Association of Paediatric Anaesthetists:

Good Practice in Postoperative and Procedural Pain

CONTENTS

1.1 Introduction

This guidance was commissioned by the Association of Paediatric Anaesthetists of Great Britain and Ireland (APA). It is intended to be used by professionals involved in the acute care of children undergoing pain management after surgery or for painful medical procedures. It is designed to provide evidence-based information on the assessment of pain and the efficacy of pain management strategies, such that an informed plan of effective analgesia can be formulated that is appropriate for the patient and clinical setting.

The document includes advice on the assessment of pain, a summary of current evidence for the efficacy of analgesic strategies including evidence-based recommendations grouped according to named procedures, and a review of some of those most frequently recommended.

The guidance will be updated biennially.

1.2 Committee

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1.3 Use, Scope and Intention

This guidance has been prepared by a committee of health professionals with the assistance of a patient representative. It was published following a period of open public consultation, including advice from representatives from patient groups and professional organisations. It is intended for use by qualified heath professionals who are involved in the management of acute pain in children. At the present time, and largely because of resource limitations, no consumer guide is planned to enable the recommendations to be easily interpreted by those who do not already possess knowledge and training in the field of children's acute pain management. In its present form it is therefore not suitable for use by other groups.

The guidance is relevant to the management of children 0-18years undergoing surgery or painful procedures in hospital settings. It includes recommendations for pain assessment, general principles of pain management and advice on the use of pharmacological and non-pharmacological pain management strategies for specific medical and surgical procedures.

Procedures
The procedures are divided into two categories, painful diagnostic and therapeutic (Medical procedures; Section 4) and surgical procedures (Postoperative pain; Section 5), they are listed at the beginning of each section. Guidance covers the management of acute pain *during* medical procedures, and that *after* surgery. It does not include advice on the intraoperative management of pain unless it is relevant to postoperative management or is otherwise stated e.g. the use of perioperative nerve blocks. Evidence-based recommendations for drug doses and frequencies for individual procedures are beyond the scope of this guideline; instead the user is referred to other resources such as the British National Formulary for Children: available at http://bnfc.org/bnfc/ , for convenience some general dosage advice is included in analgesic monographs in section 6.

The procedures that have been included in this, the first version of the guidance, are not exhaustive and were selected by the committee because they are relatively commonplace and, or, because it was expected that there would be sufficient publications to allow recommendations to be made on the basis of an adequate level of evidence. For each procedure there is a brief description, list of recommendations and 'good practice points' followed by a discussion of the relevant published evidence including ***evidence tables*** (see below) summarising evidence for the efficacy individual analgesic strategies.

Evidence tables
Tables summarising evidence have been provided for each procedure, they are intended to allow the reader a rapid assessment of the *level of supporting evidence* for individual analgesics or analgesic strategies with regard to that procedure. Evidence tabled as 'Direct' is that derived from studies which

have specifically investigated the procedure in question. ‘Indirect’ evidence is derived from studies of procedures that the committee considered to be sufficiently similar, in terms of expected pain intensity, to allow extrapolation of evidence. Recommendations have not been formulated on the basis of indirect evidence.

1.4 Methodology and Evidence Grading, Good Practice Points

Systematic methods were used to search for evidence, they are briefly summarised here and described in detail in Appendix 1, the technical report. Electronic and manual searches were performed on the published literature between January 1996 and December 2006. The bibliographies of meta-analyses, systematic reviews and review articles published during this period were also scrutinised for relevant articles. Studies in English were included if they were directly relevant to the patient population and procedures. Abstracts were obtained to confirm inclusion or exclusion where necessary. Full text versions of included articles were obtained. A tabulated data extraction method was used to summarize the articles (data extraction tables are provided in appendix 4), and they were graded level 1-4 according to the criteria shown in table 1. ***Recommendations*** were formulated, where appropriate, and graded from A-D according to the criteria described in table 2. **Good Practice Points** indicate best clinical practice, based on the clinical experience and opinion of the guideline development group; they are provided in situations where published evidence was insufficient to make a formal recommendation, but the committee wished to emphasise important aspects of good practice.

Table 1, EVIDENCE LEVELS

Level 1

1++
High quality Meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+
Well conducted Meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 -
Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

Level 2

2++
High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+

Well-conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal

2 -

Case control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal

Level 3

Non-analytic studies, e.g. case reports, case series

Level 4

Expert opinion

Table 2, GRADE OF RECOMMENDATIONS

Grade A

At least one Meta analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or
A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B

Evidence including studies rated as 2++ or better, directly applicable to the target population, and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 1++ or 1+

Grade C

Evidence including studies rated as 2+ or better, directly applicable to the target population and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 2++

Grade D

Evidence level 3 or 4; or
Extrapolated evidence from studies rated as 2+

1.5 Contact Information

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SECTION 2.0

Quick Reference Summary of Recommendations and Good Practice Points

Descriptions of levels of evidence, grading of recommendations and their associated symbols can be found in Section 1.0 and in the technical report, Appendix 1, of the supplementary materials.

I. Pain Assessment

Good Practice Point

> *In order to assess pain effective communication should occur between the child whenever feasible, their family or carers, and the professionals in the multi-disciplinary team.*

Recommendations

No individual measure can be broadly recommended for pain assessment across all children or all contexts: Grade B

Children's self-report of their pain is the preferred approach: Grade B

Children's pain should be assessed, documented and appropriate action taken as this contributes to prevention and relief of pain: Grade D

Health care professionals and parents/carers should receive information, education and training in pain assessment: Grade D

There is little evidence to recommend the clinical use of physiological measures alone to measure pain: Grade D.

II. Medical Procedures

Good Practice Point

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

Neonate: general recommendations

Breast-feeding mothers should be encouraged to breast feed during the procedure, if feasible: Grade A

Non-nutritive sucking, and /or the use of sucrose or other sweet solutions should be used for brief procedures: Grade A

Neonate: specific recommendations

1. Blood Sampling

Sucrose or other sweet solutions should be used: Grade A

Venepuncture is preferred to heel lance as it is less painful: Grade A

Topical local anaesthetics alone are insufficient for heel lance pain: Grade A

Topical local anaesthetics can be used for venepuncture pain: Grade A

Morphine alone is insufficient for heel lance pain: Grade B

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: Grade B

2. 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): Grade B

3. Ocular Examination for Retinopathy of Prematurity (ROP)

Infants should receive local anaesthetic eye drops: Grade B

Infants should be offered a pacifier: Grade B

Sucrose may contribute to pain response reduction: Grade B

4. Lumbar Puncture

Topical local anaesthesia is effective in reducing LP pain: Grade A

5. Urine Sampling

Transurethral catheterisation with LA gel is preferred as it is less painful than suprapubic catheterisation with topical LA: Grade B

6. Chest Drain (tube) Insertion and Removal

See ‘Good Practice Points’ for older children below

7. Nasogastric Tube Placement

See ‘Good Practice Points’ for older children below

Procedural Pain in Older Children

Good Practice points

Children and their parents/ carers may benefit from psychological preparation prior to painful procedures.

Pain management for procedures should include both pharmacological and non-pharmacological 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.

Older children: specific recommendations

1. Blood Sampling And Intravenous Cannulation

Topical local anaesthesia should be used for intravenous cannulation: Grade A

Psychological strategies e.g. distraction or hypnosis, to reduce pain and anxiety should be used: Grade A

Nitrous oxide is effective for pain reduction in venous cannulation: Grade A

2. Lumbar Puncture

Behavioural techniques of pain management should be used to reduce LP pain: Grade A

Topical LA and LA infiltration are effective for LP pain and do not decrease success rates: Grade B

Inhaled Entonox (50% nitrous oxide in oxygen) should be offered to children willing and able to co-operate: Grade C

3. Chest Drain (tube) Insertion and Removal

Good Practice Points

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

4. Urine Sampling

Good practice point

Lubricant, containing local anaesthesia, should be applied to the urethral mucosa prior to bladder catheterisation.

Psychological preparation and psychological and behavioural interventions should be used during bladder catheterisation and invasive investigations of the renal tract: Grade B

5. Insertion of nasogastric tubes

Good Practice Point

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.

6. Immunization and Intramuscular Injection

Good Practice Point

Intramuscular injections should be avoided in children as part of routine care. If intramuscular injection is unavoidable, pharmacological and non-pharmacological strategies should be employed to reduce pain.

Swaddling, breast feeding or pacifier, and sucrose should be considered in infants undergoing vaccination.

Psychological strategies such as distraction should be used for infants and children undergoing vaccination: Grade A

Consider additional procedure modifications such as vaccine formulation, needle size, depth of injection (25mm 25 gauge needle) or the use of vapocoolant spay: Grade A

Topical local anaesthesia may reduce immunisation pain in infants and older children in some circumstances, but there is insufficient evidence to recommend routine use: Grade B

7. Repair of Lacerations

Good Practice Point

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

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 (steri-strips): Grade A

If sutures are needed, topical anaesthetic preparations e.g. LAT (lidocaine-adrenaline-tetracaine) if available, can used in preference to injected lidocaine, as they are less painful to apply and are equi-analgesic; it is not necessary to use a preparation containing cocaine: Grade A

Buffering of injected lidocaine with sodium bicarbonate should be considered: Grade A

‘HAT’ (hair apposition technique) should be considered for scalp lacerations. It is less painful than suturing, doesn't require shaving and produces a similar outcome: Grade B

If injected lidocaine is used, pre-treatment of the wound with a topical anaesthetic preparation e.g. lidocaine-adrenaline-tetracaine (LAT) gel reduces the pain of subsequent injection: Grade B

50% nitrous oxide reduces pain and anxiety during laceration repair: Grade B

8. Change of Dressings in Children with Burns

Potent opioid analgesia given by oral, transmucosal or nasal routes according to patient preference and availability of suitable preparations should be considered for dressing changes in burned children: Grade A

Non-pharmacological therapies such as distraction, relaxation and massage should be considered as part of pain management for dressing changes in burned children: Grade B

III. POSTOPERATIVE PAIN

Good Practice Points

Paediatric anaesthetists are responsible for initiating postoperative analgesia. They should liaise with patients and their families/carers, surgeons and other members of the team providing postoperative care in order to ensure that pain is assessed and suitable ongoing analgesia is administered.

Postoperative analgesia should be appropriate to developmental age, surgical procedure and clinical setting in order to provide safe, sufficiently potent and flexible pain relief with a low incidence of side effects.

Providers of postoperative care should understand the general principles of good pain management in children; this includes knowledge of assessment techniques and the use of analgesics at different developmental ages.

Specific procedures:

ENT surgery

1. 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.

Oral paracetamol, ibuprofen or diclofenac, in suitable doses, administered 30 minutes preoperatively can achieve adequate early postoperative analgesia: Grade B

Ketorolac can provide satisfactory analgesia: Grade B

Opioids are effective but not recommended for routine use because of increased side-effects compared with minor analgesics: Grade B

2. 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.

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

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: Grade B

Tramadol can produce similar analgesia to morphine or pethidine: Grade B

Intraoperative intravenous (IV) ketamine does not provide significant postoperative advantage compared with opioid: Grade B

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 PONV: Grade C.

3. Mastoid and middle ear surgery

Great auricular nerve block can provide similar analgesia and reduced PONV compared with morphine. Pre-incision timing of the block confers no additional benefit: Grade B

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: Grade C

Opthalmology

1. Strabismus surgery

Intraoperative LA blocks (subtenon or peribulbar) reduce PONV and may improve perioperative analgesia in comparison with IV opioid: Grade B

Topical NSAIDs do not improve pain scores or postoperative analgesic requirements when compared with topical LA or placebo: Grade B

Intraoperative opioid and NSAID provide similar postoperative analgesia but opioid use is associated with increased PONV: Grade B

2. Vitreoretinal surgery

NSAID provides similar analgesia but lower rates of PONV compared with opioid: Grade C

Peribulbar block improves analgesia and reduces PONV compared with opioid: Grade C

Dental Procedures

Good practice point

NSAIDs can provide adequate analgesia for dental extractions

Swabs soaked with bupivacaine on exposed tooth sockets following extraction produce no or minor improvements in pain in the immediate postoperative period: Grade B

Intraoperative LA infiltration reduces postoperative pain following dental extractions: Grade C

General Surgery and Urology (Minor and Intermediate)

1. Subumbilical Surgery

LA wound infiltration, ilio-inguinal nerve block and caudal analgesia are effective in the early postoperative period following subumbilical surgery: Grade A

2. Circumcision

Caudal epidural and dorsal nerve block are effiective in the early postoperative period, with low rates of complications and side-effects: Grade A

Techniques using opioid alone should be avoided if possible, due to lower efficacy and higher incidence of side effects in comparison with LA techniques: Grade A

3. Neonatal Circumcision

Good practice point

> *General anaesthesia should be considered for neonatal circumcision. A multi modal analgesic approach should include a local anaesthetic technique at the time of the procedure in combination with sucrose and paracetamol.*

Local anaesthesia should be used as it is superior to other techniques for neonatal circumcision pain: Grade A

Dorsal nerve block is more effective than subcutaneous ring block or topical LA: Grade A

When using topical local anaesthetic it must be applied correctly and sufficient time allowed for it to become effective: Grade A

4. Hypospadias Repair

Caudal block is effective and reduces the need for postoperative supplementary opioid administration following hypospadias surgery: Grade A

5. Orchidopexy

Caudal block is effective for orchidopexy in the early postoperative period, with low rates of complications and side-effects: Grade A

6. Open Inguinal Hernia Repair

LA wound infiltration, ilio-inguinal nerve block or caudal analgesia are effective in the early postoperative period: Grade A

General Surgery and Urology (Major)

1. Abdominal surgery

Good Practice Point

> *Multimodal analgesia using parenteral opioids or epidural analgesia together with systemic NSAIDs and paracetamol should be used unless specifically contraindicated.*

Intravenous opioids either as continuous infusion, NCA or PCA can be effective following major abdominal surgery: Grade A

Epidural analgesia with LA is effective following major abdominal surgery. The addition of opioid or clonidine may further improve analgesia but side effects are also increased: Grade B

2. Appendicectomy (open)

Good Practice Point

Following appendicectomy infiltration of the surgical wound with local anaesthetic as part of a multimodal analgesic technique may be of benefit in the early postoperative period.

PCA combined with NSAID is effective for post-appendicectomy pain: grade B

3. Fundoplication (open)

Good Practice Point

Multimodal analgesia using parenteral opioids or epidural analgesia together with systemic NSAIDs and paracetamol should be used unless specifically contraindicated.

Epidural LA + opioid is effective and may be associated with improved clinical outcome in selected patients: grade D

4. Laparoscopic surgery

Good Practice Point

Infiltration of port sites with LA as part of a multimodal analgesic strategy may reduce postoperative pain following laparoscopy.

Although overall postoperative analgesic requirements appear to be reduced following laparoscopy, pain may be equivalent to the comparable open procedure in some circumstances, particularly during the first 24 hours.

Orthopaedics, Spinal and Plastic Surgery

1. Lower Limb Surgery

Good practice point

> *There is no evidence from human studies that NSAIDs have a deleterious effect on bone fusion. The analgesic benefit of short term NSAID use has been demonstrated and may frequently outweigh any hypothetical risk.*

Epidural opioids are effective, reduce the dose requirements of local anaesthetic and rescue IV opioids but increase the incidence of side effects: Grade B

Epidural techniques are associated with lower pain scores than intravenous opioid analgesia: Grade C

Patient controlled regional techniques (PCRA) can reduce the total dose of local anaesthetic consumed; reducing the potential for toxicity: Grade D

Systemic paracetamol & NSAID reduce intravenous opioid requirements: Grade C

Continuous peripheral nerve blocks are feasible, effective & safe: Grade D

2. Upper Limb Surgery

Brachial plexus blocks provide satisfactory analgesia for hand and forearm surgery extending into the postoperative period: Grade B

The axillary, infraclavicular & supraclavicular approach are feasible & effective: Grade B

3. Spinal Surgery

Good practice points

There is no evidence from human studies that NSAIDs have a deleterious effect on bone fusion. The analgesic benefit of short term NSAID use has been demonstrated and may outweigh any hypothetical risk.

When using an epidural technique, the timing of LA administration should be agreed in consultation with the surgical team.

Intrathecal opioids decrease intra-operative blood loss and IV opioid consumption post-operatively. The duration of action is 18-24 hours:Grade C

Dual catheter epidural techniques should be considered, as this permits coverage of multiple spinal levels: Grade C

The use of LA + lipophilic opioid in the epidural space with a single epidural catheter does not show an analgesic benefit over intravenous opioid techniques: Grade C

The use of LA + hydrophilic opioids in the epidural space has a favourable analgesic profile compared with IV opioid, but at the expense of increase adverse effects: Grade D

Plastic Surgery of Head and Neck

Infraorbital nerve block provides effective analgesia for cleft lip repair in the early postoperative period: Grade B

Cardiothoracic Surgery

1. Cardiac Surgery (sternotomy)

Epidural and intrathecal techniques with opioid and/or LA are effective for sternotomy pain but only marginal benefits have been demonstrated and there is insufficient data concerning the incidence of serious complications: Grade B

2. Thoracotomy

Good practice point

> *A multi modal analgesic approach; including a local anaesthetic technique and /or opioid with NSAID and paracetamol is suitable for post thoracotomy pain.*

Epidural analgesia is effective for post-thoracotomy pain: Grade D

Neurosurgery (5.9.0 main guideline p X)

Good practice point

> *Analgesia following neurosurgery requires good communication and close co-operation between members of the peri-operative team. Frequent pain assessments should be a routine part of postoperative care. A multi-modal analgesic approach is suitable, which may include the use of LA infiltration, paracetamol, NSAID (when indicated), and parenteral or oral opioid as determined by assessed analgesic requirements.*

Section 3.0

Pain Assessment

Children's pain should be assessed. It is an essential contribution to ensuring that pain is both prevented and relieved (Howard 2003; Finley et al. 2005) and this is enshrined in many current pain management recommendations, position statements, reports and guidelines (Canadian Paediatric Society Committee on Fetus and Newborn 2000; Anand et al. 2006; Batton et al. 2006; The Healthcare Commission 2007).

Existing guidelines: An evidence-based guideline 'The Recognition and Assessment of Pain in Children' (1999) was first produced by the Royal College of Nursing (RCN) in 1999; it is currently undergoing revision. The RCN guideline was endorsed in 2001 by the Royal College of Paediatrics and Child Health, who produced 'Guidelines for Good Practice' (RCPCH 2001) which were recommendations based on the original RCN guideline. We suggest that both these documents be consulted for further and more detailed information; the evidence and recommendations presented here are intended to support and supplement this existing guidance.

3.1 General Principles of Pain Assessment

Good pain assessment contributes to the prevention and/or early recognition of pain as well as the effective management of pain (Finley et al. 2005). There are 3 fundamental approaches to pain assessment in children:

1. Self-report: measuring expressed experience of pain.

2. Observational/ Behavioural: measuring behavioural distress associated with pain, or measuring the perceived experience of pain by parent or carer report.

3. Physiological: primarily measuring physiological arousal consequent to pain

As self-report is the only truly direct measure of pain it is often considered the 'gold standard' of measurement, however, for developmental reasons self report may be difficult or impossible in some children and therefore a proxy measure must be used. For pain to be measured as accurately as possible the principles underpinning assessment at different developmental ages and in different settings must be appreciated.

Good Practice Point

In order to assess pain effective communication should occur between the child whenever feasible, their family or carers, and the professionals in the multi-disciplinary team.

Recommendations

No individual measure can be broadly recommended for pain assessment across all children or all contexts: Grade B
(Stinson et al. 2006; von Baeyer and Spagrud 2007)

Children's self-report of their pain, is the preferred approach: Grade B
(Stinson et al. 2006)

Children's pain should be assessed, documented and appropriate action taken as this contributes to prevention and relief of pain: Grade D
(Treadwell et al. 2002; Finley et al. 2005)

Health care professionals and parents/carers should receive information, education and training in pain assessment: Grade D
(Simons et al. 2001; Simons and Roberson 2002)

There is little evidence to recommend the clinical use of physiological measures alone to measure pain: Grade D.
(Buttner and Fincke 2000; van Dijk et al. 2001)

Evidence

The results of pain assessment must be documented, acted upon, reassessed and re-evaluated to determine the effectiveness of interventions (Howard 1996; Salantera et al. 1999; Finley et al. 2005). Improved documentation can result in improved pain management (Faries et al. 1991; Treadwell et al. 2002). Studies demonstrate that pain is under-assessed, poorly documented resulting in children being under-medicated and/or their pain being poorly managed (Kohler et al. 2001). Regular pain evaluation can contribute to the safety and efficacy of management of acute pain (Falanga et al. 2006).

Children's self report of pain is regarded as the gold standard and in most circumstances it is the preferred approach. However, it needs to be recognised that self report in adults and children is complex (Stinson et al, 2006; von Baeyer, 2006; von Baeyer and Spagrud 2007). Self-report is dependent upon age and/or level of cognition (Stanford et al. 2006), is effected by a range of social and other influences (de C Williams et al. 2000) and it is subject to biases (de C Williams et al. 2000; Hodgins 2002).

No individual observational (von Baeyer and Spagrud 2007), self report (Stinson et al. 2006) or physiological measure is broadly recommended for pain assessment across all children or all contexts. Therefore health care professionals need to make informed choices about which tool to use to assess each individual child's individual pain. Composite measures using self

report and at least one other measure may be a better approach (Stinson et al. 2006).

Healthcare professionals require appropriate levels of education about pain (Simons and Roberson 2002). They also need adequate training/preparation in the use of pain assessment tools and proficiency in using them (Treadwell et al. 2002; Malviya et al. 2006). Improved working practices (Boyd and Stuart 2005), organisational commitment (Treadwell *et al.* 2002) and quality improvement strategies (Treadwell et al. 2002) have been shown to enhance pain assessment. Studies have demonstrated that health professionals assessment of children's pain is subject to a range of individual, social and contextual influences (Craig et al. 1996). Professionals need to be flexible and willing to develop more positive attitudes and beliefs regarding the attributes of children's pain (Salantera et al. 1999). . Perceptions about the pain experienced by particular groups of children, such as children with neurological impairment may need to be challenged (Breau et al. 2003).

Parents and other carers should also be given appropriate information about their child's pain (Simons et al. 2001; Polkki et al. 2002) and emotional support and clarification of their role in their child's pain (Polkki et al. 2002). Their beliefs about their child's pain need to be taken into consideration as these beliefs may impact their child's care. Parents/carers of children with cognitive impairment may have mistaken beliefs about their child's pain which need to be carefully explored (Breau et al. 2003). Parents/carers also need appropriate information, teaching and confidence in the use of pain assessment tools if they are to be effective in assessing (and managing) their child's pain (Breau et al. 2003; Voepel-Lewis et al. 2005).

3.2 Pain Assessment Tools

A bewildering number of acute pain assessment tools exist. Tools vary in relation to three broad groups of factors: child-related, user-related and structural. For example the age group, cognitive level, language, ethnic/cultural background of the child, the setting for which they are to be used and their validity and reliability in that context (Merkel et al. 2002; Mathew and Mathew 2003; Stinson et al. 2006; von Baeyer 2006b; von Baeyer and Spagrud 2007). Such factors should be taken into consideration when making choices about which acute pain assessment tool to use.

Despite the proliferation and availability of tools they are not always used consistently or well (Broome et al. 1996; Karling et al. 2002) and inconsistencies have been identified between reported assessment practice and documented practice (Simons and MacDonald 2006)**.**

The following provides a brief guide to some of the best evaluated and commonly used tools in current practice. The tools are broadly divided into self report and behavioural tools and then further sub-divided into their suitability for type of pain (acute procedural, post operative or disease related) and/or setting. Brief information of the age ranges for which the tool has been validated are presented.

A. Self Report Tools

On the basis of the evidence for the most psychometrically sound and feasible measures, based on age/developmental level and type of pain, a limited number of self-report tools have been recommended for use in clinical trials (•) (Stinson et al. 2006). However other tools, whilst not necessarily suitable for clinical trials, have been shown to have good clinical utility and have been validated.

Procedural pain

- Wong and Baker FACES Pain Scale (Wong and Baker 1988): valid for 3-18 year olds.
- Faces Pain Scale-Revised• (Hicks et al. 2001); see also (Goodenough et al. 1997; Hunter et al. 2000): valid for 4-12 year olds.
- Visual analogue• and numerical rating scales: valid for 8 years plus.
- Pieces of Hurt Tool• (Hester 1979) see also (Hester et al. 1990): valid for 3-8 year olds.
- MSPCT (The Multiple Size Poker Chip Tool) (St-Laurent-Gagnon et al. 1999): valid for 4-6 year olds.

Post operative pain

- Wong and Baker FACES Pain Scale (Wong and Baker 1988): valid for 3-18 year olds.
- Faces Pain Scale-Revised● (Hicks et al. 2001); see also (Goodenough et al. 1997; Hunter et al. 2000): valid for 4-12 year olds.
- Visual analogue● and numerical rating scales: valid for 8 years plus.
- Pieces of Hurt Tool● (Hester 1979) see also (Hester et al. 1990): valid for 3-8 year olds.

Disease related pain

- Wong and Baker FACES Pain Scale (Wong and Baker 1988): valid for 3-18 year olds.
- Faces Pain Scale-Revised● (Hicks et al. 2001); see also (Goodenough et al. 1997; Hunter et al. 2000): valid for 4-12 year olds.
- Visual analogue● and numerical rating scales: valid for 8 years plus.

B. Behavioural Measures

Premature Infants and Neonates

Most neonatal pain assessment tools have not been rigorously tested for construct validity, feasibility, and clinical utility (Stevens and Gibbins 2002). However, the following tools are widely used for neonatal pain assessment and used within neonatal intensive care/special care baby units.

Acute procedural pain

- PIPP (Premature Infant Pain Profile) (Stevens et al. 1996) see also (Ballantyne et al. 1999; Jonsdottir and Kristjansdottir 2005).
- CRIES (Krechel and Bildner 1995).
- NFCS (Neonatal Facial Coding Scale) (Grunau and Craig 1987; Grunau et al. 1998).

Post operative pain

- PIPP (Premature Infant Pain Profile) (Stevens et al. 1996) see also (McNair et al. 2004).
- CRIES (Krechel and Bildner 1995) see also (McNair et al. 2004).

- COMFORT scale (Ambuel et al. 1992; van Dijk et al. 2000; Caljouw et al. 2007).

Children and Young People without Cognitive Impairment

On the basis of the highest evidence of validity, reliability and clinical utility and use within practice settings the following behavioural tools can be recommended for children and young people (without cognitive impairment) aged 3-18 years in the following specific situations (von Baeyer and Spagrud 2007). Note that there is no specific tool that can be recommended as valid for assessment of this group. However, FLACC is widely used in practice for pain assessment of infants (neonates to under 1 year).

Procedural pain

- FLACC (Face, Legs, Arms, Cry, Consolability). (Merkel et al. 1997) ; see also (Voepel-Lewis et al. 2001; Manworren and Hynan 2003; Voepel-Lewis et al. 2003; Malviya et al. 2006): valid for 1-18 year olds.
- CHEOPS (Children's Hospital of Eastern Ontario Pain Scale) (McGrath et al. 1985); see also (Splinter et al. 1994): valid for 1-18 year olds.

Post operative pain (in the hospital setting)

- FLACC (Merkel et al. 1997): valid for 1-18 year olds.

Post operative pain (being managed by parents at home)

- PPPM (Parents Postoperative Pain Measure)(Chambers et al. 1996); see also (Chambers et al. 2003; Finley et al. 2003): valid for 1-12 year olds.

Pain in the critical care setting

- COMFORT scale (Ambuel et al. 1992): valid for newborn-17 year olds.

Children and Young People with Cognitive Impairment

Whilst there is less substantive evidence of reliability, validity, clinical utility and widespread use within practice settings the following tools are suitable for use

with children and young people with cognitive impairment in the following situations:

Procedural/disease related pain

- NCCPC-R (Non-Communicating Children's Pain Checklist) (Breau et al. 2000; Breau et al. 2001; Breau et al. 2002; Breau et al. 2003): valid for 3-18 year olds
- PPP (The Paediatric Pain Profile) (Hunt et al. 2004): valid for 1-18 year olds.

Post operative pain

- NCCPC-PV (Non-Communicating Children's Pain Checklist- Postoperative Version)(Breau et al. 2002): valid for 3-19 year olds.
- PPP (The Paediatric Pain Profile) (Hunt et al. 2004): valid for 1-18 year olds.
- Revised FLACC (Malviya et al. 2006): valid for 4-19 year olds.

Parent-report of their child's post operative pain intensity

On the basis of the evidence for the most psychometrically sound and feasible measures based on age/developmental level and type of pain the following parent-report tool has been recommended for use in clinical trials (Stinson et al. 2006) although this may not necessarily directly transfer to clinical utility and more research is needed.

- PPPM (Parents Postoperative Pain Measure)(Chambers et al. 1996); see also (Chambers et al. 2003; Finley et al. 2003).

C. Physiological Measures

Physiological parameters such as heart rate variability, changes in salivary cortisol can be used indirectly to indicate the presence of pain (Sweet and McGrath 1998; Walco et al. 2005). However, blood pressure, heart rate and respiratory rate have been shown to be unreliable indicators in newborns, infants and young children (Buttner and Fincke 2000) with wide inter-individual in behaviour–physiology correlations after major surgery in 0- 3 year old infants (van Dijk et al. 2001). Whilst physiological parameters such as cortisol changes may be measured during clinical research studies these measurements do not generally have high clinical utility. Physiological measures should be used in conjunction with other tools/measures to determine pain.

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Section 4 MEDICAL PROCEDURES

4.1 General Principles of Procedural Pain Management

4.2 Procedural Pain in the Neonate

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4.3 Procedural Pain in Infants and Older Children

4.3. 01 Blood Sampling And Intravenous Cannulation

4.3. 02 Lumbar Puncture

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4.3. 05 Insertion of nasogastric tubes

4.3. 06 Immunization and Intramuscular Injection

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Section 4.1

General Principles of procedural Pain Management

Introduction

Routine medical care involving blood sampling and other painful diagnostic and therapeutic procedures can cause great distress for children and their families. When such procedures are essential, it is important that they should be achieved with as little pain as possible. For many children who have chronic illness, procedures often need to be repeated and this can generate very high levels of anxiety and distress if their previous experience has been poor. The general principles, which apply to the management of all procedures at any age, are described on this page. Evidence based recommendations for the general and specific management of common procedures are described in section 4.2 for neonates and 4.3 for infants and older children.

Good Practice Point

Pain management for procedures should be planned taking into account the general considerations (outlined below) and include both pharmacological and non-pharmacological strategies whenever possible.

Procedural pain management: general considerations

1. Infants and children of all ages, including premature neonates are capable of feeling pain and require analgesia for painful procedures.
2. Developmental differences in the response to pain and analgesia should be considered when choosing analgesia.
3. Consider if the planned procedure is necessary, and how the information it will provide might influence care? Avoid multiple procedures if possible.
4. Are sedation or even general anaesthesia likely to be required for a safe and satisfactory outcome?
5. Would modification of the procedure reduce pain? E.g. venepuncture is less painful than heel lance.
6. Is the planned environment suitable? Ideally this should be a quiet, calm place with suitable toys and distractions.
7. Allow sufficient time for analgesic drugs and other analgesic measures to be effective.
8. Ensure that appropriate personnel are available, and enlist experienced help when necessary.
9. Formulate a clear plan of action should the procedure fail or pain become unmanageable using the techniques selected.

4.2 Procedural Pain in the Neonate

Premature neonates are able to perceive pain but the response to both pain and analgesia is dependant on developmental age. Because of this, pain assessment in this age group is particularly difficult (see section 3), and the low sensitivity of many pain measurement tools can complicate the interpretation of evidence. Clinically neonates appear to be sensitive to the adverse effects of many drugs, including analgesics; however reductions in the response to pain have been observed following non-traditional analgesia such as sucrose and to physical and environmental measures e.g. suckling or tactile stimulation which are currently not known to have potentially harmful effects. A number of documents including reviews, guideline and policy statements have been published recently on the subject of procedural pain management in the neonate (Anand et al. 2005; Mackenzie et al. 2005a; Batton et al. 2006). On the basis of the currently available evidence the following measures can be *generally* recommended for the management of procedural pain in the neonate:

Recommendations

Breast-feeding mothers should be encouraged to breast feed during the procedure, if feasible: Grade A

(Carbajal et al. 2003; Shah et al. 2006)

Non-nutritive sucking, and /or the use of sucrose or other sweet solutions should be used for brief procedures: Grade A

(Skogsdal et al. 1997; Carbajal et al. 1999; Bellieni et al. 2002; Carbajal et al. 2002; Carbajal et al. 2003; Bauer K 2004; Gradin M 2004; Stevens et al. 2004; Ling JM 2005; Ogawa S 2005; Shah et al. 2006)

Evidence

Neonatal procedural pain has been relatively well studied. Evidence relating to the specific management of a number of common procedures is listed in sections 4.2.01-4.2.07. Evidence for the benefit of sweet tasting solutions in the management of brief pain in the neonate has been accumulating over the last decade (Skogsdal et al. 1997; Stevens et al. 2004). It is becoming increasingly clear that other modalities may also modify the response to pain: especially non-nutritive sucking. Sucrose seems to be effective throughout the neonatal period, but the efficacy of non-nutritive sucking (NNS) using a pacifier has not been established in the preterm infant. Preterm infants are born

without a highly developed suck reflex: this develops around 32- 34 weeks gestation and may reduce the effectiveness of interventions involving sucking at this age (Carbajal et al. 2002). The difference between the effect of non nutritive sucking and sucrose may therefore be a feature of gestational age – this is an area that needs futher elucidation. The optimum dose of sweet tasting solutions has yet to be determined: studies have used sucrose and glucose in different concentrations and have used different assessment methods. 1ml of 30% glucose was more effective than 1 ml of either 10% glucose or 1 ml of breast milk in a study of newborns having heel prick tests who were not sucking (Skogsdal et al. 1997). Two mls of 30% glucose was more effective than 0.4 ml of the same solution prior to venepuncture in term newborns (Bauer K 2004). Studies using validated assessment methods for pre-term infants e.g. NFCS and PIPP (see section 3) have found that 0.012-0.12g i.e. 0.2-2.0 ml of 12% sucrose, is effective (Stevens et al. 2004). Recent consensus guidelines have recommended that 0.1-2.0ml 24% solution be used in the lowest effective volume 1-2 minutes prior to the procedure; upper dose limits of 0.5, 1.0 and 2.0mls for ages 27-31, 32-36 and 37+weeks respectively were also suggested (Lefrac et al. 2006). The interaction of other interventions such as pacifiers, touch and sensory stimulation is unclear for all circumstances and therefore requires further study (Bellieni et al. 2002; Stevens et al. 2004). Long term outcomes following the use of repeated doses of sucrose in preterm infants are currently unknown. See section 6.7 for advice on dosage and administration of sucrose.

4.2. 01 Blood Sampling in the Neonate

Blood sampling, particularly where frequent samples are needed in NICU, has been identified in many studies as a significant cause of pain and morbidity. Where sampling from indwelling venous access is not possible either heel lancing (heel stick) or venepuncture are options. They are not equivalent. Venepuncture pain appears to be more easily managed than pain from heel lance, but pain from heel lance can be reduced by technique modification. Venepuncture can be technically more difficult than heel lance and is therefore sometimes impractical: capillary samples are collected for blood sugars, bilirubin, newborn screening tests and capillary blood gases. Please also see sections 4.0 and 4.2 on the general management of procedural pain.

Recommendations

(See also sections 4.0 and 4.2)

Sucrose or other sweet solutions should be used: Grade A
(Skogsdal et al. 1997; Carbajal et al. 1999; Bellieni et al. 2002; Carbajal et al. 2002; Carbajal et al. 2003; Bauer K 2004; Gradin M 2004; Stevens et al. 2004; Ling JM 2005; Ogawa S 2005; Shah et al. 2006)

Venepuncture is preferred to heel lance as it is less painful: Grade A (Logan 1999; Shah and Ohlsson 2004; Ogawa S 2005)

Topical local anaesthetics alone are insufficient for heel lance pain: Grade A (A Taddio 1998)

Topical local anaesthetics can be used for venepuncture pain: Grade A
(A Taddio 1998; Jain A 2000; Gradin M 2002)

Morphine alone is insufficient for heel lance pain: Grade B
(Carbajal et al. 2005)

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: Grade B
(Bellieni et al. 2002; Johnston et al. 2003)

Evidence

Blood sampling in the neonate has been relatively well investigated, evidence for the use of sweet tasting solutions in venepuncture and heel lance pain has been accumulating over the last decade– see section 4.2. Many studies have used venepuncture as the pain stimulus: this appears to be less painful than heel lance and so when practical it is the preferred option (Logan 1999; Ogawa et al 2005). Topical local anaesthesia can reduce the pain of venepuncture (Jain 2000). However, the response to heel lance or insertion of PICC lines in preterm infants does not appear to be reduced with topical analgesia alone and this needs further study see 4.2.02 (Taddio et al. 2006). Tactile stimulation has been associated with reductions in the pain response in neonates; 'kangaroo care' reduced heel lance pain in those aged 32-36 weeks (Johnston et al. 2003) and a combination of 'multisensory stimulation'-massage, aural stimulation and eye contact - with glucose+ pacifier was more effective than glucose+ pacifier alone in another study (Bellieni et al. 2002).

Heel lance pain can be reduced by procedure modification e.g. the use of special spring-loaded devices. Studies have compared automated devices: whilst some types may improve blood collection and reduce the number of punctures required there does not seem to be a reduction in pain if collection involves squeezing of the heel(Paes et al. 1993; Shah et al. 2003). The development of local hypersensitivity from repeated sampling is reduced by widening the area of the sampling site (Barker et al. 1994).

Analgesia table 4.2.01 Blood sampling in the neonate

		Direct evidence
Local Anaesthesia	**Topical**	**1+ ***
Sucrose		**1++**
Breast feeding		**1+ ***
Non-nutritive sucking		**1+**
Tactile stimulation		**1+ ****
Procedure modifications		**1+*****

***** Venepuncture only

****** Heel lance only

******* Venepuncture by trained phlebotomist, spring loaded heel-lance device

4.2. 02 Percutaneous Central Venous Catheter Insertion (PICC) in the Neonate

Percutaneous central venous catheters are inserted for long-term venous access; the procedure can be technically difficult. Infants requiring PICC line insertion are often unwell and may be receiving ventilatory support; these infants are also likely to be receiving morphine by intravenous infusion and are the group that have been mostly studied.

Recommendations

Topical LA with tetracaine alone is insufficient to abolish pain of PICC line insertion; Tetracaine plus morphine is superior (in ventilated infants): **Grade B** (Lemyre et al. 2006; Taddio A 2006)

Evidence

In comparison with simple blood sampling or temporary venous cannulation, infants undergoing PICC line insertion need to be held in position for longer and this may contribute to the high levels of perceived distress reported in studies. There has been only limited study of this procedure, but a combination of morphine and topical local anaesthesia appears to be superior to either alone in ventilated infants (Lemyre et al. 2006; Taddio A 2006). There is little evidence to guide practice in an infant who is not ventilated: morphine in this situation may produce respiratory depression. General anaesthesia should be considered in situations where such facilities are available. Indirect evidence would suggest that a combination of topical anaesthesia and sucrose before the initial venepuncture, with the use of non nutritive sucking in the infant who is able to suck, may be helpful in reducing pain and distress.

Analgesia table 4.2.02 Percutaneous central venous catheter insertion

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical**	**1+***	
Opioids	**Intravenous**	**1+***	

Sucrose	**1++**
Non-nutritive sucking	**1+**
Tactile stimulation	**1+**

* Combined

4.2. 03 Ocular Examination for Retinopathy of Prematurity

Preterm infants 'at risk' for retinopathy (ROP) should have regular ocular examination. An eyelid speculum is inserted to hold the eye open and the retina is examined by indirect fundoscopy through a dilated pupil.

Recommendations

Infants undergoing ROP exam should receive local anaesthetic drops: Grade B
(Marsh et al. 2005).

Infants should be offered a pacifier: Grade B
(Mitchell et al. 2004; Boyle et al. 2006)

Sucrose may contribute to pain response reduction: Grade B
(Mitchell et al. 2004; Gal et al. 2005)

Evidence

A combined analgesic approach using LA, a pacifier and the addition of a sweet solution is likely to be most effective for ROP examination pain. Sucrose may have a role in reducing this pain– the frequency of dosing, and the relationship to the use of a pacifier needs further exploration. Studies of pain reduction for needle related pain suggest that sucrose is effective two minutes prior to the painful stimulus (Stevens et al. 2004). However, examination for ROP is longer in duration that either venepuncture or heel lance. For ROP, 2 ml of 24% sucrose was of some benefit in one study (Gal et al. 2005), but 1ml of 33% sucrose was not different than placebo in another (Boyle et al. 2006). The use of local anaesthesia, a pacifier and three doses of sucrose were found to reduce pain scores more than LA, pacifier and water (Mitchell et al. 2004). See section 6.7 for further information on the use of sucrose.

Analgesia table 4.2.03 Examination for retinopathy of prematurity

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical**	**1+**	
Sucrose		**1+**	
Non-nutritive sucking		**1+**	

Tactile stimulation	**1+**

4.2. 04 Lumbar Puncture in the Neonate

Sampling of cerebro-spinal fluid is often regarded as a minor procedure in infants; nevertheless it is associated with pain which can be reduced by suitable analgesia (Kaur et al. 2003).

Recommendations

Topical local anaesthesia is effective in reducing LP pain: Grade A
(Kaur et al. 2003).

Evidence

There have been few studies directly investigating LP pain in the neonate. Topical local anaesthetic has been found to be effective (Kaur et al. 2003). Indirect evidence suggests that subcutaneous infiltration of LA would also be effective, but it has not been 'consistently' shown to be superior to placebo in the neonate, in contrast to positive effects in older children and adults(Anand et al. 2005). Sucrose, NNS and other strategies have not been investigated but are also likely to be effective- see section 4.2

Analgesia table 4.2.04 Lumbar puncture in the neonate

Agent	Technique	Direct evidence	Indirect evidence
Local Anaesthesia	**Topical**	**1+**	
	Infiltration		**1+***
Sucrose			**1++**
			1+
Tactile stimulation			**1+**

* Older children and adults

4.2. 05 Urine Sampling in the Neonate

Urine sampling is important to detect urinary tract infection in infants, and must be collected so as to avoid sample contamination. Direct catheterisation of the urethra or catheterisation of the bladder by the percutaneous suprapubic route are often preferred because some types of urine collection bags have a high rate of contamination, and 'clean catch' specimens can be difficult or time consuming to collect.

Recommendations

Transurethral catheterisation with LA gel is preferred as it is less painful than suprapubic catheterisation with topical LA: Grade B
(Kozer et al. 2006)

Evidence

Pain responses were observed in neonates and infants having either urethral or suprapubic catheterisation with local anaesthesia (Kozer et al. 2006). Transurethral catheterisation appeared to be less painful (Kozer et al. 2006). Sucrose analgesia immediately before bladder catheterisation in neonates and infants up to 3 months old was not effective at abolishing pain responses; however a reduction in response was observed in a subgroup of those less than 30 days old (Rogers et al. 2006). Indirect evidence also suggests that sucrose, NNS and other strategies may be effective at reducing pain especially if used in combination with LA but this has not been directly studied-see section 4.2. See section 6.7 for advice on the use and administration of sucrose.

Analgesia table 4.2.05 Urine sampling in the neonate

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical lubricant gel***		**1+**
Sucrose		**1+**	
Non-nutritive sucking			**1+**
Procedure modification		**1+**	
Tactile stimulation			**1+**

* Urethral catheterisation

4.2. 06 Chest Drain (tube) Insertion and Removal

The management of his procedure in the neonate is discussed with that of older children in section 4.3. 03

4.2 07 Nasogastric Tube Placement

The management of his procedure in the neonate is discussed with that of older children in section 4.3. 05

4.3 Procedural Pain Management in Infants and Older Children

Painful procedures are often identified as the most feared and distressing component of medical care for children and their families. See section 4.2 for a general introduction on the management of procedural pain, and section 4.2.01 for the management of procedural pain in the neonate. When managing procedural pain in infants, older children and adolescents special emphasis should given not only to proven analgesic strategies but also to reduction in anticipatory and procedural anxiety by suitable preparatory measures. Families, play therapists, nursing staff and other team members play key roles in reducing anxiety by suitable preparation. The personality, previous experience and analgesic preferences of the child will influence management strategies. Analgesia-sedation with ENTONOX (Nitrous oxide/oxygen), by supervised self-administration should be considered where indicated, especially in children older than 6 years who can cooperate: see section 6.6. Sedation (see SIGN Guideline 58, available at: http://www.sign.ac.uk) or general anaesthesia may be needed for complex, invasive or multiple procedures. For recent reviews and guideline statements on the management of procedural pain in infants and older children see: Murat et al. 2003, Mackenzie et al. 2005b,

Good Practice points

Children and their parents/ carers may benefit from psychological preparation prior to painful procedures.

Pain management for procedures should include both pharmacological and non-pharmacological 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.

4.3. 01 Blood Sampling And Intravenous Cannulation in Children

For most children venepuncture or intravenous cannulation may be a ‘one off ‘ event but children with chronic illness are likely to require multiple procedures and this can be very distressing for the child, the family and the medical team. When managing such pain in infants, older children and adolescents, special emphasis should given not only to proven analgesic strategies but also to reduction in anticipatory anxiety by suitable preparatory measures. Venepuncture or intravenous cannulation maybe technically difficult – practitioners should not continue to try multiple cannulation sites unless the procedure is urgent or a more experienced practitioner is not available. In non-urgent cases consider whether the test can be rescheduled, and enlist the help of a more experienced practitioner. See also section 4.0: general management of procedures, and 4.3: procedural pain in infants, older children and adolescents.

Recommendations

Topical local anaesthesia should be used for intravenous cannulation: Grade A
(Hee et al. 2003; Koh JL 2004; Luhmann et al. 2004; Eidelman et al. 2005b:; Lander et al.2006)

Psychological strategies e.g. distraction or hypnosis, to reduce pain and anxiety should be used: Grade A
(Uman et al. 2006)

Nitrous oxide is effective for pain reduction in venous cannulation: Grade A
(Hee et al. 2003; Ekbom et al. 2005)

Evidence

Topical LA, such as EMLA or AMETOP, has an established place in the management of venous cannulation with high quality evidence for efficacy (Hee et al. 2003; Koh JL 2004; Luhmann et al. 2004; Eidelman et al. 2005b). Newer preparations such as liposomal encapsulated LA or newer LA delivery systems may offer advantages in some situations. Buffered injected LA (e.g. lidocaine +bicarbonate 10:1), administered with a fine 30g needle subcutaneously prior to cannulation is faster in onset and may be as acceptable and effective as topical preparations (Davies 2003; Luhmann et al. 2004; Eidelman et al. 2005b).

Nitrous oxide (50%-70%) inhalation has been used in children older than 6 years who can *self-administer* during venepuncture. 50% Nitrous oxide and EMLA have been shown to be equally effective for venepuncture with further improvements in pain reduction using a combination of the two (Hee et al. 2003; Ekbom et al. 2005). The efficacy of vapocoolant topical spray has not been clearly established, but in a study of children's preferences children who had experienced both methods selected both ethyl chloride and Ametop equally (Davies and Molloy 2006). Vapocoolant spray was not effective in reducing pain in a study of intravenous cannulation(Costello et al. 2006). Psychological strategies, particularly distraction and hypnosis, and combinations of such methods including both cognitive and behavioural elements have been shown to be effective for needle-related pain in a systematic review (Uman et al. 2006).

Analgesia table 4.3.01 Blood sampling and IV cannulation in children

		Direct evidence
Local Anaesthesia	**Topical**	**1+**
	Infiltration	**1++**
ENTONOX (Nitrous Oxide)		**1+**
Psychological Preparation		**1-**
Psychological Intervention		**1+**

4.3.02 Lumbar Puncture in Children

Lumbar puncture (LP) is necessary in acutely ill children in whom meningitis is suspected. These children are likely to be unwell and anxious and they may also undergo other painful procedures such as venepuncture as part of diagnosis and treatment.

Other children require 'elective' or 'planned' LP: this may be for diagnostic reasons, such as evaluation of possible raised intracranial pressure, or for intrathecal treatments such as chemotherapy.

Positioning of the child is very important for success and it is helpful to have assistance from trained staff with experience of correct positioning. Children who require multiple LP's may cope better with the addition of sedation (see SIGN Guideline 58, available at: www.sign.ac.uk) or general anaesthesia. See also section 4.0 and 4.3 on the general management of painful procedures.

Recommendations

Psychological techniques of pain management should be used to reduce LP pain: Grade A
(Liossi et al. 2006; Uman et al. 2006)

Topical LA and LA infiltration are effective for LP pain and do not decrease success rates: Grade B
(Carraccio et al. 1996; Juarez Gimenez et al. 1996; Eidelman et al. 2005b)

Inhaled Entonox (50% nitrous oxide in oxygen) should be offered to children willing and able to co-operate: Grade C
(Kanagasundaram et al. 2001)

Evidence

Few studies have directly examined the efficacy of analgesics in awake children undergoing lumbar puncture. Most commonly, local anaesthesia is combined with sedative agents such as midazolam, or psychological techniques such as distraction, hypnosis or other cognitive –behavioural interventions (Carraccio et al. 1996; Crock et al. 2003; Liossi et al. 2006; Uman et al. 2006). Entonox is effective for LP pain, and may also be used in combination with LA (either topical or infiltration) and other strategies (Kanagasundaram et al. 2001). Ketamine analgesia-sedation or general anaesthesia are used in emergency departments and oncology units with appropriate facilities(Ljungman et al. 2001; Evans et al. 2005; Iannalfi et al. 2005). It seems likely that older children, especially those who may only need to undergo this procedure once,

may tolerate LP with appropriate behavioural techniques and local anaesthesia. Whereas, children requiring multiple LP's should be offered sedation or GA (Crock et al. 2003)***.***

Analgesia table 4.3.02 Lumbar puncture in children

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical**	**1+**	
	Infiltration	**1-**	
Nitrous oxide		**2+**	
Psychological Interventions		**1++**	

4.3.03 Chest Drain (tube) Insertion and Removal

Chest drains are necessary in children with pneumothorax, empyema, pleural effusions, following chest trauma and surgery. Paediatricians are most likely to need to *insert* chest drains in the Neonatal Intensive Care Unit for infants with pneumothorax. This procedure is becoming increasingly rare because of improvements in the management of Respiratory Distress Syndrome e.g. the use of surfactant and ventilating infants at lower pressures. Older children require drains for management of empyema or for pneumothorax. Chest drains have become easier to insert recently with the development of small-bore Seldinger type drains that reduce the need for blunt dissection of the chest wall. They are available for both neonates and older children. Sedation (see SIGN guideline 58 available at: http://www.sign.ac.uk) or general anaesthesia should be considered for chest drain insertion; however in an emergency some children may tolerate this procedure using buffered infiltrated LA.

Studies agree that chest drain *removal* also causes significant pain. No single analgesic strategy has been shown to satisfactorily alleviate this pain in children and it is likely that the optimum effects will be achieved using a combination of strategies.

See also section 4.0 and 4.3 for advice on the general management of painful procedures.

Good Practice Points

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 a consider 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

Evidence

There is little published evidence looking at analgesic options for chest drain insertion or removal. Chest drain insertion may require general anaesthesia or sedation in combination with LA infiltration. Analgesia for removal of chest drains has included IV opioid, local anaesthetics and NSAIDs but despite the use of these analgesics significant pain is still reported (Rosen et al. 2000; Bruce et al. 2006). Inhalation agents such as Nitrous Oxide or Isoflurane may have a role in these procedures but further

study is needed (Bruce and Franck 2000; Akrofi et al. 2005). *N.B. Nitrous Oxide is contraindicated in the presence of pneumothorax and therefore cannot be recommended for chest drain insertion for this indication .* Multimodal therapy e.g. IV morphine, inhalation analgesia, topical LA and a NSAID, is likely to be superior to a single agent but such combinations, although in clinical use, have not been studied. It is important to allow enough time for the chosen agent to reach its peak effect and to use adequate doses (Bruce et al. 2006).

Analgesia table 4.3.03 Chest drain insertion and removal

	Direct evidence	Indirect evidence
Local anaesthetic: buffered lidocaine infiltration (insertion)		**1++**
Local anaesthetic: topical (removal)		**1+***
Opioids (removal)		**1+***
NSAIDS (removal)		**1+***
Entonox (removal)**	**1-* ****	
Psychological Interventions		**1++**
Procedure modification (insertion)	**3**	

* May reduce but not abolish pain of chest drain removal
** Contraindicated in presence of pneumothorax

4.3.04 Bladder Catheterisation and Related Urine Sampling Procedures

Urine specimens are usually obtained by 'clean catch' or midstream specimen (MSU). Bladder catheterisation may be required for radiological or other investigation of the renal tract e.g. Micturating Cystogram (MCUG) also known as Voiding Cystourethrogram (VCUG). Consider if MCUG is really necessary – it is a distressing procedure for the child and other less invasive techniques such as dynamic renal scanning may provide the same information. Bladder catheterisation may also be required in children who develop urinary retention, particularly those receiving epidural analgesia postoperatively. Very ill patients in ICU may also require catheterisation to monitor urine output. For children who are to receive postoperative epidural opioids after major surgery consider 'prophylactic' bladder catheterisation under general anaesthesia at the time of surgery.

Sedation may also be indicated for some children see: SIGN guideline 51 available at: www.sign.ac.uk for advice on sedation practice, and sections 4.0 and 4.3 on the general management of procedural pain.

Good practice point

Lubricant, containing local anaesthesia, should be applied to the urethral mucosa prior to bladder catheterisation.

Recommendations

Psychological preparation and psychological and behavioural interventions should be used during bladder catheterisation and invasive investigations of the renal tract: Grade B

(Phillips et al. 1998; Butler et al. 2005)

Evidence

Bladder catheterisation has been shown to cause significant pain and distress but analgesia is not part of routine care in many institutions (Vaughan et al. 2005). More complex interventions, which include bladder catheterisations such as MCUG or VCUG, have also been shown to cause significant distress, which can be reduced, by

psychological preparation, and psychological pain management techniques such as distraction or hypnosis (Phillips et al. 1998; Butler et al. 2005). Local anaesthetics incorporated into lubricant gels are frequently used in adults to reduce the pain and discomfort of catheterisation but this has not been well studied in children. Pre-treatment of the urethra with lidocaine 10 minutes before catheterisation reduced pain in a group of children (16 girls, 4 boys) with a mean age of 7.7 years(Gerard et al. 2003). However, in younger children (mean age 2 years) application of lidocaine gel to the 'genital mucosa' for only 2-3 minutes before the procedure and its subsequent use as a lubricant did not decrease pain (Vaughan et al. 2005). Techniques combining adequate preparation, local anaesthesia and psychological interventions are likely to be more effective (Stevens 2006).

Analgesia table 4.3.04

Bladder catheterisation and urine sampling in children

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical gel**	**1+***	
ENTONOX (50% Nitrous Oxide)			**1+**
Psychological Preparation		**1+**	
Psychological Intervention		**1+**	

*Applied 10 minutes before catheterisation.

4.3. 05 Nasogastric Tube Insertion

Nasogastric tube (NGT) insertion is a painful and distressing procedure frequently performed with little attention to pain relieving strategies(Juhl and Conners 2005). Infants who are unwell and unable to feed, particularly those with respiratory problems such as bronchiolitis, may need to be 'tube fed' for a short period. Nasogastric tubes are often maintained in the postoperative period and may need to be re-inserted if they become displaced. Older children may also be fed via NGT e.g. in cystic fibrosis patients who sometimes require supplementary feeding on multiple occasions. Clearly it is particularly important to optimise pain management in those patients who are likely to need repeated NGT placement.

Passing a NGT is a skilled procedure and in the UK, the Department of Health have published guidelines (CMO Update no.39, publ DoH, UK), which should be followed. See also sections 4.0, 4.2 and 4.3 for advice on the general management of painful procedures in neonates, infants and children.

Good Practice Point

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.

Evidence

NGT insertion has been little studied in children. In the adult, topical local anaesthesia and lubricants have been shown to reduce pain and facilitate placement (Singer and Konia 1999; Wolfe et al. 2000; Ozucelik et al. 2005). 10% nebulised lidocaine is effective but may also slightly increase the incidence of epistaxis (Cullen et al. 2004). The additional use of vasoconstrictors such as topical phenylephrine or cocaine may reduce this risk. These findings have not been confirmed in children. Indirect evidence also suggests that the use of psychological/ behavioural

techniques may be of benefit in older children, and that sucrose, sucking or other techniques might reduce pain responses in neonates.

Analgesia table 4.3.05 Nasogastric tube insertion

	Direct evidence	Indirect evidence
Topical Local Anaesthesia (LA)		**1++**
Sucrose		**1++***
Non nutritive sucking		**1+***
Tactile stimulation		**1+ ***
Psychological Preparation		**1+**
Psychological Intervention		**1+**

* Neonates

4.3.06 Immunization and Intramuscular Injection

Immunisation schedules result in increasing numbers of intramuscular injections being administered to infants and children. At 2, 3 months infants are offered Diptheria, Tetanus, Pertussis, Haemophilus (Hib) and Polio immunisation as one vaccination, with a separate Meningococcal or Pneumococcal vaccine. All 3 are given at 4 months. Children receive further immunisations at one year and 15 months, again at pre-school and finally at school leaving. Intramuscular administration of asparaginase to children with leukaemia, and long acting penicillin therapy are other examples. The pain of these injections is widely acknowledged and contributes to anxiety in patients and their parents/carers, particularly regarding vaccinations. There is now evidence that such pain may be reduced by a number of strategies. Knowledge that practitioners have considered the use of these strategies may help parents in their decisions about immunisation. It is important that treatable pain is not a barrier to the childhood immunisation programme.

See also sections 4.0, 4.2 and 4.3 on the general management of procedural pain.

Good Practice Point

Intramuscular injections should be avoided in children as part of routine care. If intramuscular injection is unavoidable, pharmacological and non-pharmacological strategies should be employed to reduce pain.

Swaddling, breast feeding or pacifier, and sucrose should be considered in infants undergoing vaccination.

Recommendations

Psychological strategies such as distraction should be used for infants and children undergoing vaccination: Grade A

(Cohen et al. 1999; Cohen et al. 2006; Uman et al. 2006)

Consider additional procedure modifications such as vaccine formulation, needle size, depth of injection (25mm 25 gauge needle) or the use of vapocoolant spay: Grade A

(Cohen Reis and Holubkov 1997; Mark et al. 1999; Ipp P 2004; Wood C 2004; Scheifele DW 2005; Diggle et al. 2006)

Topical local anaesthesia may reduce immunisation pain in infants and older children in some circumstances, but there is insufficient evidence to recommend routine use: Grade B

(Taddio et al. 1994; Cassidy et al. 2001; Lindh 2003; O'Brien L. Taddio A 2004)

Evidence

There are 2 phases of immunisation pain: the initial pain of the needle piercing the skin and injection of a volume of vaccine into the muscle or subcutaneous tissue, followed by a later phase of soreness and swelling at the vaccination site due to subsequent inflammatory reaction. Studies have generally investigated strategies designed to deal with the former, presumably because this is perceived to be the most unpleasant component. Children typically dread needle related pain; the use of either non-pharmacological or pharmacological pain reduction strategies may reduce subsequent negative recall (Cohen et al. 2006). There is good evidence that non-pharmacological methods, particularly distraction, can reduce immunisation pain, indeed, they may be as effective as pharmacological analgesia (Cohen Reis and Holubkov 1997; Cohen et al. 1999; Cohen et al. 2006; Uman et al. 2006). There is also evidence of benefit from non-pharmacological strategies in infants, including swaddling, non-nutritive sucking and sucrose but further study is required, especially to clarify the effectiveness of sucrose in older infants (Lewindon et al. 1998; Reis EC 2003). See section 6.7 for information on the use of sucrose.

Procedure modifications may alter pain responses. Some combined vaccine formulations (MMR-Priorix, lower dose DTP vaccine booster Tdap) appear to be less painful, and this requires further study (Ipp et al. 2004; Scheifele DW 2005; Ipp et al. 2006). Longer (25mm) needles and deeper intramuscular rather than subcutaneous injection can reduce local reactivity following immunisation (Mark et al. 1999; Diggle et al. 2006). Swab applied vapocoolant (Fluori-methane) was as effective as topical analgesia when both were combined with distraction (Cohen Reis and Holubkov 1997).

Topical local anaesthesia (EMLA, AMETOP) is clearly capable of reducing components of vaccination pain in both infants and older children but the

efficacy, and the balance of effectiveness against cost is difficult to determine from the studies presently available (Taddio et al. 1994; Cassidy et al. 2001; Lindh 2003; O'Brien L. Taddio A 2004). Lidocaine local anaesthesia added to asparaginase or benzyl penicillin injection reduced the pain response in two studies, again this approach requires further investigation (Amir et al. 1998; Albertsen et al. 2005).

Analgesia table 4.3.06 Immunisation and intramuscular injection

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical**	**1+**	
Sucrose		**1-**	
Psychological Interventions		**1++**	
Psychological Preparation			**1+**
Procedure Modifications		**1+**	

4.3.07 Repair of Lacerations In Children

Traumatic lacerations of the skin and scalp are common presentations in the emergency department. Acceptable, safe and effective repair is often a considerable challenge, general anaesthesia or sedation may be necessary (see section 4.0). For minor lacerations without general anaesthesia or sedation a combination of pharmacological and non-pharmacological techniques are likely to be most effective. There are a number of less painful alternatives to simple wound suture in the awake patient: tissue adhesives in simple low-tension wounds, and the Hair Apposition Technique (HAT) in scalp lacerations are examples.

Also see section 4.0 and 4.3 for general considerations in procedural pain management.

Good Practice Point

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 (steri-strips): Grade A
(Barnett et al. 1998; Farion et al. 2003; Zempsky et al. 2004)

If sutures are needed, topical anaesthetic preparations e.g. LAT (lidocaine-adrenaline-tetracaine) if available, can be used in preference to injected lidocaine, as they are less painful to apply and are equi-analgesic; it is not necessary to use a preparation containing cocaine: Grade A
(Ernst et al. 1997; Smith et al. 1998; White et al. 2004; Eidelman et al. 2005a)

Buffering injected lidocaine with sodium bicarbonate should be considered: Grade A
(Davies 2003)

'HAT' (hair apposition technique) should be considered for scalp lacerations. It is less painful than suturing, doesn't require shaving and produces a similar outcome: Grade B
(Hock et al. 2002)

If injected lidocaine is used, pre-treatment of the wound with a topical anaesthetic preparation e.g. lidocaine-adrenaline-tetracaine (LAT) gel reduces the pain of subsequent injection: Grade B
(Singer and Stark 2000; 2001)

50% nitrous oxide reduces pain and anxiety during laceration repair: Grade B
(Burton et al. 1998; Luhmann et al. 2001)

Evidence

Laceration repair has been relatively well studied in children. There a number of alternatives to simple wound suture in the awake patient. Tissue adhesives in simple low-tension wounds, and the Hair Apposition Technique (HAT) in scalp lacerations are less painful alternatives (Hock et al. 2002; Farion et al. 2003). A number of topical local anaesthetic mixtures are available; they can give equivalent analgesia to infiltrated local anaesthetic and are less painful to apply (Eidelman et al. 2005a). A systematic review including trials in adults and children found that 'buffering' local anaesthetics with sodium bicarbonate significantly reduces the pain of injection (Davies 2003). Nitrous oxide has been shown to be effective in reducing pain, anxiety and distress in cooperative children (Burton et al. 1998; Luhmann et al. 2001). See section 6.6 for information on the use of nitrous oxide. Psychological techniques such as distraction and relaxation are also likely to be useful (Uman et al. 2006).

Analgesia table 4.3.07 Repair of lacerations in children

		Direct evidence	Indirect evidence
Local Anaesthesia	**Topical**	**1++**	
	Infiltration	**1++**	
	Buffered infiltration	**1++**	
ENTONOX (50% Nitrous Oxide)		**1+**	
Procedure Modification		**1++**	
Psychological Intervention			**1++**

4.3.08 Dressing Changes in the Burned Child

Children with burns often require repeated, often extremely painful dressing changes. Children with severe burns are normally cared for in a specialist unit but some children will be seen in Emergency Departments. Initial dressing changes are likely to be performed under general anaesthesia, and if children remain very distressed this option may be favoured for subsequent procedures. Sedation is sometimes used to supplement analgesia for burns dressings (see SiGN guideline 58 available at: http://www.sign.ac.uk). In the early stages of burn pain management children may require continuous infusion of potent opioids such as morphine, additional analgesia will be required prior to dressing changes (Henry and Foster 2000).

Both pharmacological and non-pharmacological techniques should be used in the management of painful dressing changes, see section 4.0, 4.2 and 4.3 for advice on the general management of painful procedures.

Recommendations

Potent opioid analgesia given by oral, transmucosal or nasal routes according to patient preference and availability of suitable preparations should be considered for dressing changes in burned children: Grade A
(Sharar et al. 1998; Sharar et al. 2002; Robert et al. 2003; Borland et al. 2005)

Non-pharmacological therapies such as distraction, relaxation and massage should be considered as part of pain management for dressing changes in burned children: Grade B
(Fratianne et al. 2001; Hernandez-Reif et al. 2001; Das et al. 2005)

Evidence

The evidence base for managing burn pain in children is small and incomplete. Opioids are used extensively, and should be given as necessary by intravenous or other routes (Henry and Foster 2000). There are a number of small studies comparing different opioid formulations and routes of administration, such as transmucosal or intranasal fentanyl and hydromorphone, oxycodone morphine by the oral route (Sharar et al. 1998; Sharar et al. 2002; Robert et al. 2003; Borland et al. 2005). Nitrous oxide is used extensively for single painful procedures in children who are able to co-operate, but has not been specifically investigated for multiple or frequent administration or directly in this patient group. See section 6.6 for more information on the use of nitrous oxide.

Analgesia table 4.3.08 Dressing changes in burned child

	Direct evidence	Indirect evidence
Opioids	**1++**	
ENTONOX (Nitrous Oxide)		**1++***
Psychological Preparation		**1+**
Psychological Intervention	**1+**	

*No data for multiple administrations

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Section 5 POSTOPERATIVE PAIN

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5.1 General Principles of Postoperative Pain Management

Postoperative analgesia should be planned and organised *prior to surgery* in consultation with patients and their families or carers, and other members of the perioperative team. The paediatric anaesthetist is responsible for initiating suitable postoperative analgesia; this should be considered to be part of the overall plan of anaesthesia. Patients should not be discharged from the Postoperative Care Unit (Postanaesthesia Recovery Area) until satisfactory pain control is established and ongoing analgesia is available.

Postoperative care is frequently shared between heath professionals from different disciplines: they should be suitably qualified including an awareness of the general principles of pain assessment and pain management in children.

Prior to discharge from the hospital, patients and their families should be given clearly presented information and advice regarding the assessment of pain and the administration of analgesia at home. It is also necessary to ensure that the patient will have access to suitable analgesia.

Analgesia

Analgesia is an integral part of surgical anaesthesia and therefore potent analgesics are administered during general anaesthesia in the form of opioids, local anaesthetics and other drugs. Patients and carers should be aware that the effects of these analgesics will wear off in the postoperative period, leading to an increase in pain and the need for further analgesia.

Pain after surgery is usually most severe in the first 24-72 hours but may persist for several days or weeks. Analgesia can be given regularly (by the clock) in the early postoperative period and then ‘as required’ according to assessed pain. Drugs to counteract unwanted effects of analgesia or other side effects of surgery such as PONV should also be available and administered when necessary.

Postoperative pain should be assessed frequently: see section 3.0 for further information. Analgesic regimens should be sufficiently flexible to allow for inter-individual differences in the response to analgesics and the variation in the requirement for pain relief that occurs during the postoperative period.

Combinations of analgesics should be used unless there are specific contra-indications, for example; opioids, local anaesthetics, NSAIDs and paracetamol can be given in conjunction, not exceeding maximum recommended doses.

Good Practice Points

Paediatric anaesthetists are responsible for initiating postoperative analgesia. They should liaise with patients and their families/carers, surgeons and other members of the team providing postoperative care in order to ensure that pain is assessed and suitable ongoing analgesia is administered.

Postoperative analgesia should be appropriate to developmental age, surgical procedure and clinical setting in order to provide safe, sufficiently potent and flexible pain relief with a low incidence of side effects.

Providers of postoperative care should understand the general principles of good pain management in children; this includes knowledge of assessment techniques and the use of analgesics at different developmental ages.

5.2 ENT surgery

5.2.01 Myringotomy

Drainage of the middle ear, usually with insertion of a tube is a treatment for otitis media. Myringotomy is usually considered to be a minor procedure, undertaken on a daycase basis. See also section 5.1 for the general principles of postoperative pain management.

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 minutes preoperatively can achieve adequate early postoperative analgesia: Grade B
(Ragg and Davidson 1997; Tay and Tan 2002)

Ketorolac can provide satisfactory analgesia: Grade B
(Watcha et al. 1992; Bean-Lijewski and Stinson 1997)

Opioids are effective but not recommended for routine use because of increased side-effects compared with minor analgesics: Grade B
(Tobias et al. 1995; Ragg and Davidson 1997; Bennie et al. 1998; Galinkin et al. 2000; Pappas et al. 2003)

Evidence

Paracetamol and the NSADs have been most studied for post-myringotomy pain, but combined therapy has not been sufficiently investigated.

Paracetamol produces dose-related analgesia; 10mg/kg is no better than placebo (Watcha et al. 1992) or is associated with higher supplemental requirements (Pappas et al. 2003); whereas pain scores are low with 15-20mg/kg (Tobias et al. 1995; Bean-Lijewski and Stinson 1997; Ragg and Davidson 1997; Bolton et al. 2002; Tay and Tan 2002).

Ibuprofen and diclofenac appear to provide similar analgesia to paracetamol (Bennie et al. 1997; Tay and Tan 2002) but the combination has not been tested.

Ketorolac 1mg/kg provides minor improvements in analgesia when compared with low doses of paracetamol, 10mg/kg (Watcha et al. 1992; Pappas et al. 2003); paracetamol 10mg/kg + codeine 1mg/kg (Pappas et al. 2003); paracetamol 15mg/kg (but only first 10 minutes there was no difference at 20 minutes)(Bean-Lijewski and Stinson 1997).

Opioids e.g. codeine, butorphanol or fentanyl, have been associated with increased side-effects without clinically significant improvements in analgesia, therefore their use is not warranted for routine myringotomy:

i) increased sedation and time to discharge (oral codeine: (Ragg and Davidson 1997); nasal fentanyl(Galinkin et al. 2000); nasal butorphanol(Bennie et al. 1998)
ii) increased vomiting with oral codeine or nasal butorphanol (Pappas et al. 2003))

Analgesia table 5.2.01

	Direct evidence
Opioid*	**1-**
NSAID	**1-**
Paracetamol	**1-**

* not routinely recommended due to side effects: see text

5.2.02 Tonsillectomy

Tonsillectomy (±adenoidectomy) is one of the most common procedures performed in children. Chronic or recurrent tonsillitis with tonsillar hyperplasia leading to upper airway obstuction e.g. in sleep apnoea syndromes, is the most frequent indication for tonsillectomy. The choice of analgesia, postoperative monitoring and duration of hospital admission is influenced by the potential for serious complications such as apnoea, perioperative bleeding and postoperative nausea and vomiting (PONV). Pain after tonsillectomy can persist for many days, the use of intraoperative local anasthesia infiltration and NSAID have been controversial. See also section 5.1 for the general management of postoperative pain.

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: Grade A
(Hamunen and Kontinen 2005)

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: Grade B
(Giannoni et al. 2001; Kaygusuz and Susaman 2003; Somdas et al. 2004; Naja et al. 2005a)

Tramadol can produce similar analgesia to morphine or pethidine: Grade B
(Ozer et al. 2003; Umuroglu et al. 2004; Ozalevli et al. 2005)

Intraoperative intravenous (IV) ketamine does not provide significant postoperative advantage compared with opioid: Grade B
(Elhakim et al. 2003; O'Flaherty and Lin 2003; Ozer et al. 2003; Umuroglu et al. 2004)

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 PONV: Grade C.
(White and Nolan 2005; Ewah et al. 2006)

Evidence

Significant levels of pain, behavioural disturbance, sleep disruption and altered activity can persist for 5-8 days following tonsillectomy (Warnock and Lander 1998; Giannoni et al. 2001; Park et al. 2004; Owczarzak and Haddad 2006). Regular administration of paracetamol and NSAID is necessary for several days postoperatively, and adequate parental education about pain assessment and medication use is required.

A meta-analysis conducted in 2000 was unable to confirm benefits of **local anaesthesia infiltration**, but only six RCTs were suitable for inclusion (Hollis et al. 2000). There are conflicting results of local anaesthetic efficacy in subsequent studies. Both ropivacaine and bupivacaine injected in the tonsillar fossa reduced pain scores and supplemental analgesia for 24 hours postoperatively and increased the time to first rescue analgesia(Akoglu et al. 2006). Tonsillar fossa local anaesthetic injection reduced VAS, improved oral intake and reduced referred ear pain (Giannoni et al. 2001; Kaygusuz and Susaman 2003; Somdas et al. 2004; Naja et al. 2005a) but no difference in early VAS or time to oral intake has also been reported (Park et al. 2004). Only minor improvements in pain scores and time to oral intake have been shown with LA soaked swabs in the tonsillar fossa post tonsil removal(Hung et al. 2002).

Opioids: Tramadol produces similar analgesia and side-effects to **pethidine** (Ozer et al. 2003) and **morphine** (Hullett et al. 2006). One study reported less nausea with tramadol than morphine (Ozalevli et al. 2005). In patients with sleep apnoea tramadol was associated with fewer episodes of oxygen desaturation at one time point postoperatively (1-2hrs, no difference at earlier or later time points to 6 hrs) (Hullett et al. 2006). In other studies tramadol was less effective than ketoprofen (higher pain scores and higher postoperative PCA fentanyl) and did not differ from placebo (Antila et al. 2006).

Ketamine improves analgesia when compared with placebo (Elhakim et al. 2003; Da Conceicao et al. 2006) but provides no advantage when compared with equianalgesic opioid (Umuroglu et al. 2004) and may increase side-effects (O'Flaherty and Lin 2003)

NSAIDs improve analgesia when compared with placebo (10/11 studies), and provide similar analgesia to opioids (7/8 studies) and paracetamol (3/3 studies) (Moiniche et al. 2003). A systematic review of paediatric studies stated that heterogeneity of the data precluded meta-analysis, and many studies comparing two active treatments were not sensitive enough to show a difference(Hamunen and Kontinen 2005). Subsequent studies have reported similar analgesia with ketorolac and fentanyl (Keidan et al. 2004),

no improvement with addition of rofecoxib to opioid and paracetamol (Sheeran et al. 2004), and no difference in pain scores but increased rescue analgesic requirements with IV paracetamol compared with pethidine (Alhashemi and Daghistani 2006); and improved analgesia in the first 6 hours when comparing ketoprofen with tramadol and placebo (Antila et al. 2006).

Most meta-analyses of post-tonsillectomy analgesia have focussed on **PONV** and **bleeding** rather than analgesic efficacy. PONV following tonsillectomy is reduced by NSAID presumably due to a reduction in opioid requirement (Moiniche et al. 2003; Cardwell et al. 2005), and by intraoperative dexamethasone (Steward et al. 2003). As post-tonsillectomy bleeding is relatively rare, meta-analyses have included different trials and reached different conclusions:

1. Bleeding is increased by aspirin but not ibuprofen or diclofenac (7 trials) (Krishna et al 2003).
2. Risk of bleeding and reoperation increased (NNH 29), and NSAIDs should not be used (7 trials) (Marret et al. 2003)
3. Risk of reoperation (NNH 60) but not bleeding increased, and NSAIDs should be used cautiously (25 trials) (Moiniche et al. 2003)
4. NSAIDs do not increase risk of bleeding or reoperation but further studies required (13 paediatric trials) (Cardwell et al. 2005).

Although meta-analyses are currently inconclusive, perioperative diclofenac and ibuprofen appear to be associated with minimal risk of post-tonsillectomy bleeding. Early studies using high doses of ketorolac have been included in the meta-analyses, but there is insufficient data to assess the risks associated with different NSAIDs.

Paracetamol is more effective given orally prior to surgery than rectally after induction of anaesthesia and reduces opioid requirements and PONV (Anderson et al. 1996; Anderson et al. 1999; Anderson et al. 2000).

Analgesia table 5.2.02

Agent	Technique	Direct evidence
LA*	**Tonsillar fossa injection**	**1- ****
	Topical	**1- *****
Opioid		**1+**
	Tramadol	**1-**
Ketamine		**1-**
NSAIDs[§]		**1+**
Paracetamol		**1+**

*There are no direct comparisons of different local anaesthetic techniques, and no standardisation of dose or technique (pre vs post-incision; topical vs injection; site of injection)

**Although statistically significant, the degree of improvement is small, and some studies fail to find benefit. There is insufficient data to compare pre- or post-operative injection. Studies with follow-up for several days are more likely to show benefit.

***One study shows statistically significant improvement in pain score and time to oral intake but differences are small and of limited clinical significance.

5.2.03 Mastoid and Middle Ear Surgery

Mastoidectomy may be performed to remove infected tissue or cholesteatoma. As the incidence of chronic suppurative otitis media is declining, this surgery is now less frequently required. Middle ear surgery, such as reconstruction of a damaged tympanic membrane by placement of surgical grafts, may be associated with significant PONV. See also section 5.1 for the general management of postoperative pain.

Recommendations

Great auricular nerve block can provide similar analgesia and reduced PONV compared with morphine. Pre-incision timing of the block confers no additional benefit: Grade B
(Suresh et al. 2002)

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: Grade C
(Hasan et al. 2004)

Evidence

There are relatively few controlled trials specifically investigating pain during and after mastoidectomy and invasive middle ear surgery. As NSAIDs and paracetamol improve analgesia for middle ear procedures there is indirect evidence that they provide beneficial supplemental analgesia for mastoid surgery. In procedures that require a postauricular incision, LA block of the great auricular nerve can provide similar analgesia and reduced PONV compared with morphine (Suresh et al. 2002). No difference was found between performing the block pre-incision versus prior to the end of surgery (Suresh et al. 2004).

Analgesia table 5.2.03

Agent	Technique	Direct evidence	Indirect evidence
LA	Greater auricular nerve block	1-	
Opioid		1-	
NSAID			1-
Paracetamol			1-

5.3 Opthalmology

5.3.01 Strabismus surgery

Strabismus surgery (correction of squint) is associated with a high incidence of PONV, and intraoperative tension on ocular muscles may provoke a vagal response (oculocardiac reflex). See also section 5.1 for the general management of postoperative pain.

Recommendations

Intraoperative LA blocks (subtenon or peribulbar) reduce PONV and may improve perioperative analgesia in comparison with IV opioid: Grade B
(Deb et al. 2001; Sheard et al. 2004; Chhabra et al. 2005; Steib et al. 2005)

Topical NSAIDs do not improve pain scores or postoperative analgesic requirements when compared with topical LA or placebo: Grade B
(Morton et al. 1997; Bridge et al. 2000; Kim et al. 2003)

Intraoperative opioid and NSAID provide similar postoperative analgesia but opioid use is associated with increased PONV: Grade B
(Mendel et al. 1995; Kokki et al. 1999; Shende and Das 1999; Wennstrom and Reinsfelt 2002)

Evidence
In many trials, reduction of PONV rather than improvement in analgesia has been the primary outcome. The duration of surgery varies from 25 to 80 minutes in the reported studies, and many do not discriminate between unilateral or bilateral surgery or procedures involving single or multiple muscles. This may contribute to the variability across studies in the incidence of side-effects and analgesic requirements.

Peribulbar or **subtenon LA blocks** reduce intraoperative oculocardiac reflex responses (Deb et al. 2001; Chhabra et al. 2005; Steib et al. 2005) and PONV (Deb et al. 2001; Chhabra et al. 2005; Steib et al. 2005) when compared with intraoperative opioid. Peribulbar or subtenon blocks reduce perioperative analgesic requirements when compared with opioid in some (Deb et al. 2001; Steib et al. 2005) but not all (Sheard et al. 2004; Chhabra et al. 2005) trials. No complications of LA injections were reported in these studies but patient numbers are small.

No difference in postoperative pain scores or analgesic requirement has been detected between **topical LA** drops and **topical NSAIDs** (Morton et al. 1997; Kim et al. 2003).

Pain scores (CHEOPS) were not reduced by topical NSAIDs when compared with placebo (Kim et al. 2003; Bridge et al. 2000) but the authors questioned the sensitivity of this measure for ocular pain.
Direct comparisons of intraoperative **NSAID** and **opioid** (PR diclofenac vs IV morphine) (Wennstrom and Reinsfelt 2002); (IV ketorolac vs IV pethidine) (Shende and Das 1999) ; (IV ketorolac vs IV fentanyl) (Mendel et al. 1995) have reported no difference in postoperative pain scores or supplemental analgesic requirements but increases in PONV in patients given opioids. Comparison of intraoperative remifentanil and fentanyl reported higher early pain scores but less PONV with remifentanil (Eltzschig et al. 2002).

Comparisons of NSAID and placebo have shown minor improvements in pain score and reductions in supplemental analgesic requirements (Mikawa et al. 1997; Kokki et al. 1999).

Analgesia table 5.3.01

Agent	Technique	Direct Evidence	Indirect Evidence
LA	**Subtenon block**	**1-***	
LA	**Peribulbar**	**1-***	
LA	**Topical**	**1-***	
Opioid		**1-*****	
NSAID	**topical**	**1-****	
	systemic	**1-*****	
Paracetamol			**1-********

* no direct comparisons of different local anaesthetic techniques
** no difference confirmed between topical LA, topical NSAID or placebo
*** similar analgesia with systemic NSAID and opioid but increased PONV with opioid
****oral or rectal paracetamol given as part of multimodal analgesia to all patients in several trials but efficacy not directly compared with other agents.

5.3.02 Vitreoretinal surgery

Vitreoretinal and retinal detachment surgery are associated with significant postoperative pain and PONV, but there have been relatively few controlled trials of analgesia in children. Supplemental local anaesthetic techniques may have a role but this has not been fully evaluated. See also section 5.1 for the general management of postoperative pain.

Recommendations

NSAID can provide similar analgesia but lower rates of PONV compared with opioid: Grade C
(Subramaniam et al. 2003a)

Peribulbar block improves analgesia and reduces PONV compared with opioid: Grade C
(Deb et al. 2001; Subramaniam et al. 2003b)

Evidence

Ketoprofen and **pethidine** provided similar levels of analgesia (Subramaniam et al. 2003a). Although some advantages of **peribulbar LA block** have been shown, the studies have all been performed by the same group (Deb et al. 2001; Subramaniam et al. 2003b). Concerns have been expressed that peribulbar block represents a higher risk in children than **subtenon block** (as the eye occupies a greater volume of the bony orbit in child, and large volumes of LA were used in trials of peribulbar block). (Parulekar et al. 2002). There has been no evaluation of the risk vs. benefit of these procedures in children

Analgesia table 5.3.02

Agent	Technique	Direct evidence	Indirect evidence
LA	**Peribulbar block***	**2+**	
	Subtenon block		**1-**
Opioid		**1-**	
NSAID		**1-**	
Paracetamol			**1-**

*No analysis of risk-benefit for peribulbar block

5.4 Dental Procedures

Dental procedures in children may range from minor restoration and conservation requiring little or no postoperative analgesia, to variable numbers of extractions, and sometimes more extensive surgery leading to significant postoperative pain. See also section 5.1 for the general management of postoperative pain.

Good practice point

NSAIDs can provide adequate analgesia for dental extractions

Recommendations

Swabs soaked with bupivacaine on exposed tooth sockets following extraction produce no or minor improvements in pain in the immediate postoperative period: Grade B
(Greengrass et al. 1998; Andrzejowski and Lamb 2002; Gazal et al. 2004)

Intraoperative LA infiltration reduces postoperative pain following dental extractions: Grade C
(Anand et al. 2005)

Evidence

There are few controlled trials following dental surgery in children. In a cohort study, which included a range of dental procedures (restorations in 30%, extractions in 60%, surgical procedures in 54%), intraoperative diclofenac, codeine, paracetamol and local anaesthetic resulted in 50% of patients being pain free in the recovery room. The degree of postoperative pain correlated with the number of dental procedures performed, and moderate to severe pain persisted for at least 36 hours in 37% of patients (Atan et al. 2004).

Comparisons of **opioid** and **NSAID** for extractions have shown no difference in analgesia (Littlejohn et al. 1996; Purday et al. 1996) but opioids may produce increased PONV (Purday et al. 1996).

The role of intraoperative **local anaesthetic blocks** requires further evaluation. **LA infiltration** appears to reduce pain following extractions (Anand et al. 2005), although no difference in pain scores or in the proportion of children experiencing severe pain was found when comparing intraoperative infiltration of lignocaine or saline (Coulthard et al. 2006). LA soaked swabs placed in tooth sockets following extraction may improve early analgesia (Greengrass et al. 1998). No additional improvements in analgesia or

distress were found when LA swabs were added to paracetamol 15mg/kg (Gazal et al. 2004) or diclofenac (Andrzejowski and Lamb 2002).

Analgesia table 5.4

Agent	Technique	Direct Evidence
LA	**Local infiltration**	**2+***
	Soaked swabs	**1-****
Opioid		**1-**
NSAID		**1-**
Paracetamol		**1-**

* no difference in VAS but more children rated pain as "better" with LA
** all children received NSAID or paracetamol

5.5 General Surgery and Urology (Minor and Intermediate)

5.5.01 Subumbilical Surgery

This category has been included because many studies have used a combination of different surgical procedures from the subumbilical area as the operative model e.g. repair of inguinal hernia, orchidopexy, circumcision, phimosis, hypospadias, hydrocoele, vesico-ureteric reflux. Postoperative pain is unlikely to be equivalent following each of these different procedures (Ho and Keneally 2000), but they are not uniformly distributed between studies and the numbers of individual procedures in each study are often low, thereby making it impractical to look at each procedure in isolation. Refer to other pages in this section for more information on specific procedures, see also section 5.1 for the general management of postoperative pain.

Recommendations

LA wound infiltration, ilio-inguinal nerve block and caudal analgesia are effective in the early postoperative period following subumbilical surgery: Grade A
(Anatol et al. 1997; Ivani et al. 2002a; Ivani et al. 2002b; Suraseranivongse et al. 2003; Ivani et al. 2005)

Evidence

The majority of studies compared differing drug combinations in central or peripheral nerve blockade. **Caudal block** was the most commonly studied technique and demonstrated good efficacy in all studies with a low failure and serious complication rate. This is in agreement with a large case series of this technique (Giaufre et al. 1996). Efficacy was equivalent irrespective of the local anaesthetic agent used and there was little difference in the rate of side-effects (Ivani et al. 2002b; Breschan et al. 2005; Ivani et al. 2005). The optimal concentration and volume of LA has not been elucidated, but concentrations of levobupivacaine and ropivacaine below 0.2% have been associated with decreased efficacy in some studies (Bosenberg et al. 2002; Ivani et al. 2003).
Neuraxial analgesia: with LA: the addition of caudal S-ketamine, neostigmine, clonidine, midazolam, buprenorphine and morphine all increased analgesic efficacy and prolonged the duration of the block, with little reported increase in side-effects in most studies (Gulec et al. 1998; Ivani et al. 2000; Khan et al. 2002; Ansermino et al. 2003; Turan et al. 2003; Weber and Wulf 2003; Bano et al. 2004; Martindale et al. 2004). S-ketamine and buprenorphine were more effective when given by the caudal route compared with the intravenous route (Khan et al. 2002; Martindale et al. 2004). In direct

comparisons either caudal clonidine or midazolam were better than morphine (Gulec et al. 1998; Luz et al. 1999).
Without LA: a combination of S-ketamine and clonidine demonstrated better analgesic efficacy than S-ketamine alone via the caudal route (Passariello et al. 2004). The use of such adjunctive analgesia requires further research to better identify safety profile, risk-benefit and dose; see also section 6.0 for a further discussion of neuraxial analgesia.

Ilio-inguinal nerve block was shown to be effective, but overall efficacy was generally lower than in studies of caudal block (Anatol et al. 1997; Dalens et al. 2001). The use of ultrasound to place the ilioinguinal block improved the quality of the block, decreased supplementary opioid use and decreased the amount of local anaesthetic used (Willschke et al. 2005). No benefit was seen from adding clonidine to the local anaesthetic in ilio-inguinal nerve block (Ivani et al. 2002a; Kaabachi et al. 2005).

Wound infiltration was equivalent to ilio-inguinal block with no further benefit from using them in combination. (Anatol et al. 1997; Suraseranivongse et al. 2003).

Analgesia table 5.5.01 Subumbilical Surgery

Agent	Technique	Direct evidence	Indirect evidence
LA	**Wound infiltration***	**1+**	
LA	**Ilio-inguinal nerve block***	**1+**	
LA	**Caudal epidural**	**1+**	
LA+ Ketamine	**Caudal epidural**	**1+**	
LA+ Clonidine	**Caudal epidural**	**1+**	
Opioid**			**1+**

NSAID**	**1+**
Paracetamol**	**1+**

* possibly lower efficacy than caudal block: more studies are required.
** as part of a multi-modal technique

5.5.02 Circumcision

Circumcision is regarded as a relatively minor surgical procedure but it may be associated with significant postoperative pain and distress. It is usually undertaken on an out-patient or day case basis. Circumcision in the neonate is considered separately in section 5.5.03. See sections 5.1 for the general management of postoperative pain and 5.5.01 for a discussion of subumbilical surgery.

Recommendations

Caudal epidural and dorsal nerve block are effective in the early postoperative period, with low rates of complications and side-effects: Grade A
(Allan et al. 2003)

Techniques using opioid alone should be avoided if possible, due to lower efficacy and higher incidence of side effects in comparison with LA techniques: Grade A
(Allan et al. 2003)

Evidence

Local anaesthetic techniques involving a regional block or topical application can provide good analgesic efficacy in the early postoperative period (McGowan et al. 1998; Allan et al. 2003; Matsota and Papageorgiou-Brousta 2004). This approach can decrease postoperative nausea and vomiting by reducing the need for supplementary opioids (Allan et al. 2003).

Analgesia following **caudal** or **dorsal nerve block** was equivalent and was superior to subcutaneous 'ring' block (Irwin and Cheng 1996; Holder et al. 1997; Allan et al. 2003; Gauntlett 2003; Weksler et al. 2005). Caudal and dorsal nerve block demonstrated a low failure and serious complication rate in all studies. This is in agreement with larger case series of both techniques (Giaufre et al. 1996; Soh et al. 2003). In some studies a caudal block reportedly increased the time to micturition and incidence of motor block compared with dorsal nerve block and subcutaneous ring block but this finding was not seen in other investigations (Irwin and Cheng 1996; Holder et al. 1997; Allan et al. 2003; Gauntlett 2003; Weksler et al. 2005). The ideal agent, dose or concentration for a caudal block has not been elucidated.

The use of **subcutaneous ring block** was associated with a higher failure and complication rate than caudal or dorsal nerve block (Irwin and Cheng 1996; Holder et al. 1997). One study compared **topical local anaesthesia** with dorsal nerve block for six hours postoperatively and showed no difference in analgesia between the two (Choi et al. 2003).

The use of adjuncts to LA e.g. clonidine, ketamine in caudal block for circumcision still requires further research to identify safety profile, risk-benefit and dose: they may decrease the need for supplementary analgesia, but there is insufficient evidence to compare benefits with risks (Lee and Sanders 2000; Sharpe et al. 2001).

The use of **opioid** is associated with lower analgesic efficacy and increased postoperative nausea and vomiting compared with LA techniques (Allan et al. 2003; Matsota and Papageorgiou-Brousta 2004).

NSAID (Diclofenac) as a sole agent was inferior to dorsal nerve block but the combination may decrease supplementary analgesic use compared with either technique in isolation (McGowan et al. 1998).

Analgesia table 5.5.02 Circumcision

Agent	Technique	Direct Evidence
LA	**Topical***	**1+**
LA	**Subcutaneous 'ring' block***	**1-**
LA	**Dorsal n. block**	**1+**
LA	**Caudal epidural**	**1+**
Opioid**		**1+**
NSAIDS**		**1+**
Paracetamol**		**1+**

* lower efficacy than caudal epidural or dorsal nerve block
**as part of a multi-modal technique

5.5.03 Neonatal Circumcision

Neonatal circumcision is considered separately from circumcision in older children due to differences in clinical practice and evidence base. Premature neonates can experience pain and therefore require good perioperative analgesia for surgical interventions. Many circumcisions are done in the *awake* neonate in the first few hours or days of life; this is reflected in the literature as studies have generally evaluated pain during the procedure. However, for neonatal circumcision no single technique has been shown to reliably alleviate pain in the awake patient, which therefore presents a clinical challenge. Circumcision in infants and older children is invariably performed under general anaesthesia (see section 5.5.01), the debate regarding the necessity for general anaesthesia in the neonate remains unresolved. See sections 5.1 for the general management of postoperative pain and 5.5.01 for a futher discussion of subumbilical surgery.

Good practice point

General anaesthesia should be considered for neonatal circumcision. A multi modal analgesic approach should include a local anaesthetic technique at the time of the procedure in combination with sucrose and paracetamol.

Recommendations

Local anaesthesia should be used as it is superior to other techniques for circumcision pain: Grade A
(Brady-Fryer et al. 2004)

Dorsal nerve block is more effective than subcutaneous ring block or topical LA: Grade A
(Brady-Fryer et al. 2004)

When using topical local anaesthetic it must be applied correctly and sufficient time allowed for it to become effective: Grade A
(Brady-Fryer et al. 2004)

Evidence

Post-operative pain after circumcision in the neonate has not been well investigated and available studies have all examined pain *during* the procedure in awake neonates. For all techniques studied there was a significant failure rate (Taeusch et al. 2002; Brady-Fryer et al. 2004). The use of local anaesthesia was superior to either placebo or simple

analgesics and sucrose (Brady-Fryer et al. 2004). **Dorsal nerve block** appears to be superior to **subcutaneous ring block** or **topical local anaesthesia** (caudal epidural analgesia has not been studied) and was associated with lower cortisol levels in one study, but was operator dependent and not totally reliable (Taeusch et al. 2002; Brady-Fryer et al. 2004). Efficacy of topical local anaesthetic agents was very dependent on the time allowed and success of application (Taddio et al. 1998; Brady-Fryer et al. 2004; Lehr et al. 2005).

No increased incidence of complications was seen in one technique compared with another (Brady-Fryer et al. 2004). The duration of surgery (and therefore intra operative pain) was dependent on the surgical technique with the 'Mogen Clamp' associated with faster procedures (Taeusch et al. 2002; Brady-Fryer et al. 2004).

Analgesia table 5.5.03 Neonatal Circumcision

Agent	Technique	Direct evidence	Indirect evidence
LA	**Topical**	**1++**	
LA	**Subcutaneous "ring' block**	**1++**	
LA	**Dorsal nerve block**	**1++**	
LA	**Caudal epidural**		**1+**
Paracetamol*			**1+**
Sucrose**			**1+**

* for post-procedure pain

** as part of multimodal technique

5.5.04 Hypospadias Repair

Hypospadias surgery may be either relatively superficial and minor, or more major reconstructive surgery involving the entire penile urethra may be undertaken which will influence postoperative analgesia requirements. Some procedures are suitable for day case surgery whilst others require hospital admission overnight or longer, with the possibility of prolonged urethral catheterisation and painful postoperative dressing changes. See sections 5.1 and 5.5.01 for the general management of postoperative pain and for a futher discussion of subumbilical surgery.

Recommendations

Caudal block is effective and reduces the need for postoperative supplementary opioid administration following hypospadias surgery: Grade A
(Prosser et al. 1997; Abdulatif and El-Sanabary 2002; Gunes et al. 2004a; Hansen et al. 2004; Mahajan et al. 2004)

Evidence

Caudal local anaesthesia was most commonly investigated for hypospadias repair. Good efficacy for the technique was demonstrated with a low failure and serious complication rate; this is in agreement with a large case series of this technique (Giaufre et al. 1996). Bupivacaine 0.25%, 0.5ml/kg was most frequently studied, but there were few comparisons with other local anaesthetics or between different concentrations or volumes. One study found that caudal ropivacaine 0.1%, 1.8ml/kg was more effective with less motor block than ropivacaine 0.375%, 0.5ml/kg (Silvani et al. 2006)

Neuraxial analgesics: i) With LA: the addition of neostigmine or diamorphine to caudal bupivacaine increased analgesic efficacy (Kelleher et al. 1996; Abdulatif and El-Sanabary 2002; Mahajan et al. 2004) but also increased the rate of nausea and vomiting in two of the studies (Kelleher et al. 1996; Abdulatif and El-Sanabary 2002). The addition of tramadol, clonidine or sufentinil showed no increase in efficacy (Prosser et al. 1997; De Mey et al. 2000; Hansen et al. 2004). Increasing the dose of clonidine by 100% (to 2mcg/kg) did not increase efficacy or side-effects if given either intravenously or caudally; this study did not use a plain local anaesthetic control (Hansen et al. 2004).

ii) Without LA: ketamine or mixture of ketamine/alfentanil was superior to alfentanil alone, and higher doses of neostigmine increased efficacy but also increased nausea and vomiting (Ozbek et al. 2002; Batra et al. 2003). In general the use of neuraxial analgesics has not been comprehensively studied, further research to identify safety profile, risk-benefit and dose are required (see also section 6.0). Only one study compared different techniques and showed that tramadol given by the caudal route

(alone) demonstrated better analgesic efficacy and less postoperative nausea and vomiting than when given by the intravenous route (Gunes et al. 2004a).

Epidural analgesia was shown to provide good analgesia both intra- and postoperatively irrespective of the local anaesthetic agent used: bupivacaine, levobupivacaine or ropivacaine ; there was an exclusion rate of 10% in one study (De Negri et al. 2004) and patients having an abdominal incision were included in another (Lerman et al. 2003).

An investigation of the timing of **dorsal nerve block** either pre or post surgery; found that placing the block pre surgery improved analgesic efficacy (Chhibber et al. 1997). The use of supplementary analgesia in studies was also low.

Paracetamol given alongside a caudal block showed no analgesic benefit in the first six postoperative hours compared with a caudal block alone in one study (Ozyuvaci et al. 2004). Overall, there is insufficient data to evaluate the use of supplementary analgesia in either the early or late postoperative period. In clinical practice, a multi-modal analgesic technique for this procedure with regular supplementary analgesia given in the postoperative period is suggested.

Analgesia table 5.5.04 Hypospadias Repair

Agent	Technique	Direct evidence	Indirect evidence
LA	**Dorsal n. block**	**1+**	
LA	**Caudal epidural**	**1+**	
LA	**Lumbar epidural**	**1+**	
LA+neostigmine*	**Caudal epidural**	**1+**	
LA+opioid*	**Caudal epidural**	**1+**	
Opioid**			**1+**
NSAID**			**1+**
Paracetamol**			**1+**

* small improvements in efficacy must be balanced against increased PONV
** as part of a multimodal technique

5.5.05 Orchidopexy

Orchidopexy usually involves surgical exploration of the inguinal region, dissection and traction of the spermatic cord and scrotal incision may also be required. Orchidopexy is generally performed on a day case basis. See sections 5.1 and 5.5.01 for the general management of postoperative pain and for a futher discussion of subumbilical surgery.

Recommendations

Caudal block is effective for orchidopexy in the early postoperative period, with low rates of complications and side-effects: Grade A
(Findlow et al. 1997; Somri et al. 2002; Verghese et al. 2002)

Evidence

There are few studies investigating analgesia for orchidopexy alone. Postoperative analgesia requirements may be greater than that required for inguinal hernia repair (Ho and Keneally 2000)
Caudal block using 1ml/kg of 0.125-0.25% bupivacaine showed good efficacy (Findlow et al. 1997; Somri et al. 2002; Verghese et al. 2002). In agreement with the findings of a large case series (Giaufre et al. 1996). It was associated with greater efficacy, less supplementary analgesic use and lower levels of stress hormones when compared with **ilioinguinal nerve block** plus **local infiltration** (Findlow et al. 1997; Somri et al. 2002). There was also no difference in complications (time to micturition, motor block or nausea and vomiting) between the two techniques (Findlow et al. 1997). Caudal block was also associated with a low failure and serious complication rate in all studies, again this is in agreement with a large case series (Giaufre et al. 1996). Bupivacaine was used in all the studies with good efficacy but it has not been compared with other local anaesthetic agents.

A higher volume of local anaesthetic (1mlkg) was associated with less response to cord traction but not with improved postoperative analgesia (Verghese et al. 2002).
Neuraxial analgesia: the addition of ketamine 0.25 - 1mg/kg as an adjunct to bupivacaine increased analgesic efficacy but was associated with ‘short -lived psychomotor effects’ at higher doses (Semple et al. 1996).

Analgesia table 5.5.05 Orchidopexy

Agent	Technique	Direct evidence	Indirect evidence
LA	**Wound infiltration***	**1+**	
LA	**Ilioinguinal Block***	**1+**	
LA	**Caudal Epidural**	**1+**	
Opioid**			**1+**
NSAID**			**1+**
Paracetamol**			**1+**

* less effective (in combination) than caudal block
** as part of a multi-modal technique

5.5.06 Inguinal Hernia Repair (Open)

Surgical repair of inguinal hernia is generally performed on a day case basis. The following refers to the conventional 'open' technique, rather than laparoscopic repair which is becoming more popular. See sections 5.1 and 5.5.01 for the general management of postoperative pain and for a futher discussion of subumbilical surgery.

Recommendations

LA wound infiltration, ilio-inguinal nerve block or caudal analgesia are effective in the early postoperative period: Grade A
(Machotta et al. 2003; Sakellaris et al. 2004; Kumar et al. 2005; Sasaoka et al. 2005; Naja et al. 2006)

Evidence

Caudal block was the most commonly studied technique with good efficacy and a low failure complication rate in all studies. This is in agreement with a large case series of this technique (Giaufre et al. 1996). Bupivacaine 0.25% was the most studied LA, and the concentration with which others were generally compared; ropivacaine 0.25% was found to be equivalent in one study (Koinig et al. 1999). Another study comparing different concentrations of bupivacaine with and without adjunctive opioid showed lower efficacy for 0.125% bupivacaine (Joshi et al. 1999). In a study of bupivacaine 0.175% (+adrenaline 1:10,000) there was no difference in efficacy or side-effects at volumes of between 0.7 and 1.3ml/kg (Schrock and Jones 2003).

Neuraxial analgesia: i) With LA; midazolam, ketamine, clonidine, fentanyl, neostigmine, adrenaline, morphine and tramadol have all been studied as adjuncts to local anaesthesia for caudal block. They all show good efficacy but evidence of overall benefit is equivocal as in most studies, few patients required further analgesia following caudal block with plain LA (Klimscha et al. 1998; Gaitini et al. 2000; Ozcengiz et al. 2001; Senel et al. 2001; Baris et al. 2003; Memis et al. 2003; Gunes et al. 2004b; Kumar et al. 2005). In studies where no comparison was made with plain LA: increasing the dose of ketamine also increased efficacy, but behavioural effects were seen at higher doses (Panjabi et al. 2004). Increasing clonidine dose from 1-2 microgm/kg had equivocal effects on efficacy, prolonging time to 1st analgesia in one study but not in another (Yildiz et al. 2006; Klimscha et al. 1998).

ii) Without LA: S(+) ketamine without local anaesthetic was equivalent to bupivacaine+adrenaline mixture, and S (+) ketamine+clonidine mixture (no local anaesthetic) showed increased efficacy over ketamine alone (Marhofer et al. 2000; Hager et al. 2002). Another study comparing the use of caudal with intramuscular S-ketamine showed increased efficacy in the caudal group (Koinig et al. 2000). Tramadol

without local anaesthetic showed reduced efficacy compared with plain bupivacaine or a bupivacaine+tramadol mixture (Senel et al. 2001).

Placement of the caudal block prior to surgery was also shown to have better efficacy in the postoperative period than placement at the end of surgery (Kundra et al. 1998).

Comparison of **paravertebral block** with intraoperative opioid (fentanyl) showed increased postoperative analgesic efficacy, patient satisfaction and earlier hospital discharge with the block (Naja et al. 2005b).

Ilioinguinal nerve block also shows good efficacy and safety, although a preferred agent, dose or volume has not been demonstrated (Lim et al. 2002; Tsuchiya et al. 2004; Sasaoka et al. 2005). No postoperative advantage was seen with adding **genitofemoral nerve block** or with using a 'double shot technique' (Lim et al. 2002; Sasaoka et al. 2005). In one study the success rate of the block was quoted as only 72% (Lim et al. 2002).

Wound infiltration is effective when compared to caudal block with plain LA or placebo, although in one study postoperative opioid use was comparatively high (Dahl et al. 1996; Machotta et al. 2003; Sakellaris et al. 2004). The timing of wound infiltration, either pre or post surgery, did not influence efficacy (Dahl et al. 1996; Sakellaris et al. 2004).

Analgesia table 5.5.06 Inguinal Hernia Repair (Open)

Agent	Technique	Direct Evidence	Indirect evidence
LA	**Wound infiltration**	**1+**	
LA	**Ilioinguinal Block**	**1+**	
LA	**Paravertebral Block**	**1-**	
LA	**Caudal Epidural**	**1+**	
Opioid**			**1+**

NSAID**	**1+**
Paracetamol**	**1+**

** as part of a multi-modal technique

5.6 General Surgery and Urology (Major)

5.6.01 Abdominal surgery

This group includes a heterogeneous mixture of abdominal procedures on the gastro-intestinal (GI) and genitourinary (GU) tracts including nephrectomy, pyeloplasty, ureteric reimplantation and cystoplasty for all of which a significant level of postoperative pain is expected. Intravenous opioid techniques or epidural analgesia are acceptable for postoperative pain; in clinical practice supplementary analgesia with NSAID and paracetamol is usually also administered.

Appendicectomy and fundoplication are considered separately in sections 5.6.02, 5.6.03 and laparoscopic techniques in section 5.7. See also section 5.1 for general management of postoperative pain.

Good Practice Point

Multimodal analgesia using parenteral opioids or epidural analgesia together with systemic NSAIDs and paracetamol should be used unless specifically contraindicated.

Recommendations

Intravenous opioids either as continuous infusion, NCA or PCA can be effective following major abdominal surgery: Grade A
(Bray et al. 1996; Peters et al. 1999; Monitto et al. 2000; van Dijk et al. 2002)

Epidural analgesia with LA is effective following major abdominal surgery. The addition of opioid or clonidine may further improve analgesia but side effects are also increased: Grade B
(Kart et al. 1997; Bosenberg 1998; Moriarty 1999; Bosenberg et al. 2003; Cucchiaro et al. 2003; Lerman et al. 2003).

Evidence

There is a considerable descriptive literature (pre-dating the time limits of this guideline 1996-2006) describing the use of opioid infusions, PCA, NCA and LA epidural infusion with or without opioid for major surgery such that these techniques have become part of everyday practice. For suitable regimens see section 6. Paravertebral LA block has also

been described and is a feasible alternative. There are very few well-designed clinical trials comparing these analgesic techniques. A variety of surgical procedures are included in most studies, the exact surgical incision employed is frequently not stated.

Intravenous **opioids** as a continuous infusion, PCA or NCA are effective for abdominal surgery: the analgesic response is a function of dose and developmental age (Bray et al. 1996; Peters et al. 1999; Monitto et al. 2000; van Dijk et al. 2002). See Section 6.0 for information on doses and regimens.

Epidural analgesia with **LA** is acceptable. Bupivacaine, ropivacaine and levobupivacaine have been shown to be effective in a variety of infusion concentrations and dose rates (Kart et al. 1997; Ivani et al. 1999; Moriarty 1999; Lerman et al. 2003; Bosenberg et al. 2005).

Epidural **LA + opioid** also provides good analgesia. Morphine, fentanyl, hydromorphone and diamorphine have been the most frequently described; the side effect profile depends on the dose and particular opioid which is used (Lerman et al. 2003; Moriarty 1999; Cucchiaro et al. 2003).

Epidural **LA+clonidine** has been compared to LA+opioid and epidural clonidine alone. Clonidine causes dose-dependant sedation and hypotension. Clonidine or clonidine+LA were equally effective as part of a multimodal strategy in combination with ketoprofen (Klamt et al. 2003). The efficacy of clonidine+LA was inferior to morphine+LA in another study, but PONV and pruritis were absent with clonidine (Cucchiaro et al. 2003).

Epidural **opioid** (without LA)
Single doses of epidural opioid can improve postoperative analgesia and reduce requirements for ongoing analgesia (Bozkurt et al. 1997; Kiffer et al. 2001). Intermittent epidural morphine was superior to intramuscular morphine in one study (Chabas et al. 1998), but less effective than bupivacaine+fentanyl infusion (Kart et al. 1997).

Analgesia table 5.6.01 Abdominal surgery

Agent	Technique	Direct evidence	Indirect evidence
LA	**Epidural**	**1+**	
LA	**Paravertebral block**		**1+**
LA+opioid	**Epidural**	**1+**	
LA+clonidine	**Epidural**	**1-**	
Opioid	**Epidural**	**1+**	
Clonidine	**Epidural**	**1-**	
Opioid	**Intravenous**	**1+**	
NSAID*		**1-**	
Paracetamol*			**1+**

See notes below
*as part of a multimodal technique

5.6.02 Appendicectomy (open)

Appendicectomy is the most common indication for laparotomy in children. Under normal circumstances this procedure is performed through a right lower quadrant incision. In the majority of cases appendicectomy will be performed as an emergency or unplanned procedure. See also sections 5.6.00 and 5.6.01 for information on the general management of postoperative pain, and a further discussion of analgesia following abdominal surgery.

Good Practice Point

Following appendicectomy infiltration of the surgical wound with local anaesthetic as part of a multimodal analgesic technique may be of benefit in the early postoperative period.

Recommendations

PCA combined with NSAID is effective for post-appendicectomy pain: grade B (Morton and O'Brien 1999)

Evidence

Intravenous opioids as a continuous infusion, PCA or NCA, together with a multimodal analgesic strategy including wound infiltration, NSAID and paracetamol is current suggested practice following appendicectomy (Till et al. 1996; Morton and O'Brien 1999; Munro et al. 2002; Dix et al. 2003; Yildiz et al. 2003; Jensen et al. 2004).

Morphine PCA has been previously shown to be effective, supplementation with NSAID improves analgesia, particularly for pain on movement (Morton and O'Brien 1999). The addition of ketamine to morphine did not improve analgesia in one study and neurobehavioural side effects were increased (Dix et al. 2003). Antiemetic additives to the opioid such as droperidol or ondansetron offered no advantage but may increase side effects (Habre et al. 1999; Munro et al. 2002).

Wound Infiltration with LA has previously been investigated (Wright 1993) but results from current studies are inconclusive. Neither pre nor post incision Bupivacaine 0.25-0.5% reduced postoperative morphine requirement in the first 24hrs when compared with placebo (saline) or no infiltration (Ko et al. 1997; Jensen et al. 2004). However, pre-incision bupivacaine followed by infiltration of the muscle layer on closure reduced pain scores for up to 48hr in another study which included children and adults (Lohsiriwat et al. 2004).

Analgesia table 5.6.02 Appendicectomy

Agent	Technique	Direct evidence	Indirect evidence
LA*	**Wound infiltration**	**1-**	
Opioid	**Intravenous**	**1+**	
NSAID*		**1+**	
Paracetamol*			**1+**

See notes below
* as part of a multimodal technique

5.6.03 Fundoplication (open)

This procedure usually involves an incision of the upper abdomen utilising either a midline, transverse supra-umbilical or left sub-costal approach. Increasingly laparoscopic techniques have been used for fundoplication; see section 5.7.0. The patient population is diverse, including significant numbers of children with neurodevelopmental delay and communication difficulties, which may influence the choice of analgesic regime. See also sections 5.1 and 5.6.01 for information on the general management of postoperative pain, and a further discussion of analgesia following abdominal surgery.

Good Practice Point

Multimodal analgesia using parenteral opioids or epidural analgesia together with systemic NSAIDs and paracetamol should be used unless specifically contraindicated.

Recommendations

Epidural LA + opioid is effective and may be associated with improved clinical outcome in selected patients: grade D
(McNeely et al. 1997; Lejus et al. 2001; Wilson et al. 2001)

Evidence

Some of the studies quoted have included other major procedures as well as fundoplication. There is no grade 1 evidence to indicate the most effective post-operative analgesic strategy after open fundoplication.

Epidural analgesia has been favoured following fundoplication as this group of patients is at high risk of respiratory complications, and includes significant numbers with neurodevelopmental delay (Brenn et al. 1998; Tsui et al. 2001; Wilson et al. 2001).
Epidural LA: Ropivacaine without opioid provided satisfactory analgesia for neonates and infants after major thoracic and abdominal surgery including 4 patients following fundoplication(Bosenberg et al. 2005).
Epidural LA +opioid: buivacaine + fentanyl appears to be effective; higher pain scores were noted in patients who had had fundoplication in one of the studies but overall the regimen was considered to be ‘satisfactory’ (Lejus et al. 2001; Tsui et al. 2001).
Epidural Clonidine or LA +clonidine: both were found to be effective for a mixed surgical group as part of a multimodal strategy including ketoprofen, although after fundoplication (n=9) there was an increased need for supplementary opioid on the first postoperative night (Klamt et al. 2003).

Intravenous opioid appears to be effective in studies, but may be inferior for non-pain outcomes: see below (McNeely et al. 1997; Dick et al. 1998).

Epidural analgesia vs. parenteral opioid
Two retrospective observational studies have found that duration of hospital stay is prolonged in patients selected for opioid analgesia even when spinal deformity patients (scoliosis) were excluded in one study(McNeely et al. 1997; Wilson et al. 2001).

Analgesia table 5.6.03 Fundoplication (open)

Agent	Technique	Direct evidence	Indirect evidence
LA		**3**	
LA+opioid		**3**	
LA+clonidine*		**3**	
Clonidine*		**3**	
Opioid	**Intravenous**	**3**	
NSAID*		**3**	
Paracetamol*			**1+**

*as part of a multimodal technique

5.7 Laparoscopic surgery

There has been a dramatic increase in the amount of paediatric laparoscopic surgery in the last decade. This is performed mainly through the body cavities (chest and abdomen) or potential spaces. Inguinal hernia repair, appendicecomy, fundoplication, renal and adrenal surgery are examples. For general management of postoperative pain see section 5.1.

Good Practice Point

Infiltration of port sites with LA as part of a multimodal analgesic strategy may reduce postoperative pain following laparoscopy.

Although overall postoperative analgesic requirements appear to be reduced following laparoscopy, pain may be equivalent to the comparable open procedure in some circumstances, particularly during the first 24 hours.

Evidence

One of the advantages of laparoscopic surgery may be an overall reduction in pain in comparison with the open surgical counterpart (Till et al. 1996; Rowney and Aldridge 2000; Sekaran et al. 2006). The duration of postoperative pain appears to be reduced, but analgesic requirements may be at least as great on the first postoperative day (Dick et al. 1998; Dick and Potts 1999; Rowney and Aldridge 2000). Multimodal analgesia including LA infiltration, opioid, NSAID and paracetamol is suitable. Demand-led opioid regimens such as PCA may be effective and require further evaluation (Till et al. 1996). Little good evidence exists with regards to the optimum analgesic regimen.

LA infiltration of port sites when combined with NSAID provided equivalent analgesia to caudal block for minor diagnostic and therapeutic laparoscopic procedures (Borkar and Dave 2005).

Analgesia table 5.7 Laparoscopic surgery

Agent	Technique	Direct evidence	Indirect evidence
LA*	**Infiltration**	**1-**	
LA	**Caudal**	**1-**	
Opioid	**Parenteral /oral**	**3**	
NSAID*		**1-**	
Paracetamol*		**3**	

*as part of a multimodal technique

5.8 Orthopaedics, Spinal and Plastic Surgery

5.8.01 Lower Limb Surgery

The surgery covered in this section ranges from relatively minor single site orthopaedic surgery to more major procedures such as multiple level osteotomies.
The population of patients requiring femoral and pelvic osteotomies includes those suffering from cerebral palsy; pain in this population can also precipitate painful muscle spasm requiring specific management with benzodiazepines.
Multimodal analgesia is suitable: there is particularly extensive experience of the use of local anaesthetic techniques for this type of surgery. Concerns have been expressed that NSAIDs may inhibit new bone growth following orthopaedic surgery; this is addressed below.

Good practice point

There is no evidence from human studies that NSAIDs have a deleterious effect on bone fusion. The analgesic benefit of short term NSAID use has been demonstrated and may frequently outweigh any hypothetical risk.

Recommendations

Epidural opioids are effective, reduce the dose requirements of local anaesthetic and rescue IV opioids but increase the incidence of side effects: Grade B
(Brenn et al. 1998; Goodarzi 1999; Lovstad and Stoen 2001)

Epidural techniques are associated with lower pain scores than intravenous opioid analgesia: Grade C
(Lovstad et al. 1997; Kiffer et al. 2001; Lejus et al. 2001; Bai et al. 2004)

Patient controlled regional techniques (PCRA) can reduce the total dose of local anaesthetic consumed; reducing the potential for toxicity: Grade D
(Antok et al. 2003; Duflo et al. 2006)

Systemic paracetamol & NSAID reduce intravenous opioid requirements: Grade C
(Eberson et al. 1999; Hiller et al. 2006)

Continuous peripheral nerve blocks are feasible, effective & safe: Grade D
(Dadure et al. 2004; Duflo et al. 2004; Vas 2005; Dadure et al. 2006)

Evidence

Studies have shown **epidural analgesia** using opioids, local anaesthesia or a mixture of the two are effective but differences in efficacy and side effects between regimens are observed. **Epidural opioids** improve analgesia but side effects are more frequent. The side-effect profile may be related to the individual properties of specific opioids**:** morphine, fentanyl & hydromorphone were of comparable analgesic efficacy in one study; respiratory depression, somnolence and retention of urine were higher in the morphine group; PONV & urinary retention had the lowest incidence with hydromorphone (Goodarzi 1999). Single dose epidural morphine was equianalgesic with increasing dose (11.2mcg/kg, 15mcg/kg and 20mcg/kg) but the incidence of PONV increased with dose (Castillo-Zamora et al. 2005). In a study comparing bupivacaine +fentanyl with bupivacaine (both with adrenaline), the fentanyl group had superior analgesia and did not require rescue opioid but had a higher incidence of PONV, whereas the bupivacaine group required more bupivacaine and 10/26 (38%) required rescue opiates and antiemetic therapy, itching only occurred in the fentanyl group (Lovstad and Stoen 2001).

Epidural versus Peripheral nerve block:
A comparison of continuous epidural block with continuous popliteal nerve block for major foot surgery, showed no difference in pain or rescue analgesia, but adverse effects and patient satisfaction were improved with peripheral nerve block (Dadure et al. 2006).

Epidural compared with Intravenous techniques:
In a comparison between patient controlled epidural analgesia (PCEA) with lidocaine, and nurse controlled IV fentanyl, pain scores (unvalidated method), and PONV were lower in the epidural group (Bai et al. 2004). A single dose of epidural morphine 30mcg/kg reduced postoperative PCA morphine use and VAS scores were also lower in the epidural morphine group, there was no difference in the incidence of side effects (severe pruritis and PONV) (Kiffer et al. 2001).

A number of successful series of **peripheral nerve blocks** have been described, including popliteal nerve block (Duflo et al. 2004; Dadure et al. 2006; Duflo et al. 2006), fascia iliaca compartment block (Duflo et al. 2004; Duflo et al. 2006), sciatic nerve block(Vas 2005) and psoas compartment block (Dadure et al. 2004).

*Continuous LA infusion versus **PCRA/PCEA**:*
PCRA (Ropivacaine 0.2%) showed similar efficacy to a continuous regional technique, with a lower total dose of LA for popliteal and fascia iliaca blocks (Duflo et al. 2006). In a comparison of PCEA vs. CEA, again efficacy was similar and a lower dose of LA used (Antok et al. 2003).

Systemic analgesia with **NSAID** and **paracetamol** can be combined with intravenous opioid or regional analgesia. In one study a combination of paracetamol & ketoprofen significantly decreased pain scores & IV morphine requirements compared to either drug alone (Hiller et al. 2006). In a case series of patients undergoing club foot surgery & long bone osteotomy, ketorolac reduced IV morphine usage and associated GI effects (Eberson et al. 1999).

Analgesia table 5.8.01 Lower Limb surgery

Agent	Technique	Direct evidence	Indirect evidence
LA	**Peripheral nerve block**	**1-**	
LA	**Caudal Epidural**		**1-**
LA	**Lumbar Epidural**	**1+**	
Opioid	**IV infusion**	**1+**	
NSAID**		**1+**	
Paracetamol**		**1+**	

** as part of a multi-modal technique

5.8.02 Upper Limb Surgery

Surgery on the upper limb is most commonly performed for plastic and orthopaedic procedures of hand and forearm, often following trauma. Local anaesthesia of the brachial plexus prior to surgery is frequently used. There is some controversy regarding the most safe and reliable approach to the brachial plexus. See section 5.1 for the general management of postoperative pain.

Recommendations

Brachial plexus blocks provide satisfactory analgesia for hand and forearm surgery extending into the postoperative period: Grade B
(Fisher et al. 1999; Altintas et al. 2000; Pande et al. 2000; Fleischmann et al. 2003; Thornton et al. 2003; de Jose Maria and Tielens 2004).

The axillary, infraclavicular & supraclavicular approach are feasible & effective: Grade B
(Fisher et al. 1999; Pande et al. 2000; Fleischmann et al. 2003; Thornton et al. 2003; de Jose Maria and Tielens 2004).

Evidence

Analgesia following upper limb surgery has not been well studied and few investigations of postoperative pain management have been undertaken. Brachial plexus block appears to be effective but differences between techniques have not been investigated. The axilliary approach to the brachial plexus is theoretically less likely to lead to accidental pneumothorax. There are no comparisons between brachial plexus block and other alternatives such as intravenous opioid.
Axilliary brachial plexus block was the most studied approach; postoperatively patients were generally managed with oral analgesia. There was no difference in postoperative efficacy (time to 1st analgesia, analgesic consumption, pain score) between 0.2% ropivacaine & 0.25% bupivacaine when used for axillary brachial plexus block(Thornton et al. 2003). There was no benefit to using a fractionated dose of LA compared to a single injection for axillary brachial plexus block, nor in placing the block prior to or after surgery (Altintas et al. 2000; Carre et al. 2000).
Other studies have examined the feasibility of the different approaches to brachial plexus block. The infraclavicular (Fleischmann et al. 2003; de Jose Maria and Tielens 2004) and the supraclavicular approach (Pande et al. 2000) are effective, there were no incidences of pneumothorax in these studies (275 patients).

Analgesia table 5.8.02 Upper Limb surgery

Agent	Technique	Direct evidence	Indirect evidence
LA	**Brachial plexus block**	**1+**	
Opioid	**Intravenous**		**1+**
	Oral		**1+**
NSAID**			**1+**
Paracetamol**			**1+**

** as part of a multi-modal technique

5.8.03 Spinal Surgery

Surgery to correct spinal deformity requires extensive exposure of the spine which may be achieved posteriorly, anteriorly via thoracotomy or thoraco-abdominal approach or by a combined anterior- posterior approach. Postoperative pain can be severe and prolonged, necessitating the use of potent intravenous or neuraxial analgesic techniques for 3 – 5 days postoperatively. The use of intravenous opioid analgesia has not been well studied, however the success of neuraxial techniques in controlling post-operative pain in children has led to an interest in their use for spinal surgery.

The patient population requiring spinal surgery includes healthy adolescents and patients with severe underlying medical conditions such as Duchenne's muscular dystrophy and cerebral palsy. The choice of analgesic technique will be influenced by both patient and surgical factors in addition to local circumstances e.g. neuraxial techniques are not suitable for some patients. The involvement of the surgeon in the choice of analgesic technique is especially important in spinal surgery as it must also enable early & frequent assessment of neurological function, Epidural LA is not usually administered following surgery until normal neurological function has been demonstrated. See section 5.1 for the general management of postoperative pain.

Good practice points

There is no evidence from human studies that NSAIDs have a deleterious effect on bone fusion. The analgesic benefit of short term NSAID use has been demonstrated and may outweigh any hypothetical risk.

When using an epidural technique, the timing of LA administration should be agreed in consultation with the surgical team.

Recommendations

Intrathecal opioids decrease intra-operative blood loss and IV opioid consumption post-operatively. The duration of action is 18-24 hours: Grade C
(Goodarzi 1998; Gall et al. 2001)

Dual catheter epidural techniques should be considered, as this permits coverage of multiple spinal levels: Grade C
(Tobias et al. 2001; Ekatodramis et al. 2002; Blumenthal et al. 2005; Blumenthal et al. 2006)

The use of LA + lipophilic opioid in the epidural space with a single epidural catheter does not show an analgesic benefit over intravenous opioid techniques: Grade C
(Cassady et al. 2000; O'Hara et al. 2004)

The use of LA + hydrophilic opioids in the epidural space has a favourable analgesic profile compared with IV opioid, but at the expense of increase adverse effects: Grade D
(Arms et al. 1998; Sucato et al. 2005)

Evidence:

The majority of studies have been conducted in adolescents, some studies have also included young adults up to the age of 22 years. Neuraxial techniques have been the most investigated. **Intrathecal opioids**: single doses of intrathecal (IT) opioids can reduce intraoperative blood loss and postoperative analgesic requirements. IT morphine plus sufentanil decreased intra-operative blood loss compared with IV sufentanil (Goodarzi 1998). IT morphine 5mcg/kg also decreased intra-operative blood loss compared with 2mcg/kg IT or saline controls (Gall et al. 2001). The time to first analgesic use, 6-24 hours postoperative, was significantly increased in proportion to dose of IT morphine in these studies (Goodarzi 1998; Gall et al. 2001). Pain scores were also lower with intrathecal morphine (Gall et al. 2001).
Studies have found no increase in respiratory depression with IT opiates compared with intravenous techniques (Goodarzi 1998; Gall et al. 2001), and no difference in level of sedation, nausea & vomiting or pruritus (Gall et al. 2001). IT opiates did not affect the ability to monitor spinal sensory evoked potentials (SSEPs) (Goodarzi et al. 1996).

Epidural analgesia appears to be effective but differences in efficacy and side effects are observed depending upon the regimen used, none has been clearly shown to be superior. In a retrospective series (613 patients) a single epidural catheter infusing bupivacaine with hydromorphone provided lower pain scores compared with a group receiving PCA morphine; the epidural group had a higher incidence of side effects (Sucato et al. 2005). However, a single catheter midthoracic epidural infusion of bupivacaine + fentanyl showed no difference in pain scores compared with PCA morphine (Cassady et al. 2000; O'Hara et al. 2004). Case series have demonstrated effective analgesia with the following regimes: bupivacaine 0.0625% - 0.1% with fentanyl, hydromorphone or morphine, 0.1% ropivacaine with hydromorphone, bupivacaine 0.0625% - 0.125% with morphine (Shaw et al. 1996; Arms et al. 1998; Turner et al. 2000; Lowry et al. 2001). Several authors commented that placement of the epidural catheter by direct visualisation during surgery was important.
Using a **dual epidural catheter** technique, also placed under direct vision may have benefits. Infusion of ropivacaine, without opioid, showed significantly lower pain scores compared with continuous IV infusion of morphine in both posterior (Blumenthal et al.

2005) and anterior spinal surgery (Blumenthal et al. 2006). Both 0.0625% bupivacaine with fentanyl and with clonidine, and ropivacaine with hydromorphone have also been reported as successful using a dual catheter technique (Tobias et al. 2001; Ekatodramis et al. 2002). Epidural analgesia may be associated with a more rapid return in GI function (Cassady et al. 2000). The use of an epidural technique did not compromise neurological assessment (Shaw et al. 1996). There was one report of a wound infection occurring in a patient receiving epidural analgesia (Cassady et al. 2000) but no reports of epidural haematoma or abscess (881 patients).

NSAIDS: no difference in the incidence of non-fusion nor in the amount of post-operative bleeding was found in patients who had received ketorolac (60 patients) compared to controls (148 patients) in a retrospective review (Vitale et al. 2003).

Analgesia table 5.8.03 Spinal surgery

Agent	Technique	Direct evidence	Indirect evidence
LA	**Lumbar Epidural**	**1-**	
LA	**Thoracic Epidural**	**1-**	
LA	**Lumbo-thoracic 2 Catheter**	**1+**	
Opioid	**Intrathecal**	**1+**	
Opioid	**IV infusion**	**1+**	
NSAID**			**1+**
Paracetamol**			**1+**

** as part of a multi-modal technique

5.8.04 Plastic Surgical Procedures of Head and Neck

This section includes a range of procedures such as repair of Cleft Lip and Palate, Otoplasty, and Alveolar bone grafting. See section 5.1 for the general management of postoperative pain.

Recommendations

Infraorbital nerve block provides effective analgesia for cleft lip repair in the early postoperative period: Grade B

(Prabhu et al. 1999; Eipe et al. 2006)

Evidence

The evidence base supporting the efficacy of analgesic strategies is weak for this group of procedures and postoperative analgesic requirements are not clear. Many patients appear to be successfully managed with intraoperative local anaesthesia followed by NSAID's, paracetamol and low doses of opioid postoperatively.

Cleft Lip Repair: **infra-orbital nerve block** for cleft lip surgery is feasible and one study has demonstrated lower pain scores in patients who received infra-orbital nerve block compared with peri-incisional infiltration of local anaesthetic (Prabhu et al. 1999; Eipe et al. 2006).

Cleft Palate Surgery: effect of **NSAID**s on peri-operative bleeding was reviewed in one small case series (20 patients) there was no effect associated with diclofenac 1mg/kg b.d. (Sylaidis and O'Neill 1998)

Alveolar Bone Graft: low morphine PCA requirements (less than 0.4mg/kg), no improvement in analgesic efficacy with IV ketorolac 0.5mg/kg qid (Dawson et al. 1996).

Otoplasty: regional nerve blockade with bupivacaine 0.5% showed no improvement in analgesia compared with local infiltration of the operative field with Lidocaine 1% and adrenaline (Cregg et al. 1996).

Analgesia table 5.8.04 Plastic surgery procedures of head and neck

Agent	Technique	Direct evidence	Indirect evidence
LA	**Local infiltration**	**1+**	
LA	**Infraorbital nerve block**	**1+***	
Opioid**			**1+**
NSAID**			**1+**
Paracetamol**			**1+**

* repair of cleft lip alone
** as part of a multi-modal technique

5.9 Cardiothoracic Surgery

5.9.01 Cardiac Surgery (sternotomy)

Classically, cardiac surgery with cardiopulmonary by-pass (CPB) will involve division of the bony sternum to obtain access to the heart and great vessels. Anticoagulation with heparin is maintained throughout CPB, which has implications for the use of regional techniques. Postoperative patients are nursed in ICU areas, often with a short period of mechanical ventilation prior to extubation of the trachea. Postoperative analgesia with intravenous opioids, most frequently morphine or fentanyl, has been standard practice for more than 20 years in most institututions. See section 5.1 for the general management of postoperative pain.

Recommendations

Epidural and intrathecal techniques with opioid and/or LA are effective for sternotomy pain but only marginal benefits have been demonstrated and there is insufficient data concerning the incidence of serious complications: Grade B (Shayevitz et al. 1996; Hammer et al. 2000; Peterson et al. 2000; Finkel et al. 2002; Pirat et al. 2002; Suominen et al. 2004; Hammer et al. 2005; Leyvi et al. 2005)

Evidence

Intravenous opioids are the standard to which other analgesic techniques are to be compared. A comparison of morphine and tramadol NCA found no difference in efficacy between the two, although tramadol caused less sedation in the early postoperative period (Chu et al. 2006).

There has been increasing interest in **regional analgesic techniques** because of their potential to reduce stress responses and facilitate earlier tracheal extubation with possible improvements in clinical outcome and economic cost reduction. The relatively small size of studies precludes accurate prediction of very rare but serious side effects such as epidural haematoma and consequent neurological damage.

Intrathecal opioid: morphine or fentanyl produce equivalent analgesia (and side effects) to intravenous morphine with lower overall analgesic consumption (Pirat et al. 2002; Suominen et al. 2004)
Intrathecal opioid + LA: improved pain scores compared with bolus IV fentanyl alone with lower overall fentanyl consumption but no difference in opioid related side effects (Hammer et al. 2005).

Epidural: case series have demonstrated the feasibility and efficacy of epidural catheter techniques from caudal, lumbar or thoracic approaches with few and modest improvements in outcomes (Shayevitz et al. 1996; Hammer et al. 2000; Peterson et al. 2000). There is a single case report of epidural haematoma requiring surgical decompression in an 18year old with TEB who remained anticoagulated following aortic valve surgery (Rosen et al. 2004).

NSAIDS: ketorolac commenced 6 hrs postoperatively did not increase postoperative bleeding, nor affect IV morphine requirements or reduce time to extubation in one study (Gupta et al. 2004).

Analgesia table 5.9.01 Cardiac Surgery (sternotomy)

Agent	Technique	Direct evidence	Indirect evidence
LA	**Caudal Epidural Catheter**	**3**	
LA	**Thoracic Epidural (TEB)**	**1-**	
LA	**Intrathecal (SAB)**	**1-**	
Opioid	**IV infusion**	**1+**	
Opioid	**Caudal**	**2-**	
Opioid	**Thoracic Epidural (TEB)**	**2-**	
Opioid	**Intrathecal**	**1+**	
NSAID**			**1+**
Paracetamol**			**1+**

** as part of a multi-modal technique

5.9.02 Thoracotomy

Access to the lungs, pleura and intrathoracic structures is obtained by an intercostals incision and separation and retraction of the ribs. Typical procedures include ligation of PDA (patent ductus arteriosus), resection of aortic co-arctation, lung biopsy or partial resection, pneumonectomy, repair of tracheoesphageal fistula. Considerable pain can be expected following classical thoracotomy incision. Recently VATS (video assisted thoracoscopic surgery) a minimally invasive technique has been used for some relatively minor thoracic procedures e.g. lung biopsy or smaller lung resections.

Good practice point

A multi modal analgesic approach; including a local anaesthetic technique and /or opioid with NSAID and paracetamol is suitable for post thoracotomy pain.

Recommendations

Epidural analgesia is effective for post-thoracotomy pain: Grade D
(Bosenberg 1998; Moriarty 1999; Lejus et al. 2001; Birmingham et al. 2003; Bosenberg et al. 2005).

Evidence

Thoracotomy is frequently included in studies of analgesia for major surgery in combination with other procedures such as abdominal and spinal surgery, making interpretation of findings difficult. Either epidural analgesia or intravenous opioids as part of a multimodal strategy including NSAID and paracetamol have been used extensively for post thoracotomy pain. Paravertebral block has also been described. There are few studies comparing regional and systemic techniques directly, or with other more novel regimens. Although it might be anticipated that pain following VATS would differ from classical thoracotomy; there are no studies exploring this issue.

Epidural Analgesia is frequently recommended for post-thoracotomy pain, however there is no conclusive evidence that any particular regimen is more effective.
Epidural LA: plain bupivacaine and ropivacaine solutions have been found to be effective for major abdominal and thoracic surgery in neonates and infants (Bosenberg 1998; Bosenberg et al. 2005). Analgesia was reported as equivalent in a case series (272 patients, 29 thoracic) comparing children who received either plain ropivacaine or bupivacaine+diamorphine as part of a multimodal analgesic strategy (Moriarty 1999).
LA+opioid: bupivacaine with fentanyl, morphine, diamorphine or other opioids is effective for post-thoracotomy pain, by continuous infusion or PCEA (Lin et al. 1999; Moriarty 1999; Lejus et al. 2001; Birmingham et al. 2003).

Epidural opioid (no LA)**:** single dose thoracic epidural morphine was equivalent to intravenous morphine infusion in the first 24hrs after thoracotomy (Bozkurt et al. 2004). Single dose caudal morphine with or without LA was less effective than thoracic epidural Morphine+LA infusion; infusion patients also had better non-pain outcomes e.g. earlier oral intake, less PONV and shorter ICU stay (Lin et al. 1999).
Intrathecal opioid as part of a multimodal technique has been described in a small case series (Ioscovich et al. 2004).
Paravertebral block has been described as effective in a number of small case series of neonates, infants and children (Karmakar et al. 1996; Cheung et al. 1997; Downs and Cooper 1997; Karmakar et al. 1997; Shah et al. 1997; Karmakar and Critchley 1998; Gibson et al. 1999). There have been no comparisons with other techniques.
Intercostal nerve block: increased the time to further analgesia when compared with a single dose of pethidine at skin closure(Matsota et al. 2001).
Opioids: intravenous infusion of opioid is frequently used for severe postoperative pain including post thoracotomy (Lynn et al. 2003). PCA/NCA has been described in studies which have included a small number of post thoracotomy patients (Peters et al. 1999; Monitto et al. 2000). Data on the efficacy of opioids for thoracotomy are inadequate to allow conclusive evaluation, the role of multimodal analgesia has also not been sufficiently evaluated. In a comparison of PCA and continuous infusion of morphine without supplementary NSAID and paracetamol there was no difference between the groups but 20-40% of patients in each group had pain scores in the 'severe' range on the first postoperative day (Peters et al. 1999).

Analgesia table 5.9.02 Thoracotomy

Agent	Technique	Direct evidence	Indirect evidence
LA	**Thoracic epidural***	**3**	
LA	**Paravertebral block**	**3**	
LA	**Intercostal block*****	**3**	

LA+opioid	**Thoracic epidural***	**3**	
Opioid	**Thoracic epidural****	**1-**	
Opioid	**Intrathecal*****	**3**	
Opioid	**Intravenous**	**2-**	
NSAID***			**1+**
Paracetamol***			**1+**

* caudal, lumbar and thoracic catheter insertion sites
** 1st 24 hrs
***as part of a multi-modal technique

5.9 Neurosurgery

Neurosurgical procedures in children include drainage of hydrocephalus and insertion or replacement of an extra cranial shunt, craniotomy, craniofacial surgery and surgery for intracranial aneurism or other vascular malformation. There has been little investigation of analgesic requirements or analgesia for this group of patients, but it is frequently asserted that severe postoperative pain is not a prominent feature even following major neurosurgical interventions. Postoperatively, many neurosurgical patients are admitted to ICU or high dependency areas for monitoring; opioid analgesia must be used judiciously as excessive sedation may mask signs of acute changes in intracranial pressure or interfere with the patient's ability to co-operate with neurological assessments. As the risk of postoperative bleeding is relatively high and potentially disastrous following some procedures, NSAID's are sometimes withheld during the first 24hours. See also section 5.1 on the general management of postoperative pain, and section 5.20.01 for the management of craniotomy and major neurosurgery.

Good practice point

Analgesia following neurosurgery requires good communication and close co-operation between members of the peri-operative team. Frequent pain assessments should be a routine part of postoperative care. A multi-modal analgesic approach is suitable, which may include the use of LA infiltration, paracetamol, NSAID (when indicated), and parenteral or oral opioid as determined by assessed analgesic requirements.

5.20.01 Craniotomy and major neurosurgery

Craniotomy is most frequently performed for tumour surgery, repair of vascular anomalies and surgery for epilepsy. Posterior fossa craniotomy, a relatively invasive approach, is more frequently indicated in children than adults yet in common with other paediatric neurosurgical procedures postoperative pain and analgesia requirements 2000postoperative and neurosurgical pain respectively.

Evidence

The literature informing the management of postoperative pain after neurosurgery is scarce. There have been few studies comparing standard analgesic regimens. **Opioids:** the use of parenteral opioids following craniotomy and major neurosurgery has been described. NCA was reportedly used successfully in a small number of patients less than 6 years old following neurosurgical procedures as part of a large case series, but results for these patients were not reported separately (Monitto et al. 2000). In a pharmacokinetic study comparing IM and PR codeine following craniotomy high pain scores were reported for both groups (Mc Ewan et al. 2000).

Intrathecal opioid: intrathecal morphine 20microgm/kg reduced postoperative analgesic requirements and the lengthened the time to first analgesia following bi frontal craniotomy in retrospective comparison with a group who received intravenous opioid only.

Analgesia table 5.20.01 Craniotomy and major neurosurgery

Agent	Technique	Direct evidence	Indirect evidence
LA	**Infiltration**		**1-**
Opioid	**IV infusion**	**3**	
Opioid	**Intrathecal**	**2-**	
NSAID*			**1+**
Paracetamol*			**1+**

*as part of a multi-modal technique

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Section 6.0 Analgesia

Contents

Section 6.0 Analgesia

This section describes some of the important properties, dosing regimens, interactions and adverse effects of analgesics for acute pain in children.

Local anaesthetics, opioids, NSAIDs, and paracetamol form the pharmacological basis for the majority of analgesic regimens. Ketamine, a dissociative anaesthetic with analgesic properties and clonidine, an alpha-2-agonist are used to provide systemic or neuraxial analgesia alone or as adjuncts to other agents. For painful procedures, inhaled nitrous oxide has an important role, and in neonatology intra-oral sucrose solution is used. The availability of specific opioids, NSAIDs and local anaesthetics can vary from country to country.

The detailed pharmacology and formulations of these drugs are available in standard textbooks, and from resources such as Martindale® (Sweetman 2007)available at: https://www.medicinescomplete.com/mc/martindale/current/ For more comprehensive prescribing information, summaries of product characteristics and licence status of specfic agents for children in the UK please consult resources such as the British National Formulary for Children(2006) available at: http://bnfc.org/bnfc and the Electronic Medicines Compendium available at: http://emc.medicines.org.uk/

6.8 Local Anaesthetics

(Morton 2000; Berde 2004; Bosenberg 2004; Mazoit and Dalens 2004)

Most widely used local anaesthetics are amides with the exception of tetracaine (amethocaine), which is an ester. They all act by reversibly blocking sodium channels in nerves. They vary in onset, potency, potential for toxicity and duration of effect. Formulations are available for topical application to mucosae or intact skin, for local installation or infiltration, for peripheral nerve or plexus blockade, for epidural injection or infusion and for subarachnoid administration. Vasoconstrictors may be added to reduce the systemic absorption of local anaesthetic and to prolong the neural blockade. Neuraxial analgesics such as the α-2-agonist clonidine, the phencyclidine derivative ketamine or opioids such as fentanyl may be co-administered with the local anaesthetic to prolong the effect of central nerve blocks.

6.1.01 Bupivacaine, levobupivacaine, ropivacaine

(i) Preparations and routes

Bupivacaine is an amide LA with a slow onset and a long duration of action which may be prolonged by the addition of a vasoconstrictor. It is used mainly for infiltration anaesthesia and regional nerve blocks, particularly epidural block, but is contra-indicated for intravenous regional anaesthesia (Bier's block). Bupivacaine is a racemic mixture but the S(-)-isomer levobupivacaine is also commonly used (see below). A carbonated solution of bupivacaine, with faster onset of action, is also available for injection in some countries. Bupivacaine is used in solutions containing the equivalent of 0.0625 to 0.75% (0.625-7.5mg/ml). In recommended doses bupivacaine produces complete sensory blockade and the extent of motor blockade depends on concentration. 0.0625% or 0.125% solutions are associated with a very low incidence of motor block, a 0.25% solution generally produces incomplete motor block, a 0.5% solution will usually produce more extensive motor block, and complete motor block and muscle relaxation can be achieved with a 0.75% solution. Hyperbaric solutions of 0.5% bupivacaine may be used for spinal intrathecal block.

Levobupivacaine is the S-enantiomer of bupivacaine, it is equipotent but toxicity is slightly less. It is available in the same concentrations as bupivacaine and is used for similar indications, like bupivacaine it is contra-indicated for use in intravenous regional anaesthesia (Bier's block).

Ropivacaine Is an amide LA with an onset and duration of sensory block which is generally similar to that obtained with bupivacaine but motor block may be slower in onset, shorter in duration, and less intense. It is available in solutions of 0.2%. 0.75% and 1%.

(ii) Dosage, side effects and toxicity

The dosage of **bupivacaine, levobupivacaine, and ropivacaine** depend on the site of injection, the procedure and the status of the patient: suggested maxima are given in table 6.1.1. A test dose may help to detect inadvertent intravascular injection and doses should be given in small increments. Slow accumulation occurs with repeat administration and continuous infusions, especially in neonates.

Table 6.1.1
Suggested maximum dosages of bupivacaine, levobupivacaine, and ropivacaine

Single bolus injection	**Maximum dosage**
Neonates	2 mg kg-1
Children	2.5 mg kg-1
Continuous postoperative infusion	**Maximum infusion rate**
Neonates	0.2 mg kg-1 h-1
Children	0.4 mg kg-1 h-1

Bupivacaine is 95% bound to plasma proteins with a half-life of 1.5-5.5 hours in adults and 8 hours in neonates. It is metabolised in the liver and is excreted in the urine mainly as metabolites with only 5 to 6% as unchanged drug. Bupivacaine is distributed into breast milk in small quantities. It crosses the placenta but the ratio of fetal concentrations to maternal concentrations is relatively low. Bupivacaine also diffuses into the CSF.
The toxic threshold for bupivacaine is in the plasma concentration range of 2-4 micrograms/mL. The two major binding proteins for bupivacaine in the blood are α1-acid glycoprotein, the influence of which is predominant at low concentrations, and albumin, which plays the major role at high concentrations. Reduction in pH from 7.4 to 7.0 decreases the affinity of the α1-acid glycoprotein for bupivacaine but has no effect on albumin affinity. For epidural infusion techniques in neonates, the reduced hepatic clearance of amide local anaesthetics is the more important factor causing accumulation of bupivacaine than reduced protein binding capacity, particularly as protein levels tend to increase in response to surgery.

Bupivacaine is more cardio toxic than other amide local anaesthetics and there is an increased risk of myocardial depression in overdose and when bupivacaine and antiarrhythmics are given together. Propranolol reduces the clearance of bupivacaine. **Levobupivacaine** is slightly less cardio toxic and therefore safer but maximum recommended doses are similar to those of buivacaine

Ropivacaine is about 94% bound to plasma proteins. The terminal elimination half-life is around 1.8 hours and it is extensively metabolised in the liver by the cytochrome P450 isoenzyme CYP1A2. Prolonged use of ropivacaine should be avoided in patients treated with potent CYP1A2 inhibitors, such as the selective serotonin reuptake inhibitor (SSRI) fluvoxamine. Plasma concentrations of ropivacaine may be reduced by enzyme-inducing drugs such as rifampicin. Metabolites are excreted mainly in the urine; about 1% of a dose is excreted as unchanged drug. Some metabolites also have a local anaesthetic effect but less than that of ropivacaine. Ropivacaine crosses the placenta.

6.1.02 Lidocaine, Prilocaine and EMLA

(i) Preparations

Lidocaine is an amide LA, it is used for infiltration anaesthesia and regional nerve blocks. It has a rapid onset of action and anaesthesia is obtained within a few minutes; it has an intermediate duration of action. Addition of a vasoconstrictor reduces systemic absorption and increases both the speed of onset and duration of action. Lidocaine is a useful surface anaesthetic but it may be rapidly and extensively absorbed following topical application to mucous membranes, and systemic effects may occur. Hyaluronidase may enhance systemic absorption. Lidocaine is included in some injections, such as depot corticosteroids, to prevent pain and itching due to local irritation.

Prilocaine is an amide local anaesthetic with a similar potency to lidocaine. However, it has a slower onset of action, less vasodilator activity, and a slightly longer duration of action; it is also less toxic. Prilocaine is used for infiltration anaesthesia and nerve blocks in solutions of 0.5%, 1%, and 2%. A 1% or 2% solution is used for epidural anaesthesia; for intravenous regional anaesthesia 0.5% solutions are used. For dental procedures a 3% solution with the vasoconstrictor felypressin or a 4% solution without, are used. A 4% solution with adrenaline 1 in 200 000 is also used for dentistry in some countries. Carbonated solutions of prilocaine have also been used for epidural and brachial plexus nerve blocks. Prilocaine is used for surface anaesthesia in a eutectic mixture with lidocaine **EMLA** (see below).

(ii) Doses, side effects and toxicity

The dose of **lidocaine** depends on the site of injection and the procedure but in general the maximum dose should not exceed 3mg/kg (maximum 200mg) unless vasoconstrictor is also used. Lidocaine hydrochloride solutions containing adrenaline 1 in 200 000 for infiltration anaesthesia and nerve blocks are available; higher concentrations of adrenaline are seldom necessary, except in dentistry, where solutions of lidocaine hydrochloride with adrenaline 1 in 80 000 are traditionally used. The maximum dose of adrenaline should be 5micrograms/kg and of lidocaine 5mg/kg. Adrenaline containing solutions should not be used near extremities such as for digital or penile blocks. Lidocaine may be used in a variety of formulations for surface anaesthesia. Lidocaine ointment is used for anaesthesia of skin and mucous membranes. Gels are used for anaesthesia of the urinary tract and for analgesia of aphthous ulcers. Topical solutions are used for surface anaesthesia of mucous membranes of the mouth, throat, and upper gastrointestinal tract. For painful conditions of the mouth and throat a 2% solution may be used or a 10% spray can be applied to mucous membranes. Eye drops containing lidocaine hydrochloride 4% with fluorescein are used in tonometry. Other methods of dermal delivery include a transdermal patch of lidocaine 5% for the treatment of pain associated with postherpetic neuralgia, and an iontophoretic drug delivery system incorporating lidocaine and adrenaline.

Lidocaine is bound to plasma proteins, including α1-acid glycoprotein (AAG). The extent of binding is variable but is about 66%. Plasma protein binding of lidocaine depends in part on the concentrations of both lidocaine and AAG. Any alteration in the concentration of AAG can greatly affect plasma concentrations of lidocaine. Plasma concentrations decline rapidly after an intravenous dose with an initial half-life of less than 30 minutes; the elimination half-life is 1 to 2 hours but may be prolonged if infusions are given for longer than 24 hours or if hepatic blood flow is reduced. Lidocaine is largely metabolised in the liver and any alteration in liver function or hepatic blood flow can have a significant effect on its pharmacokinetics and dosage requirements. First-pass metabolism is extensive and bioavailability is about 35% after oral doses. Metabolism in the liver is rapid and about 90% of a given dose is dealkylated to form monoethylglycinexylidide and glycinexylidide. Both of these metabolites may contribute to the therapeutic and toxic effects of lidocaine and since their half-lives are longer than that of lidocaine, accumulation, particularly of glycinexylidide, may occur during prolonged infusions. Further metabolism occurs and metabolites are excreted in the urine with less than 10% of unchanged lidocaine. Reduced clearance of lidocaine has been found in patients with heart failure, or severe liver disease. Drugs that alter hepatic blood flow or induce drug-metabolising microsomal enzymes can also affect the clearance of lidocaine. Renal impairment does not affect the clearance of lidocaine but accumulation of its active metabolites can occur. Lidocaine crosses the placenta and blood-brain barrier; it is distributed into breast milk. Lidocaine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in animals.

The clearance of lidocaine may be reduced by propranolol and cimetidine. The cardiac depressant effects of lidocaine are additive with those of beta blockers and of other antiarrhythmics. Additive cardiac effects may also occur when lidocaine is given with intravenous phenytoin, mexilitene or amiodarone; however, the long-term use of phenytoin and other enzyme-inducers such as barbiturates may increase dosage requirements of lidocaine. Hypokalaemia produced by acetazolamide, loop diuretics, and thiazides antagonises the effect of lidocaine.

Prilocaine dosage for children over 6 months of age is up to 5 mg/kg. For dental infiltration or dental nerve blocks the 4% solution with adrenaline (1:200 000) is often used. Children under 10 years generally require about 40 mg (1 mL). The dose of prilocaine hydrochloride with felypressin 0.03 international units/mL as a 3% solution for children under 10 years is 30 to 60 mg (1 to 2 mL).
Prilocaine has relatively low toxicity compared with most amide-type local anaesthetics. It is 55% bound to plasma proteins and is rapidly metabolised mainly in the liver and kidneys and is excreted in the urine. One of the principal metabolites is o-toluidine, which is believed to cause the methaemoglobinaemia observed after large doses. It crosses the placenta and during prolonged epidural anaesthesia may produce methaemoglobinaemia in the fetus. It is distributed into breast milk. The peak serum concentration of prilocaine associated with CNS toxicity is

20 micrograms/mL. Symptoms usually occur when doses of prilocaine hydrochloride exceed about 8 mg/kg but the very young may be more susceptible. Methaemoglobinaemia has been observed in neonates whose mothers received prilocaine shortly before delivery and it has also been reported after prolonged topical application of a prilocaine/lidocaine eutectic mixture in children. Methaemoglobinaemia may be treated by giving oxygen followed, if necessary, by IV methylthioninium chloride.
Prilocaine should be used with caution in patients with anaemia, congenital or acquired methaemoglobinaemia, cardiac or ventilatory failure, or hypoxia. Prilocaine has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients. Methaemoglobinaemia may occur at lower doses of prilocaine in patients receiving therapy with other drugs known to cause such conditions (e.g. sulfonamides such as sulfamethoxazole in co-trimoxazole).

(iii) EMLA

Lidocaine forms a mixture with prilocaine that has a melting point lower than that of either ingredient. This eutectic mixture containing lidocaine 2.5% and prilocaine 2.5% can produce local anaesthesia when applied to intact skin as a cream. It is used extensively for procedural pain including venepuncture, intravenous or arterial cannulation, lumbar puncture, minor dermatological procedures and others (see section 4.0). The eutectic cream is usually applied to skin under an occlusive dressing for at least 60 minutes and a maximum of 5 hours. Transient paleness, redness, and oedema of the skin may occur following application.

Eutectic mixtures of lidocaine and prilocaine are used in neonates and are safe in single doses. There has been concern that excessive absorption (particularly of prilocaine) might lead to methaemoglobinaemia particularly after multiple applications. For this reason the maximum number of doses/day should be limited in the neonate. In some countries EMLA has been licensed for use in neonates provided that their gestational age is at least 37 weeks, and that methaemoglobin values are monitored in those aged 3 months or less. In fact systemic absorption of both drugs from the eutectic cream appears to be minimal across intact skin even after prolonged or extensive use. However, EMLA should not be used in infants under 1 year who are receiving methaemoglobin-inducing drugs; it should not be used on wounds or mucous membranes or for atopic dermatitis. EMLA should not be applied to or near the eyes because it causes corneal irritation, and it should not be instilled into the middle ear. It should be used with caution in patients with anaemia or congenital or acquired methaemoglobinaemia.

6.1.03 Tetracaine (amethocaine)

(i) Preparations

Tetracaine is a potent, para-aminobenzoic acid ester local anaesthetic used for surface anaesthesia and spinal block. It is highly lipophillic and can penetrate intact skin. Its use in other local anaesthetic techniques is restricted by its systemic toxicity.
For anaesthesia of the eye, solutions containing 0.5 to 1% tetracaine hydrochloride and ointments containing 0.5% tetracaine have been used. Instillation of a 0.5% solution produces anaesthesia within 25 seconds that lasts for 15 minutes or longer and is suitable for use before minor surgical procedures.
A **4% gel** (Ametop) is used as a percutaneous local anaesthetic. This formulation of tetracaine 4% produces more rapid and prolonged surface anaesthesia than EMLA and is significantly better in reducing pain caused by laser treatment of port wine stains and for venous cannulation. A transdermal patch is effective and patches containing a mixture of lidocaine and tetracaine have also been tried. Tetracaine has been incorporated into a mucosa-adhesive polymer film to relieve the pain of oral lesions resulting from radiation and antineoplastic therapy. Liposome-encapsulated tetracaine can provide adequate surface anaesthesia.

LAT (LET) 4% lidocaine, 0.1% adrenaline and 0.5% tetracaine have been combined in a gel and applied as a surface anaesthetic to lacerations of the skin especially the face and scalp. It is less a painful alternative to LA infiltration prior to suture of lacerations.

(ii) Dosage side effects and toxicity

Tetracaine A stinging sensation may occur when tetracaine is used in the eye. Absorption of tetracaine from mucous membranes is rapid and adverse reactions can occur abruptly without the appearance of prodromal signs or convulsions; systemic toxicity is high and fatalities have occurred. It should not be applied to inflamed, traumatised, or highly vascular surfaces and should not be used to provide anaesthesia for bronchoscopy or cystoscopy, as there are safer alternatives, such as lidocaine.

Tetracaine Gel: The gel is applied to the centre of the area to be anaesthetised and covered with an occlusive dressing. Gel and dressing are removed after 30 minutes for venepuncture and 45 minutes for venous cannulation. A single application provides anaesthesia for 4 to 6 hours. Tetracaine is 15% bioavailable after application of 4% gel to intact skin, with a mean absorption and elimination half-life of about 75 minutes. It is rapidly metabolised by esterases in the skin, in plasma, and on red cells. Mild erythema at the site of application is frequently seen with topical use; slight

oedema or pruritus occur less commonly and blistering of the skin may occur. It has been used safely in the neonate.

LAT: 1-3ml of the solution is applied directly to the wound for 15-30 minutes using a cotton-tipped applicator. The solution and gel have been used in children from 1 year old and above. There are no reports of toxicity but application of preparations of tetracaine to highly vascular surfaces, mucous membranes and wounds larger than 6cm is not recommended. If lidocaine is injected following LAT the maximum dose of lidocaine (5mg/kg) should not be exceeded.

6.2 Neuraxial Analgesic Drugs

(Ansermino et al. 2003; de Beer and Thomas 2003; Peutrell and Lonnqvist 2003; Dalens 2006)

Drugs that produce a specific spinally mediated analgesic effect following epidural or intrathecal administration are referred to as neuraxial analgesic drugs (other terms include spinal adjuvants, caudal additives). Analgesia is not mediated by systemic absorption of the drug as spinal dose requirements and associated plasma concentrations are lower than those required for an analgesic effect following systemic administration. These agents modulate pain transmission in the spinal cord by:

- reducing excitation e.g. ketamine (NMDA antagonist)
- enhancing inhibition e.g. opioids; clonidine (alpha2 agonist); neostigmine (anticholinesterase); midazolam ($GABA_A$ agonist)

In paediatric practice, these drugs are most commonly administered as single dose caudal injections, and are often used in combination with local anaesthesia in order to improve and prolong analgesia, reducing the dose requirement for local anaesthetic and thereby unwanted effects such as motor block or urinary retention. There is conflicting data about the ability to produce a selective spinally mediated effect in children. No improvement in analgesia was reported when caudal clonidine was compared with peripheral nerve block or IV administration (Ivani et al. 2002; Hansen et al. 2004). Caudal administration of tramadol has been reported to produce lower serum concentrations of metabolites but no difference in analgesia when compared with IV administration (Murthy et al. 2000). Many studies which compare the effect of neuraxial drugs are hampered by poor study design, such as:

- inadequate power and sample size. If the sample size is small it is difficult to confirm any change in the incidence of side effects, particularly those that are less common.
- insensitive outcome measures. No difference may be found between two active treatments (e.g. LA ± additive; different doses; different routes such as caudal versus systemic) if pain scores and supplemental analgesic requirements are low in both groups. Measures of side effects such as sedation and respiratory depression are often insensitive and not standardised.

A number of compounds have been used for neuraxial analgesia, table 6.2.1 gives doses for neuraxial analgesia. The use of ketamine and clonidine is described here: tramadol, and other opioids are discussed in section 6.3.

Table 6.2.1
Doses of epidural neuraxial analgesics

Drug	Single dose	Infusion	Side-effects
clondine	1-2mcg/kg	0.08-0.2mcg/kg/hr	sedation; dose related hypotension and bradycardia (5mcg/kg); delayed respiratory depression and bradycardia in neonates

ketamine	0.25-1mg/kg		hallucinations at higher doses
morphine	15-50mcg/kg	0.2-0.4 mcg/kg/hr	nausea and vomiting; urinary retention; pruritis; delayed respiratory depression
fentanyl	0.5-1mcg/kg	0.3-0.8 mcg/kg/hr	nausea and vomiting
tramadol	0.5-2mg/kg		nausea and vomiting

6.2.01 Ketamine and Clonidine

(i) Preparations

Ketamine

(Marhofer et al. 2000; Koinig and Marhofer 2003)

Ketamine is an anaesthetic agent given by intravenous injection, intravenous infusion, intramuscular injection or orally. It can also be given by the epidural route for neuraxial analgesia. Ketamine produces dissociative anaesthesia characterised by a trance-like state, amnesia, and marked analgesia which may persist into the recovery period. There is often an increase in muscle tone and the patient's eyes may remain open for all or part of the period of anaesthesia. It has been found that ketamine has good analgesic properties in subanaesthetic IV doses and when used neuraxially. Ketamine can produce unpleasant emergence phenomena, including hallucinations. Ketamine is a racemic mixture, the S-isomer, has approximately twice the analgesic potency of the racemate and is available as a preservative-free solution for epidural use.

Clonidine

(Jamali et al. 1994)

Clonidine is an imidazoline and stimulates alpha2 adrenoceptors and central imidazoline receptors. It has analgesic, antiemetic and sedative properties and can produce hypotension and bradycardia. It can be used to treat opioid withdrawal. Clonidine can be given orally, transdermally, intravenously or epidurally.

(ii) Doses, side effects and toxicity

Ketamine: for anaesthesia 2 mg/kg given intravenously over 60 seconds usually produces surgical anaesthesia within 30 seconds of the end of the injection and lasting for 5 to 10 minutes. Caudal epidural administration of

preservative-free racemic ketamine has been extensively studied and the usual dose is 0.5mg/kg when given with a local anaesthetic. The S-isomer, has approximately twice the analgesic potency of the racemate and is available as a preservative-free solution. Typical dose for caudal epidural block is 0.25-0.5mg/kg, CNS stimulatory effects and neurobehavioural phenomena may be reduced by the lower dose. Ketamine undergoes hepatic biotransformation to an active metabolite norketamine and is excreted mainly in the urine as metabolites.

Clonidine: a typical dose for children when added to a caudal epidural local anaesthetic injection is 1-2 micrograms/kg. Clonidine is about 20 to 40% protein bound. About 50% of a dose is metabolised in the liver. It is excreted in the urine as unchanged drug and metabolites, 40 to 60% of an oral dose being excreted in 24 hours as unchanged drug; about 20% of a dose is excreted in the faeces, probably via enterohepatic circulation. The elimination half-life has been variously reported to range between 6 and 24 hours, extended to up to 41 hours in patients with renal impairment. Clonidine crosses the placenta and is distributed into breast milk. Caution is required in neonates as oversedation and respiratory depression and apnoea can occur. The hypotensive effect of clonidine may be enhanced by diuretics, other antihypertensives, and drugs that cause hypotension. The sedative effect of clonidine may be enhanced by CNS depressants. Clonidine has been associated with impaired atrioventricular conduction in a few patients, although some of these may have had underlying conduction defects and had previously received digitalis, which may have contributed to their condition. Clonidine hydrochloride has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Neuroxicity: issues relating to the potential neurotoxicity of some spinally administered drugs and the ethical use of unlicensed routes of administration has been debated for many years (Hodgson et al. 1999; Cousins and Miller 2004). The safety of spinally administered analgesic agents has not been conclusively confirmed and none has been specifically evaluated in children. In particular the effects of developmental age on the potential for neurotoxicity with neuraxial analgesics has also not been evaluated. The preservatives contained in many drug preparations have been implicated as a cause for neurotoxicity.

Ketamine with preservative has been associated with neurotoxicity. A preservative-free solution of S-ketamine (2-3 times as effective as racemate) is available in some countries, but again safety has not been unequivocally established (Dalens 2006).

The neurotoxicity of epidural **clonidine** has been more extensively studied, but licensing of this route is limited and does not encompass paediatric use.

6.3 Opioids

Opioids remain the most powerful and widely used group of analgesics. They can be given by many routes of administration and are considered safe, provided accepted dosing regimens are used and appropriate monitoring and staff education are in place. Morphine is the prototype opioid, diamorphine, tramadol, oxycodone, and hydromorphone are alternatives to morphine in the postoperative period. Fentanyl, sufentanil, alfentanil, and remifentanil have a role during and after major surgery and in intensive care practice and can be used to ameliorate the stress response to surgery. Codeine and dihydrocodeine can be used for short-term treatment of moderate pain. Pethidine (meperidine) is not recommended in children due to the adverse effects of its main metabolite, nor-pethidine. Opioid infusions can provide adequate analgesia with an acceptable level of side effects, Patient-controlled opioid analgesia is now widely used in children as young as age 5 years and compares favourably with continuous morphine infusion in the older child. NCA where a nurse is allowed to press the demand button within strictly set guidelines can provide flexible analgesia for children who are too young or unable to use PCA. This technology can also be used in neonates where a bolus dose without a background infusion allows the nurse to titrate the child to analgesia or to anticipate painful episodes while producing a prolonged effect due to the slower clearance of morphine. Neuraxial administration of opioids has a place where extensive analgesia is needed, for example after major abdominal surgery, spinal surgery or when adequate spread of epidural local anaesthetic blockade cannot be achieved within dosage limits.

Table 6.3.1
Relative potency of opioids

Drug	***Potency relative to morphine***	***Single dose (oral)***	***Continuous infusion (IV)***
Tramadol	0.1	1-2 mg/kg	100-400microgm/kg/hr
Codeine	0.1-0.12	0.5-1 mg/kg	N/A
Morphine	1	200-400 microgram/kg	10-40 micrograms/kg/h
Hydromorphone	5	40-80 microgram/kg	2-8 micrograms/kg/hr
Fentanyl	50-100	N/A	0.1-0.2 micrograms/kg/min or use TCI* system
Remifentanil	50-100	N/A	0.05-4 mcg/kg/min or use TCI* system

* target controlled infusion

6.3.01 Opioid preparations, dosages and routes

Morphine

(Kart et al. 1997b; a)

Morphine is the most widely used and studied opioid in children. Its agonist activity is mainly at μ opioid receptors. It can be given by the oral, subcutaneous, intramuscular, intravenous, epidural, intraspinal, and rectal routes. Parenteral administration may be intermittent injection, continuous or intermittent infusion the dose is adjusted according to individual analgesic requirements. Using accepted dosing regimens morphine has been shown to be safe and effective in children of all ages.

The pharmacokinetics of morphine in children is generally considered similar to those in adults but in neonates and into early infancy the clearance and protein binding are reduced and the half-life is increased. These differences, which are dependent on gestational age and birth weight, are mainly due to reduced metabolism and immature renal function in the developing child. This younger age group demonstrate an enhanced susceptibility to the effects and side effects of morphine and dosing schedules must be altered to take this into account. Morphine has poor oral bioavailability since it undergoes extensive first-pass metabolism in the liver and gut.

Morphine dosing schedules:
An appropriate monitoring protocol should be used dependent on the route of administration and age of the child. For neuraxial dosing see section 6.2.

Oral:
Neonate: 80mcg/kg 4-6 hourly
Child: 200-500mcg/kg 4 hourly

intravenous or subcutaneous loading dose: (titrated according to response}
Neonate: 25 mcg/kg increments
Child: 50 mcg/kg increments

Intravenous or subcutaneous infusion: 10-40 mcg/kg/hr

Patient Controlled Analgesia (PCA):
Bolus (demand) dose: 10-20mcg/kg
Lockout interval: 5-10 minutes
Background infusion: 0-4micrograms/kg/hr

Nurse Controlled Analgesia (NCA):
Bolus (demand) dose: 10-20mcg/kg
Lockout interval: 20-30 minutes
Background infusion: 0-20micrograms/kg/hr (<5kg use no background)

Diamorphine

Diamorphine hydrochloride is an acetylated morphine derivative and is a more potent opioid analgesic than morphine. It is much more lipid-soluble and has a more rapid onset and shorter duration of action than morphine. Diamorphine can be given by the oral, intranasal, subcutaneous, intramuscular, intravenous, and epidural and intrathecal routes. Due to its abuse potential the supply of diamorphine is carefully controlled and in many countries it is not available for clinical use.

On injection diamorphine is rapidly converted to the active metabolite 6-O-monoacetylmorphine (6-acetylmorphine) in the blood and then to morphine. Oral doses are subject to extensive first-pass metabolism to morphine. As with morphine, neonates and infants have altered pharmacokinetics and an increased susceptibility to the opioid effects of diamorphine.

Diamorphine dosing schedules:
An appropriate monitoring protocol should be used dependent on the route of administration and age of the child.

Oral: >1yr 100-200 mcg/kg 4 hourly

intravenous or subcutaneous loading dose: (titrated according to response}
Neonate: 10-25 mcg/kg increments
Child: 25-100 mcg/kg increments

Intravenous or subcutaneous infusion: 2.5-25 mcg/kg/hr

Intranasal: 100mcg/kg in 0.2ml sterile water instilled in to one nostril.

Hydromorphone

Hydromorphone is an opioid analgesic related to morphine but with a greater analgesic potency and is used for the relief of moderate to severe pain. It is a useful alternative to morphine for subcutaneous use since its greater solubility in water allows a smaller dose volume.

Hydromorphone dosing schedules:

Oral: 40-80micrograms/kg 4 hourly

intravenous or subcutaneous loading dose: (titrated according to response}
Child<50kg: 10-20 microgram/kg increments

Intravenous or subcutaneous infusion: 2-8 micrograms/kg/hr

Codeine

Codeine is much less efficacious than morphine and is used for the relief of mild to moderate pain. It is often given in combination with NSAIDs or paracetamol. Codeine can also given by intramuscular injection, in doses similar to those by mouth, the intravenous route should not be used as severe hypotension may occur.

The analgesic effect of codeine is unpredictable. Its effects may be wholly or mainly due to metabolism to morphine. The enzyme responsible for this conversion, CYP2D6, shows significant genetic variation and across populations the amount of codeine converted to morphine is very variable (Williams et al. 2002). Development may also affect CYP2D6 activity with lower levels of activity found in neonates and infants.

Codeine dosing schedules:

Oral, intramuscular or rectal:
Neonate or Child: 0.5-1 mg/kg 4-6 hourly (care with repeated doses in neonates)

Dihydrocodeine

Dihydrocodeine is an opioid analgesic related to codeine. It is used for relief of moderate to severe pain, often in combination with paracetamol. The analgesic effect of dihydrocodeine appears to be primarily due to the parent compound (unlike codeine), it is metabolised in the liver via the cytochrome P450 isoenzyme CYP2D6, to dihydromorphine which has potent analgesic activity, some is also converted via CYP3A4 to nordihydrocodeine.

Dihydrocodeine dosing schedules:

Oral or intramuscular: >1yr: 0.5-1mg/kg 4-6 hourly

Oxycodone

(Kalso 2005)

Oxycodone can be given by mouth or by subcutaneous or intravenous injection for the relief of moderate to severe pain. It can be given by continuous infusion or PCA. The oral potency is about twice that of morphine, whereas intravenously it is about 1.5 times as potent. Although not widely

used at present in the United Kingdom it may be a useful and safe alternative to morphine and codeine as an oral opioid.

Oxycodone dosing schedules:
Oral: 100-200micrograms/kg 4-6 hourly

Tramadol

(Grond and Sablotzki 2004; Allegaert et al. 2005)

Tramadol hydrochloride is an opioid analgesic with noradrenergic and serotonergic properties that may contribute to its analgesic activity. Tramadol can be given by mouth, intravenously, or as a rectal suppository. It has also been given by infusion or as part of a PCA system.

Tramadol is increasingly used in children of all ages and has been shown to be effective against mild to moderate pain. It may produce fewer typical opioid adverse effects such as respiratory depression, sedation and constipation though it demonstrates a relatively high rate of nausea and vomiting.

Tramadol dosing schedules: For neuraxial dosing see section 6.2.

Oral, rectal or intravenous: 1-2mg/kg 4-6 hourly

Fentanyl

Fentanyl is a potent opioid analgesic related to pethidine and is primarily a μ-opioid agonist. It is more lipid soluble than morphine and it has a rapid onset and short duration of action. Due to its high lipophilicity fentanyl can also be delivered via the transdermal (+/- iontophoresis) or transmucosal routes. Small intravenous bolus doses can be injected immediately after surgery for postoperative analgesia and PCA systems have been used.

After transmucosal delivery, about 25% of the dose is rapidly absorbed from the buccal mucosa; the remaining 75% is swallowed and slowly absorbed from the gastrointestinal tract. Some first-pass metabolism occurs via this route. The absolute bioavailability of transmucosal delivery is 50% of that for intravenous fentanyl. Absorption is slow after transdermal application.

The clearance is decreased and the half-life of fentanyl is prolonged in neonates. As with morphine, neonates are more susceptible to the adverse effects of fentanyl and appropriate monitoring and safety protocols should be implemented when fentanyl is used in this age group. There are differences in pharmacokinetics between bolus doses and prolonged infusion with highly lipophilic drugs such as fentanyl; the context sensitive half time progressively increases with the duration of infusion.

Fentanyl dosing schedules:

An appropriate monitoring protocol should be used dependent on the route of administration and age of the child. For neuraxial dosing see section 6.2.

intravenous dose: titrated according to response
0.5-1.0 mcg/kg (decrease in neonates)

Intravenous infusion: 0.5-2.5 mcg/kg/hr

Transdermal: 12.5-100 mcg/hr

Remifentanil

Remifentanil is a potent short-acting μ-receptor opioid agonist used for analgesia during induction and/or maintenance of general anaesthesia. It has also been used to provide analgesia into the immediate postoperative period. Remifentanil is given intravenously, usually by infusion. Its onset of action is within 1 minute and the duration of action is 5 to 10 minutes. Remifentanil is metabolised by esterases and so its half-life is independent of the dose, duration of infusion and age of child.

Remifantanil is a strong respiratory depressant. It can be used in the spontaneously breathing patient as a low dose infusion but the child must be nursed in an appropriate area with adequate monitoring. When appropriate, alternative analgesics should be given before stopping remifentanil, in sufficient time to provide continuous and more prolonged pain relief.

Remifentanil dosing schedules:
An appropriate monitoring protocol should be used.

Anaesthesia: 0.1-0.5mcg/kg/min

Spontaneously Breathing: 0.025-0.1mcg/kg/min

6.3.02 Opioid toxicity and side-effects

Opioids have a wide range of effects on a number of different organ systems (See table 6.3.02). These provide not only clinically desirable analgesic effects but also the wide range of adverse effects associated with opioid use.

The profile of side-effects is not uniform between the opioids or even between patients taking the same opioid. The incidence and severity of side-effects in an individual patient are influenced by a number of genetic and developmental factors and therefore appropriate monitoring and adverse effect management should be instituted for patients who are prescribed opioids.

Table 6.3.02
Physiological Effects of Opioids

1. Central Nervous System
    - Analgesia
    - Sedation
    - Dysphoria and euphoria
    - Nausea and vomiting
    - Miosis
    - Seizures
    - Pruritis
    - Psychomimetic behaviours, excitation

2. Respiratory System
    - Antitussive
    - Respiratory Depression
        - ↓ respiratory rate
        - ↓ tidal volume
        - ↓ ventilatory response to carbon dioxide
3. Cardiovascular System
    - Minimal effects on cardiac output
    - Heart rate
        - Bradycardia seen on most occasions
    - Vasodilation, venodilation
        - Morphine >> other opioids ?histamine effect
4. Gastrointestinal System
    - ↓ intestinal motility and peristalsis
    - ↑ sphincter tone
        - Sphincter of Oddi
        - Ileocolic
5. Urinary System
    - ↑ tone
        - Uterus
        - Bladder
        - Detrusor muscles of the bladder
6. Musculoskeletal System
    - ↑ chest wall rigidity

6.4 Non Steroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs are effective for the treatment of mild or moderate pain in children. In addition to analgesia they have anti-inflammatory and anti-pyretic effects. They are opioid sparing. The combination of NSAIDs and paracetamol produces better analgesia than either drug alone. Their mechanism of action is the inhibition of cyclo-oxygenase (COX) activity, thereby blocking the synthesis of prostaglandins and thromboxane. Aspirin, a related compound, is not used in children because of the potential to cause Reye's syndrome.

6.4.01 NSAID preparations, dose and routes

A number of convenient NSAID formulations are available:

- Ibuprofen tablet and syrup formulations for oral administration and a dispersible tablet for sublingual administration
- Diclofenac tablet (dispersible and enteric coated), suppository and parenteral formulations
- Ketorolac for intravenous use
- Naproxen oral tablets
- Piroxicam oral tablets and a dispersible sublingual formulation
- Ketoprofen oral tablets and syrup, parenteral formulations

Selective COX 2 inhibitors have been developed with the expectation that the analgesic & anti-inflammatory effects of NSAIDs would be retained while reducing the risk of gastric irritation & bleeding. However in adult studies potential improvements in safety have been offset by an increase in the incidence of adverse cerebral & cardiac thrombotic events. Reports of the use of selective COX-2 inhibitors in children are appearing in the literature which demonstrate equal efficacy with non selective NSAIDs. However their role in paediatric practice is yet to be established. Pharmacokinetic data for the neonatal use of ibuprofen has been established from its use in patent ductus arteriosus closure. Clearance is reduced and the volume of distribution is increased. However its use as an analgesic below age 3 months is not recommended, see section 6.4.03

NSAID	Dose mg/kg	Interval hours	Maximum Daily dose mg/kg/day	Licensed from age
Ibuprofen	5-10	6-8	30	3 months
Diclofenac	1	8	3	6 months
Ketorolac*	0.5	6	2	
Naproxen	7.5	12	15	
Piroxicam*	0.5	24	0.5	Not licensed for acute pain.

Ketoprofen*	1	6	4	

***High incidence of GI complications.**

6.4.02 NSAID toxicity and Side effects

Because of their mechanism of action NSAIDs have the potential to cause adverse effects at therapeutic plasma levels.

- Hypersensitivity reactions
- NSAIDs reduce platelet aggregation and prolong bleeding time. Therefore they are usually contra-indicated in children with coagulation disorders or in those who are receiving anti-coagulant therapy.
- NSAIDs can inhibit prostaglandin mediated renal function, this effect is greater in the presence of renal disease and dehydration. Ibuprofen has been shown to reduce the glomerular filtration rate in neonates by 20%. NSAIDs should not be administered concurrently with nephrotoxic agents. Renal toxicity is low in healthy children.
- NSAIDs can cause gastric irritation and bleeding. They are therefore relatively contra-indicated in children with a history of **peptic ulcer disease**. Ibuprofen has the lowest potential for gastric irritation. The risk of adverse GI effects is low when NSAID use is limited to 1-3 days in the post-operative period, it may be further reduced by co-prescription of proton pump inhibitors e.g. omeprazole and H2 anatagonists in patients at higher risk. Piroxicam, ketorolac and ketoprofen are known to be especially likely to cause GI side effects particularly in the elderly. In the UK, piroxicam is no longer licensed for acute indications and is subject to special prescribing and monitoring restrictions.
- Owing to excess leukotriene production NSAIDs have the potential to exacerbate **asthma** in a predisposed subset of asthmatics. It is estimated that 2% of asthmatic children are susceptible to aspirin induced bronchospasm, 5% of this subgroup are likely to be cross sensitive to other NSAIDs i.e. 1:1000. The incidence of asthma in children is increasing, and it is important that children who are not sensitive are not denied the benefits of NSAIDs. History of previous uneventful NSAID exposure should be established in asthmatic children whenever possible. Studies by Lesko and Short have provided some reassuring data regarding the safety of short term use of ibuprofen and diclofenac in asthmatic children (Short et al. 2000; Lesko et al. 2002). NSAIDs should be avoided in children with severe acute asthma.
- NSAiDs should be used with caution in children with severe eczema, multiple allergies and in those with nasal polyps. NSAIDs should be avoided in liver failure
- Animal studies using high doses of Ketorolac demonstrated delayed bone fusion. This has led to concern that the use of NSAIDs in children may delay bone healing following fracture or surgery. This has

not been supported by human studies and the analgesic benefits of short term NSAID use outweigh the hypothetical risk of delayed bone healing: see section 5.7.

- NSAIDs are not currently recommended for analgesia in neonates due to concerns that they may adversely affect cerebral and pulmonary blood flow regulation.

Of the NSAIDs currently available ibuprofen has the fewest side effects and the greatest evidence to support its safe use in children. In a large community based study in children with fever the risk of hospitalisation for GI bleeding, renal failure and anaphylaxis was no greater for children given ibuprofen than those given paracetamol(Lesko and Mitchell 1995).

6.5 Paracetamol

(Anderson et al. 1996; Anderson et al. 2001)

Paracetamol is a weak analgesic. On its own it can be used to treat mild pain, in combination with NSAIDs or a weak opioid such as codeine it can be used to treat moderate pain. Studies have demonstrated an opioid sparing effect when it is administered post-operatively.

6.5.01 Paracetamol preparations, doses and routes

Paracetamol is available for oral administration in syrup, tablet and dispersible forms. Following oral administration maximum serum concentrations are reached in 30-60 minutes. As the mechanism of action is central there is a further delay before maximum analgesia is achieved. Suppositories are available, however there is wide variation in the bioavailability of paracetamol following rectal administration. Studies have demonstrated the need for higher loading doses (of the order of 40mg/kg) to achieve target plasma concentrations of 10mg/l following rectal administration. The time to reach maximum serum concentration following rectal administration varies between 1 and 2.5 hours. Rectal administration of drugs is contra-indicated in neutropaenic patients because of the risk of causing sepsis. Recently an intravenous preparation of paracetamol has become available. Initial experience with IV paracetamol is that the higher effect site concentration achieved following intravenous administration is associated with higher analgesic potency. When administered IV it should be given as an infusion over 15 minutes.

There are several published dosage regimens for paracetamol (perhaps indicating that the optimum regimen is still to be determined). The regimen used will depend on the age of the child, the route of administration and the duration of treatment. The clearance in neonates is reduced and the volume of distribution is increased. The dose of paracetamol therefore needs to be reduced in neonates – see Table 1. Bioavailability following rectal administration is higher in the neonate. The current recommendations stated in the BNFc are shown in tables 1 and 2.

Table 1
Paracetamol dosing guide – oral and rectal administration

Age	Route	Loading dose	Maintenance dose	Interval	Maximum daily dose	Duration at maximum dose
28-32 weeks PCA	Oral	20 mg/kg	10 – 15 mg/kg	8 – 12 h	30 mg/kg	48 hours
	Rectal	20 mg/kg	15 mg/kg	12 h		
32 - 52 weeks PCA	Oral	20 mg/kg	10 – 15 mg/kg	6 – 8 h	60 mg/kg	48 hours
	Rectal	30 mg/kg	20 mg/kg	8 h		
> 3	Oral	20 mg/kg	15 mg/kg	4 h	90 mg/kg	48 hours

months	Rectal	40 mg/kg	20 mg/kg	6 h		

PCA = Post Conceptual Age

Table 2
IV Paracetamol dosing guide

Weight (kg)	Dose	Interval	Maximum daily dose
<5 (term neonate)	7.5mg/kg	4-6 h	30 mg/kg
5-10	7.5mg/kg	4-6 h	30 mg/kg
10-50	15mg/kg	4-6 h	60 mg/kg
>50	1 g	4-6 h	4 g

6.5.02 Paracetamol toxicity and side effects

When the maximum daily dose of paracetamol is observed it is well tolerated. The maximum daily dose is limited by the potential for hepatotoxicity which can occur following overdose (exceeding 150mg/kg). Multiple doses may lead to accumulation in children who are malnourished or dehydrated. The mechanism of toxicity in overdosage is the production of N-acetyl-p-benzoquinoneimine (NABQI). The amount of NABQI produced following therapeutic doses of paracetamol is completely detoxified by conjugation with glutathione. In overdosage glutathione stores become depleted allowing NABQI to accumulate and damage hepatocytes. Acetylcysteine and methionine replenish stores of glutathione and are therefore used in the treatment of toxicity.

6.6 Nitrous oxide (N2O)

(Bruce and Franck 2000)

6.6.01 Preparations, dosage and administration

Nitrous oxide is supplied compressed in metal cylinders labelled and marked according to national standards. It is a weak anaesthetic with analgesic properties rapidly absorbed on inhalation. The blood/gas partition coefficient is low and most of the inhaled N2O is rapidly eliminated unchanged through the lungs. Premixed cylinders with 50% N2O in oxygen are available, but it is also occasionally administered at inspired concentrations up to 70% with oxygen.
Nitrous oxide inhalation using a self administration with a face mask or mouthpiece and 'demand valve' system is widely used for analgesia during procedures such as dressing changes, venepuncture, as an aid to postoperative physiotherapy, and for acute pain in emergency situations, see section 4.0. It is also used in dentistry. The system is only suitable for children able to understand and operate the valve, generally those over 5 years of age. Heathcare workers must be specifically trained in the safe and correct technique of administration of N2O.

Nitrous oxide is given using a self-administration demand flow system operated by the patient unaided such that sedation leads to cessation of inhalation. Analgesia is usually achieved after 3 or 4 breaths. Recovery is rapid once the gas is discontinued.

Continuous flow techniques of administration, where the facemask is held by a healthcare worker rather than the patient, is capable of producing deep sedation and unconsciousness and therefore the use of this method is not included in this guideline. For information on sedation-analgesia see SIGN Guideline 58 available at: http://www.sign.ac.uk

6.6.02 Side effects and toxicity

Nitrous oxide potentiates the CNS depressant effects of other sedative agents. There is a risk of increased pressure and volume from the diffusion of nitrous oxide into closed air-containing cavities and is therefore contra-indicated in the presence of pneumothorax. Frequent side effects include euphoria, disinhibition, dizziness, dry mouth and disorientation. Nausea and vomiting can occur. Excessive sedation is managed by discontinuation of the gas, oxygen administration and basic airway management. Prolonged or frequent use may affect folate metabolism leading to megaloblastic changes in the bone marrow, megaloblastic anaemia and peripheral neuropathy. Depression of white cell formation may also occur. Patients who receive N20 more frequently than twice every 4 days should have regular blood cell examination for megaloblastic changes and neutrophil hypersegmentation.
Exposure to prolonged high concentrations of N2O has been associated with reduced fertility in men and women. It should only be used in a well ventilated environment which should be monitored and maintained below the UK

Occupational Exposure Standard for atmospheric levels of N_2O which is less than 100ppm.

6.7 Sucrose

(Lefrak et al. 2006)

Sucrose solutions reduce physiological and behavioural indicators of stress and pain in neonates. The effects of sucrose appear to be directly related to the sweet taste of the solution with very low volumes (0.05-2ml) in concentrations of 12-24% being effective within 2 minutes of administration.

6.7.01 Sucrose dosage and administration

Sucrose should be administered in a 24% solution 1-2 minutes before a painful stimulus, and may be repeated during the painful procedure if necessary. It can be given using a pacifier or directly dripped (one drop at at time) onto the tongue using a syringe, the number of applications is decided according to the infant's response. Upper volume limits per procedure have been suggested according to the gestational age in weeks:

27-31 0.5ml maximum
32-36 1.0ml maximum
>37 2.0ml maximum
each 'dip' of the pacifier is estimated to be 0.2ml.

The effectiveness of sucrose appears to decrease with age, at present it's use as a primary analgesic should be confined to the neonatal period until further information is available.

6.7.02 Sucrose side effects and toxicity

Coughing, choking, gagging and transient oxygen desaturations have been reported: when using the syringe method the solution should be applied carefully to the tongue one drop at a time. There is some evidence that adverse effects of sucrose, including a temporary increase in "Neurobiologic Risk' score, is more frequent in very premature infants, particularly those <27, and 28-31 weeks gestational age.

6.8 Non-pharmacological strategies

There is increasing interest in the use of non-pharmacological pain management strategies in acute pain. Skin to skin contact and other forms of tactile stimulation have been shown to be effective for needle related procedural pain in neonates (Bellieni et al. 2002; Johnston et al. 2003). There is growing evidence supporting the use of psychological interventions for a variety of acute pain indications. Psychological interventions for acute pain include a wide variety of physiological, behavioural and cognitive techniques aimed at reducing pain and pain related distress through the modulation of thoughts, behaviours and sensory information. Some of the most strongly supported are guided imagery, distraction and hypnosis (Uman et al. 2006. Liossi 2007). Some of the terms most commonly used to describe these techniques are detailed below:

- Behavioural interventions are defined as interventions based on principles of behavioural science as well as learning principles by targeting specific behaviours.

- Cognitive interventions are defined as interventions which involve identifying and altering negative thinking styles related to anxiety about the painful situation, and replacing them with more positive beliefs and attitudes, leading to more adaptive behaviour and coping styles.

- Distraction includes cognitive techniques to shift attention away from the pain or specific counter activities (e.g., counting, listening to music, playing videogames, talking about something else other than pain or the medical procedure).

- Hypnosis is a psychological state of heightened awareness and focused attention, in which critical faculties are reduced and susceptibility and receptiveness to ideas is greatly enhanced.

- Psychological preparation refers to specific interventions designed to provide information about the procedure and reduce anxiety. Often three types of information is provided: information about the procedure itself (i.e. steps that children must perform and steps that health care professionals will perform); the sensations the patient can expect to feel (e.g. sharp scratch, numbness); and about how to cope with the procedure.

- Relaxation is a state of relative freedom from anxiety and skeletal muscle tension, a quieting or calming of the mind and muscles.

Further Reading

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