute migraine and this may prove useful in the future (currently cannot be recommended as yet).
23. NSAIDs are effective in treating acute migraine, but alone are less effective than triptans or anti-emetics.
24. Combination of an NSAID with an anti-emetic and caffeine was more effective than a triptan in a single study.
25. Aspirin, ibuprofen and indomethacin orally and intravenous ketorolac have all been used successfully for acute migraine headache. NSAIDs can also be given by suppository should vomiting be a problem.
26. In emergency department therapy intravenous ketorolac would be the NSAID drug of choice and should be combined with an intravenous anti-emetic.
27. A coxib could be substituted for ketorolac should there be a major contra-indication to non-selective NSAID therapy.
28. Overall parenteral triptan therapy is the therapy of choice for the current emergency department treatment of acute migraine (unless a major contra-indication exists).
29. Therapy of migraine in children is similar to that in adults with the following provisos:
    a. Triptans are effective and the drugs of choice for children over the age of 12 years of age.
    b. Nasal sumatriptan is well tolerated.
    c. No evidence is as yet available supporting the safety and usage of triptans in younger children.
    d. Paracetamol and NSAIDs are effective and safe for acute therapy in younger children.
    e. Aspirin should not be used in young children due to the rare but real danger of Reye's syndrome.
    f. Anti-emetics should be used with care due to the higher incidence of extra-pyramidal side effects.

11.13.2 Tension headache

1. Tension-type headaches may be episodic or chronically recurrent in nature.
2. Tension-type headaches are classically bilateral and characterised by a pressing or tightness cranial sensation.
3. Tension-type headaches are not generally exacerbated by movement and not associated with nausea.
4. Paracetamol and aspirin have both been shown to be effective agents, alone and in combination with other NSAIDs.
5. NSAIDs alone are more effective than paracetamol alone. Ibuprofen, naproxen and ketoprofen have all been shown to be effective therapy for tension-type headaches.

11.13.3 Cluster headache

1. Cluster headaches occur almost exclusively in males and are characterised by recurrent brief attacks of severe, unilateral, peri-orbital pain often associated with tear formation and conjunctival injection.
2. Triptan therapy is the treatment of choice for cluster headaches and has been proven effective.
3. Oxygen therapy is effective second-line therapy and is indicated for patients unable to use triptans and patients who experience multiple attacks per day.
4. Ergot derivatives are also effective, but have largely been replaced by triptans.

11.13.4 Post-dural puncture headache

1. Acute headache post-dural puncture warrants special mention. This may occur after spinal anaesthesia, spinal taps, blocks and lumbar punctures.
2. The incidence is higher in younger patients and in pregnancy.
3. These headaches are usually postural in nature and may be relieved by lying flat. Bedrest *per se* does not prevent headache, but difficulty in mobilisation once there is onset of headache is common.
4. Prevention of headache is better than cure and there is a lower incidence of headache if small gauge needles are used for the puncture and if the said needles are of the non-cutting/non-bevelled type.
5. Blood patch remains the standard treatment using 15 ml of the patient's blood, although evidence for efficacy is scanty.
6. Blood patch is contra-indicated in sepsis, HIV, coagulopathy and malignant blood dyscrasias.
7. Routine oral analgesic agents of opioid and non-opioid types provide temporary relief. Caffeine too has been shown to be effective in this regard.
8. Complete resolution of headache occurs in the vast majority of patients within 10 days.
9. There is no evidence-based medicine to support the use of triptans, neuraxial opioids, epidurally administered fluids or fibrin glue in these patients.

11.14 Neurological disorders

1. Acute pain associated with neurological disorders is often neuropathic in nature but may have a nociceptive component as well.
2. Neurological origin pain may be acute or chronic with acute exacerbations.
3. The pain may be peripheral in origin (e.g. peripheral neuropathy) or central (e.g. multiple sclerosis).
4. Nociceptive pain components, e.g. due to muscle spasm, is treated with routine analgesics. Data is still lacking on the use of muscle relaxants and anti-spasticity agents (e.g. baclofen).
5. Neuropathic pain is treated with an array of agents, in different combinations and with differing responses. These regimens are extrapolated from the treatment of chronic neuropathic pain states with varying success. Agents which may be used are tricyclic antidepressants, anti-convulsant drugs, membrane-stabilising drugs, NMDA-receptor antagonists and opioids.
6. Agents used for neuropathic pain include carbamazepine for trigeminal neuralgia, various anti-convulsants in pain associated with multiple sclerosis and tricyclic antidepressants, lamotrigine and gabapentin for pain following stroke.

11.15 Acute orofacial pain

1. No specific evidence exists for comparing analgesics for therapy of pain due to sinusitis or otitis media.
2. Therapeutic decisions are derived from evidence of treating other causes of orofacial pain, such as dental pain.
3. NSAIDs, coxibs, paracetamol, aspirin, tramadol and codeine are all useful agents in treating acute orofacial pain. Combination preparations are widely and effectively used in these scenarios in South Africa, although various combinations have never been compared in an evidence-based manner. Popular combinations include paracetamol with ibuprofen and codeine, paracetamol with tramadol and aspirin with codeine.
4. Other medications commonly utilised are those which give symptomatic relief in these conditions and which may secondarily augment pain relief, although not actually analgesic themselves. No trials exist assessing the added benefits of these agents. These include anti-histamines, decongestants and beta-stimulants. Various preparations are available on the market combining these agents with genuine analgesics (paracetamol, aspirin and/or ibuprofen most commonly) and are actively marketed for the symptomatic treatment of sinusitis and otitis media.
5. In the treatment of pharyngitis and tonsillitis, additional pain relief may be achieved by adding mouth washes and gargle solutions containing topical local anaesthetic agents.
6. In acute oral mucosal ulceration due to trauma, burns, infection or drugs, antiseptic and local anaesthetic solutions, pastes, lozenges and gels may add analgesia.

11.16 Herpes zoster infection

1. Acute shingles (herpes zoster infection) is associated with acute, severe pain in the dermatome distribution of the affected nerve roots.
2. Spinal and cranial nerves can be infected by the varicella-zoster virus and hence involved in the distribution of the severe zoster pain.
3. Shingles pain may progress to a chronic pain syndrome, post-herpetic neuralgia (PHN), which is pain that persists for more than 3 months after the onset of the disease. This is more common in elderly and immunocompromised patients.
4. Early management of the zoster infection has been shown to decrease the incidence of developing PHN.
5. Antiviral therapy given early after the onset of the rash (within 3 days) has been demonstrated to effectively decrease the duration and severity of the attack. This results in earlier resolution of skin lesions, less pain and a lower risk for the development of PHN. Acyclovir, famcyclovir and valacyclovir have all demonstrated efficacy.
6. Amitriptyline started at the onset of the disease and continued for 90 days, has been shown to decrease the incidence of developing PNH.
7. Corticosteroids acutely have been shown to decrease the acute pain of shingles, but not alter the incidence of developing PNH. Corticosteroids should only be used in combination with an antiviral agent, as use alone may immunosuppress the patient and aid dissemination of infection.
8. Topical application of aspirin to lesions has been effective for acute pain relief. Topical NSAIDs have not been effective. Systemic aspirin and NSAIDs do not offer effective analgesia.
9. Anticonvulsants have been ineffectual at decreasing acute zoster pain, but are efficacious in diminishing pain associated with chronic PHN.

11.17 Acute pain in patients with HIV infection

Pain is a common symptom in people infected with the human immunodeficiency virus (HIV), with the prevalence ranging from about 30% in the early stages of infection to 80% in those with acquired immunodeficiency syndrome (AIDS). Pain related to HIV/AIDS may be due to:

1. Effects of the human immunodeficiency virus on the peripheral or central nervous system, or
2. Opportunistic infections or neoplasms as a result of immunosuppression.
3. Side effects of treatment. *Note:* Despite the potential neurotoxic effect of certain ARV agents, the prolonged use of highly active antiretroviral therapy (HAART) has been shown to result in a decrease in neuropathic pain incidence and severity.

Principles of management

The treatment of pain in patients with HIV/AIDS should be based on similar principles to those for the management of cancer and chronic pain. It has been well documented that pain in HIV patients is frequently under-treated and this should be rectified. Multiple clinician-, patient- and system-related barriers to adequate pain management account for this. Amongst these are underestimation

of the patient's pain by the clinician, fear of analgesic side effects by both clinician and patient and the problem of polypharmacy in patients, who are already using several disease-specific agents. A meticulous clinical assessment is essential to determine the likely cause of the pain and the most appropriate treatment:

1. Treat the HIV infection with HAART,
2. the associated disease complicating the HIV
3. and the pain itself.

Based on the WHO analgesic ladder, moderate to severe pain should be managed with opioid agents (in addition to non-opioids such as paracetamol and NSAIDS). Tramadol, morphine and fentanyl are the most frequent opioid agents used. Opioids should be administered by the least invasive and safest route capable of providing adequate analgesia. Adjuvant agents, where appropriate, can be used at any level of the analgesic ladder. These include agents such as antidepressants, anticonvulsants and corticosteroids. Explanation, reassurance and acceptance are of particular importance in the management of acute HIV-related pain, since aspects such as stigma, fear and poor socio-economic conditions frequently aggravate the pain experience in patients with HIV/AIDS.

Drug interactions between analgesics and antiretrovirals

Drugs that inhibit the cytochrome P450 (3A4) enzymes, such as ritonavir, nelfinavir, ketoconazole, itraconazole and clarithromycin can reduce the clearance of fentanyl and lead to severe respiratory depression. Therefore, ritonavir-treated patients receiving intravenous bolus fentanyl require longer respiratory monitoring. Those receiving continuous dosing with fentanyl should have their doses reduced.

The antiretroviral agent, ritonavir, also inhibits the cytochrome P450 (2D6) enzyme which is involved in converting tramadol from a pro-drug to an active metabolite. Concomitant use of ritonavir with tramadol may lead to decreased analgesic efficacy of tramadol.

Rifampicin, used in the treatment of tuberculosis, may decrease the analgesic effect of morphine and increased doses may be required.

Approach to pain in HIV/AIDS

Pain in HIV/AIDS	Aetiology	Treatment
Neuropathic pain: Frequently due to a distal sensory polyneuropathy (DSP): Burning pain, pins and needles, numbness and allodynia. Begin in both feet and progress to legs with loss of sensory function, particularly pain and vibration sense. Also due to postherpetic neuralgia	HIV HAART: stavudine and didanosine Isoniazid Cancer Cancer therapy Herpes zoster	The following are based on their efficacy for neuropathic pain due to other diseases. Tricyclic anti-depressants (TCAs), calcium channel $\alpha 2$-δ ligands such as gabapentin or pregabalin and SSNRIs such as duloxetine and venlafaxine. Lamotrigine is useful as second line or for neuropathy associated with ARV therapy. Patients with acute severe neuropathic pain will require rapid pain relief, during titration of one of these first line agents. Oral or parenteral tramadol or a strong opioid (morphine or fentanyl) is suggested in this situation or as second line.

Pain in HIV/AIDS	Aetiology	Treatment
Abdominal pain and headaches	Infections and neoplasmas	Progressively stronger analgesics
Oral and pharyngeal pain	Aphthous ulcers, herpes simplex- and cytomegalo virus ulcers and acute necrotising gingivitis	Antibiotics for gingivitis, oral or intravenous acyclovir or oral valacyclovir is used for HSV. For minor aphthous ulcers use rinse containing benzydamine and topical corticosteroids.
Genital ulceration	Usually HSV	Acyclovir or valacyclovir plus standard analgesia.
Patients with stroke have pain related to muscle spasticity	Muscle spasms	Oral baclofen as first choice, alternatively diazepam and dantrolene
Brain-related central neuropathic pain	Following stroke or intracranial neoplasmas	TCAs, calcium channel $\alpha 2$-δ ligands and SSNRIs are considered first and second choice in the management of this pain. In acute severe central neuropathic pain, consider intravenous morphine
Oesophageal pain Odynophagia	Oesophagitis most commonly caused by candida infection. Other causes: cytomegalovirus infection, idiopathic aphthous ulcers and less commonly herpes simplex virus (HSV) infection	Start with empiric antifungal therapy: fluconazole 200–400 mg daily for 14–21 days, IV required in patients who are unable to swallow. Upper endoscopy ulcer appearance, biopsy and viral cultures help to make a definitive diagnosis if it does not improve. Treat HSV with acyclovir 15 mg/kg/day IV or 200 mg 5 times daily PO, provided the patient can swallow, for 14–21 days. IV ganciclovir is used to treat CMV but has many side effects.
Kaposi's sarcoma	Malignancy	Pain medication and radiotherapy
Acute herpes zoster infection (This is covered under neuropathic pain section)	Herpes zoster	Treat early and aggressively to limit post-herpetic neuralgia. Antiviral therapy such as acyclovir, valacyclovir or famcyclovir should be initiated within 72 hours after the onset of pain or rash plus aggressive use of analgesics, which may include opioids. Consider amitriptyline 25 mg daily for 90 days

11.18 Cancer acute pain

1. Acute pain in cancer patients is commonly an acute exacerbation of underlying chronic pain.
2. Acute exacerbations of pain should be treated aggressively and expediently.
3. Practitioners should be aware that acute changes in pain levels may signify a progression of the underlying disease locally or in terms of metastases. Every incident should be appropriately investigated and treated.
4. Cancer patients are frequently on chronic slow-release opioid maintenance analgesia. The correct management in acute exacerbations of pain is the urgent administration of rapid-release narcotics, repeated every half hour until complete pain resolution is achieved. Appropriate patient monitoring is required to prevent adverse effects. This is in effect a titration of opioid therapy.

5. A general guide to proper analgesia for cancer patients is to use increments of analgesic dose equal to one-sixth of the usual daily maintenance opioid requirement.
6. Intravenous fentanyl is the standard therapy in this scenario and is effective and reliable.
7. Nausea and vomiting are common in this situation and anti-emetic therapy should be routinely considered. Serotonin inhibitors such as ondansetron and granisetron are effective. Morphine small volume parenterals for injection are also available which include a combination anti-emetic, viz cyclizine (Cyclimorph®).

11.19 The pregnant patient

Analgesia during pregnancy, childbirth, the puerperium and lactation

Pregnant women and new mothers are at high risk for experiencing pain. For example, physiological changes of pregnancy can result in increased headaches. The changing anatomy can bring on back pain, and an altered centre of gravity, predisposing the woman to falls and other injuries. Giving birth is painful, and the puerperium takes some recovery, regardless of how the infant was delivered. Breastfeeding is associated with new changes, which may also be painful.

As such, these women frequently require for analgesia. However, this is often neglected. Parturients (and inexperienced health-care providers) fear the effects of drugs on the developing foetus, and the breastfeeding infant. The coding of drugs in terms of safety during pregnancy is complicated, and the use of many drugs is restricted by a lack of conclusive data, resulting in many health-care providers incorrectly labelling them all as unsafe.

Poorly managed pain in this group may interfere with the experience of pregnancy, and there could be issues around maternal-infant bonding. Postnatal depression is increased in mothers with a poor experience of pregnancy. The benefits of breastfeeding may be lost if the mother stops breastfeeding because of pain.

Pregnancy

First trimester

This is the highest risk period for foetal abnormalities, as this is the period during which organogenesis occurs. However, this is also the period which carries the highest risk for miscarriage during times of stress, as may happen following injury.

Analgesia following termination of pregnancy should include NSAIDs and paracetamol. Short-acting opiates can be used for the procedure itself.

Second trimester

There is a lower risk of foetal abnormalities occurring during this period, as well as a lower risk of miscarriage following stress. This is considered the safest period in which to perform emergency procedures.

Third trimester

There is no risk of developmental abnormalities occurring during this period, as this is the period during which growth occurs. However, all drugs given to the mother may cross into the foetus, and as such the side effects of drugs must be taken into account. There is a high risk of the onset of premature labour during this period, and the wellbeing of the foetus should be considered after all stressful experiences.

Analgesia throughout pregnancy:

- Paracetamol (1g 6 hrly po)
- Short course opiates (codeine 15-40 mg 4-6 hrly or propoxyphene 65 mg 4 hrly, for up to 5 days). Codeine should be prescribed along with symptomatic relief for constipation.
- Avoid NSAIDs during all stages.

Childbirth

All women should be offered methods of managing pain regularly throughout giving birth. All institutions with birthing facilities should have appropriate options for analgesia available.

Analgesia for vaginal delivery

Non-pharmacological methods

Mothers should be allowed to choose methods that improve their experience. This will be subjective. Distraction techniques (e.g. breathing exercises, white noise) may be effective. Labouring in a bath is often helpful. The presence of a birthing partner is helpful, e.g. a mother, sister or friend, a partner.

Systemic analgesia

Opiates – traditionally pethidine is offered, however the analgesia it provides is relatively ineffective, and the perceived benefit comes from the sedation and euphoria caused by it. It causes respiratory depression in both mother and baby. It is not recommended for use during labour or delivery. Morphine provides good analgesia during labour, however it should not be given within four hours of delivery, and there should be naloxone available for the infant immediately after delivery, if required.

PCA pump – usually using morphine. Analgesia quality is slightly better, although the side effects are similar to pethidine.

Regional analgesia

Epidural – this provides high quality analgesia, and the use of low doses allows minimal motor block, rendering the mother more mobile. Hypotension may occur (especially during initiation of the block), and the mother should be regularly monitored (every 5 minutes for 30 minutes after initiation or top-up, thereafter every 30 minutes). Mothers should be encouraged to sit or lie in a position that is comfortable for them (although avoiding aortocaval compression, in other words not fully supine unless a wedge is used to raise the right side at least 15 degrees). Walking should not be allowed unaided, as there may be some motor block, and proprioception (position sense) is lost. Mothers can walk if supported on both sides.

Combined spinal-epidural (CSE) – an intrathecal injection of opiate is given before the epidural is sited and used. This allows faster onset of analgesia, but no other benefits, and requires special sets and added skill.

Analgesia during vaginal delivery:

1. Non-pharmacological methods
2. Morphine 5-10 mg IMI 4 hrly
3. PCA pump morphine 1mg bolus, 6 min lockout
4. Epidural 0.1% bupivacaine + fentanyl 2 µg/ml, at 8-10 ml/hr
   - Top-up with 5-10 ml 0.25% bupivacaine
   - If for Caesarean section, top up with 5-15 ml 0.5% bupivacaine, or 5-15 ml 1% lignocaine
   - CSE – intrathecal injection 25-50 µg fentanyl, epidural mix as above
5. Nitrous oxide in oxygen (1:1), self-administered via face mask

Inhalational analgesia

Nitrous oxide is useful during labour in areas near to sea level. It does not completely eliminate the pain of contractions, and should be administered from the very beginning of the contraction, until the very end of it. It should be provided in a 1:1 ratio with oxygen, preferably premixed as Entonox. It should only be administered by the parturient herself, in order to avoid overdose and excessive sedation. It should be avoided in parturients with respiratory compromise, neurological injury (acute or chronic), and pulmonary hypertension.

Analgesia for Caesarean section

- Neuraxial block
  This technique is recommended for all mothers, unless there are contraindications (e.g. severe hypotension, coagulopathy, raised intracranial pressure, local sepsis). This will provide analgesia for the operation itself and for approximately 2-3 hours postoperatively.
  The addition of fentanyl improves and prolongs the quality of the block, and allows for less bupivacaine to be used, hence less haemodynamic fluctuations.
- General anaesthesia
  Analgesia is often forgotten in the rush of an emergency. The same level of analgesia should be given to mothers as would be given to any patient having abdominal surgery.
  If the intubation response is required to be blunted (e.g. pre-eclampsia), try to avoid opiates if possible. Recommendations are magnesium sulphate (not necessary if the patient has recently been loaded with magnesium), or ketorolac. If opiates are the only option, choose alfentanil.
  From incision until delivery of the infant, the infant will be exposed to all drugs given to the mother. Keep the mother deep, and use short-acting opiates (e.g.) if necessary. Inform the person receiving the baby if you have used opiates, and they should have naloxone ready.
  Once the baby has been delivered, the mother should be given multimodal analgesia, as with all abdominal surgery. Local anaesthetic can be infiltrated into the wound at the end of the procedure.

Analgesia for Caesarean section:

Neuraxial block:

Recommended intrathecal injections are:

- 2.0-2.5 ml 0.5% heavy bupivacaine (i.e. bupivacaine with dextrose)
- 1.8-2.0 ml 0.5% heavy bupivacaine with 12.5-20 µg fentanyl added

General anaesthesia:

Bluntening intubation response:

- Magnesium sulphate 2 g IV infusion over 10 minutes pre-induction
- Ketorolac 10-20 mg IVI
- Alfentanil 0.5-1 mg 0.5-1 mg IVI

Intraoperative analgesia following delivery of baby:

- Fentanyl 50-200 µg IVI
- Morphine 5-10 mg IVI
- NSAIDs (diclofenac 50-75 mg or indomethacin 100 mg suppositories),
- Paracetamol (1 g IVI or suppositories)
- Local anaesthetic infiltration into wound 0.25% bupivacaine, not exceeding total dose of 2.5 mg/kg – about 50-100 ml).

The puerperium

Analgesia following vaginal delivery

Mothers will experience pain from ongoing contractions, vaginal tears and episiotomies. They may also have headaches (from prolonged labour, emotion, prolonged pushing, or even from accidental dural puncture during insertion of an epidural), and breast pain.

Perineal pain is acute, and may be severe. It may be alleviated by sitting in iced water, or by using ice packs, in combination with multimodal analgesia.

Other forms of pain can be managed using combinations of paracetamol and ibuprofen (the combination is very effective), adding short-course opiates only if necessary. The breastfeeding infant should be monitored for sedation if high doses of opiates are used.

Analgesia following Caesarean section

As with all abdominal surgery, the pain postoperatively is considerable. Again, multimodal analgesia is the most effective way of alleviating this pain. Patients should be discharged with oral medication and/or suppositories

Analgesia during the puerperium:

Following normal vaginal delivery:

- NSAID (e.g. ibuprofen 200-400 mg 8 hrly or diclofenac 50-100 mg 8 hrly)
- Paracetamol (1 g 6 hrly)
- Short source opiates (e.g .codeine 15-40 mg 4-6 hrly, or propoxyphene 65 mg 4 hrly).
- Combination tablets are available – check the relative doses of each component, and supplement with individual components rather than increasing the doses of all of them.

Analgesia following Caesarean section:

- Paracetamol (1g 6 hrly)
- NSAIDs (ibuprofen 200-400 mg 8 hrly)
- Short-course opiates: nurse administered (e.g. morphine 10 mg 4 hrly/PRN), or patient administered (PCA morphine 1 mg bolus with 6 min lockout) while in hospital, then oral opiates (codeine 15-40 mg 4-6 hrly or propoxyphene 65 mg 4 hrly) at home, for a few days. Codeine should be given along with symptom relief for constipation.

Lactation

Mothers can experience pain for a variety of reasons while they are breastfeeding. Breast pain is common (especially after the first few days), from engorgement as well as cracked nipples. Headaches are commonly experienced. Abdominal and perineal pain can continue for several days. As with anyone, the mother may experience injury, which may be painful.

While most drugs will cross into breastmilk, the concentrations are usually far too small to be of concern for the wellbeing of the baby.

Multimodal analgesia is recommended, with the choice of combination to be appropriate for the level of pain experienced.

Analgesia for lactating mothers:

- Mild pain – paracetamol 1 g 6 hrly, with possible addition of NSAID (e.g. ibuprofen 200-400 mg 8 hrly).
- Moderate pain – paracetamol + NSAID in regular intervals.
- Severe pain – paracetamol + NSAID + short-course opiate (codeine or propoxyphene). Large doses of opiates may cause the infant to become drowsy.

11.20 Specific patients with medical conditions

11.20.1 Respiratory patients, including asthmatics

1. In respiratory patients (restrictive or obstructive disease) it is advised to use analgesics which may be respiratory-depressive agents cautiously.
2. The agents that are most dangerous in these patients are potent narcotic opioids.

3. It is assumed that the intravenous administration of opioids is the most risky and this is true if large or repeat doses are given, and in elderly patients.
4. With proper monitoring and supervision, intravenous administration is in fact the safest way to give potent opioids, in that this allows careful titration of dosing versus clinical response and side effects. Intravenous opioid titration gives the most consistent and predictable dose to serum blood level ratio.
5. All other modes of opioid administration have a variable absorption rate which varies according to the individual and according to a host of other factors (e.g. body mass index, time of last meal, activity level after administration and concomitant medications). These result in variations in duration of onset of action, efficacy and adverse effects. The half-life and hence, duration of activity, may also vary in different patients according to similar parameters (e.g. volume of distribution, organ function, etc).
6. Oral administration and intra-muscular injection are the least predictable modes of opioid administration.

The asthmatic

1. Of particular importance in managing acute pain in asthmatic patients, is to avoid precipitating or exacerbating acute bronchospasm.
2. Aspirin and all non-selective NSAIDs should be avoided in all asthmatic patients. These agents may precipitate bronchospasm directly or via cross allergy which is not uncommon.
3. Aspirin may directly induce an acute severe asthmatic attack.
4. Cross hyper-sensitivity has been reported to almost all non-selective NSAIDs.
5. The sensitivity appears to be related to COX I inhibition and the less the COX I selective, the less is the risk for inducing asthma.
6. Selective COX II inhibitors (coxibs) have also been reported to occasionally induce bronchospasm, but the risk is far lower and these agents should be preferentially used in asthmatic patients, where NSAID therapy is deemed necessary.
7. Paracetamol too has rarely been reported to cause bronchospasm in these patients, but represents the safest overall option of a cyclo-oxygenase-inhibiting agent.
8. Opioids should also be avoided whenever possible in asthmatic patients.
9. Morphine, codeine and tramadol have all been reported to induce acute asthma or worsen current bronchospasm.
10. Hypersensitivity and bronchospasm are related to the histamine release which often accompanies opioid administration. This is common and, as such, opioids should only be used in asthmatic patients when really justified.
11. Anti-histamine premedication (diphenhydramine) may attenuate the response and should be given when possible.

12. Sensitivity to opioids appears to be class-specific within opioids as a group, with phenanthrenes (morphine, codeine, dihydro-codeinone) the most common culprits, followed by phenylpiperadines (fentanyl, pethidine). Patients reacting to these drugs may still tolerate phenylheptanes (propoxyphene), however alternate classes should be trialled cautiously. True major allergy and anaphylaxis to opioids is rare in all patients.
13. Regional and neuraxial blockade where possible, are useful tools in asthmatic patients undergoing surgery and in those who sustain injury.

11.20.2 Cardiac patients

1. All NSAID drugs should be used cautiously in all cardiac patients.
2. Paracetamol represents the only truly safe cyclo-oxygenase inhibiting agent in these patients.
3. NSAIDs are known to exacerbate hypertension in certain patients and to diminish efficacy of certain anti-hypertensive medications. NSAIDs may exacerbate known hypertension or unmask previously unknown borderline new onset cases.
4. Loop diuretics and thiazide diuretics may have a diminished efficacy with the concomitant administration of NSAIDs.
5. Much attention recently has been focussed on the negative cardiac effects of coxibs, with several agents (rofecoxib 'Vioxx®', valdecoxib 'Bextra®' and lumaricoxib 'Prexige®') being withdrawn from the South African market due to these concerns. It would appear that true selective COX II inhibition with minimal COX I activity does increase the cardiac risks of these agents. This is mainly in hypertensive, ischaemic and cardiac failure patients and predominantly in the elderly. In other patients, coxib cardiac risks are similar to those of other non-selective NSAIDs.
6. NSAIDs may also worsen other vascular pathologies which are common in cardiac patients. They may occasionally precipitate stroke in patients with cerebro-vascular disease, may cause a deterioration in renal function in renal vascular (atherosclerotic or hypertensive) disease and prostaglandin inhibition may worsen critical ischaemic peripheral vascular disease.
7. Opioids are generally safe in cardiac patients, except in those at risk for dropping their blood pressure. Careful titration of intravenous opioids is advocated in severe pain in these patients, in order to avoid hypotension.
8. Caution is required in analgesia given to patients on any concomitant anti-coagulation therapy.
9. Aspirin and NSAIDs should be avoided in patients on other anti-coagulant therapies due to their own cumulative anti-coagulant effect. This includes oral clotting factor inhibiting agents of the coumadin group (Warfarin®), injectable heparins (including newer low molecular weight heparins), other newer clotting factor inhibitor agents to soon be released (dabigatran, abigatran), oral anti-platelet agents such as dipyridamole (Persantin®) and the newer IIIa/IIb glycoprotein inhibiting agents such as clopidogrel (Plavix®).
10. Opioids are generally safe in patients on anti-coagulants, as are coxibs and paracetamol (providing none of the cardiac risk factors above are present).

11. NSAIDs and aspirin should also be avoided in patients receiving thrombolytic therapy, due to the increased risk of major haemorrhage. This includes patients receiving streptokinase, urokinase or tissue plasminogen activator (Actalyse®).

11.20.3 Analgesia in the presence of liver and kidney dysfunction

The liver and kidneys are central in the metabolism and excretion of drugs.

The main role of the liver is converting lipid soluble analgesic and anti-hyperalgesic drugs into a more soluble form for renal or, less commonly, biliary excretion. Liver failure thus tends to result in accumulation of unmetabolised drug.

The kidney has a limited role in biotransformation of drugs but a major role in excretion of both metabolised lipid-soluble drugs and non-metabolised water-soluble drugs. Kidney failure thus tends to result in the accumulation of water-soluble hepatic drug metabolites that are occasionally more active than the parent compound.

Organ system failure changes the composition of the body's fluid compartments with consequent alterations in drug pharmacokinetics, particularly on initial administration.

Principles of analgesic/anti-hyperalgesic prescription with organ failure:

1. Define the pain experienced:
    a. Likely aetiology
    b. Nociceptive vs neuropathic
    c. Intensity
    d. Duration
    e. Response to previous therapy
2. Quantify the degree of organ dysfunction
    a. Kidney
        - Urine output, serum creatinine, creatinine clearance
    b. Liver
        - Childs-Pugh criteria
3. Review current medications to avoid interactions between the pain relieving drugs to be prescribed and the medication the patient already requires.
4. Appropriate analgesics/anti-hyperalgesics will have:
    a. Minimal metabolism with inactive metabolites
    b. Organ independent elimination
    c. Limited drug interactions
    d. Short duration of action

5. Start low and go slow – commence pain therapy with the lowest effective dose and escalate over weeks rather than days.
6. Monitor
    a. Response to therapy with downward titration or withdrawal if possible
    b. Occurrence of side effects with prophylaxis if predictable
    c. Progression of organ failure

Paracetamol

Liver failure

The recommended dose of paracetamol of no more than 20 mg/kg (1 g in adults) as a single dose and no more than 80 mg/kg (4 g) in a single day should be reduced by at least 20% in the presence of clinically detectable liver failure.

In the postoperative setting, intravenous paracetamol is preferred as liver exposure is reduced by 80%, compared with oral or rectal dosing where 100% of the paracetamol administered has to pass through the liver before reaching the systemic circulation.

Kidney failure

Paracetamol, unlike phenacetin, does not cause renal failure when taken at recommended doses for less than 3 months. Prolonged exposure at doses that exceed recommendations have been associated with the development of renal failure. In established renal failure paracetamol remains the foundation of the WHO pain ladder with no requirement for dose adjustment.

NSAIDs (including COXIBs)

Liver failure

Aspirin has been associated with Reye's syndrome, which includes liver damage, leading to the recommendation that aspirin be withheld from infants and children.

Liver failure may be precipitated by NSAIDs due to genetically determined variations in hepatic metabolism. Diclofenac hepatocyte toxicity as well as cholestasis with sulindac has been described. Lumiracoxib was withdrawn after reports of hepatotoxicity following clinical release.

Non-selective NSAIDs (nsNSAIDs) and coxibs are relatively contraindicated in liver failure because cirrhotic patients have a reduced intravascular volume. Administration of an nsNSAID or coxib is likely to result in the development of renal failure and/or precipitation of the hepatorenal syndrome.

nsNSAIDs have the added disadvantage of platelet inhibition which, together with the defects in the clotting cascade due to impaired factor synthesis, can precipitate bleeding.

Kidney failure

All NSAIDs can precipitate renal failure, particularly in hypovolaemic patients and should thus be avoided in patients with renal dysfunction who do not require dialysis, particularly where the creatinine clearance is less than 30 ml/min.

However, in established chronic renal failure where patients are already on dialysis, NSAIDs may be used, particularly for postoperative pain and soft tissue injury. The coxibs are preferred as they do not affect the platelets and are thus unlikely to cause bleeding complications in the face of uraemic platelet dysfunction and the requirement for anticoagulation during dialysis.

Opioids

Liver failure

Severe liver failure will result in a reduction of the conversion of opioids to their water soluble metabolites with accumulation of the opioid administered. The dose of opioid should be reduced and the dose interval prolonged in established liver failure.

Tramadol and buprenorphine have theoretical advantages in liver failure due to their lack of active metabolites and limited potential to cause respiratory depression.

Codeine is not converted to active metabolites in liver failure so will be ineffective. Pethidine and propoxyphene should not be used in liver failure due to unpredictable metabolite levels.

Kidney failure

Opioids are converted to water-soluble metabolites in the liver to be excreted in the urine.

The two commonest metabolites are:

1. Demethylation to the nor- metabolite. These may be toxic (nor-pethidine and nor-propoxyphene) reducing seizure threshold and thus predisposing to seizures.
2. Glucuronidation. The resulting metabolites are commonly inactive. However, morphine-6-glucuronide is more potent than morphine, has better CNS penetration and a longer half life.

Buprenorphine and tramadol are preferred in renal failure due to their lack of active metabolites and limited potential to cause respiratory depression.

If more potent opioid analgesia is required, fentanyl is preferred to morphine as, while fentanyl clearance is reduced in renal dysfunction, nor-fentanyl is an inactive metabolite. However, dosage formulations of fentanyl in South Africa are limited to intravenous and transdermal formulations. This means that in the outpatient setting, morphine is still going to be used. The drug should be titrated to effect with dose reduction and extension of dosage interval.

Adjuvant drugs

Liver failure

Drugs that the manufacturers' recommend be avoided in liver failure include: clonazepam and sodium valproate.

Dosages of the following drugs should be reduced in liver failure, according to the manufacturers: fluoxetine, lamotrigine, valproic acid, venlafaxine, tramadol, topiramate, duloxetine.

Amitryptiline is hepatically metabolised so will persist for longer periods in liver failure.

Gabapentin and pregabalin are excreted unchanged in the urine and are thus unaffected by changes in liver function.

Kidney failure

The nor- and glucuronide metabolites of amitryptiline and the other tricyclic antidepressants accumulate in renal failure and may contribute to excessive sedation and arrhythmias.

Both gabapentin and pregabalin are excreted unchanged via the kidneys and thus also accumulate in renal failure.

Carbamazepine undergoes hepatic metabolism with inactive metabolites so no dosage adjustment is required in renal failure.

Experience with newer drugs such as venlafaxine and duloxetine is limited but the principle of starting at the lowest dose likely to be effective and only titrating upwards in the absence of side effects should be applied.

11.21 Acute pain management in the patient with obstructive sleep apnoea

Mild obstructive sleep apnoea (OSA) affects one in five people, whereas moderate to severe OSA affects one in fifteen people. Anaesthesia in the presence of OSA presents a multidimensional problem, and analgesia is just as challenging, particularly as OSA is often undiagnosed in many patients requiring pain relief.

The evidence available to us on the risks of opiates in patients with OSA is limited. Nevertheless in many cases where complications occur in these patients, opiates appear to be a common factor. To date, there are no studies comparing opioid with non-opioid techniques in patients with obstructive sleep apnoea.

Therefore the recommendations for pain management in patients with OSA are as follows:

- The patient should preferably be managed in a high dependency area;
- Supplemental oxygen is recommended; not necessarily CPAP, unless the patient has severe OSA;
- Opioid-sparing analgesia techniques are recommended; thus non-opioid multi-modal therapy is the order of the day, including local and regional techniques.

11.22 Analgesic options for patients with opioid tolerance

Opioid analgesics are used extensively in the treatment of acute and chronic as well as cancer and non-cancer pain. Opioids provide excellent pain relief but may provide insufficient analgesia in a small but significant number of patients.The major risk factor for inadequate opioid analgesia is prior exposure to opioids, particularly as sole analgesic agents, resulting in tolerance.

Tolerance may be a result of:

a. Alterations in G-protein coupling to the opioid receptor

b. Changes in receptor trafficking between the neuronal surface and cytoplasm

c. An increase in the number and sensitivity of NMDA receptors as a result of central sensitisation.

Tolerance is only seen in a small proportion of patients (< 5%) receiving opioids but in these patients any or all of the above mechanisms may be active.

Management of opioid tolerance

Multimodal approach

Anti-hyperalgesic drugs

Patients with acute or chronic pain deemed to be nociceptive/inflammatory in nature will benefit from the institution of paracetamol and an NSAID appropriate for the patient in the absence of contraindications.

Continue/add appropriate adjuvant drugs

Patients who have not previously been assessed by clinicians familiar with chronic pain are commonly treated with opioids alone or with NSAIDs. There is often an element of neuropathic pain in a patient with chronic pain that will need to be addressed by appropriate adjuvant drugs as discussed in the appropriate sections of this guideline and summarised briefly below:

- Tricyclic antidepressants – e.g. amitryptiline 10–75 mg at night
- Anticonvulsants: e.g. gabapentin100–1200 mg BD-TDS; pregabalin 25–300 mg daily or clonazepam 0.5–3 mg BD

Consider addition of a regional block

This approach is particularly useful in the perioperative period where neuraxial, regional or nerve blocks can be employed. Continuous wound infiltration is now possible with at least two wound infiltration catheters available in South Africa.

In patients receiving systemic opioid therapy, neuraxial opioids should not be used but the systemic opioids should be continued.

A small subgroup of patients may benefit from implantation of a continuous epidural or spinal catheter that can be refilled as an outpatient. These patients need to managed under the supervision of a pain specialist who is familiar with the technique.

Additional opioid medication

Patients should be continued on their usual dose of opioid by the usual route. If oral administration is not possible, particularly perioperatively, systemic administration will be required. This may be given transcutaneously by means of an opioid patch, avoiding the need for an infusion device, or subcutaneously using a continuous infusion, which may be administered using a mechanical or disposable infusion device. Intravenous administration may be used in the perioperative period, particularly if a central line has been placed.

Opioid "re-sensitisers"

Opioid rotation

There are significant differences in the interaction between different mu agonists and the mu receptor that go beyond the effect on second messenger systems after binding and include the rate of receptor

trafficking and possibly even effects on receptor synthesis an affinity. In view of this, a patient who is experiencing inadequate analgesia from one opioid drug may be switched to e.g. slow release morphine to transdermal fentanyl in the hope that the patient will achieve better analgesia with the different opioid. Should analgesia on the new drug become inadequate over time a switch back to the previous drug may prove effective.

In the perioperative setting, a patient on maintenance opioids for chronic pain should be managed with a different opioid for perioperative analgesia.

Ketamine

NMDA receptors are central in the pathogenesis and maintenance of chronic pain states. One of the best accepted mechanisms for tolerance to opioids is chronic up-regulation of NMDA receptors. Administration of low dose ketamine to patients with inadequate opioid analgesia has been shown to restore opioid sensitivity for prolonged periods. Doses that have been demonstrated to be effective are as follows:

- Perioperative dose: 0.5 mg/kg on induction, repeated 30minutes prior to estimated emergence for operations lasting longer than 2 hours.
- PCA: Ketamine may be mixed with an appropriate opioid at a concentration of 1–3 mg/ml: e.g. ketamine 100 mg + morphine 100 mg in 50 ml with saline given as a 1 ml bolus with a 10 minute lockout .
- OR
- fentanyl 2.5 mg + ketamine 250 mg in 50 ml with saline given as a 1 ml bolus with a 10 minute lockout.
- Oral: Ketamine undergoes extensive first pass metabolism so a dose of 5 mg/kg is required for the drug to be effective. A typical mixture is morphine 5 mg/ml with ketamine 10 mg/ml given as a dose of 5 ml 1–4 hourly as needed.

Alpha-2 agonists

Activation of alpha-2 receptors results in hyperpolarisation of presynaptic neurons involved in pain transmission. This reduction in input to the dorsal horn and thalamus results in improved analgesia. Alpha-2 agonists provide analgesia independent of opioid receptors by facilitating descending inhibition of pain transmission mediated by noradrenalin from the peri-aqueductal grey matter and nucleus raphe magnus.

Both clonidine and dexmedetomidine are effective adjuvants to neuraxial anaesthesia. Dexmedetomidine is also effective when administered systemically as a component of a multimodal PCA regimen as follows:

- Dexmedetomidine 200 mcg + ketamine 250 mcg + fentanyl 2.5 mg + granisetron 3 mg dosed with a 1 mg bolus and 10 minute lockout.
- Dexmedetomidine 200 mcg + ketamine 250 mcg + morphine 500 mg + granisetron 3 mg dosed with a 1 mg bolus and 10 minute lockout.

DRUGS AND DOSES USED IN EPIDURAL ANALGESIA (From Table IV, page 77)

(Recommendations only, scientific evidence as such not available)

Drug	Dose	Onset	Duration	Remarks
Lipophilic opioids:				
Fentanyl Sufentanil	Dilute single dose in 10 ml normal saline 50–100 µg 25–100 µg/hr 10–50 µg 10–20 µg/hr	5–10 min	2–4 h	Limited spread in CSF. Early respiratory depression most likely. Opioids alone via the epidural route seem to be of limited benefit.
Hydrophilic				
Morphine	1–5 mg 0.1–1 mg/hr	30–60 min	6–24 h	Extensive spread in CSF. Early and delayed respiratory depression possible.
Local anaesthetics				
Bupivacaine Not commonly used alone in analgesic infusion	5–8 ml/h 1.2 mg/ml or Incremental doses of 3–5 ml of 1.25–2.50 mg/ml	10–20 min, 30 min for optimal	3–4 h	Establish the block with 0.5% bolus 15–30 ml. Recommendation: limit to 2 mg / kg in 4 h and 400 mg/24 h
L-bupivacaine	10–15 ml/h of 1.25 mg/ml Or 5–7.5 ml/h of 2.5 mg/ml		150 (–240) min	Minimal to moderate motor block, dilution stable for up to 7 days at 20°C. Maximum dose over 24 h of 400 mg.
Ropivacaine	2 mg/ml Bolus:10–20 ml 6–14 ml/h	15–20 min	140 (–200) min	Establish the block for surgery with 15–25 ml of 7.5 mg/ml for lumbar or 5–15 ml for thoracic epidural.
Combinations				
Ropivacaine 2 mg/mL + fentanyl 4 µg/ml	6–14 ml/ h			This combination is marketed as a polybag in some countries.
Bupivacaine 1 mg/ml + fentanyl 4 µg/ml	Bolus 1(–2) µg/kg fentanyl + infuse 0.5 (–2) µg/kg/h			Prepare by adding 5 x 10 ml 5 mg/ml bupivacaine + 2 x 10 ml fentanyl to 180 ml normal saline.
Patient (PCEA)- controlled epidural analgesia	**Continuous infusion in ml/h**	**Demand dose in ml**	**Lockout in minutes**	
Levobupivacaine 1,25 mg/ml + fentanyl 4 µg/ml	Initial rate of 4 ml/h	2	10	Stability proven for up to 40 hours at 20°C.
1 mg/ml bupivacaine + 5 µg/ml fentanyl	6 (3–4 ml/h for thoracic)	2	10–15	
1–2 mg/ml ropivacaine + 2–5 µg/ml fentanyl	3–5	2	10–20	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