Association of Paediatric Anaesthetists:

Good Practice in Postoperative and Procedural Pain

i) 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 efficacy of analgesic strategies such that an informed choice of analgesics that are appropriate for the patient and clinical setting can be made. 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 resume of analgesic pharmacology. The guidance will be updated biennially.

ii) Committee

Richard Howard	**Paediatric Anaesthetist** Chair
Bernadette Carter	**Professor of Children's Nursing** Representing RCN (UK)
Joe Curry	**Paediatric Surgeon** Representing BAPS
Neil Morton	**Paediatric Anaesthetist** Pain management specialist
Kate Rivett	**Lay Representative**
Mary Rose	**Paediatric Anaesthetist** Representing BPS
Jennifer Tyrrell	**Paediatrician** Representing RCPCH
Suellen Walker	**Paediatric Anaesthetist** Sen. Lecturer in Pain Medicine
Glyn Williams	**Paediatric Anaesthetist** Pain management specialist

Special thanks to:

Jean Craig	**Evidence Based Medicine**
Linda Whiteford	**Paediatrician**

iii) 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. In its present form it is not suitable for use by other groups. 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.

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 analgesia for specific procedures.

Procedures

The procedures are divided into two categories, painful diagnostic and therapeutic (Medical procedures; Section 4) and surgical procedures (Postoperative pain; Section 5). 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.

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 summarising the level of evidence available for the efficacy individual analgesic strategies.

Recommendations
Recommendations were formulated with the help of guidance published by the Scottish Intercollegiate Guidelines Network (SIGN) which are available at: www.sign.ac.uk/methodology/index.html and the National Institute of Clinical Evidence (NICE) http://guidance.nice.org.uk.

Good Practice Points
'Good practice points' have been included In situations where published evidence does not reflect current best practice, or where the committee wished to emphasise certain elements of good practice.

Evidence tables
Evidence tables are intended to allow the reader a rapid assessment of the strength of supporting evidence for individual analgesics or analgesic strategies relevant to the procedure in question. 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.

iv) Methodology and Evidence Grading

Systematic methods were used to search for evidence. Electronic searches were performed on the published literature between January 1996 and December 2006. Search strategies including databases and keywords are described in detail in Appendix 1, the technical report. 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, and they were graded from 1-4 according to the criteria below:

GRADE 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

GRADE 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

GRADE 3

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

GRADE 4

Expert opinion

Recommendations were formulated, where appropriate, and graded from A-D according to the criteria described below:

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

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

Grade C

A body of evidence including studies rated as 2+, 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+

Good practice points

Recommended best practice based on the clinical experience of the guideline development group, but not necessarily supported by research evidence.

SECTION 2.0

Summary of Recommendations and Good Practice Points

More detailed information and a summary of evidence for each procedure is available in the relevant section of the guidance.

Pain Assessment

(Section 3.0)

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

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)

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.

MEDICAL PROCEDURES

(section 4.0)

Good Practice Point

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

4.1 Procedural Pain in the Neonate

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, 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)

Specific procedures in the neonate:

4.1. 01 Blood Sampling

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 B
(A Taddio 1998; Jain A 2000; Gradin M 2002)

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

Multisensory stimulation including tactile stimulation, such as holding or stroking, should be combined with sucrose where feasible, as it may further reduce the pain response: Grade B
(Bellieni et al. 2002)

4.1. 02 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
(Lemyre et al. 2006; Taddio A 2006)

4.1. 03 Ocular Examination for Retinopathy of Prematurity

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)

4.1. 04 Lumbar Puncture

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

4.1. 05 Urine Sampling

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

4.1. 06 Chest Drain (tube) Insertion and Removal

(see 4.2. 03)

4.1 07 Nasogastric Tube Placement

(see 4.2. 05)

4.2 Procedural Pain in Infants and Older Children

Good Practice points

Children and their parents/ carers 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.

Specific procedures in infants and older children:

4.2. 01 Blood Sampling And Intravenous Cannulation

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)

Psychological strategies 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)

4.2. 02 Lumbar Puncture

Behavioural 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)

4.2. 03 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

4.2. 04 Urine Sampling

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)

Good practice point

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

4.2. 05 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.

4.2. 06 Immunization and Intramuscular Injection

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)

Swaddling, breast feeding or pacifier, and sucrose should be considered in infants undergoing vaccination: Grade B

(Lewindon et al. 1998; Reis EC 2003)

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.

4.2. 07 Repair of Lacerations

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 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)

Good Practice Point

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

4.2. 08 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
(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)

POSTOPERATIVE PAIN

(Section 5)

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

5.1.01 Myringotomy

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)

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.

5.1.02 Tonsillectomy

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 and pethidine: Grade B
(Ozer et al. 2003; Umuroglu et al. 2004; Ozalevli et al. 2005)

Intraoperative intravenous (IV) ketamine does not provide significant 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)

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.

5.1.03 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
(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)

Opthalmology

5.2.01 Strabismus surgery

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)

5.2.02 Vitreoretinal surgery

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

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

Dental Procedures

NSAIDs can provide adequate analgesia for dental extractions: Grade B
(Littlejohn et al. 1996; Purday et al. 1996; Roelofse and Payne 1999)

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)

General Surgery and Urology (Minor and Intermediate)

5.4.01 Subumbilical Surgery

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)

5.4.02 Circumcision

Caudal epidural and dorsal nerve block are effiective 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)

5.4.03 Neonatal Circumcision

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)

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.

5.4.04 Hypospadias Repair

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)

5.4.05 Orchidopexy

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)

5.4.06 Open Inguinal Hernia Repair

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)

General Surgery and Urology (Major)

5.5.1 Abdominal surgery

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).

Good Practice Point

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

5.5.2 Appendicectomy (open)

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

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.

5.5.3 Fundoplication (open)

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)

Good Practice Point

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

5.6 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.

5.7 Orthopaedics, Spinal and Plastic Surgery

5.7.01 Lower Limb Surgery

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 C
(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)

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.

5.7.02 Upper Limb Surgery

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

5.7.03 Spinal Surgery

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. 2006)

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

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.

5.7.04 Plastic Surgery of Head and Neck

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)

5.8 Cardiothoracic Surgery

5.8.01 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
(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)

5.8.02 Thoracotomy

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).

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.

5.9 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.

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 (Committee on Fetus and Newborn and Canadian Paediatric Society 2000; Anand et al. 2006; Batton et al. 2006; 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 UK 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 recommend 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 assessment 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 2006a)

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 1997; 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 2006b). 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 2006; 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

4.0 General Guidance on Procedural Pain Management

4.1 Procedural Pain in the Neonate

4.1. 01 Blood Sampling

4.1. 02 Percutaneous Central Venous Catheter Insertion (PICC)

4.1. 03 Ocular Examination for Retinopathy of Prematurity

4.1. 04 Lumbar Puncture

4.1. 05 Urine Sampling

4.1. 06 Chest Drain (tube) Insertion and Removal (see 4.2. 03)

4.1 07 Nasogastric Tube Placement (see 4.2. 05)

4.2 Procedural Pain in Infants and Older Children

4.2. 01 Blood Sampling And Intravenous Cannulation

4.2. 02 Lumbar Puncture

4.2. 03 Chest Drain (tube) Insertion and Removal

4.2. 04 Urine Sampling

4.2. 05 Insertion of nasogastric tubes

4.2. 06 Immunization and Intramuscular Injection

4.2. 07 Repair of Lacerations

4.2. 08 Change of Dressings in Children with Burns

Section 4.0 MEDICAL PROCEDURES

General Guidance

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, these 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. Further advice for use in specific age groups, and specifically for some of the most common procedures are described in sections 4.1 and 4.2.

Good Practice Point

Pain management for procedures should 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.

4.1 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. 2005; 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, 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 4.1.01-4.1.07. 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 be a feature of gestational age – this is an area that needs more research. 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). 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.

4.1. 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 4.1 on the general management of procedural pain.

Recommendations

(See also sections 4.0 and 4.1)

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 B
(A Taddio 1998; Jain A 2000; Gradin M 2002)

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

Multisensory stimulation including tactile stimulation, such as holding or stroking, should be combined with sucrose where feasible, as it may further reduce the pain response: Grade B
(Bellieni et al. 2002)

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 4.1. 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 S 2005). Topical local anaesthesia can reduce the pain of venepuncture (Jain A 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 4.1.02 (Taddio A 2006). 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 4.1.01 Blood sampling in the neonate

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

***** Venepuncture only

****** Heel lance only

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

4.1. 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 4.1.02 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

4.1. 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 venepuncture suggest doses of 0.012-0.12g of sucrose i.e. 0.2-2.0 ml of 12% 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 4.1.03 Examination for retinopathy of prematurity

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

4.1. 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 4.1

Analgesia table 4.1.04 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

4.1. 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 4.1. See section 6.7 for advice on the use and administration of sucrose.

Analgesia table 4.1.05 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

4.1. 06 Chest Drain (tube) Insertion and Removal

The management of his procedure in the neonate is discussed with that of older children in section 4.2. 03

4.1 07 Nasogastric Tube Placement

The management of his procedure in the neonate is discussed with that of older children in section 4.2. 05

4.2 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 4.1 for a general introduction on the management of procedural pain, and section 4.1.01 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.

Good Practice points

Children and their parents/ carers 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.

4.2. 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 4.2: 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)

Psychological strategies 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).

Analgesia table 4.2.01 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+**

4.2.02 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 4.2 on the general management of painful procedures.

Recommendations

Behavioural 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 bio behavioural techniques such as distraction 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 4.2.02 Lumbar puncture in children

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

4.2.03 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 4.2 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.* Multimodal therapy e.g. IV morphine, Nitrous Oxide, 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 4.2.03 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

4.2.04 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 4.2 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 behavioural 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 behavioural interventions are likely to be more effective (Stevens 2006).

Analgesia table 4.2.04

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.

4.2. 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, 4.1 and 4.2 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 4.2.05 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

4.2.06 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, 4.1 and 4.2 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.

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)

Swaddling, breast feeding or pacifier, and sucrose should be considered in infants undergoing vaccination: Grade B

(Lewindon et al. 1998; Reis EC 2003)

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 4.2.06 Immunisation and intramuscular injection

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

4.2.07 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. 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 4.2 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 4.2.07 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++**

4.2.08 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, 4.1 and 4.2 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 4.2.08 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

Contents

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5.0 General Management of Postoperative Pain

Postoperative pain management 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

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 which occurs during the postoperative period.

Intraoperative 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.

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.

5.1 ENT surgery

5.1.01 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 5.0 for the general management of postoperative pain.

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).

As **opioids** e.g. codeine, butorphanol or fentanyl, have been associated with increased side-effects without clinically significant improvements in analgesia, 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 (oral codeine, nasal butorphanol (Pappas et al. 2003))

Analgesia table 5.1.01

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

* not routinely recommended due to side effects: see text

5.1.02 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 5.0 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 and pethidine: Grade B
(Ozer et al. 2003; Umuroglu et al. 2004; Ozalevli et al. 2005)

Intraoperative intravenous (IV) ketamine does not provide significant 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 and Lee 2001).
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 5.1.02

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.

5.1.03 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 5.0 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 5.1.03

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

5.2 Opthalmology

5.2.01 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 5.0 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 5.2.01

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.

5.2.02 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 5.0 for the general management of postoperative pain.

Recommendations

NSAID provides similar analgesia but lower rates of PONV compared with opioid: Grade B
(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 5.2.02

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

5.3 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 5.0 for the general management of postoperative pain.

Recommendations

NSAIDs can provide adequate analgesia for dental extractions: Grade B
(Littlejohn et al. 1996; Purday et al. 1996; Roelofse and Payne 1999)

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 painfree 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). **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 5.3

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

5.4 General Surgery and Urology (Minor and Intermediate)

5.4.01 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 5.0 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 (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 5.4.01 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

5.4.02 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 daycase basis. Circumcision in the neonate is considered separately in section 5.4.03. See sections 5.0 for the general management of postoperative pain and 5.4.01 for a discussion of subumbilical surgery.

Recommendations

Caudal epidural and dorsal nerve block are effiective 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 5.4.02 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

5.4.03 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 5.4.01), the debate regarding the necessity for general anaesthesia in the neonate remains unresolved. See sections 5.0 for the general management of postoperative pain and 5.4.01 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 5.4.03 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 mutimodal technique

5.4.04 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 daycase surgery whilst others require hospital admission overnight or longer, with the possibility of prolonged urethral catheterisation and painful postoperative dressing changes. See sections 5.0 and 5.4.01 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 no comparisons with other local anaesthetics or between different concentrations or volumes.

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, levobupivaciane or ropivacaine), there was an exclusion rate of 10% in this study, and there has been no comparison between caudal or lumbar epidural approaches(De Negri et al. 2004). 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 5.4.04 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

5.4.05 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 5.0 and 5.4.01 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 5.4.05 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

5.4.06 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 5.0 and 5.4.01 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 however, did not improve efficacy (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 5.4.06 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

5.5 General Surgery and Urology (Major)

5.5.01 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 5.5.02, 5.5.03 and laparoscopic techniques in section 5.6. See also section 5.0 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, although the exact surgical incision employed is infrequently 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 5.5.01 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

5.5.02 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 5.5.00 and 5.5.01 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, particulary 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 5.5.02 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

5.5.03 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 5.6.0. 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 5.5.00 and 5.5.01 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 (scoloiosis) were excluded in one study(McNeely et al. 1997; Wilson et al. 2001).

Analgesia table 5.5.03 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

5.6 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 5.0.

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 5.6 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

5.7 Orthopaedics, Spinal and Plastic Surgery

5.7.01 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 specfic 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 C
(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 5.7.01 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

5.7.02 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 5.0 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 D
(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 D
(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 5.7.02 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

5.7.03 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 5.0 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. 2006)

The use of 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 hydrophilic opioids in the epidural space has a favourable analgesic profile 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 visualistion during surgery was important.
Using a **dual epidural catheter** technique, also placed under direct vision may have benfits. 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 5.7.03 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

5.7.04 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 5.0 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 5.7.04 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

5.8 Cardiothoracic Surgery

5.8.01 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 5.0 for the general mangement 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. 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 5.8.01 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

5.8.02 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 supplemantary 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 5.8.02 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 extracranial 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 patients 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 5.0 on the general management of postoperative pain, and section 5.9.01 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.

5.9.01 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 have not been studied. See also sections 5.0 and 5.9 for the general management of postoperative 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).

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 5.9.01 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 cardiotoxic 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 cardiotoxic 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 portwine 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 eg. ketamine (NMDA antagonist)
- enhancing inhibition eg. 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 (eg. 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 favorably 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. It's 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 are 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, epidural and intraspinal 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 efficaceous 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.

Anaestheisa: 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.

NSAID	Dose mg/kg	Interval hours	Maximum Daily dose mg/kg/day	Licensed from age
Ibuprofen	5-10	6-8	40	3 months
Diclofenac	1	8	3	6 months
Ketorolac	0.5	6	2	
Naproxen	7.5	12	15	
Piroxicam	0.5	24	0.5	
Ketoprofen	1	6	4	

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 is not recommended below 3 months, see section 6.4.03

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.
- 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	72 hours

months	Rectal	40 mg/kg	20 mg/kg	6		

PCA = Post Conceptual Age

Table 2
IV Paracetamol dosing guide

Weight (kg)	Dose	Interval	Maximum daily dose
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, disinhinbition, 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 N2O 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.

Further Reading

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Technical Report

1.0 Search strategy

Systematic methods were used to search for studies relevant to the three evidence-based sections of the guideline:
Section 3.0 Pain Assessment
Section 4.0 Medical Procedures
Section 5.0 Postoperative Pain

General searches were performed for human studies between the dates of 1st January 1996- 31st December 2006, in children, 0-18 years. Intervention studies including meta-analyses and systematic reviews evaluating the efficacy/ validity of pain management techniques and assessment tools for acute postoperative and procedural pain were identified and included by keyword search and appraisal of abstracts. Databases consulted were Pubmed/Medline, Ovid, Cinahl, Embase, Psychlit, Ingenta, Web of Science, British Nursing Index and Cochrane Library as appropriate.
For pain assessment, the list of articles obtained was also compared to those obtained by the RCN in conjunction with Bazian in developing the upcoming revision of the guideline 'Recognising and assessing the intensity of acute pain in children' as part of a collaboration process.

For procedure-related and postoperative pain, intervention studies including meta-analyses and systematic reviews of interventions, examining the efficacy of analgesics or analgesic strategies were identified and included by keyword search and appraisal of citations, abstracts or full text articles as appropraite. See figure 1 for search example.

Review articles and published guidelines relevant to the above were also identified and appraised, the latter using the AGREE instrument (available at: http://www.agreecollaboration.org/1/agreeguide/sign/index.html) including a bibliography review in order to confirm that searches had identified all relevant publications.

Table 1: Existing Guidelines

Year	Title	Source	AGREE compliant
1999	The recognition and assessment of acute pain in children	RCN (UK)	Y
2001	The recognition and assessment of acute pain in children	RCPCH (UK)	n/a
2005	Guideline Statement: the management of procedure-related pain in neonates	RACP (Australia) Paediatrics and Child Health Division	N
2005	Guideline Statement: management of procedure related pain in children and adolescents	RACP (Australia) Paediatrics and Child Health Division	N
2005	Acute Pain Management: Scientific Evidence*	ANZCA (Australia)	Y

*adults and children

Fig. 1 Search Strategy Example: Pubmed

1. **PubMed**
   http://www.ncbi.nlm.nih.gov/entrez/query.fcgi

2. **Limits**
   i) "**English**"
   ii) "**Humans**"
   iii) "**All Child: 0 -18 years**"

3. General Searches obtained using criteria:
   i) **child or children or paediatric or pediatric**
   ii) **acute pain or postoperative pain or analgesia**
   iii) specific procedure or keyword eg. "**tonsillectomy or tonsil"**

4. Searches i) - iii) combined using search "**History"** function.

5. Citations assessed for inclusion.

6. Expand function ("find related articles") used for key articles to broaden search.

7. Abstracts obtained and reviewed.

8. Full text articles obtained except where otherwise specified in data extraction tables

2.0 Appraisal of studies

Efficacy studies or other studies reporting efficacy data were appraised and graded for quality using the grading system recommended by the Scottish Intercolleageate Guideline Network (SIGN), shown below:

GRADE 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

GRADE 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

GRADE 3

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

GRADE 4

Expert opinion

This process was assisted by the use of study quality checklists: available from SIGN at www.sign.ac.uk/methodology/index.html. And using the 'Oxford Bias Guide' for the evaluation of clinical trials available at: http://www.jr2.ox.ac.uk/bandolier/Extraforbando/Bias.pdf .

3.0 Formulation of recommendations

Recommendations were formulated and graded according to the following criteria:

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

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

Grade C

A body of evidence including studies rated as 2+, 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+

This process was assisted by reference to published guidance from the National Institute for Clinical Excellence (NICE) on creating guideline recommendations available at: http://www.nice.org.uk/page.aspx?o=423027

4.0 Good practice points

Good practice points are recommendations for best practice based on the clinical experience of the guideline development group, but not necessarily supported by research evidence.

5.0 Data Extraction Tables

1. Pain Assessment (see attached file)
2. Medical Procedures (see attached file)
3. Postoperative Pain (see attached file)

Pain Assessment I (Procedural/Post-Operative)

Author/Yr/ Paper Code/Jrnal	Paper title	Study Design/ Type	No. of patients /partics	Patient/Part. Characteristics	Pain Tools Used	Result & Conclusion	Limitations	Problems	Grade. Cmmnts
Vetter, TR & Heiner, EJ (1996) Journal of Clinical Anesthesia USA	Discordance between patient self-reported visual analog scale pain scores and observed pain-related behaviour in older children after surgery	Prospective, comparative study. To assess the correlation in an older pediatric population between, patient self-reported visual analog scale (VAS) p ain scores and observational pain-related behavior scores. Inpatient surgical units of a free-standing children's hospital. 3 health care providers (a CNS, RN, &child life specialist) did independent observation using pain-related behavioural score.	n=30	30 ASA physical status I and II outpatients, 8 to 16 years of age, undergoing a variety of orthopedic, plastic, urologic, and general surgical procedures.	VAS (0-10) with **smiling anchor** as 0. 10cm slide-rule. Independent pain-related behaviour score (0-100)	When compared with a patient's self-reported VAS score, the 3 pain-related behavioral scores generated by each HCP for a given patient exhibited both variable and minimal correlation. It appears that a tenuous relationship may exist between an older child's own perception of pain intensity and his or her behavioral expression of that pain as interpreted by a HCP.	The pain related bahviour tool was not validated. Other studies show that self-report is usually different to behavioural assessment. NO limitations identified in the paper.	The pain behaviour score not validated; just clinical impression based on facial expression, activity level and breathing pattern	2-

Foster, R.L. & Varni, J.W. 2002 Journal of Pain and Symptom Management. USA	Measuring the Quality of Children's Postoperative Pain Management: Initial Validation of the Child/Parent Total Quality Pain Management (TQPM™) Instruments	A descriptive, correlational design guided this two-phase study conducted at 2 sites. Phase 1 – initial testing; Phase 2: instrument testing The purpose of this study was to address one aspect of pain management for children, the postoperative period.	Phase 1: n=5 (child/parent dyads) Phase 2 n=50 (parent/child dyads)	Phase 1: 8 - 12 yrs. Phase 2: 8-12 yrs 50% boys/50% girls Range of backgrounds.	The Child TQPM And Parent TQPM (they modified both from the adult tool)	The pain intensity scale adapted for the Child and Parent TQPM instruments demonstrated good criterion-related validity. Beginning support for construct validity was demonstrated	Uses a smiling face as the anchor for no pain – so is it valid? Needs larger more diverse population to be tested on.	Further research is needed	2+
Myatt, HM. & Myatt, RA. (1998) International Journal of Pediatric Otorhinolaryngology UK	The development of a paediatric quality of life questionnaire to measure post-operative pain following tonsillecto	Development of a Paediatric Quality of Life Questionnaire to assess pain amongst children following tonsillectomy. The nine item questionnaire was completed by parents at 4,8 and 24 hours post operatively. A descriptive cross sectional study.	n=48 (aged 2 –13 years)	Patient underwent elective dissection tonsillectomy by the same surgeon.	A Paediatric Quality of Life questionnaire to measure postoperative pain following tonsillectomy.	Item nine was deleted to improve internal consistency of the questionnaire. No significant correlations were found between the amount of post operative analgesia dispensed and QoL scores.	Unable to perform construct validity because there was no gold standard in which the new questionnaire could be compared. The criterion	Problems with the questionnaire not being a self report scale but an observational instrument. Wide age range from very young to adolescence Numerous problems with the research process in terms of consistency in the process	2-

my					Nevertheless the QoL scores significantly increased over time which is in clinical accordance that pain decreases over time. Suggests the eight item questionnaire will provide HCP with an accurate way of measuring post tonsillectomy children.		validity using amount of post-operative analgesia prescribed might not be reliable, or results could reflect the instrument does not measure the amount of pain. Problems with validity due to subjective phenomenon – has face validity Criterion validated by comparing pain score with analgesia administered, though variables still make this inaccurate i.e. delay/timing in

							administering analgesics will affect scoring so time is a factor		
De Jong, AEE, Bremer, M, Schouten, M, Tuinebrieje r, WE, Faber, AW. 2005 Burns Netherland s	Reliability and validity of the pain observatio n scale for young children and the visual analogue scale in children with burns	Aim to assess if the POCIS and the VAS are reliable and valid instruments to measure procedural and background pain in burned children. Videos taken in 1st week of admission, to decrease the influence of wound care procedures on pain behaviour. A total of 24 fragments (18 during wound care and 6 during periods of rest) of 2 min each was randomly selected. Ragments then viewed by nurses and rate on (1) impression, (2) VAS, then (3) POCIS. One fragment = practice, then rest = real.	N=18 children N=73 nurses from	Children in 3 Dutch burns units Aged 0–4 years.	POCIS (pain observation scale for young children – derived from CHEOPS) and VAS (used by nurses)	VAS ratings for fragments in group Poor intra-rater reliability for background & procedural pain. Low minimum value confidence interval for both types of pain together. Construct validity not obtained due to poor inter-rater reliability in both scales. POCIS scores = poor to moderate interrater reliability, moderate to good intra-rater reliability and an acceptable internal consistency.	Convenience sample. Nurses may not have been trained adequately (ie, only one practice fragment) so this may have thrown results.	VAS deemed unsuitable for assessing pain by nurses of burned children	2-
Blount, R.L.,	The Child–Adult	Purpose: to examine the validity of the	N=60 (child/p	N=32 boys, 28 girls	*CAMPSIS-SF* CAMPIS-R,	This study suggests that the	Faces scale used smiling		2-

Bunke, V., Cohen, L.L., Forbes. C.J. 2001 Journal of Pain and Symptom Management. USA	Medical Procedure Interaction Scale-Short Form (CAMPIS-SF): Validation of a Rating Scale for Children's and Adults' Behaviors During Painful Medical Procedures	CAMPIS-SF (against other tools) All four observational measures were coded using videotaped recordings of the immunizations. Coding spanned from up to 3 minutes prior to the cleaning of the child's arm for injection until 2 minutes post-injection or the child left the room. Other validity measures included parent-report of child fear and pain, staff-report of child distress and cooperation, and child self-report of fear and pain. Parent and staff reports were assessed VAS	arent/nurse triads)	Age 3-7yrs	Observational Scale of Behavioral Distress (OSBD), Behavioral Approach-Avoidance Distress Scale (BAADS) FACES Scale for child self report. And VAS (parents and staff)	CAMPISSF is a valid measure as evidenced by numerous significant correlations with three other valid, reliable, and recognized pediatric pain observational measures, and with several parent-report, staff-report, and child-report inventories.	face. all participants were of a narrow age range; only one type of acute painful medical procedure, immunizations, was used; and all of the children were healthy.		
Bosenberg, A., Thomas, J., Lopez, T., Kokinsky, E., Larsson, L.E. 2003	Validation of a six-graded faces scale for evaluation of postoperative pain in children	Aim to evaluate the validity of a six-graded faces pain scale after surgery by comparing the level of agreement between the children's report of faces pain scores and experienced nurses' assessment of pain by observation of behaviour. Postoperative pain	N=110	N=110 boys, 10 girls Aged: 4-12 yrs Two settings (one urban, one rural)	*6 graded faces pain scale for children (Smiley one) Four graded observer scale for nurse – no pain – severe pain)*	For the whole material, the correlation coefficient was 0.76. (0.70 seen in other studies as requirement for validity of pain tool when comparing 2 diff methods for self-report in same	Differences between 2 setting - possibly dye to (1) cultural differences, (2) anaesthetic technique differences, or (3) nurses' ability to	Children asleep were considered not to be in pain	2-

Pediatric Anesthesia South Africa		assessments were undertaken every hour for 8 h after the injection of ropivacaine unless the patient was asleep and in addition if the child reported pain between the observation points. In every patient, the result of the four-graded scale was recorded before the evaluation with the faces scale. Total of 753 pain assessments made.				pt). the findings in the study support the six faces scale to be a valid instrument for measuring postoperative pain in children.	assess.	
Suraserani vongse, S., Santawat, U., Kraiprasit, K., Petchharat ana, S., Prakkamad om, S., and Muntraporn , N. (2001) British Journal of Anaesthesi	Cross validation of a composite pain scale for preschool children within 24 hours of surgery	Cross validation of a composite measure of pain scales for preschool children with 24 hours of surgery in Thailand. Videotaped children's behaviour before and after surgery (before analgesia was administered) and observers rated pain behaviour	n=167 (aged 1-5.5 years). 30 nurses rated the behaviours of children on videotape and evaluated the practical	Children were undergoing anaesthesia and surgery at hospitals in Bangkok, Thailand.	Children's Hospital of Eastern Ontario Pain Scale (CHEOPS), Objective Pain Scale (OPS), Toddler Preschool Postoperative Pain Scale (TPPPS) and Face, Legs, Activity, Cry, Consolability (FLACC).	CHEOP is recommended as a valid, reliable and practical tool for clinical use. The content validity of OPS and FLACC was accepted but some problems detected in CHEOPS and TPPPS. Inter rate and intra rater reliabilities of the four observers were excellent and construct or	The videotape methodology could be an inaccurate way to observe behaviour. CHEOPS is recommended above FLACC (which has similar psychometric properties) although CHEOP	Some problems with missing data e.g.18 had missing PACU data and 28 had missing ward data.	2+

a. Thailand			ities of using the tools			discriminant validity clearly demonstrated significant differences in pain after surgery. The agreement of CHEOPS with the clinical decision to treat pain was the highest among all scales both in PACU and on the ward. A cut off point of 6 for CHEOPS in the PACU yielded good agreement with the decision to treat pain and a cut off point of 5 on the ward.	takes 14 seconds longer to complete. The reason for this is not discussed. Problems with behaviour identification in Thai children, which not comparable with Western children	
Versloot, J., Veerkamp, Hoogstraten Community Dent Oral Epidemiol. 2006 Netherlands	Dental Discomfort Questionnaire: assessment of dental discomfort and/or pain in very young children	Aim to present and analyse the DDQ for very young children and to assess the possible differences in pain-related behaviours displayed by children with or without reported toothache, and by children with or without decayed teeth. Parental interviews generated data for the development of the DDQ.	N=146	Parents on behalf of toddlers. 94 referred to special dental care centre (decayed teeth) and 52 from day care centre. Mean age 47 mnths	Dental Discomfort Questionnaire (DDQ)	Preliminary validation of the questionnaire if four (of 12) items removed. One-third of children with decayed teeth without toothache according to the parent had a relative high score on the DDQ,	Sample was referred.	2-

						suggesting there might be children in this subsample with unrecognized toothache.		
Suominen, P., Caffin, C., Linton, S., McKinley, D., Ragg, P., Davie, G., Eyres, R. 2004 Pediatric Anesthesia	The cardiac analgesic assessment scale (CAAS): a pain assessment tool for intubated and ventilated children after cardiac surgery	Evaluated the reliability and validity of the Cardiac Analgesic Assessment Scale (CAAS) as a postoperative pain instrument for children after cardiac surgery. Two prospective studies Four concurrent observers performed paired observations with the CAAS or the VAS once for every patients. Three different CAAS values were analysed to study the changes in the CAAS values and response to analgesia over time: (i) CAAS value before the administration of i.v. morphine; (ii) the highest CAAS score indicating the need for i.v. morphine; and (iii) the CAAS score following the intervention. Scoring was performed at least every 2 h. The data	N=69. (Part 1= 32, Part 2 = 37)	69 children (aged 0–16 years) admitted to the intensive care following cardiac surgery with a sternotomy incision.	Cardiac Analgesic Assessment Scale (CAAS) VAS	VAS had low interrater reliability. A CAAS score of four or more is interpreted as the appropriate level of pain at which medication is required. The CAAS was shown to be internally consistent. The CAAS variables and the total CAAS score had almost perfect interrater reliability. In 97% of cases the nurses agreed as to whether there was an indication for treatment of pain or not. CAAS	The time difference after the administration of pain medication to the next CAAS scoring was delayed in some cases making the interpretation of the efficacy of the intervention more difficult.	2-

		of 37 patients from the ITM study who had these three scores, was used to evaluate the ability of the CAAS to detect changes in pain status and responses to analgesia over time.				significantly reflects changes in pain status over time. CAAS more consistent measurement of postop pain in ventilated and sedated children than subjective assessment using the VAS.		
Ramritu, PL 2000 Journal of Clinical Nursing Australia	Use of the Oucher Numeric and the Word Graphic Scale in children aged 9±14 years with post-operative pain	Construct validity. Purpose of this study was to further examine the construct validity of the Oucher Numeric and the Word Graphic Scales AND to investigate the clinical applicability of the two scales. The children used the Oucher Numeric Scale and the Word Graphic Scale to report on the intensity of pain before and at each of the 4 h following admin. of analgesia. At the end of 4 hours following the administration of analgesia, or just before	N=81	35 (42.7%) girls; 46 (56.8%) boys, Ages 9 -14 years (mean 11 years).	Oucher Numeric Word Graphic Scales	Forty-four children (54.3%) preferred the Oucher Numeric Scale, 53% of parents preferred WGS Nurses (65%) preferred Oucher NS. Both the Oucher Numeric and the Word Graphic Scales are valid scales and useful in assessing children's pain. Since the scales provide two different methods of conceptualizing pain (numbers or words), their use	non-randomized sample of the study limits the generalizability Usually children were discharged on day 1, which meant that data sometimes couldn't be collected for all of the 4 h following the admin. of analgesia or the child could not be included in the study if	2-

discharge in instances where the child was discharged during data collection, the child, parent and nurse were asked to identify their preference of scale and reason for their preference.		in clinical settings would give children a choice in methods of reporting the intensity of their pain.	analgesia was not admin. very early in the morning. The ethical considerations of not waking children who were sleeping also led to the loss of some valuable data.

INTERVENTION Pain Assessment (Child)

Author/Yr/ Paper Code/Journal	Paper title	Study Design/ Type	No. of patients /participants	Patient/Part. Characteristics	Pain Tools Used	Result & Conclusion	Limitations	Problems	Evidence Grade and Comments
Chambers, CT and Craig, KD. (1998) Pain USA	An intrusive impact of anchors in children's faces pain scales	Cross sectional/ comparative study. To examine the potential biasing impact of a smiling face anchor compared to a neutral face in a face pain scale in response to a series of vignettes. Allocated randomly to one of three groups. Children were tested in a quiet area of their day care centre after responding to a letter sent to their homes.	n=100 (children aged 5-12 years stratified into three groups. 5-6 years (n=32) 7-8 year (n=34) and 9-12 years (n=34). n=49 boys, n=51 females.	Children recruited from child care centres in Vancouver. Variety of socioeconomic backgrounds. Command of the English language.	Faces pain scales were used and presented to children either to measure sensory pain (presence of pain) or affective pain (feeling happy or sad). A child's emotion was also measured using vignettes and a VAS used to rate the level of pain on each vignette.	The children completed a faces scale, a VAS and emotions scale in response to four scenarios. Format of scale and not the accompanying instructions should be considered when choosing a tool to use. Children using the smiling scale had significantly higher pain scores for no pain and pain /negative emotions vignettes and lower faces scale scores for	Small sample sizes when divided into subgroups. The use of hypothetical vignettes may not be generalisable to clinical pain scenarios. Use of vignettes meant the children were not actually experiencing pain at the time of scoring. The faces scales were developed specifically for the study and their psychometric properties are not well	Use of VAS scales assumes same value to each interval + 'no pain' = 'smiley face' n=8 children did not understand the VAS scale.	2-

		ANOVA of scores.				pain/positive vignettes than children who used neutral scales. Using a rating pain with smiling faces may alter children's concepts of pain. Younger children rated negative emotion vignettes as more painful than older children.	explored. Research bias? (no blinding evident).		
Chambers, CT., Hardial, J., Craig, KD., Court, C. and Montgomery, C. (2005) Clinical Journal of Pain USA	Faces Scales for the Measurement of Postoperative Pain Intensity in Children Following Minor Surgery	Comparative study. Used 5 successively administered faces scales and the Colored Analog Scale (CAS). Aim to determine whether faces scales beginning with a smiling rather than a	n=78 children aged 5-13 years, (39 boys, 39 girls), n=78 parents/guardians (55 mothers, 20 fathers and 3 others)) and n=31 postoperative care nurse)	Children, parents/carers and their post-op care nurse. Children were undergoing surgery and were recruited from the surgical unit at a Children's Hospital. They were scheduled for day/overnight stay surgery. All from middle	Five faces scales were used of which 3 were neutral and 2 were smiling (specified and in addition the Coloured Analogue scale (CAS) was used as the independent measure. All scales administered	Parents and nurses rated significantly more pain when using scales with a smiling rather than a neutral face. The pattern was not as clear for the children's ratings although their highest ratings were provided using a smiling scale. CAS	Number of scales used – variability in terms of number of faces per scale/interval scales. CAS excluded in children's rating of preference. Further work needed to examine the statistically	Effects of having undergone surgery on children's performance.	2+

neutral (no pain) face would produce higher ratings in the assessment of postoperative pain intensity in children and compare this to reports from scales using an additional independent measure of pain intensity. Children given five scales to complete and the CAS around 40 minutes after surgery.		socioeconomic status, English speaking.	to child in PACU. Order of admin randomised to each child but same order used for matched parent/nurse. Child asked which scale they liked best and why. Pearson correlation coefficients were used to examine the relations among the 5 scales and the CAS for children's, parents', and nurses' ratings. As correlational analyses do not disclose mean differences among measures, analyses of	ratings were more similar to ratings using a neutral scale. The Wong and Baker scale was the most popular amongst all three subgroups (which collected the higher pain ratings). There were no age or sex differences in ratings of pain scales.	significant differences among faces scales in children's pain.

					variance (ANOVA) were also undertaken. Parents/nurse blind to all of child's scores/responses				
Van Cleve, L., Munoz, C., Bossert, EA. And Savedra, MC. (2001) Pain Management Nursing, USA	Children's and Adolescents' Pain Language in Spanish: Translation of a Measure	Aim to have tool available for Spanish speaking children (from range of countries of origin where Spanish is spoken with different dialects etc. 3 Pilot studies undertaken with well children aiming to translate APPT into Spanish. Final aim to enable collection of data from	n=17 (pilot 1 n=5, 10-14 years, pilot 2 n=5, 10-17 years, pilot 3 n=7, 7-14 years and n=5 for the Leukaemia study, 8-17 years).	Patients for the pilot studies were from schools and community church and were Spanish speaking children from Mexico, South America and Central America). The Leukaemia study featured all children who were newly diagnosed with acute lymphocytic leukaemia.	Adolescent Paediatric Pain Tool (APPT)	Content validity of APPT was supported as 51/66 words in the Spanish APPT was selected by at least one child to describe pain. Evidence to support the Spanish speaking children understand and use the words on the Spanish translation of APPT. The APPT Spanish translation has not undergone enough testing	Very small sample size and further work needs to be conducted so that statistical tests can be performed to evaluate the validity of APPT. Newly diagnosed children might not be the best choice in terms of participation in project + no clear explanation of why this particular sample	The translation of APPT followed strict guidelines but the content was not evaluated by Spanish speaking children for different parts of the world (i.e.Spain, Puerto Rico)	2-

		Spanish speaking children with Leukaemia. Pain interviews in Spanish took place amongst children with Leukaemia. Standardised translation and back translation used.				for it to be deemed useful in clinical practice.	chosen in terms of pain experience.		
Crombez, G., Bijttebier, P., Eccleston, C., Mascagni, T., Mertens, G., Goubert, L/ and Verstraeten, K. (2003) Pain Belgium	The child version of the pain catastrophizing scale (PCS-C): a preliminary validation	Cross sectional study. The testing of the PCS-C for its construct and predictive validity in both a community and clinical child sample. Undertaken as 2 studies.	n=858 aged 8-16 years. (n=814 for the community sample from four Flemish schools) (n=43 in clinical sample)	814 children from four Flemish schools (400 boys and 414 girls). 43 children from a child psychiatric unit of a university hospital (23 girls 20 boys).	Pain Catastrophizing Scale for Children (PCS-C), Short Depression Questionnaire for children (SDQC), trait versions of the state-trait anxiety inventory for children (STAIC-trait), Functional Disability Inventory (FDI) and a pain	From the community sample the factor structure of PCS-C was acceptable across gender and age and subscales were internally consistent. PCS-C scales were highly correlated with depressive mood and trait anxiety. Girls had higher scores on PCS-C than	Differences in age and gender could be due to age and gender differences in reporting in self report scale and not just the level of catastrophizing. Also the instrument is an adult scale attempted to be adapted for use amongst children which might overlook some	Needs further exploration	2++)

					intensity VAS.	boys on all scales. The predictive validity of PCS-C in predicting pain severity and disability was shown. Catastrophic pain predicted pain related disability beyond age, gender and pain intensity. Can be used in children as young as 9.	children's experiences. Adult focus might not be generalisable across child population.		
Crow, CS. (1997) Pain USA	Children's Pain Perspectives Inventory (CPPI): developmental assessment.	Descriptive cross sectional study designed to evaluate the psychometric properties of CPPI, a tool to assess the developmental progression of children's pain perspectives. Six of the 10 children in phase one were	n=88 (aged 5-13 years) a convenience sample including children from families known by the investigators	Phase one n=10 to determine the usefulness and comprehension of items of CPPI. Phase two, n=30 from two orthopaedic outpatient clinics. Phase three, n=48 same recruitment procedure as	Children's Pain Perspective Inventory (CPPI) and the Cartoon Conservation Scale (CCS).	Crow conducted a descriptive correlation study which showed that children's pain perspective could be developmentally ordered, coded, reliable and valid. CPPI has acceptable interrater, intrarater, test-	Low sample sizes for each phase of the study effects the generalisability of findings. Bias injected with the interview schedule as difficulty in achieving uniform administration across respondents.	Convenience sampling, greater risk of bias.	2-

		interviewed twice with a two week interval between interviews.		phase 2.		retest and internal consistency reliability. Criterion validity of the CPPI compared to the CCS, were also good. This suggested a correlation between children's pain perspectives and cognitive development. The responses of the children to 12 interview items showed the highest item-scale correlations and were consistent to Piaget's theory of cognitive development progression.			
Gilbert, CA., Lilley, CM., Craig, KD., McGrath, PJ., Court, C.,	Postoperative Pain Expression in Preschool Children:	To determine whether a measurement system based on facial	n=100 (aged 13-74 months)	100 families in which children were undergoing minor surgery	Child Facial Coding System (CFCS). It has been applied	CFCS serves as a valid measurement tool for persistent pain	Videotape methodology may create bias and sometimes the	How easy is this to use? Whilst the researchers indicated that this	2+

Bennett, S. and Montgomery, CJ. (1999) Clinical Journal of Pain Canada	Validation of the Child Facial Coding System	expression (CFCS) would be useful in the assessment of post operative pain in young children to examine construct validity and concurrent validity of the CFCS. Patients were videotaped in the post anaesthesia care unit (PACU). Observational, cross sectional study.	(requiring anaesthesia) participated from a Children's Hospital tertiary care facility in Vancouver.	to a variety of types of pain in the past.	in children but needs further validation in psychometric properties of facial coding systems. The frequency of occurrence of each facial action was recorded with the most frequent action being open lips. The PCA of facial activity was conducted which indicated the best solution was a single factors accounting for 55% of variance in CFCS actions. Mean facial action summary scores were compared to global ratings of pain with 25/30	face of the child was obstructed (missing data 27% of the total). Analysis of medication status looked only at the classes of drugs and not for the use or timing of administration. Problems differentiating distress form pain- were the team actually measuring the pain experienced by the child	tool has some validity, this in addition to reliability and transferability needs further testing.

						correlations being significant. There were no significant differences between facial action summary scores by gender and use of intravenous opioids pr surgery type. Detailed analysis of actial expression does indicate a realiotnship topt he apin expreicne post operatively and is particularly useful for this pre-school age group.			
Goodenough, B., van Dongen, K., Brouwer, N., Adu-Saad, HH. And Champion, GD.	A comparison of the Faces Pain Scale and the Facial Affective Scale for children's	Measuring intensity of pain, affective state and pain unpleasantnes s during blood sampling for	n= 80 (4-6 and 7-10 years old).	Children with scheduled for blood testing (both venepuncture and finger prick needle	Faces Pain Scale (FPS) Facial Affective Scale (FAS) and a paired mechanical	The FPS showed significantly higher correlation with CASi rather than	Small scale study which is unable to determine whether small effects in the data are	No discussion with child prior to venepuncture/fing er prick The order the face scales presented will	2-

(1999) European Journal of Pain Australia	estimates of the intensity and unpleasantness of needle pain during blood sampling	children, using a variety of different questionnaires. Administered within five minutes of the procedure ending.	types). Australian study Following criteria for inclusion applied: First language English No topical anaesthetic used Children knew how to apply pain scales and concepts and only one needle insertion/ finger prick attempted	visual analogue scale for pain intensity and the Mechanical visual analogue scale of pain unpleasantness.	CASu and the FAS correlated significantly more highly with CASu. Correlations between pairs of scales measuring different dimensions of pain remained strong. The MVAS-intensity measure could proportionately explain more variance compared to the other three measures. Findings show facial expression scales are the most age appropriate choice in helping children to separately estimate both intensity and unpleasantness of pain.	meaningful. Unsure of clinical meaningfulness in terms of utility in determining treatment options. Many variables are being tested i.e. not only the correlation between the pain tools used in terms of measuring emotional versus sensory aspects of pain, but how this relates to age of child, as well as needle history, family structured etc. Did the registered paediatric nurse use any distraction	have an effect All the children had previous experience of venepuncture/finger pricks

Hicks, CL., von Baeyer, CL., Spafford, PA., van Korlaar, I. and Goodenough, B. (2001) Pain Canada	The Faces Pain Scale ± Revised: toward a common metric in pediatric pain measurement	Cross modality matching methodology with the aim psychometrically refining pre-existing pain assessment tools. Revision of FPS from 7 to 6 faces and to evaluate validity of FPS-R amongst children in pain situations in clinical and non clinical settings. Compared scores from CAS and VAS to assess reliability of FPS-R. Build on previous study evaluated above.	Study 1, n=15 (adults), study 2, n=76 (aged 5-12 years divided up into 5-6, 7-8 and 9-12 years), study 3, n=90 (, 4-12 years divided into 4-6, 7-9 and 10-12 years).	Adults students from the University of Saskatchewan who had extensive experience with children between the ages of 5-12. Study 2 sample were children requesting ear piercing and sample 3 inpatients from children's hospital	Faces Pain Scale-Revised (FPS-R) and the Sydney Animated Facial Expressions Scale (SAFE) computerised animation. The coloured Analogue Scale (CAS), the visual analogue scale (VAS).	The FPS-R can be used with the 0-5 or 0-10 system which will be useful in clinical practice. Study one shows suitable psychometric properties for the revised scale. Study two showed a positive correlation between ratings of pain on VAS and FPS-R amongst all three age groups. No difference between age and gender ratings of pain were found although no 10-12 year olds rated pain higher than 3. Similar findings in	techniques? Use of adults to help match pain intensity represented by a face to a number. Assumption that parents would be approach the task more seriously. Sample two contained more females than males (57/19) and the males were only having one ear pierced. This procedure is desired by the children, which will affect the way pain is perceived and affects its transferability to the acute setting	Young children do tend to choose the extremes in terms of pain scores which did affect the results. Need to use a VAS to check understanding and clarify which measure should be used as a means of calibrating the scale – complex scale to use.	2+

						study 3. Excellent inter-scale agreement in the youngest age group which suggests it is useful for clinical practice.			
Hunter, M., McDowell, L., Hennessy, R. and Cassey, J. (2000) *Journal of Pain and Symptom Management* *Australia*	An Evaluation of the Faces Pain Scale with Young Children	Observation of children's responses to the 7 faces of FPS. Exploring the psychometric characteristics of FPS and evaluating its usefulness with young children. Extending on the work of Bieri et al (1990)	n=135 Group1 (n=45) aged 3.5-4.5 years, group 2 (n=45) 4.5-5.5 years, group 3 (n=45) aged 5.5-6.5 years	Children with healthy girls and boys recruited from kindergartens and primary schools. Australian study	Faces Pain Scale (FPS)	The aims and intentions of the scale were understood by even the youngest age group making it an appealing clinical instrument. FPS was found to be sensitive and discriminating, however difficulties in discriminating between faces 3-6 suggests FPS does not qualify as an interval scale. Few significant differences between	Small sample size for test retest reliability as there was a large degree of variability children's responses when they were asked to imagine what pain would be involved in a particular event. Quanititavie results are not entirely clear in relation to conclusion drawn Test re-test reliability is not	Vague conclusions drawn from what was a potentially well designed and implemented study.	2+/-

						gender and response to pain. Accuracy of reporting pain was poorest for the youngest children. FPS should be reserved for school age children.	clear – is I worthwhile testing children in this way when they have not had the experience offered as examples and can young children speculate in this way?		
McGrath, PA., Seifert, CE., Speechly, KN., Booth, JC., Stitt, L. and Gibson, MC. (1996) Pain	A new analogue scale for assessing children's pain: an initial validation study	The development and validity of a practical clinical measure to assess children's pain intensity and affect (the CAS and a facial affective scale). Comparative study (with some randomisation within the chosen group)	n=104 aged 5-16 years. (n=51 healthy group and n=53 headache group)	Groups were randomised to either CAS or VAS scales. Ability to speak English Canadian study	Coloured Analogue scale (CAS) to assess pain intensity), Facial affective Scale (FAS, to measure affective component of pain). VAS and Children's Pain Inventory to aid validation.	Children's CAS and VAS scores on the CPI were similar and there was no difference in intensity or affective rating by scale type. The mean number of painful events experienced by children increased significantly with age. But affective ratings did not. The CAS had similar psychometric	Some children basing their pain assessment on hypothetical situation in absence of direct pain experience i.e. the calibration task is not as accurate as adult experience where pain actually experienced	Only one five year old was recruited so can not be generalised to 5 year olds. Need further formal definitive test for construct validity in different clinical settings Large age range means that age related trends identified might not be significant i.e. 5-7 age group only 27 children in total where only 1 5 year	2+

						properties to the VAS was rated as easier to administer and score than the VAS therefore it may be more practical for routine clinical use. Psychophysical properties and discriminant validity was shown.			
Miro, J. and Huguet, A. (2004) Pain Spain	Evaluation of reliability, validity, and preference for a pediatric pain intensity scale: the Catalan version of the faces pain scale – revised	Cohort study testing the construct and criterion validity and test retest reliability of the Catalan version of FPS-R on the Catalan population. Questionnaires completed twice with one month interval. Developing the	n=371 aged 7-15 years (hospitalised patients n=124 and school children, n=247)	Children in the hospitalised group included those with surgical and non surgical painful conditions Catalan speaking children with not cognitive impairment	Faces Pain Scale – Revised (FPS-R), Catalan version (FPS-R-C), Faces Affective Scale (FAS) and Coloured Analogue Scale (CAS). Measuring affective state and intensity of pain.	The children significantly preferred the FPS-R-C to the CAS. It was proven to be a practical measure for use in clinical settings. Psychometric properties were regarded strong.	Test retest results appeared weak despite the conclusions ranging from 0.26-0.7. Statistical significance might not reflect clinical relevance. Healthy children again asked to base pain assessment on	Need further studies especially targeting the younger age groups <7	2+

		work by Baeyar et al (2001) above in a population where cultural background and language are different.					hypothetical situations rather than actual pain experience, though this tested at beginning of study and one month later which will increase reliability and validity of tools used For hospitalised children variability in pain experience due to cause of pain not reflected	
Newman, CJ., Lolekha, R., Limkittikul, K., Luangxay, K., Chotpitayasundh, T. and Chanthavanich ,P. (2005)	A comparison of pain scales in Thai children	The validity of the VAS, the Wong Baker Faces Pain Scale and the Faces Pain scale revised were assessed for validity amongst Thai	n=122 Thai children aged 4-15 years (children with HIV, n=61 and age matched controls with no chronic disease, n=61).	Patients with HIV were recruited from the outpatient clinic in the Queen Sirikit National Institute of Child Health in Bangkok.	Visual Analogue Scale for pain (VAS), The Wong Baker Faces Pain scale (WBFPS) and the Faces Pain Scale Revised	The three pain scales were significantly correlated to one another on overall analyses and. On analysis of gender and amongst	No cross cultural validation conducted on the expression of pain which may differ between cultures. Also the conclusion	2+/-

ADC Online Thailand		children. Case control study.			(FPS-R).	children with /without HIV. Correlation between the VAS and WBFPS was low in four year old children and the highest coefficients in all subgroups were those correlating the two face pain scales. Nearly 30% of 4 year olds presented more than 2 points difference between the VAS and WBFPS. Suggests tools suitable for clinical use.	does not highlight that the tool appears unsuitable for children aged four. This requires further examination. Other validation is needed e.g. Factor analysis, discriminant ability?		
Peden, V., Vater, M. and Choonara, I. (2003) Paediatric Anesthesia	Validating the Derbyshire Children's Hospital Pain Tool: a pilot study	Cohort? Single centred study. Exploratory pilot study preceding above study. Known groups validity, convergent	n=40 (aged 1-5)	Children undergoing minor and intermediate surgery. Research nurse and nursing staff	The Derbyshire Children's Hospital Paediatric Pain Chart (DPC- not validated) and the	The DPC is said to hold construct, convergent and known groups' validity. Could be useful in clinical	Small sample size. Biased sample (those with minor surgery). Some areas of validity not tested.	Small pilot study where 8 children scored '0' post operatively Parental involvement not considered at all – are nurses always	2- small sample

UK		validity and inter rater reliability Preoperative and postoperative measurement of pain measured hourly up to four hours postoperatively by nurse.		performing pain assessment	Preschooler Postoperative Pain Scale	practice with further testing. Correlation between research nurse and nursing staff in terms of joint pain assessment.	There is consistency in terms of one nurse carrying out all the pain assessments, though this may lead to bias in terms of her influence on nursing colleagues even though she was blinded to nurses scores. Recommended that an independent external supervisor validate her scores.	the most skilled in terms of assessing pain, especially in terms of behavioural factors?	
Peden, V., Choonara, I. and Vater, M. (2005). Journal of Child Health Care UK	Validating the Derbyshire Children's Hospital Pain Tool in children aged 6–12 years	Cohort? Single centred study. Exploratory study Inter rater reliability between staff and construct and concurrent validity tested. Preoperative and	n=60 (aged 6-12) 24 female and 36 male	Children undergoing minor and intermediate surgery Children, as well as research nurse. Nursing staff carrying out pain	The Derbyshire Children's Hospital Paediatric Pain Chart (partially validated) and Oucher Scale (previously validated). Pain indicators	Known groups construct validity, concurrent validity and inter-rater reliability was supported. The tool will be useful in clinical practice with	Small sample size as 17 postoperative patients were unable to provide pain assessment due to anaesthesia. Some areas of validity not addressed	A prior study (detailed below) identified the need for external supervision to reduce researcher bias, though this did not take place in this study either	2- small sample

		postoperative measurement of pain measured hourly by nurses up to four hours postoperatively.		assessment.	were facial expression, verbal and body movement.	further testing.	(e.g. discriminant) Bias because this is a locally produced tool where Oucher or other faces scales may be more relevant for this age group. There were inconsistencies in post operative scoring for a variety of reasons Consistency between child and nursing staff not clear		
Perrott, DA., Goodenough, B. and Champion, GD. (2004) European Journal of Pain Australia	Children_s ratings of the intensity and unpleasantness of post-operative pain using facial expression scales	Explored if global uni dimensional self-report, facial expression, pain scales help children estimate the sensory and affective magnitude of	n=90 (aged 5-15 years)	Inpatients at Sydney Children's Hospital undergoing a range of elective surgeries (tonsillectomy (31%) orthopaedic (34%)	Faces Pain Scale (FPS), Facial Affective Scale (FAS) and Coloured Analogue Scale for intensity (CASi) and CAS for unpleasantnes	Ratings on FPS correlated more highly with those on the analogue scale for unpleasantness than with intensity. Correlations between pairs of scales	The administration of the four pain scales in a fixed order may have influenced the outcome of the study. (e.g force a relationship between the	118 children consented to study but only 90 complete data sets for both child and parent. Problems with scoring in terms of Day 1 and Day 2 and administration of	2++

		post-operative pain. Patients were given four pain scales to estimate their pain intensity and affect during the first 2 days post surgery. Exploratory study to examine feasibility of paring to facial scales.		abdominal (17%) oral (8%) and thoracic (9%). All children used the 4 scales in the same order. Australian study	s (CASu)	purporting to measure different dimensions of pain were high. Factor analysis showed all measures loaded on a single dimension of distress (not two separate measures of pain) although an additional weaker factor corresponded to a unique contribution of the FAS. No age differences were observed. Clinical relevance of findings yet to be determined.	FACES and CASi. Use of scales problematic – 2 facial scales clearly different to one another whilst CAS not which makes them more difficult to use Order of scales also problematic – FPS as anchor point Findings only robust over two days of post-operative pain.	analgesia and pain reduction Children's ability to use scales not discussed	
Stanford, EA., Chambers, CT. and Craig, KD. (2006)	The role of developmental factors in predicting young children's	Examined young children's ability to use the FPS-R for pain in	n=112 children aged 4-6 years (n=28 in each subgroup, 3-4 years, 4-5 years 5-6	Children were recruited from the community using posters and newspaper	Faces Pain Scale Revised (FPS-R) and the Charleston Paediatric Pain Pictures	3 year olds responses to FPS-R were consistent with what would be expected by	Almost half of the patients (46% had an income level of greater that $80 000 CDN	Need further research with children who are actually in pain.	2++

Pain Canada	use of a self-report scale for pain	response to vignettes depicting pain scenarios common in childhood. Parents provided demographic information. Children completed a range of tasks taken approximately 90 mins. Cross sectional study.	years and 6 years).	notices.	(CPPP). Both have been previously validated	chance. There was a significant difference in children's ability to complete FPS-R in response to the CPPP vignettes by age; 3 year olds made significantly more errors than four year olds who made significantly more errors than 5 and 6 year olds. The effect of gender was not significant. 5 and 6 year olds still made errors close to 40%. Further work needs to be done to rectify this problem. Numerical reasoning development, language	which could bias the results. The use of hypothetical vignettes with healthy children are subject to lower levels of external validity (children not experiencing pain which could prove difficult). Attention, memory, previous experience of pain or temperament could all affect the way they score.

						development and general intellectual development are related to ability to use FPS-R in relation of vignettes Study highlights the importance of using a developmental framework for understanding and improving pain assessment in young children			
St-Laurent-Gagnon, T., Bernard-Bonnin, AC. And Villeneuve, E. (1999) Acta Paediatr Canada	Pain evaluation in preschool children and by their parents	To determine the validity of a MSPCT in preschool children and to compare ratings of children's pain obtained from both the child and parent.	n=104 children (aged 4-6 years) and their parents. (47 boys and 57 girls, 4 year olds =54, 5 year olds, n-34 and 6 year olds, n=16.	Children were undergoing an immunization procedure in the outpatient department of a tertiary paediatric care hospital.	McGrath Facial affective Scale (FAS), the Hester Poker Chip Tool (HPCT) and the Multiple Size Poker Chip Tool (MSPCT).	Intra rater correlations were very high in both parent and children's when comparing pain scores obtained from the HPCT and the MSPCT but correlations were low between the FAS and either	There was a comparatively low sample size for 6 year olds and results might not be generalisable to this age group. The presence of the parent in the room when both child and parent were	Young children tend to go to extremes of scales when self assessing so it might be that parents are not underestimating their child's pain at all	2+

			the HPCT or MSPCT. Inter rater comparisons between children/parents were obtained for all three scales. Little differences between pain scores were found based on age, gender and previous hospitalisation. The MCPCT appears to have good concurrent validity and discriminant validity. Parent's underestimated their child's pain when using HPCT or MSPCT (which appear to measure a similar dimension of pain). Parent	completing the questionnaires could seriously bias the results.

and child ratings of pain were better correlated with the FAS, esp in the younger age group.

INTERVENTION Pain Assessment (infant/toddler)
COMPILED BY: Bernie Carter/Cassie Ogden/Elaine Hill

Author/Yr /Jnl/Country	**Article title**	**Study Design/ Type**	**No. of ptnts/ptcpnt**	**Ptnt/Participant Characteristics**	**Pain Tools Used**	**Result & Conclusion**	**Limitations**	**Problems**	**Evidence Grade and Comments**
Breu, LM McGrath, PJ Craig, KD Santor, D. Cassidy, KL, Reid, GJ (2001) The Clinical Journal of Pain Canada	Facial Expression of Children Receiving Immunizations: A Principal Components Analysis of the Child Facial Coding System	To identify the structure of facial reaction to procedural pain and to determine the subset of facial actions that best describe the response. Observational, video recording. . Randomly assigned to receive Emla cream or placebo. The Faces Pain Scale (FPS)26 was completed by children. This consisted of seven faces depicting neutral to extreme pain expressions, anchored on the left by 0 (no pain) and on the right by 6 (worst pain possible). This scale has demonstrable reliability and clinical	n=123 (52-80 month) 54% male and 46% female.	Preschool vaccinations varying 'medical' experiences in the past. Canadian population.	Child Facial Coding System (CFC) (containing 13 facial actions).VAS (used by parents). Faces Pain Scale (used by children).	Parents', children's and technicians' ratings correlate. Facial actions change according to pain.	Who is using the tool and what is their experience? Unclear whether Emla affected pain ratings.	.	2-

		utility.27 Parents and a technician completed a visual analog scale (VAS) of pain consisting of a 100-mm horizontal line anchored on the left by “no pain” and the right by “worst pain ever.” A VAS anchored by “no anxiety” and “worst anxiety imaginable” was also used by parents to rate their child’s anxiety before immunization.							
Van Dijk, M., de Boer, JB., Koot, HM, Tibboel, D., Passichier, J. and Duivenvoorden, HJ. (2000) Pain Netherlands	The reliability and validity of the COMFORT scale as a postoperative pain instrument in 0 to 3-year-old infants	Testing the reliability and validity of the COMFORT scale as a postoperative pain instrument for children aged 0-3 years. Observational study with trained nurses rating the children’s pain at 3, 6 and 9 hour postoperative.	n=158 (0-4 months, n=56, 1-6 months, n=47, 7-12 months, n=23, 1-3 years, n=32)	Neonates and toddlers from the Paediatric Surgical Intensive Care Unit in Sophia Children’s Hospital, Rotterdam. Patients requiring superficial, abdominal or thoracic surgery. Not included if they received medication which could affect behavioural	COMFORT scale (behavioural and physiological) and VAS for pain.	Interrater reliability of COMFORT proved to be good for all items except ‘respiratory response’. COMFORT data best represented by three latent variables: comfort behaviour, heart rate baseline and mean arterial blood pressure. The heart rate	The statistical tests may be affected by the relatively small sample size and multiple testing. The sample was skewed with more infants than 1-3 year olds the conclusions are limited. Some nurses rated children on both scales		2- because of small sample size and multiple testing. High risk of bias in this sense but not in terms of having trained nurses

				assessment.		and blood pressure measurement had limited validity as measures of postoperative pain. COMFORT behaviour and VAS pain were highly interrelated. Indicating congruent validity. Results support use of COMFORT to assess postoperative pain in neonates and infants.	which could bias results.		as observers.
Hartrick, CT. and Kovan, JP. (2002) Journal of Clinical Anesthesia USA	Pain Assessment Following General Anesthesia Using the Toddler Preschooler Postoperative Pain Scale: A Comparative Study	Evaluate the reliability of the TPPPS following general anaesthesia and to compare the validity of the scale with other observational measures of pain in children. Prospective single blinded observational study. Patients emerging from general anaesthesia following different procedures were observed for pain	n=51 (subgroups stage one postoperative pain n=20, stage two comparison to non painful events n=23 and stage three comparison of three scales n=12).	All were patients of the William Beaumont Hospital Human Investigation Committee, USA, requiring general anaesthesia	Toddler Preschooler Postoperative Pain Scale (TPPPS), Faces, Legs, Activity, Crying, Consolability scale (FLACC) and a modified COMFORT scale.	Following painful procedures TPPPS, FLACC and the modified COMFORT scale used purely as a behavioural tool can be recommended for postoperative assessment of patients aged 1-5 years. The TPPPS may be preferred as it	The act of scoring each tool may affect the scoring of the other tools. Only small sample so reduces power of statistical tests. Greater risk of type II error (rejecting null hypothesis when it is true). Did not show		2-

		scores during recovery before and after anaesthesia and at discharge. Compared the clinical utility of TPPPS to that of FLACC and COMFORT				discriminates between painful and non painful scales. All three scales reported significant reductions following analgesic administration, the TPPPS demonstrated significantly better performance in discriminating between painful and non painful situations.	patient characteristics. Do they use same observer in all three groups?		
Lilley, CM., Craig, KD and Grunau, RE. (1997) Pain Canada	The expression of pain in infants and toddlers: developmental changes in facial expression.	Observational study into facial expression of pain during the first 18 months of life. Infants were video recorded when given the injection and afterwards their parent was asked to complete questionnaires consisting of a demographic form, the Infant Characteristics Questionnaire and measure of temperament. Coders blind to temperament	n=75 (stratified into five age groups (n=15 in each), 2-4 months, 4-6 months, 6-12 months, 12-18 and 18 months)	Canadian infants undergoing routine immunization injections. Exclusions: if not receiving injections within 31 days of median age. If accompanying parent did not speak English	Infant Characteristics Questionnaire (ICQ), Neonatal Facial Coding System (NFCS) and baby FACS.	There were consistencies in facial displays over age groups but differences on both measures of facial activity. Least pain was expressed by four month age group and temperament was not related to the degree of pain expressed.	The presence of video recorder may have affected the infants' responses (i.e. made them confused). At times the face of the child was also obstructed. The sub sample sizes of 15 are too low to infer statistical power to tests.		2-

		score and exact age of child. Groups balanced for age and sex.					Age groups do not contain equal intervals. The effect of excluding non English speaking parents may exclude ethnic minorities.		
Lyon, F. and Dawson, D. (2003) EMJ ?UK	Oucher or CHEOPS for pain assessment in children	A review of the literature to evaluate whether the Oucher or the CHEOPS is better at assessing pain in children.	n/a (literature review)	n/a	Oucher (self report measure) and Children's Hospital of Eastern Ontario Pain Scale, a behavioural pain measure(CHEOPS)	12 papers were found with three addressing the subject indirectly. Some disagreement as to whether the CHEOPS correlates to the Oucher score. No agreement as to whether the CHEOPS is more/less reliable in different age groups. Further studies are needed using a larger sample ub a range of clinical situations.	No evidence was found to show whether CHEOPS or Oucher was better at assessing pain in children. Theoretical scenario does not contribute to new evidence.		4
Merkel, S. (2002)	Pain Assessment in Infants and Young	Evaluating the use of the finger span scale in terms of analgesia administration.	n/a	n/a	Finger Span Scale	Discussion of using the Finger Span scale for children possibly	No evidence, merely an article explaining the		4

AJN USA	Children: The Finger Span Scale					aged 2-3 who understand pain but find it difficult to understand rank order. It is suggested that this self report measure could be used with children alongside a comprehensive pain assessment (e.g. FLACC)	possible benefits of the finger span scale backed up with no empirical evidence. Still a problem for pain self assessment in children that don't know the difference between a lot and a little.		
Yeh, C-H. (2005) The Journal of Pain, Taiwan	Development and Validation of the Asian Version of the Oucher: A Pain Intensity Scale for Children	Design and development of the Asian version of the Oucher Pain intensity scale the content, convergent, discriminant and clinical validity of the scale was tested in the new population of Asian children. For study three pain was measured before surgery, 10 minutes after surgery and 60 minutes later.	n=370 (study one n=53 , study 2, n= 220 for content validity and study 3, n=149 to examine validity further)	Children Taiwanese, aged 3-7 years. Study 2, children were from the day care centre. Study three were patient who had general anaesthetic for outpatient clinic surgery	The Asian version of the Oucher Pain Intensity Scale (OPIS), the VAS, Hester's Poker Chip Tool (HPCT), Child Medical Fears Scale – 17 items (CMFS), Faces, legs activity, cry and consolability Pain Scale (FLACC) and	Agreement levels of photos selected for the Oucher scale (Asian version) were between 60-100%. A female and male version was created. Children preferred to use the picture Oucher scale, differences in scores obtained during the pain episode for each	Final decision of the pictures were made by 'experts' and not the children who will use the scale. Did not assess the effect of completing all the instruments on the Asian Oucher. Will it work with other Asian groups?		2++

					the Scare scale.	of the four pain scales were statistically significant. The Asian Oucher, VAS, PCT and FLACC showed different pain levels which demonstrates the clinical validity of Asian Oucher.The VAS, PCt and Asian Oucher deomstrated good convergent validity. Medical fear correlated very poorly with Asian Oucher indicating it measured pain and not fear.Convergent, discriminant and clinical validity was proven for male and female version of Asian Oucher.			

INTERVENTION Pain Assessment (Parent tool – the Parent Postoperative Pain Measure)									
COMPILED BY (Bernie Carter/Anne Hunt/Angela Edmonds				CHECKED BY					
Author/Yr/	Article title	Study Design/Type	No. of patients/ participants	Pt/Part. Chrct	Pain Tools Used	Result & Conclusion	Limitations	Problems	Evidence Grade & Comments
Chambers et al., 1996 Pain Canada	Development and preliminary validation of a postoperative pain measure for parents	The purpose of the present study was to develop and validate this measure by examining the relation between parent-report of child behaviors and child-rated pain. Scale development and testing	N= 110 children and one of their parents	56.4% male Age 7-12 years undergoing day surgery at a tertiary-care children's hospital	Parent's Postoperative Pain Measure & Faces Pain Scale (Bieri).	Evidence of validity for 15-item PPPM provided. (see attached table) This study provides preliminary evidence for the use of the PPMP as a valid assessment tool with children between the ages of 7–12 years following day surgery. It is internally consistent and strongly related to child-rated pain.	External (inter-rater) reliability not assessed. Future research should explore the use of this measure with a younger sample and children with developmental delays.		2-
Chambers et al., 2003 Pain	The parents' postoperative pain measure: replication and extension to 2–6-year-old children	Replication of above validation study and extension to younger age group	N=158 children and one of their parents.	51 children 7-12 years undergoing day-surgery. (22 girls and 29 boys)	Parent's Postoperative Pain Measure & Faces Pain Scale (FPS) (Bieri). Children 7-12 used FPS to self-report. For children 2-6	Evidence of validity for 15-item PPPM provided. (see attached table) The results of this study provide evidence of the reliability and validity	External (inter-rater) reliability not assessed.		2-

USA				107 children 2-6 years (69 boys and 38 girls)	years parents used FPS as proxies.	of the PPPM as a measure of postoperative pain among children aged 2 through to 12 years.			
Finley et al., 2003. The Clinical Journal of Pain Canada .	Construct Validity of the Parents' Postoperative Pain Measure	Study 1: Examination of relative specificity of PPPM to pain versus anxiety	75 children and one of their parents	Children aged 7-12 years undergoing day surgery likely to be associated with at least moderate pain.	Parent's Postoperative Pain Measure & Faces Pain Scale (Bieri). + Stait-trait Anxiety Inventory for Children(STAIC).	Evidence of validity for 15-item PPPM provided. (see attached table). PPPM can differentiate pain from anxiety. provide further support for the construct validity of the PPPM and confirm that the measure is a valid pain assessment tool for use by parents at home following children's surgeries.	External (inter-rater) reliability not assessed.		2-

		Study 2: to examine responsiveness of PPPM to analgesic treatment.	28 children and one of their parents	Children aged 7-12 years 21 boys, 7 girls		Evidence of validity for 15-item PPPM provided. (see attached table). PPPM follows pattern of children's self-report and was significantly lower after 3/6 analgesic administrations. FPS significantly less after 4.	External (inter-rater) reliability not assessed.		
Overall re PPPM						Overall there is good evidence that the PPPM is a valid measure of children's acute pain following day case surgery.	There is no evidence of inter-rater reliability. Would it make a difference which parent uses the PPPM? Mothers vs fathers for instance. Parents using the PPPM were reported to be in middle to upper socioeconomic status. There is a need to evaluate behaviour		Uncertain as system does not adequately incorporate scale development studies but would say level of evidence is 2- to 2+ and recommendation level C.

							changes and parent's perceptions in different cultural settings. Unsure whether the tool has been used / validated in the UK. UK validation might be needed. Validation has been limited to relatively minor surgery. Evaluation of measure by parents in more longstanding or recurrent pain situations might be worthwhile.		
Kankkunen et al 2003 European Journal of Pain Finland	Parents_ perceptions of their 1–6-year-old children_s pain	Purpose: To describe parents_perceptions of 1–6-year-old children's pain. Questionnaire survey	a convenience sample of 1000 children (4.4% of the population) were selected to represent the population (19 wards, 10 hosp)	Children's day surgery	VAS (filled in by parents) Children_s pain behaviours were measured by using the Finnish version of Parents_ Postoperative	Parents seemed to have both adequate and misleading perceptions of children's pain. Fathers accepted children's pain more than mothers. Boys expected to tolerate pain more than girls.	Rating the intensity of children_s postoperative pain in VAS scores may have been difficult for some parents.	Drs went on strike during study period; reduced questionnaire distribution. !!	2-

					Pain Measure (PPPM). And a questionnaire	Adequate info needed to decrease misleading perceptions of children's pain tolerance. Parents of boys should be encouraged to alleviate the child's postoperative pain. Fathers could be taught to protect their children from pain.	the sample did not present the population in a satisfactory level.	Children's day surgeries were cancelled in the hospitals participating in the strike.	
Kokki et al 2003 Scand J Caring Sci; Finland	Validation of the Parents' Postoperative Pain Measure in Finnish children aged 1–6 years	The purpose of this study was to test validity and reliability of this measure in 1–6-year-old Finnish children at home after minor day surgery. Survey. Parents completed questionnaire & PPPM & VAS during the day	Children (n = 85) and their parents Nonrandom sampling,	From 4 hospitals. Day surgery	Questionnaire including PPPM during the day of operation, and the first and second postoperative days. Parents (n ¼ 85) rated the presence or absence of behavioural changes from a checklist and also the child's worst pain during each day (using a Visual Analogue Scale, VAS).	The findings showed that construct validity of the measure was satisfactory. The PPPM was successful in discriminating between children who had no/low pain and children who had a clinically significant pain measured by VAS (convergence validity). Scores on the PPPM decreased from days 0 to 1 and from days 1 to 2 (predictive validity). Internal consistency of the measure and correlations with the			2-

		of operation, and the first and second postoperative days.				pain scores on VAS were high on all days following surgery (equivalence). Sensitivity was satisfactory only when specificity was weaker. The results provide pilot information on the cultural differences in children's pain expressions and assessment between these two countries. It seems that Canadian children express their pain fairly quietly and parents identify their pain by using cues related to children's outlook. In Finland, the children seemed to be very verbal in their pain expressions and their pain-related action is more visible			

Scale name	Parent's Postoperative Pain Measure (PPPM)
Authors	Reid et al., 1995 Chambers et al., 1996, Chambers et al., 2003. Finlay et al., 2003 Kokki et al., 2003 (for Finnish children)
Country of origin	Canada
Population	Children undergoing day surgery and their parents.
Generation of items	29 Items generated from parent (n=) reports and reviewed for content validity by psychologists (2), anaesthetist (1), advanced psychology students and parents (5). All items retained (Reid et al 1995). Chambers et la., 1996): Correlation between parent PPPM items and child reported Faces Pain Scale (Bieri et al., 1990). Items with correlation < 0.30 dropped.- leaving 15 items.
Scale – latest versions	15 items, scored as present or not present.
Setting of assessments	3 surgery classes – high, moderate and no/low pain (derived from Finlay et al 1996). Parents completed the measure on one of three periods on each of two days.
Age groups	Children 7-12 (Reid et al 1995, Chambers et al 1996) Children 7-12 and 2-7 (Chambers et al 2003), Children 7-12 (Finlay et al 2003).
Developmental level	Not reported.
Validation	Chambers et al., 1996: ANOVA demonstrated no significant interactions or main effects of age or sex. Significant differences between high / moderate pain classed surgery and no/low pain surgery groups (ANOVA $p<0.0001$), but not between high and moderate pain classes. Validation in two age groups (Chambers et al., 2003): Eta Correlation coefficients – in older group 9 of 15 items significantly correlated with child's own report. In younger group 13 of 15 items significantly correlated with parent global (Faces) report. Significant decrease in PPPM scores and FPS scores on day 2 for both age groups (paired t-test $p<0.05$). Scores differed significantly between

	surgical pain classes low – moderate pain and high pain on both post-surgery days (independent t-test). Discrimination from anxiety (Finley et al., 2003). Parents used PPPM and State-Trait Anxiety Inventory to score children on 2 days preceding and 2 days following surgery for 1 of 3 randomly assigned time periods. Low FPS and PPPM scores pre-op then significant increase in both scores on first post-op day, decreasing significantly on second post-op day. (ANOVA with post-hoc tests) . Anxiety scores remained constant across 2 pre-op days and first post-op day, with significant decrease on 2nd post-op day.
Internal reliability	Cronbach's alpha 0.88 and 0.87 on days 1 & 2 respectively. Principal axis factor analysis – one factor solution provided best solution. Spearman correlation between child rated pain and PPPM 0.61 on both days ($p<0.0001$).
External reliability	Not reported
Responsiveness	Lower PPPM on day 2 than day 1 for child reported FPS ($p< 0.0001$) and parent PPPM ($p< 0.0001$). Finley et al., 2003: Children (n=28) and parents used FPS and PPPM respectively at 2 points on day of surgery and two post-op days for two-hour period before and 2-hour period after administration of analgesic. Significant difference between pre and post analgesic PPPM score on 3 out of 6 assessments. FPS scale lower post-analgesic in 4 out of 6 assessments, overlapping with the 3 significant parent assessment episodes.
Sensitivity and specificity	Cut-off of score of 6 out of 15 had sensitivity of 0.88 on day 1 and 0.80 day 2; and specificity of 0.80 on day 1 and 0.84 on day 2.

INTERVENTION: Blood sampling, Venepuncture, and heel prick in neonates

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Jain A, 2000}	RCT 27-41 weeks(med 33) 2 – 17 days n=40 (1 exclusion)	Amethocaine gel 1.5 g vs placebo for 1 hour prior to Venepuncture	Video recording of facial features and cry at 1 second intervals for 5 secs pre and post Venepuncture (neonatal facial coding system)	16/19 amethocaine treated infants showed little or no pain compared with 6/20 in the placebo group (p=0.001) Topical amethocaine provides effective pain relief during venepuncture in the newborn.	No local reaction seen	1 + (Tapes assessed by 2 observers)
{Skogsdal Y, 1997}	RCT Newborn N=120	1ml of 30% glucose vs breast milk and 10% glucose infants having heel prick. Not sucking		30% glucose alleviates mild pain		Grade 1+
{Ogawa S, 2005}	RCT 5 days N=100	Heel lance alone Heel lance with pre treatment with oral sucrose Venepuncture alone Venepuncture with sucrose Used 50% sucrose	Video recordings Neonatal facial coding system Crying response	Venepuncture is less painful and more effective than heel lance for blood sampling in newborn infants.($p<0.001$). Pre-treatment with sucrose significantly reduced ($p<0.01$)NCFS score for heel lance, but this remained significantly more painful during blood sampling than venepuncture alone($p<0.01$) Sucrose pre-treatment tended still further to reduce the NCFS score for venepuncture, but this was not significant	None	Grade 1+ Single blinded investigator

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Shah V, 2004}	Syst rev Term infants 4 trials included **(Cochrane)**	Venepuncture vs heel lance for blood sampling	Validated pain meaures	Venepuncture when performed by a skilled phlebotomist, appears to be the method of choice in term neonates	Needs more research in settings with multiple phlebotomists	!++
{Logan, 1999}	Controlled Clinical trial 36 newborns	Venepuncture vs heel lance for blood sampling	Audiotape of cry	Venepuncture: shorter sample collection time, length and duration of cry: $p<0.05$		2+ (Potential confounder is that midwives at 2 centres each did only 1 technique)
{Taddio, 1998}	Systematic review **Venepuncture** 2 studies: RCCT(n= 60) and nonrandomized (n=116) CCT Neonates **Heelprick** 2RCCT's: 67 infants	**Venepuncture**: after application of EMLA or placebo Cohort design: EMLA vs no intervention **Heelprick** 0.5 g EMLA in 7 term infants vs placebo 0.5g EMLA in 60 preterm vs placebo	Heart rate and cry Used Pain scores Crying during procedure PIPP profile	EMLA associated with less pain as judged by HR and cry – no significance stated Pre-treatment with EMLA associated with a higher frequency of lower pain scores ($p<0.01$) No significant difference	Emla diminishes pain for circumcision but not heel prick. It may diminish pain for venepuncture, arterial puncture and percutaneous venous placement	1+

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Carbajal-Ricardo, 2005}	RCCT Preterm: 27+/-1.7weeks N=42	Infants randomised to receive either morphine in a loading dose and then maintenance dose vs placebo: responses x 3 heel pricks before loading dose, 2 hours later and 24 hours later	Used Premature Infant Pain profile	No significant difference in pain profile response to heel prick. Morphine does not provide adequate analgesia for acute procedural pain among preterm neonates		1+
{Ling JM, 2005}	RCCT Newborns admitted with jaundice N=52	Infants randomised to 2 ml oral 30% dextrose or 2 ml water pre venepuncture	Videotaped. Used Neonatal Infant Pain score and duration of cry	Dextrose group significantly less cry and pain as evinced by score (p0.03)		1+
{Gradin, 2005}	RCCT Newborns N=70	Heart rate monitored whilst infants given 30% glucose or water without painful stimulus	Observed heart rate	Significant increase in heart rate during glucose administration (p=0.002)	Important to recognise that effects of increase in heart rate during venepuncture may not be due to pain alone	1+

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Bauer K, 2004}	RCT Newborn(31 – 42 weeks) N=58	Randomised to 2 ml 30% glucose, 0.4 ml 30% glucose, or water.	Videotaped pain profile, , cry duration, indirect calorimetry and heart rate before venepuncture	2ml glucose reduced pain score compared with 0.4 ml and water but did not prevent rise on oxygen consumption, energy expenditure or heart rate	Suggests non painful handling causes stress – this may be reason for rise in 02 consumption despite 30% glucose	Grade 1+
{Carbajal, 2003}	RCT Newborn – term N=180	Gp 1: breast fed, gp 2: held in mothers arms , gp3 – given water, gp 4: 1ml 30%glucose followed by pacifier prior to venepuncture	Aigue Nouveau-ne scale and Premature infant pain profile	Breast feeding and 30% glucose group both significantly better than other groups($p<0.0001$). No difference between these 2 groups	Breast feeding equivalent to 30% glucose + pacifier in terms of analgesia	Grade 1 +
{Gradin M, 2002}	RCT Newborns N=201	Compared EMLA on skin +oral placebo, with Placebo on the skin and 30% glucose orally for venepuncture	Premature Infant Pain profile, heart rate and crying time	Pain scores and duration of crying were significantly lower in the glucose group than the EMLA group	Did not control for pacifier	Grade 1-

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Gradin M, 2004}	RCT Full term newborns N=120	During venepuncture: Gp 1 : breast fed and 1ml placebo, gp2 breast fed and 1 ml 30% glucose, gp3: fasting and placebo, gp4: fasting and 1ml 30% glucose	Premature infant Pain profile Crying time Parents rating on a Visual Analogue score	PIPP score significantly lower in infants receiving glucose(p-0.004) Breast feeding before venepuncture had no major impact on the pain score but reduced the crying time		1+
{Carbajal, 2002}	RCT – crossover trial Preterm neonates(< 32 weeks) N=40 (25 in trial1, 15 in trial2)	During sc injections of erythropoietin Trial 1: 0.3ml 30%glucose vs placebo Trial 2 0.3 mo 30% glucose with or without a pacifier	Pain using the Douleur Aigue Nouveau ne score	Significantly less pain with glucose vs placebo No additional effect of using a pacifier NB: 7 neonates in glucose group had slight but brief O2 desaturation.	These are very pre term infants – this could account for differences with sucking Recommend continous monitoring of preterm neonates receiving intervention	1+
{Bellieni CV, 2002}	RCT Newborn N=120	During heel prick: Gp A: Control Gp B:1ml 33% oral glucose+ sucking 2 mins before procedure Gp C: Sucking Gp D:1ml glucose +sucking GpE: Multisensory massage including 1 ml glucose+ sucking GpF: Multisensory massage and placebo (mulit sensory massage massaging infant, talking to infant, allowing infant to smell perfume on therapists hands)	Video Assessment of pain using Douleur Aigue Nouveau ne score	Gp D and Gp E the most effective E> effective than D	(Pacifiers not used but syringe giving fluid used to stimulate sucking)	1+

INTERVENTION: heelprick and venepuncture in infants

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Stevens B, 2004}	Sys Rev (Cochrane) RCT's in term and preterm infants – up to 28 days post 40 weeks gestational age Sucrose for analgesia in newborn infants	44 studies identified for inclusion in review 21 actually included (1616 infants) 9 evaluated preterm infants 11 term 1 both		Sucrose is safe and effective for reducing procedural pain from single painful events (heel lance, venepuncture). There was inconsistency in the dose of sucrose that was effective (dose range of 0.012 g to 0.12 g), and therefore an optimal dose to be used in preterm and/or term infants could not be identified. The use of repeated administrations of sucrose in neonates needs to be investigated as does the use of sucrose in combination with other behavioural (e.g., facilitated tucking, kangaroo care) and pharmacologic (e.g., morphine, fentanyl) interventions. Use of sucrose in neonates who are of very low birth weight, unstable and/or ventilated also needs to be addressed.	Suggested sucrose had greater analgesic effect when given 2 mins before painful stimulus	1++
{Johnston CC, 2000}	RCT Preterm infants <31 weeks at birth N=107	Sucrose (0.1ml of 24%) or water given up to 3 times, 2 minutes apart for every invasive procedure over a 7 day period	Neurobehavioural Assessment of the Preterm Infant at 32, 36, and 40 week Neurobiological Risk score(NBRS) at 2 weeks of age and at discharge	**No significant differences between the groups on any outcomes** but in sucrose group only higher numbers of doses predicted lower scores on motor development and vigour. In placebo group only higher numbers of interventions led to higher NBRS scores	Not examined post discharge. Could only examine those not discharged to other centres at term.Concerns that < 32 week infants might potentially be at neurodevelopmental risk from too many doses of sucrose	1-
{Stevens B, 2005}	RCT Preterm infants N=66	Gp1: standard care : positioning and swaddling Gp2: sterile water +pacifier Gp 3:sucrose 24% + pacifier Prior to all painful procedures	Clinical outcome data and neurobiological risk at 28 days of NICU discharge	No group differences for adverse effects or clinical outcomes or neurobiological risk status. Sucrose+ pacifier was effective and safe	Need further exploration of consistent pain management on clinical, developmental and	1+

					neurobiological outcomes	

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Taddio A, 2006}	RCT.Double blind. 132 neonates (mean gestation 30.6 weeks)	Randomized to receive tetracaine, morphine or both for alleviating pain in ventilated neonates prior to central line insertion. Separate non randomised control group	Pain score during different phases of procedure – and observed effect of drugs on need for ventilatory supposrt and skin reactions	Morphine and Morphine + tetracaine groups lower pain scores than tetracaine alone.	Morphine infants needed more ventilatory support, 30% tetracaine patients had skin reactions	1+
{Carbajal R, 1999}	RCT 150 newborns having newborn screening(venepuncture)	Compared: no treatment Placebo(2ml water) 2ml glucose 30% 2 ml 30% sucrose pacifier 2 ml 30% sucrose + pacifier	DAN score (a behavioural pain score)	Pacifiers more effective than sweet solutions alone. Sucrose+ pacifier showed trend to lower score than pacifier alone		1+
{Lemyre, 2006}	RCT 54 infants 27+/- 2 weeks gestation requiring PICC lines	Tetracaine 4 % gel (Ametop ®) compared with placebo	PIPP score during initial venepuncture and then during insertion phase	No difference between the 2 groups	Infants PIPP scores were in the 'moderate' range suggesting that infants felt discomfort	1+

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Shah, 2006}	Cochrane review Effectiveness of breast feeding or breast milk in reducing procedural pain in neonates	11 studies identified		If available, breast feeding or breast milk should be used to alleviate procedural pain in infants undergoing a single painful procedure, compared to placebo, positioning or no intervention.Glucose/sucrose had similar effectiveness as breast feeding for reducing pain.	The effectiveness of breast feeding for repeated painful procedures is not established and further research is needed.	1++
{Shah, 1998}	RCT Double blind 75 term neonates undergoing heel prick	Randomised to receive 20 mg/ kg paracetamol or placebo 60 – 90 minutes before heel prick for newborn screening	Infant facial and cry duration.	No difference between the two groups – paracetamol does not reduce the pain of heel lance		1+
{Cignacco, 2007}	Systematic literature review of non pharmacological interventions management of procedural pain in preterm and term neonates	13 RCCT and 2 meta analyses were studied including: Nutritive and non nutritive sucking (5 papers). Music (2), facilitated tucking (3), swaddling(3), positioning (3), olfactory stimulation/multifactorial stimulation(2), kangaroo care/maternal touch(2)		There is evidence that the methods of 'non nutritive sucking', 'swaddling' and 'facilitated tucking' have a pain relieving effect in neonates	Conclusions: Some of the non-pharmacological interventions have an evident favourable effect on pulse rate, respiration and oxygen saturation, on the reduction of motor activity, and on the excitation states after invasive measures. However, unambiguous evidence of this still remains to be presented. Further research should emphasise the use of validated pain assessment instruments for the valuation of the pain-alleviating effect of non-pharmacological interventions.	1++
{Barker, 1994}	187 heel prick procedures in 47	Randomly assigned 2 different lancet types - Autolet2 or	Behavioural responses.	No significant difference in behavioural response or times for	expensive	1-

	infants	Tenderfoot Preemie	Collection times.	collection of small to medium amounts of blood, but Tenderfoot device superior for large volumes(>1ml)		
{Paes, 1993}	40 health full term infants for newborn screening test	Randomized trial comparing automated lancet for heel pricks with manual device	Total blood, blood sampling times,pain (measured by crying times) and degree of bruising	Total volume and blood sampling time significantly better with automated lancet ($p<0.001$)	No difference in crying time	1-
{Shepherd, 2006}	340 healthy newborns undergoing screening test	Randomly assigned to heel prick via Tenderfoot or Genie-Lancet	Quality of sample Time taken No of heel pricks If needed to squeeze heel Pain expressed by infant bruising	Tenderfoot device saved significant time, fewer no of heel pricks needed .	Pain assessed by length of cry only	1+
{Harpin, 1983}	36 newborns undergoing routine blood sampling for Guthrie Test	Compared Autolet (automated lancet) with manual heel prick		Equally effective in obtaining blood but Autolet less painful		1-
{Shah, 2003}	80 neonates – healthy undergoing newborn screening test	Compared BD safety flow lancet with BF QuikHeel	Facial grimacing score during puncture and heel squeeze Cry duration, duration of the procedure, number of punctures required	QH group required fewer punctures and less crying. Pain scores during squeezing did not differ		1-

INTERVENTION: Examination for retinopathy of prematurity.

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Mitchell, 2004 #171}	RCT 30 preterm infants having ROP exams	Randomized to either: local anaesthetic eye drops+ pacifier+ 3 doses of sterile water or : local anaesthetic eye drops+ pacifier+ 3 doses of 24% sucrose during eye exam	Premature Infant Pain Profile (PIPP) measures physiological variables and behavioural state	During exam less distress in sucrose group but no difference after exam	Sucrose and a pacifier may be helpful during eye exam in infants who have already had local anaesthetic eye drops	1+
{Grabska, 2005 #172}	32 infants RCT	Randomized to receive either sucrose or sterile water during eye exam	PIPP. Crying time	No significant difference between groups Sucrose group had small but significant drop in O2 sats after admin	Sucrose alone not sufficient Potential bias: infants described as being offered a pacifier but those receiving this intervention not separately considered	1-
{Marsh, 2005 #174}	RCT 22 infants, < or = 30 weeks gestation	Randomized to either saline or proparacaine 0.5 % eye drops, receiving alternate treatment at second scheduled eye exam	PIPP – at 1 and 5 minutes before and after the eye exam and at insertion of the speculum	Significantly less pain at speculum insertion than with saline	Local anaesthetic drops should become routine practice	1+
{Gal, 2005 #173}	RCT 23 infants < or = to 30 weeks	All had local anaesthetic drops. Randomized to receive either 2 ml of sucrose or 2 ml or water orally immediately prior to eye exam.	PIPP – at 1 and 5 minutes before and after the eye exam and at insertion of the speculum	For 3 of 5 responses significantly less pain at speculum insertion with sucrose than with placebo	Oral sucrose may reduce immediate pain response to eye exam	1+

{Boyle, 2006 #175}	RCT 40 infants < 32 weeks gestation or birth weight blinded to study drug but not to pacifier	2 mins before first screening exam: either (i) 1 ml sterile water-syringe (ii) 1 ml sucrose 33% - syringe (iii) 1 ml sterile water – syringe +pacifier (iv) 1ml sucrose syringe+pacifier	Videotaped during exam and until 2 mins after. PIPP for 1st eye, physiological variables thereafter	Infants randomised to pacifiers scored significantly less than those without. Sucrose did not appear to have a synergistic effect in this study	Possible that a synergistic effect might be seen if repeated doses of sucrose given (see Mitchell)	1+

INTERVENTION: Lumbar puncture

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AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Crock, 2003 #185}	Questionnaire survey of children (< 18 years)with cancer and families undergoing repeated painful procedures eg LP or bone marrow (96 children)	Either midazolam sedation and local anaesthetic or GA	Questionnaire to children and parents about the procedure and which they preferred	GA: 106 procedures: restraint needed 4%. 25% reported distressed Sedation and LA: 94% procedures restraint needed, 90% reported distress	90% parents wished for GA for future procedures	Not further discussed in these tables but included to emphasise that children requiring repeated painful procedures should be offered GA option 3
{Kanagasundaram, 2001 #186}	Observational study	Observational study of children receiving nitrous oxide in relieving pain and anxiety during painful procedures. 90 children requiring bone marrows, LP's, venous cannulation, dressing change	Observational Scale of behavioural distress scores pre, during and post procedure	Scores highest (most distress) during induction phase, with subsequesnt lower scores Most suitable for children over 6 and for short procedures	Few side effects . mean recovery time 3 minutes	2+
{Kaur, 2003 #187}	Sixty consecutive newborns (gestational age, ≥ 34 weeks) undergoing diagnostic lumbar puncture	Topical application of 1 g of EMLA or placebo 60 to 90 minutes before lumbar puncture.	Heart rate, transcutaneous oxygen saturation level, and total behavioral score recorded on a video camera and graded according to the Neonatal Facial Coding System.	Lumbar puncture in newborns produces pain responses. Eutectic mixture of local anesthetics is an efficacious agent for reducing the pain associated with needle insertion and withdrawal during lumbar puncture in newborns.		1+
{Carraccio, 1996 #193}	RCCT 100 infants less than 3 years requiring LP	Randomized to receiving lidocaine subcutaneously or placebo prior to LP	Comparison of number of attempts needed to obtain CSF and no of traumatic taps	No difference between groups in ease of obtaining CSF,. Slightly more traumatic taps in lidocaine group		1

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Uman, 2006 #188}	Cochrane review: Psychological interventions for needle related procedural pain and distress in children and adolescents	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a psychological intervention group with a control or comparison group were eligible.		Largest effect sizes seen for treatment improvement over control exist for distraction, hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating psychological strategies for procedural pain and distress into practice with children	1++
{Eidelman, 2005 #188}	Systematic review of randomised controlled trial 25 trials identified – 2096 subjects	Compared the analgesic efficacy of topical anaesthetics for dermal instrumentation with conventional local anaesthesia. Also compared other LA agents to EMLA		EMLA vs intradermal LA: no significant difference but EMLA advantageous because less painful to apply EMLA compared with tetracaine, liposome encapsulated tetracaine and liposome encapsulated lidocaine (ELA Max)	Liposomal lidocaine in the US is less expensive than EMLA and has a more rapid onset of action	**1++**
{Stevens B, 2004 #131}	Sys Rev (Cochrane) RCT's in term and preterm infants – up to 28 days post 40 weeks gestational age Sucrose for analgesia in newborn infants	44 studies identified for inclusion in review 21 actually included (1616 infants) 9 evaluated preterm infants 11 term 1 both		Sucrose is safe and effective for reducing procedural pain from single painful events (heel lance, venepuncture). There was inconsistency in the dose of sucrose that was effective (dose range of 0.012 g to 0.12 g), and therefore an optimal dose to be used in preterm and/or term infants could	Suggested sucrose had greater analgesic effect when given 2 mins before painful stimulus	1++

				not be identified. The use of repeated administrations of sucrose in neonates needs to be investigated as does the use of sucrose in combination with other behavioural (e.g., facilitated tucking, kangaroo care) and pharmacologic (e.g., morphine, fentanyl) interventions. Use of sucrose in neonates who are of very low birth weight, unstable and/or ventilated also needs to be addressed.		
{Liossi, 2006 #196}	RCT Pediatric cancer patients requiring LP 45 children age 6 – 16 years	LP with 1. Local anaesthetic (LA) 2. LA + hypnosis 3. LA+ attention		LA + hypnosis group had less anticipatory anxiety and less procedure related pain and anxiety		

INTERVENTION: Chest Drain Removal

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Rosen 2000 {Rosen, 2000 #2}	RCT n=120 children	0.1mg/Kg (10mg max) IV morphine v EMLA for CT removal EMLA on for 3hrs	pain assessed by observer using visual analogue scale 10cm	Before removal pain scores lower in morphine group. During procedure no difference between morphine (7.16) and EMLA (7.4) groups. Scores during procedure mod to severe pain.	no adverse events.	1+
Valenzuela 1999 {Valenzuela, 1999 #1}	double blind RCT adults n=100	0.1mg/Kg (10mg max) IV morphine v EMLA for CT removal EMLA on for 3 hrs	Increase in pain from before to during CT removal Assessed by observer looking at pain behaviour VAS 10cm	No differences between the groups pre(morphine 0.4 EMLA 0.9) and post procedure Increase in pain during procedure less in EMLA (4.4 v 6.0 for morphine) group Conclude EMLA cream more effective than IV morphine in relieving pain of CT removal		1- 48 dropouts – no details. Implied that CT removed without observer present fewer patients able to complete questionnaire in morphine group
Bruce E 2006 {Bruce, 2006 #134}	1 and 2 observational studies children study 3 pilot RCT	1. prevalence and clinical characteristics of pain and analgesic practices during CTR. N=135	Pain	1. prevalence mod to severe pain 76%. Morphine commonest used analgesic, varying dose.		Studies 1 and 2 grade 3. Study 3 grade 1- (score 3), only pilot study. May not have been big

	children n=14	2. efficacy and safety entonox for CTR. N=30 3. IV morphine versus entonox for CTR		2. Entonox safe still had pain despite also having morphine and/or diclofenac 3. no differences between morphine or entonox. Children still had pain. Morphine or entonox alone unlikely to provide adequate analgesia.		enough to show difference
Akrofi M 2005 {Akrofi, 2005 #135}	RCT Adults Post cardiac surgery N=66	0.1mg/KgIV morphine v 20ml 0.5% bupivicaine infiltrated subcutaneously v inhaled entonox for CTR	Pain measured on VAS 100mm	Pain scores: bupivicaine 9.5mm, entonox 37mm, morphine 15mm. Bupivicaine and morphine produce lower pain scores.	No differences in BP, heart rate, $PaCO_2$, oxygenation or sedation	1- Pain scores low compared to other studies. All groups also had background morphine.
Puntillo K 2004 {Puntillo, 2004 #136}	RCT Adults post cardiac surgery. N=74	4mg IV Morphine + procedural information v 30mg IV keterolac + procedural information v 4mg Iv morphine + procedural and sensory info v 30mg IV keterolac + procedural and sensory info. For CTR.	Pain intensity and distress before and straight after CTR.	No difference between groups. Pain level low in all groups. Either opiod or NSAID can successfully reduce pain during CTR if used correctly i.e big enough dose and given time to work.	No differences in sedation	1+ mean pain intensity score 3.26, Pain distress score 2.98. These are low.
Bruce 2006 {Bruce, 2006 #137}	Literature review 14 studies 5 descriptive 3 non-pharmological intervention 6 RCT (includes Rosen and Valenzuela) of morphine ,LA and entonox only 2 involved children.	Conclusions: Descriptive studies: 4 of adults. Suggest patients experience moderate to severe pain during chest drain removal. Type and dose analgesia given not reported. 1 of children didn't measure pain looked at behaviour, found displayed number of coping behaviours and concluded procedure frightening and painful. Non-pharmacological interventions: white noise, patients own music and no music – no difference. Relaxation technique v normal care – no difference. Ice v no ice – no difference. Patients given analgesia as well mainly opiates all experienced significant pain. Analgesic interventions: 3 morphine v LA, morphine v subfacial lidocaine – no difference. 2 morphine v EMLA (1 adult, 1 children) – EMLA group less pain. 1 LA (intrapleural bupivacaine via chest drain) v placebo - no difference both groups significant pain. Subgroup received IV keterolac – pain significantly lower in this group; 2 inhalation studies, entonox v entonox and 0.25% isoflurane – entonox only more pain, entonox v 0.25% isoflurane and 1% desflurane and 60% 02 – no difference. Pain mild but studies only briefly reported. Chest drain removal painful procedure. Non- pharmacological interventions not helpful. 4 of the 6 analgesic studies showed patients experienced mod to severe pain despite strong analgesics such as morphine and LA used. Morphine alone insufficient. Inhalation agents , NSAIDS and LAs may provide more effective analgesia. Multimodal therapy need more research.				1++

{Taddio A, 2006 #91}	RCT.Double blind. 132 neonates (mean gestation 30.6 weeks)	Randomized to receive tetracaine, morphine or both for alleviating pain in ventilated neonates prior to central line insertion. Separate non randomised control group	Pain score during different phases of procedure – and observed effect of drugs on need for ventilatory supposrt and skin reactions	Morphine and Morphine + tetracaine groups lower pain scores than tetracaine alone.	Morphine infants needed more ventilatory support, 30% tetracaine patients had skin reactions	1+
{Horsley, 2006 #201}	Cohort study of adults with small bore chest drains using historical controls			Seldinger drains were well tolerated and effective method of draining pneumothoraces and uncomplicated efdusion		Have sent for paper Will be grade 3

INTERVENTION: NGT insertion

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Wolfe, 2000}	double blind RCT adults n=40	atomized 4% lidocaine v saline to nasopharynx and oropharynx prior to NGT placement. all patients also received topical 2% lidocaine jelly intranasally.	Pain of NGT placement VAS 100mm	mean pain scores 37.4mm for lidocaine group and 64.5mm for placebo group. atomized 4% lidocaine results in clinically and statistically significant reductions in pain during NGT placement		1++ No children in this study
{Singer, 1999}	RCT Adults N=40	Topical anaesthetics and vasoconstrictors v surgical lubricants alone for NGT insertion. 0.5% phenylephrine spray to nose followed by 5ml 2% lidocaine gel. Throats sprayed with 2% tetracaine and 14% benzocaine	Pain NGT insertion measured on VAS Nasal pain, gagging, Vomiting , choking and epistaxis	Experimental group significantly less pain, discomfort and gagging. No difference in adverse effects	Use of topical lidocaine and phenylephrine to nose and tetracaine and benzocaine to throat significantly reduces pain and discomfort NGT insertion. Recommend widespread use.	1+ all adults ?children tolerate so much preparation
{Ozucelik, 2005}	RCT double blind Adults N=100	10mg metoclopramide IV versus saline IV as placebo for NGT insertion	Pain, nausea and discomfort VAS	Initaial VAS scores similar. Consequent scores sig lower in metoclopramide group.	Mean VAS scores for pain, nausea and discomfort significantly lower following IV metoclopramide	1++ Score 4 need IV access. no children
{Cullen, 2004}	RCT double blind Adults N=50	Nebulized lidocaine (4ml 10%) versus neb saline	Discomfort 100mm VAS	Lidocaine group mean VAS scores 37.7mm. Saline group mean VAS scores 59.3mm.	No difference in difficulty of procedure	1++ no children

{Ducharme, 2003}	Double blind double dummy randomized triple crossover Adults N=30	Healthy volunteers had 3 NGT placed acting as own controls for 3 medications: 1.5ml 4% atomized lidocaine, 1.5ml atomized cocaine, 5ml 2% lidocaine gel.	Pain of tube insertion and "global discomfort" Which do participants prefer?	No significant difference in pain scores. "global discomfort" less with lidocaine gel (p=0.17) Participants preferred gel	Epistaxis occurred more frequently in lidocaine group 17% v 0%. Neb lidocaine decreases discomfort of NGT insertion 2% lidocaine gel appeared to provide best option.	1++ statistically but not clinically significant.
{Stevens B, 2004 #131}	Sys Rev (Cochrane) RCT's in term and preterm infants – up to 28 days post 40 weeks gestational age Sucrose for analgesia in newborn infants	44 studies identified for inclusion in review 21 actually included (1616 infants) 9 evaluated preterm infants 11 term 1 both		Sucrose is safe and effective for reducing procedural pain from single painful events (heel lance, venepuncture). There was inconsistency in the dose of sucrose that was effective (dose range of 0.012 g to 0.12 g), and therefore an optimal dose to be used in preterm and/or term infants could not be identified. The use of repeated administrations of sucrose in neonates needs to be investigated as does the use of sucrose in combination with other behavioural (e.g., facilitated tucking, kangaroo care) and pharmacologic (e.g., morphine, fentanyl) interventions. Use of sucrose in neonates who are of very low birth weight, unstable and/or ventilated also needs to be addressed.	Suggested sucrose had greater analgesic effect when given 2 mins before painful stimulus	1++

INTERVENTION: Venepuncture and intravenous cannulation in older children

AUTHOR	**DESIGN (?RCT/?DB)** (Ages) (n=…)	**TREATMENT**	**OUTCOME MEASURE** (include evaluation times)	**RESULT & CONCLUSION**	**SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION**	**EVIDENCE GRADE / COMMENTS**
{Eidelman, 2005 #188}	Systematic review of randomised controlled trial 25 trials identified – 2096 subjects	Compared the analgesic efficacy of topical anaesthetics for dermal instrumentation with conventional local anaesthesia. Also compared other LA agents to EMLA		EMLA vs intradermal LA: no significant difference but EMLA advantageous because less painful to apply EMLA compared with tetracaine, liposome encapsulated tetracaine and liposome encapsulated lidocaine (ELA Max)	Liposomal lidocaine in the US is less expensive than EMLA and has a more rapid onset of action	**1++**
Koh JL, Harrison D, Myers R, Dembinski R, Turner H, McGraw T{Koh JL, 2004 #87}	RCT 8-17 years n=60	Comparison of 2 different topical anaesthetics: EMLA vs new ELA-Max	Children rated pain using visual analog scale. Anaesthetist rated presence of blanching and difficulty in siting iv	30 min application of ELA-Max as effective as 60 min application of EMLA. No difference in ease of venous access but less blanching with ELA-Max	ELA Max contains no prilocaine so that the theoretical problems of methaemoglobinaemia (not in practice a problem) – not a problem	1+
Luhmann J,{Luhmann J, 2004 #88} Hurt S, Shootman M, Kennedy R.	RCT 4-17 years n=69	Comparison of ELA-Max with 0.1-0.2ml sub cut buffered lidocaine in peripheral intravenous catheter placement	Self reported visual analog scale questionnaires for patients and parents, nurse and blinded observer	No difference between buffered lidocaine and ELA-Max in termsof pain, anxiety, technical difficulty		1+

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Hee HI, Goy RW, Ng AS.{Hee HI, 2003 #82}	RCT 8-15 years n=120	Day surgery patients needing iv's: Gp1:EMLA+air/O2 GP2:50%N2O/50%O2 Gp3:Emla +N2O	Childrens Hospital of E Ontario pain scale by observer, VAS by patien. Heart rate, O2 sats, ease of cannulation	EMLA and 50% nitrous oxide equally effective for pain reduction whilst combination provides superior analgesia and satisfaction	No difference in time or ease of cannulation	1-
Andrew M, Barker D, Laing R. {Andrew M, 2002 #80}	RCT 5-15 years n=80	Day surgery patients EMLA cream on each hand After removal and 10 mins prior to cannula, application of Glyceryl Trinitrate (GTN) ointment or placebo (each child their own control)	Hand with visually best quality vein selected and cannulated – primary outcome was which hand was selected	GTN hand was chosen in 70% of children suggesting that GTN cream may aid in cannula placement		1-
Taddio A, Soin HK, Schuh S, Koren G, Scolnik D. {Taddio A, 2005 #92}	RCT 1 month – 17 years n=142	Liposomal lidocaine or placebo prior to cannulation	Children<5 years pain evaluated by parents and research assistant(Face Pain Scale0 Over 5 years included child	Liposomal lidocaine associates with higher intravenous cannulation success rate	less pain , shorter procedure time and minor dermal changes with liposomal lidocaine	1+

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Ekbom K, Jakobsson J, Marcus C{Ekbom, 2005 #169}	RCT 6-18 years n=70 (50 with difficult venous access) 20 who very anxious	All had EMLA Randomized to N2O (NO) or conventional treatment	No of attempts at cannulation Time required for procedure Pain (VAS) Satisfaction score – parents, children and nurse	Highly significant results in both anxious children and difficult access children being easier and less painful in N2O group	Children held their own mask. Only suitable therefore over 6. Only tested very fit children (American Soc of Anaes – grade1). No problems – suggested gr 2 would also do well	1-
Kleiber C, Craft-Rosenberg M, Harper DC. {Kleiber C, 2001 #85}	RCT Pre school children 44	Iv catheters placed for tests Parents received distraction education vs standard care	Observation of child and parent	No group differences in reports of behavioural distress. Parents who had been taught distraction were more likely to use it		1-
MacLaren Jill, Cohen Lindsey L {MacLaren, 2005 #189}	RCT 1-7 years n=88	Gp1: interactive toy distraction Gp2: passive movie distraction Gp3 : standard care	Parent, nurse, child over 4 self report; observational coding	Children in the passive condition were more distracted and less distressed than those either with interactive toy distraction of standard care – there were no differences between these groups (this was watching a movie rather than playing with an interactive toy)	Suggests a passive strategy is more effective method of distracting children than an active one – suggests children's distress interfered with their ability to engage with the distractor	1-
{Uman, 2006 #188}	Cochrane review: Psychological interventions for needle related procedural pain and distress in children and adolescents	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a psychological intervention group with a control or comparison group were eligible.		Largest effect sizes seen for treatment improvement over control exist for distraction, hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating psychological strategies for procedural pain and distress into practice with children	1++

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Fanurik Debra, Koh Jeffrey L, Schmitz Michael {Fanurik, 2000 #170}	RCT 2-26 years in age blocks 2-4,5-8,9-12,13-16 n=160	Iv insertion in OP pre endoscopy All had EMLA Randomised to 'distraction' or 'usual coping strategy'	Pain ratings Behavioural distress ratings	Pain ratings not influenced by distraction but children's behavioural distress lower for older children and those who were provided distraction		1-
{Kolk AM, 2000 #118} Kolk AMM, Van Hoof R, Fiedeldij-Dop MJC	RCT 3-8 years n=31	Children with local anaesthetic were randomly assigned to a have preparation before the Venepuncture or not	Groniger Distress Scale	Prepared children showed significantly less distress than those who had not been prepared		1-(small study)
McErlean M, {McErlean M, 2003 #89}Bartfield JM, Karunakar TA, Whitman MC, Turley DM.	RCT 9months to 6 years n=46	Midazolam syrup pre placement of PIC	Parents and observers rated childrens pain scores	Median parents pain scores less in miazolam rather than placebo group (p=0.002) Observers scores not significantly different	No adverse effects in this small study	1-
{Kanagasundaram, 2001 #190}	Cohort study Observational 90 children requiring repeated painful procedures	Gave between 50 and 70% NO to children between 1 and 11 years. Used OBSD-R scores during timed phases pre, during and post procedure	OBSD-R score	Increased level of distress during admin of NO – but this is less in children more than 6 years suggesting that those who can understand the procedure will benefit most	Children having dressing changes had higher scores than those having shorter procedures	2-

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Costello, 2006 #197}	RCT 127 children between 9 and 18 years requiring intravenous cannulation	37 had ethyl vinyl chloride vapocoolant spray 48 received isopropyl alcohol (placebo) spray 42 no pre-treatment	Used children's VAS score	No difference between groups for the pain of venepuncture		1+
{Davies, 2006 #197}	RCT 77 children requiring venepuncture for assessment of GFR. Age 5 – 13 years	Compared ethyl chloride spray pre venepuncture with ametop	Childs preferred choice for third venepuncture having had one of each	Equal preference		

INTERVENTION: Immunisationand IM injection

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Scheifele DW, 2005 }	RCT 4 – 5.5 years n=288	Compared local reactions at 48 hours and daily parental pain reports after 2 different diptheria-tetanus- pertussis vaccine booster doses at 4 – 6 years. The standard (DtaP) vaccine was compared with a vaccine containing a lower diptheria and pertussis doses (Tdap)	Daily parental pain reports. Assessment of degree of redness and swelling by nurse observer at 48 hours. Serological response pre and 4 weeks post vaccine	Less redness and swelling in the Tdap group at 48 hours. (p=0.004)Children with large reactions more likely to have higher levels of pre immunization ab levels. BOOSTER RESPONSES TO Tdap were reduced with the smaller antigen doses but generally satisfactory .	(No IPV in Tda	1++
{Wood C, 2004}	Multi centre survey 4-6 years olds 28 paediatricians enrolled 620 children	Compared children pain scores post either ‘Priorix’ MMR vaccine of ‘RORVax’ MMR vaccine in children receiving their 2nd routine MMR vaccine. Children used a standardised ‘faces pain scale’	Parents and childrens reports over 4 days post vaccination	Priorix less painful that RORVax – p<0.001) This persisted over 4 days		1- if all else equal , choice of vaccine influences degree of pain
{Ipp M, 2004}	RCT Age = 12 months N=49	Random allocation to receive ‘Priorix’ or MMR-II .	Pain responses recorded before and 15 secs after immunization by parent and paediatrician,. Also recorded whether cried and length of cry	Paediatrician (p=0.001)and parents (p=0.007) both scored pain scores significantly less for Priorix than for MMRII		1++
{Ipp, 2006 }	RCT Double blind 4-6 years 60 children	Participants received either Priorix® or M-M-RII®	Children self reported ‘Oucher ‘ scale. Parents and paediatricians completed VAS scores	MMRII group had higher median pain scores, crying and paediatrician reported pain		1+

{Diggle, 2006 }	RCT 696 infants 2,3,4 months of age	Random allocation to immunisation with 23/25 mm needle, or 25 gauge 16mm needle; or 25 gauge 25 mm	Parental records of local and general reactions 6 hours post and 3 following days. Antibody response	No difference in antibody response Long needles reduce vaccine reactogenicity without compromising immunogenicity		1+
{Uman, 2006 }	Cochrane review: Psychological interventions for needle related procedural pain and distress in children and adolescents	28 trials with 1951 participants age 2- 19 years. Only used RCT's with at least 5 participants in each arm comparing a psychological intervention group with a control or comparison group were eligible.		Largest effect sizes seen for treatment improvement over control exist for distraction, hypnosis, combined cognitive – behavioural interactions .	Health professionals should be aware of the value of incorporating psychological strategies for procedural pain and distress into practice with children	1++

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Albertsen BK, 2005}	RCT 12 children with ALL 17 treatment courses evaluated	Children receiving asparaginase. 4 different combinations: 2 where asparaginase dissolved in lidocaine and 2 in water	Pain intensity (Pain Visual Analog Scale, VAS score) and drug pharmokinetics evaluated	Pain scores showed significantly less pain if asparaginase dissolved in lidocaine ($p<0.0001$)	Did not affect bioavailability or absorbtion rate of the enzyme	1+
{Amir J, 1998}	RCT Children receiving 2 doses of im benzathine penicillin for secondary prophylaxis of rheumatic fever 1 month apart N=18	2 groups: 1: benzathine penicillin diluted with sterile water, followed 1 month later with penicillin diluted with lidocaine 2: same regime in reverse order	Serum penicillin concentrations after each injection	Pain score significantly lower after lidocaine(? significance level)	No difference in serum penicillin levels	1-
{Reis EC, 2003}	RCT Infants receiving their routine 2 month immunizations (4 injections) N= 116	Intervention group: received sucrose, oral tactile stimulation with a pacifier or bottle, and were held by their parents during immunization. Control group did not receive these interventions (standard practice)	Blinded assessment of audiotaped crying, heart rate , parent preference for further use of injection technique, nurse rated ease of vaccine administration	Combining sucrose, oral tactile stimulation and parental holding was associated with significantly reduced crying ($p=0.002$).Parent preference for the intervention :$p<0.001$ (NB this part of the study not blinded)	Nurse rated ease of vaccine administration equivalent for both groups	1-

| AUTHOR | DESIGN (?RCT/?DB) (Ages) (n=…) | TREATMENT | OUTCOME MEASURE (include evaluation times) | RESULT & CONCLUSION | SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION | EVIDENCE GRADE / COMMENTS |

{Lewindon PJ, 1998}	RCT 2,4, 6 months 107 infants	Received either 2ml 75% sucrose or 2 ml water pre immunisation	Duration of infant crying Infant distress assessed by visual analogue scale (Oucher)	Sucrose reduced infant crying time Mean duration of first cry reduced from 42 – 29 seconds.		1 -
{O'Brien L. Taddio A, 2004}	RCT 1 year old infants n=120	1g amethocaine or placebo 30 mins before vaccination	Pain assessed by Modified Behavioural Pain Scale	4 %amethocaine reduces pain of immunisation (p = 0.29). Amethocaine produced local(non serious) side effects	No difference in immunization success. Needed applying 30 mins pre immunisation	1++
{Taddio A, 1994}	RCT 0-1 years n=96	2.5 gm EMLA or placebo applied 60 minutes pre immunisation	Modified Behavioural Pain Scale and duration of infants cry	Time to cry longer with EMLA: p=0.0004 Total crying time shorter with EMLA: p = 0.027	EMLA group had more local skin reactions P<0.0001	!+

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Lewkowski MD, 2003 #68}	RCT 9-11 years during immunisation 7-12 years during venepuncture	Compared: sweetened chewing gum Unsweetened chewing gum Sweet taste control	Ratings of pain intensity (not specified)	Variable correlation. Peer response may have affected girls ratings		2-
{Cohen LL, 2002 #61}	Controlled trial 3-7 years n=61	Compared procedural coping and stress behaviour in group of children trained in these skills compared to group who had not	Observation of children's ability to cope with immunization pain	Children understood coping skills but did not use them.	Observation showed that parents behaviour tended to comfort child distress, whearas nurse behaviour encouraged child coping	2
{Cohen, 2002 #58}	RCT Infants receiving immunization N=90	Compared nurse directed distraction to standard care during immunization (not blinded)	Observational scale Parent and nurse ratings Heart rate	Infants engaged in distraction and distraction reduced behavioural distress (? Significance level) Difference between ratings and heart rate inconclusive	Infants exhibited elevated stress prior to and during injection but this seemed to be fleeting	1-

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Sparks, 2001 #76}	RCT 4 – 6 years n=105	Children needing DPT immunization.Randomly assigned to receive: Touch Bubble blowing Standard care	Child medical fear scale prior to injection. Pain of injection using Oucher scale	Both forms of distraction significantly reduced pain perception. Fear not a significant covariate but distraction effective when fear was not constant		1+
{Cohen LL, 1999 #60}	RCT 10 year olds(4th graders) n=39 having 3 immunizations over a 6 month period	Compared distraction, EMLA, , typical care during immunization	Child and Adult medical Procedures Interaction	All children low distress despite moderate anxiety or pain. Distraction more child coping, less child distress. No difference in participant rating and heart rate with all treatments		2
{Jackson, 2006 #202}	RCT 372 children, age 4 years, having 4th DtaP vaccine	Compared pre and ongoing treatment with either acataminophen(paracetamol) or ibuprofen or placebo to see if the local reaction could be modified	Size of local reaction to vaccine	No change between groups		1+

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Mark A, 1999 #70}	RCT 10 year old n=252	Compared DT vaccine given subcutaneously or intramuscularly in upper arm	Observed redness, itching, swelling, pain over 2 week period. Serology to look for ab levels	IM injection significantly less redness , swelling or pain. No difference in antibody responses.	Girls had lower response to diphtheria toxoid than boys	1+
{Sweet SD, 1999 #77}	Observational study Infants at 6 or 18 months N=60	Video recorded immunizations to see how different patterns of maternal and staff behaviour influenced prediction of pain	Neonatal Facial Action Coding System Child Adult Medical procedure Interaction scale	'Reassurance' ('mother's distress promoting behavior') predicted increased infant pain behaviour, whilst 'distraction'('staff coping promoting behaviour' predicted decreased infant pain behaviour		3
{Cohen Reis E, 1997 #62}	RCT School age children: 4 – 6years N=62	Immunization in following groups: Gp!: EMLA+distraction Gp2:Vapocoolant spray + distraction Gp 3 distraction	Videotape: cry duration Pain Behaviours as measured by Observational scale of Behavioural distress	EMLA and spray both significantly and equally better than control Children preferred vapocoolant	Vapocoolant much cheaper than EMLA	1+

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Lindh V, 2003 #69}	RCT 3 months n=90	Children receiving immunization EMLA + glucose Or placebo	ECG Video – modified behavioural pain scales (MBPS) Latent of first cry total crying time	ECG – transient heart rate slowing followed by acceleration significantly more in placebo group Cry and MBPS scores significantly less in EMLA+glucose group		1+
{Cassidy KL, 2001 #57}	RCT 4-6 years n=161	Routine immunization EMLA patch vs placebo	Childs self report on a Faces Pain scale Child Facial Coding system Children's Hospital of E Ontario pain scale Parent and Technician ratings	EMLA patch group had significantly less pain on all 4 measures compared with placebo (17% vs 43 % in placebo group)		1+
{Cohen, 2006 #193}	RCT 136 infants 1-24 months	Routine immunization Parents received coaching in distraction (watching 'Sesame Street' or 'Teletubbies' video versus standard care	MAISD (Measure of Adult and Infant Soothing and Distress) Parents and nurse rating using VAS	MAISD: infants in distraction group significantly less distress than control ($p<0.05$) No difference in parent and nurse report		1-
{Jackson, 2006 #195}	RCT Blinded 372 children	Routine immunization with 5th Dtap vaccine – compared pre treatment with paracetamol, ibuprofen or placebo	Local reaction with area of redness or limb swelling 48 post vaccination	No difference between groups		

INTERVENTION: Laceration repair

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Farion, 2003}	Systematic review. 8 papers. Adults and children.	Tissue adhesives v standard wound closure. Acute, linear, low tension wounds.	Cosmesis Pain Procedure time	No difference in cosmesis. TAs less pain and quicker.	TAs slight increased risk of dehiscence.	1++ Same author and data as Cochrane review 2001. CD003326.
{Barnett, 1998}	RCT Children> 4yrs N=163	Glue versus sutures for repair linear lacerations ,5cm, ,12hrs old not involving eyelids or mucous membranes	Cosmetic outcome at 3 and 12 months	Cosmetic outcome the same.	Length time – glue group faster. Pain – doctors, nurses and parents but not children rated glue as less distressing	1-
{Zempsky, 2004}	RCT Ages 1-18 N=100	Steristrip versus dermabond for facial lacerations	Cosmesis at 2 months Pain.	No difference in cosmesis or pain scores	More dehiscence in dermabond group Equivalent techniques. Steri strips cheaper	1+
{Hock MO 2002}	RCT Children 1-18 N=189	HAT v sutures	Procedure time Wound healing Scarring Pain complications	HAT quicker, less scarring, pain and complications, trend towards better healing	HAT equally acceptable and perhaps superior to standard suturing	1+ score 3 not blinded
{Eidelman, 2004}	Systematic review. 22 trials	Topical v infiltrated anesthesia	Efficacy Cost ?need for cocaine	Topical as good or better analgesia than infiltrated anesthesia. Cocaine containing products costly and use not justified as equivalent efficacy		1++ scored studies using same scoring system as us.
{Ernst, 1997}	RCT N=66 Only 13 were children (5-17yrs)	LAT v injected buffered lidocaine	Pain application or injection Analgesic efficacy	LAT less painful than injection. Equal efficacy. Trend towards LAT working better	LAT gel compares favourably with injected lidocaine interms of anesthesia	1+

				on scalp and face lacerations cf extremities	and considerably less painful to apply.	
{White NJ, 2004}	Prospective case series. N=67 Ages 5-18	Lat for repair simple finger lacerations	LAT success/failure	53.7% success rate. Better anesthesia on dorsal than ventral surface.	No digital ischaemia. Safe and effective	3
{Smith, 1998}	RCT N=90 >1 year	Tetralidophen v lidocaine infiltration in repair mucous membranes.	Pain	Suture technician, research assistant and video reviewer scored lidocaine infiltration better. Patients and parents no significant difference in scores	Infiltrated lidocaine better but differences in pain scores were small and may not be clinically significant. Also pain of injection not taken into account	1-
{Singer AJ 2001}	RCT double blind Age 1-59 years N=60	Pretreat lacerations with either LET or Emla	Adequacy of anesthesia to needlestick. Pain of infiltration of lidocaine.	LET better at anesthesia to needlestick. No difference between the two in decreasing pain of infiltration.	Pretreatment with LET or EMLA results in similar amounts of pain of subsequent lidocaine infiltration. LET cheaper and not contraindicated in open wounds.	1++ 2/3 patients <18yrs
{Singer AJ 2000}	Double blind RCT N=43 Ages >1 year mean age 13yrs	Pretreatment with LET V placebo	Adequacey of anaesthesia to needlestick. Pain of infiltration of lidocaine.	LET group better anaesthesia to needlestick and significantly less pain on infiltration of lidocaine	Pre-treatment with topical LET significantly reduces pain of subsequent lidocaine injection	1++
Stewart GM 1998(Stewart, Simpson et al. 1998)	Double blind RCT N=100 Ages 5-16 years	Aqueous 1% lidocaine or saline soaked pad applied to wound 10 min prior to infiltration of lidocaine.	Pain response from patient and parent	No difference	Topical lidocaine ineffective at relieving pain of injection.	1++
Luhmann JD	RCT	Standard care (topical +/-	Distress during	Groups that received N_2O had lower	Regimens including	1+

2001(Luhmann, Kennedy et al. 2001)	Ages 2-6 years N=204	infiltrated anesthesia) v standard + N_2O v standard + oral midazolam v standard + N_2O and midazolam	procedure scored by observer (OSBD-R) Adverse events	distress scores. Groups that received midazolam had more adverse events and longer recovery times.	N_2O more effective at reducing distress during suturing of facial lacerations in 2-6 year olds	
Burton JH 1998 (Burton, Auble et al. 1998)	Double blind RCT N=30 Ages 2-7 years	50% NO/ 50% oxygen versus 100% oxygen for laceration repair.	Change in Pain (CHEOPS) and anxiety scores before and during laceration repair	Pain and anxiety scores went up in control group and down in NO group.	NO/oxygen mix significant decrease in anxiety during laceration repair	1+
{Davies, 2003}	Systematic review. 63 publications. 22 RCTs	Buffering local anaesthetic with sodium bicarbonate	Pain of infiltration	Buffering significantly reduces pain of LA injection	Buffering significantly reduces pain of injection. Particularly useful for large or sensitive areas and in children.	1++
(Bar-Meir, Zaslansky et al. 2006)	Observational study 60 patients between 1 and 16 years requiring suturing	15 received standard care and 45 had nitrous oxide in addition to lidocaine infiltration	Pain scores evaluated by surgeon and nurse at end of procedure using FLACC scale	FLACC scores lower in nitrous oxide group	.3% of children had mild side effects – mostly nausea and vomiting	2-
{Sinha, 2006 #200}	240 children between 6 and 18 years requiring suturing	Age appropriate distractors or a control group	Facial Pain scale State trait anxiety inventory in over 10 year olds	Nodifference in facial pain scores in children less than 10 although parents perceived less distress. Older children had reduced situational anxiety but not pain intensity or parents perception of pain distress	Older children may benefit from distraction in terms of anxiety but need further pain management	1 -

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Das DA, 2005 {Das, 2005 #138}	RCT 7 children acted as own controls. 11 episodes studied ages 5-18	Playing a vitual reality game + analgesia versus analgesia alone during burn dressing changes	Pain during removal and application of dressing. Parent and nurses view of child's anxiety and perception of pain.	VR significantly reduced pain during dressing change – by at least 2 on FACES scale. Parents and nurses agreed VR reduced anxiety and pain.	No side effects	1+ Small study Some children studied more than once.
Fratianne RB, 2001 {Fratianne, 2001 #139}	RCT crossover N=25 Ages 7+	Music therapy versus no music therapy during dressing changes	Patients perception pain and anxiety. Nurses observation of patient's tension	Significant reduction in self-reporting of pain in those who received music therapy. Biggest difference at beginning and end of treatment. During debridement less effective.		1- not blinded. Need therapist present.
Hernadez-Reif M, 2001 {Hernandez-Reif, 2001 #140}	RCT n=24 age – mean 2.5 years	Massage therapy versus no massage therapy in addition to standard care during dressing changes.	Observers perception of distress behaviours (CHEOPS) Nurses perception of ease in completing procedure	Massage therapy group showed less distress (facial grimacing, torso movement, crying, leg movement and reaching out) Nurses reported easier to complete dressing		1+ Massage 15min prior to dressing change.
Robert R, 2003 {Robert, 2003 #141}	RCT double blind reverse crossover. N=8 Age 5 -/+ 2	Oral Morphine versus transmucosal fetanyl citrate during tubbing	Pain (FACES scale) and anxiety (FEAR Thermometer)	Pain and anxiety better managed with fetanyl		1+ no details randomization or double blinding. Small study.
Borland M, 2005 {Borland, 2005	RCT double blind crossover N=24	Oral morphine versus intranasal fetanyl	Pain scores	No significant difference in pain scores	Time to resumption normal activities. No significant	1++

#142}	Median age 4.5 years (max 15 years)				difference. Fewer side effects with INF. INF suitable analgesic	no details randomization.
Sharar SR, 1998 {Sharar, 1998 #143}	RCT double blind crossover N=14 Ages 4-17 years	Transmucosal fetanyl versusoral hydromorphone for wound care	Patient pain scores. Observer scores for co-operation, anxiety and sedation.	Fetanyl improved pain and anxiety scores during wound care.	No significant difference in vital signs, n&v, pulse oximetry, sedation , cooperation or time to normal activites. Fetanyl safe and effective. Minor improvements in analgesia and anxiolysis.	1+
Sharar SR, 2002 {Sharar, 2002 #144}	Double blind RCT placebo controlled N= 22 Ages 5-14 years	Oral transmucosal fetanyl citrate versus oral oxycodone for outpatient wound care procedures.	Patient pain scores. Observer scores for cooperation, anxiety and sedation.	No significant differences	No significant side effects.OTFC and oral oxycodone safe and effective in outpatient setting. Fetanyl improved palatability	1+ no details randomization. Dropouts not discussed.
Heinrich M, 2004{Heinrich, 2004 #145}	Case Series N=47 dressing changes (30 children)	PR S(+)-ketamine and midazolam for dressing changes in outpatient setting.	Pain Patient satisfaction	94% adequate sedation and analgesia Return to normal after 30 min All children had anterograde amnesia No complications	Conscious sedation with rectal S(+) ketamine and midazolam safe and effective	3 sedation

INTERVENTION: myringotomy

AUTHOR	DESIGN	TREATMENT	OUTCOME	RESULT	S-EFFECT / 2^0 OUT.	SIGN GRADE / COM
{Bean-Lijewski, 1997 #144}	DB RCT 6/12-9yrs n=125	Paracetamol 15mg/kg Ketorolac 1mg/kg Oral 30 mins preop	Obj Pain Scale 5, 10, 20mins	K pain score lwr 5 and 10 min only (both below extra treatment trigger); No diff at D/c or post D/c analgesia	No diff	1+
{Bennie, 1997 #129}	DB RCT >6/12 n=43 (13-16 each grp)	Paracetamol 15mg/kg Ibuprofen 10mg/kg Saline Oral 30 mins preop	CHEOPS 5,10,15,30,45,60 mins after surgery	No diff in pain scores cf. placebo; no diff in rescue cf. placebo	No diff	1- Small sample
{Bolton, 2002 #131}	Open label (mainly ph'kinetic study) 17-72 mths n=30	Paracetamol 40mg/kg oral 30 mins preop	CHEOPS 10,20,30 mins	57% no further analgesia		2-
{Bennie, 1998 #130}	DB RCT >6/12 n=60 (15 each grp)	Transnasal butorphanol 5, 15, or 25mcg/kg saline	CHEOPS 5,10,15,30,45,60 mins after surgery	25mcg: lwr pain score, incr time to analgesia; lwr doses no diff from placebo	No diff in vomiting; incr sedation and time to oral intake with 25mcg	1- small sample size
{Galinkin, 2000 #132}	Randomised not blinded (mainly ph'kinetic) 9/12-6yrs n=265	Intranasal fentanyl 2mcg/kg; Saline; [+ paracetamol 10mg/kg all grps]	CHEOPS 5 then 15 minutely until 2hrs	Decr CHEOPS	Incr time to discharge from recovery; no diff vomiting	2+ Minor decr pain score – not clin significant
{Pappas, 2003 #133}	RCT single blinded 6/12-6yrs; n=120	Paracetamol 10mg/kg; Parac 10mg/kg + codeine 1mg/kg; Nasal butorphanol 25mcg/kg; IM ketorolac 1mg/kg	Obj pain score (0-10)	Higher pain score in P and P+C cf. B and K; incr rescue in P; no diff in analgesia at home	Incr vomiting in P+C and B	1- statistical not clinically significant difference in pain scores
{Tobias, 1995 #134}	Rand ?blinded 6-60mths n=50	Paracetamol 15mg/kg; paracet 10mg/kg + codeine 1mg/kg; Oral 30mins preop	Observer pain scale (0-10) 5 and 30 mins	Decrease pain score P+C; decr suppt analgesia		2+ Statist ?clinical sig decr score
{Watcha, 1992 #135}	DB RCT n=90	Paracetamol 10mg/kg; Ketorolac 1mg/kg; Saline. Oral 30 mins preop	Obj pain scale	K: lwr pain score and less suppt analgesia; P no different from placebo		1-
{Tay, 2002 #136}	DB RCT >1yr n=63	Paracetamol 15mg/kg; Diclofenac 0.5mg/kg [all fent 1mcg/kg]	CHEOPS	Pain scores low and no diff; 20-27% req rescue		1- all received fentanyl

{Ragg, 1997 #137}	DB RCT 1-12 yrs n=95	Paracetamol 20mg/kg; parac 12mg/kg + codeine 0.5mg/kg + promethazine 0.65mg/kg		Pain scores low and similar both grps	sedation and time to oral intake increase with combination	1-
{Bhananker, 2006 #154}	DB RCT (comp gen.) 6mths-8yrs n=124 (52/72)	Paracetamol 30mg/kg preop + saline ear drops vs placebo + 2%lignocaine ear drops	CHEOPS (0-10) 5 minutely in PACU; Paracetamol 15mg/kg rescue score >6 - codeine if no response; parent VAS at home at home, going to bed, next morning	Pain scores no diff; %requiring supplt analgesia no diff		1-
{Derkay, 1998 #152}	DB RCT (?method) Age: 4mths-18yrs n=200	Paracetamol 10mg/kg; Paracet 10mg/kg + codeine 1mg/kg; Ibuprofen 10mg/kg; Placebo (all preop) ALL: 4% lignocaine	Obj Pain score 0-10 arrival, 15 & 30 mins	Pain scores no diff in PACU and 24hrs; Suppt analgesia 24hrs: no diff	No facial nerve palsy, 1/200 vertigo	2+
{Lawhorn, 1996 #153}	DB RCT Children N=122	4% lignocaine drops at end BSM		Decr pain score; decr % req. suppt paracetamol	No vertigo or tinnitus	

INTERVENTION: tonsillectomy meta-analyses

AUTHOR	DESIGN	TREATMENT	OUTCOME	RESULT	COMMENTS	Gr
{Cardwell, 2005 #2}	Meta-analysis Cochrane	NSAID and tonsillectomy 13 trials, n=955 children	Bleeding requiring surgical intervention	NSAIDs did not significantly alter no. of periop bleeding events needing surgery OR no. of bleeding events not requiring surgery	Bleeding req. surgery rare – large CI (0.42-4.28) suggests need further studies Subgroup analysis ketorolac: no significant diff in bleeding	1++
{Marret, 2003 #4}	Meta-analysis	NSAID and bleeding Adult and paed 7 studies. Adult and paed	Postop bleeding No. reoperation	Bleeding incr 5.3 to 9.2% OR 1.8(0.9-3.4) Reop incr 0.8 to 4.2%; OR 3.8(1.3-11.5) NNH 29	"NSAID should not be used" 114/262 receiving NSAID = ketorolac 1mg/kg	1++
{Krishna, 2001 #7}	Meta-analysis	Aspirin vs NSAID (ibuprofen & diclofenac) 7 studies, Adult and paed	Postop bleeding	aspirin OR 1.94 (1.09-3.42) significantly higher than NSAID OR 0.93(0.44-1.95)	limited literature review – mainly ENT journals	1-
{Moiniche, 2003 #6}	Quantitative systematic review	NSAID and tonsillectomy 25 studies, NSAID n=970, nonNSAID or placebo n=833. Adult and paed	Intraop blood loss Postop bleeding Hospital admission Reoperation for bleeding	Postoperative bleeding: ns Only reoperation happened significantly more often with NSAID OR: 1.12-4.83; NNH: 60(34-277)	"should be used cautiously…further research needed rather than clinical recommendations"	1++
{Moiniche, 2003 #6}	Quantitative systematic review	NSAID vs opioid Adult and paed	PONV	Risk of emesis signif. decreased: 31.6% vs 48.8% RR 0.73 (0.63-0.85), NNT 9		1++
{Cardwell, 2005 #2}	Meta-analysis Cochrane	NSAID and tonsillectomy 10 trials, n=837 children	PONV	Less nausea and vomiting when NSAID part of analgesic regime		1++
{Steward, 2003 #5}	Meta-analysis Cochrane	Single intraop dose dexamethasone and post-tonsil morbidity; Paed	PONV	Single intraop dose (0.15-1mg/kg; max dose 8-25mg) 2 times less likely to vomit; NNT 4 More likely soft/solid diet on day 1 (RR 1.69; 1.02-2.79)	Missing data and variant measurement tools – unable to assess effect on pain	1++
{Moiniche, 2003 #6}	Quantitative systematic review	NSAID vs placebo and vs opioid Adult and paed	Analgesia	NSAID vs placebo: 10/11 studies improved pain relief NSAID vs opioid: 8 studies: NSAID > opioid in 2; equianalgesic in 5; NSAID < opioid in 1 NSAID vs paracetamol: 3 studies : all no diff NSAID vs paracetamol & codeine: 3 studies: 1 each <,>,=	Opioids: morph 0.1-0.2mg/kg; papaveretum 0.2-0.3mg/kg; pethidine 1mg/kg; tilidine 2.5mg/kg; orqal tramadol 1mg/kg)	1++

{Hollis, 2000 #18}	Meta-analysis Cochrane 6 trails	LA either injected before or after removal (5); spray after removal (1)	Pain score Supplemental analgesia	No significant difference	Small no. of trials and small sample sizes	1+
{Hamunen, 2005 #19}	Systematic review 36 studies 16/36 sensitive	Pain after tonsillectomy: paracetamol, NSAIDs, opioids. Age 1-16yrs	Analgesia	See summary and table below	Heterogeneity of data precluded meta-analysis	1++

Summary Table from {Hamunen, 2005 #19}

AUTHOR	STUDY ANALGESIC	ROUTINE ADDITIONAL ANALGESIC	MAIN RESULT
{Bone, 1988 #161}	Diclofenac 2mg/kg PR vs. papaveretum 0.2mg/kg IM vs placebo	No	Decrease rescue analgesia with diclofenac
{Ozkose, 2000 #162}	Tramadol 0.5mg/kg vs. tramadol 1mg/kg vs placebo	No	No difference in rescue analgesia or pain intensity
{Sutters, 1995 #163}	Ketorolac 1mg/kg IM vs. placebo	No	Ketorolac reduced rescue analgesia and pain intensity
{Watters, 1988 #164}	Pethidine 1mg/kg IM vs diclofenac 1mg/kg IM vs control	No	Pethidine and diclofenac equal need for and time to rescue, and pain intensity
{Anderson, 1996 #148}	Paracetamol 40mg/kg oral preop vs 40mg/kg PR at induction	No	Oral: less rescue morphine in PACU and lower pain scores
{Habre, 1997 #166}	Nalbuphine 0.1mg/kg IV vs. pethidine 1mg/kg IV	Paracetamol 15mg/kg po preop	Nalbuphine: higher pain scores and more rescue in PACU
{Mather, 1995 #167}	Paracetamol 20mg/kg po preop vs morphine 0.1mg/kg IV vs. paracetamol 20mg/kg preop + ketorolac 0.5mg/kg IM during	No	Paracetamol alone: more morphine compared to other groups
{Mendham, 1996 #168}	Diclofenac 1mg/kg PR vs. diclofenac 1mg/kg PR + fentanyl 0.75mcg/kg IV vs. tenoxicam 0.4mg/kg IV vs. tenoxicam 0.4mg/kg + fentanyl 0.75mcg/kg IV	Paracetamol 15mg/kg qid + diclofenac 1mg/kg tds	Tenoxicam alone: higher pain score in PACU and more rescue cf. diclofenac alone
{Moore, 1988 #169}	Fentanyl 1mcg/kg vs. nil	Pethidine 1mg/kg IM preop	Fentanyl: pain score lower at 10 and 20 mins; less rescue analgesia
{Oztekin, 2002 #50}	Diclofenac 1mg/kg PR vs nil	Remifentnil infusion, morphine 50mcg/kg at end + PCA postop (bolus+4mcg/kg background)	Diclofenac: lower pain score first hour, lower total morphine consumption
{Pendeville, 2000 #72}	Tramadol 3mg/kg IV +2.5mg/kg po at 6hrs postop then tds vs. Propacetamol 30mg/kg IV + 15mg/kg 6hrs postop then tds	Sufentanil 0.25mcg/kg IV	Tramadol: lower pain scores (PACU, ward & home); less rescue
{Pickering, 2002 #56}	Ibuprofen 5mg/kg po vs. rofecoxib 0.625mg/kg po vs. placebo (1/24 preop)	Paracetamol 20mg/kg po 1/24 preop + fentanyl 2mcg/kg IV	Ibuprofen: less early rescue. No diff in time to first rescue, pain score at 4/24, total analgesic

			consumption
{Romsing, 1998 #172}	Ketorolac 1mg/kg at induction vs. after surgery vs. placebo	Fentanyl 3mcg/kg IV, paracetamol 20mg/kg	Preop ketorolac less rescue in PACU vs postop ketorolac. No difference in rescue during first 5/24 in ketorolac grps. No difference in paracetamol during 24/24
{Sutherland, 1998 #173}	Tenoxicam 0.2mg/kg IM vs morphine 0.2mg/kg IM	No	Tenoxicam: increase rescue morphine
{Williams, 2002 #51}	Codeine 1.5mg/kg IM vs morphine 0.15mg/kg IM	Diclofenac 1mg/kg PR	Codeine: more rescue during first 2 and 4 hrs; no difference in pain scores

INTERVENTION: tonsillectomy + systemic analgesia (post meta-analysis)

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	SIGN GRADE / COMMENTS
{Antila, 2006 #145}	DB RCT (comp. generated) N=45 Age: 9-15yrs	T:tramadol 1mg/kg bolus +6hr infusion Ket: ketoprofen 2mg/kg bolus + infusion S: saline ALL: fent 3mcg/kg	VAS during swallowing (0-100) at 30,60,90mins & 2,6,24hrs PCA fentanyl	Ket: lower pain scores first 6hrs; decr PCA reqt 0-6hrs only; minor diff 24hr PCA No diff between T and S	Ket: higher bld loss intraop (vs placebo, no diff cf. T) No diff PONV	1- statistical rather than clinically significant diff
{Hullett, 2006 #158}	DB RCT (?method) N=66 (28/32) Age: 1-8yrs	M: 0.1mg/kg morphine T: 2mg/kg tramadol ALL: oral paracetamol 30mg/kg; ondans; dexameth	PMH (local) pain score 0-10 Rescue	No diff pain scores or suppt analgesic reqt	Only one pt PONV Minor decr in episodes of desat at 1-2hrs postop but not other times	OSA patients
{Alhashemi, 2006 #26}	DB RCT (computer rand.) Age: 3-16 yrs N=80	IV paracetamol 15mg/kg + IM saline OR IM pethidine 1mg/kg + IV saline ALL: fentanyl 1mcg/kg	Obj Pain Score (0-10) every 5 mins in PACU until discharge (40 mins) Rescue: morphine 50mcg/kg (OPS>5)	OPS not sign diff (ns) : one point lwr in pethidine grp (~2/10 vs 3/10) Rescue (ns) : 7/40 paracetamol; 0/40 pethidine	PONV (in PACU only): 3/40 both grps Ready for discharge: 15 vs 25 mins (paracet vs peth)	1- Inadequate power for difference in pain score Very short follow up (40 mins)
{Ozalevli, 2005 #28}	DB RCT (consecutive "rand.") Age: 6-12yrs N=60	Postop PCA bolus M: 20mcg/kg morphine bolus (0.1mg/kg loading) T: 0.2mg/kg bolus (1mg/kg loading)	CHEOPS (0-10) 5,15,30mins and 1,2,4,6,24hrs	Pain scores : ns fist 60 mins; M:lower at 1,2 and 4hrs. PCA median dose M: 11.8mg(9.7-14); T:80mg(57-127)	Nausea score higher with M at 4,6,24hrs; nausea: T 3/30; M 11/30	1- inappropriate randomisation method
{Keidan, 2004 #41}	DB RCT age 1.7-10yrs n= 60 day case	K: ketorolac 1mg/kg F: fentanyl 2mcg/kg ALL: paracet 30mg/kg PR; dexamethasone 1mg/kg (max 25mg); ibuprofen 10mg/kg postop	PONV : score 1=none to 4=multiple Objective Pain Scale every 30 mins until discharge Agitation postop; sleep pattern at home Parent at home: pain none, moderate, severe	No diff in pain score K: increased agitation in recovery No diff in vomiting High incidence behavioural change and sleep disturbance at home	No bleeding any grp	1- very high dose ketorolac; small numbers no difference

{Sheeran, 2004 #38}	DB RCT Age >3 yrs (mean 7 yrs) N=45 (23/22)	R: rofecoxib 1mg/kg oral (max 25mg) P: placebo ALL: morphine 50mcg/kg; paracet 30mg/kg PR; dexameth 0.5mg/kg; ondansetron 0.1mg/kg	CHEOPS on arrival, before rescue (morph 25mcg/kg), and every 30mins in PACU; Wong-Baker faces on discharge and at rest and with swallowing (parent every 4hrs for 24hrs)	No difference : pain scores, PONV, PACU time or morphine	Parent – too few returned data – R: trend to lower pain score	1- Max CHEOPS or Faces score used to calculate diff b/w grps Small groups
{MJ, 2006 #146}	DB RCT (?method) N=90 Age: 5-7yrs	Saline (I) Ketamine 0.5mg/kg preop (II) or end of procedure (III) All: PR diclofenac 1mg/kg; dexameth, ondansetron	Oucher (0-100) every 20mins in PACU, 2hrly on ward Score >30 morphine 1mcg/kg(?) All regular paracetamol 20mg/kg	Decr pain scores with ketamine (no diff pre vs post) 1-8hrs; decr suppt analgesia	No diff in side-effects; only one pt PONV	1- Sleep apnoea pts Very low dose morphine
{Umuroglu, 2004 #39}	DB RCT (envelope method rand.) N=60 (15 per grp) Age: 5-12yrs	K: IV ketamine 0.5mg/kg M: IV morphine 0.1mg/kg T: IV tramadol1.5mg/kg S: IV N saline	Numeric Rating Pain Scale (NRS: 0-5, no-severe pain) & CHEOPS at 1,5,10,15,20,30, 45mins & 1,2,4,6hrs Time to first analgesic Intraop resuce: alfentanil Postop rescue: peth 1mg/kg in PACU, paracetamol on ward	Pain scores lower in M grp only at some time points Rescue analgesia: M 6/15; K 11/15; T 9/15, S 15/15 Time to first analgesic: longer in M grp	PONV: M 20%, T 20%, K 40%, S 6.6%	1-- very small sample size, wide variability in time to first analgesic high rate PONV
{O'Flaherty, 2003 #45}	DB RCT age 3-12 yrs n=80 (20/20/20/20)	K: 0.15mg/kg; M: MgSO4 30mg/kg; K+M; P: placebo ALL: fentanyl 2mcg/kg; dexamethasone 0.2mg/kg	Objective Pain Scale (0-10) on arrival in PACU, 30, 60 and 120mins; fentanyl if OPS>4	OPS : no diff – tended to be low in all groups Trend to higher score and incr PACU analgesic use in placebo grp but not significant	No diff in vomiting; no bleeding any group. Dreaming in 3 receiving ketamine, 2 in no ketamine grps	1- small sample groups
{Elhakim, 2003 #46}	DB RCT (envelope method) N=50 Age: 5-12yrs	K: ketamine 0.1mg/kg IM OR placebo 20mins before All: preop PR diclofenac 2mg/kg; intraop fentanyl 1mcg/kg	Visual analogue (animals increasing size) 0-10 in PACU & 6,12,24 hrs CHEOPS at 30mins, 1,2,3hrs Nurse observer VAS at rest & drinking (6hrs) Time to first analgesia Rescue: morphine to 0.2mg/kg in PACU; rectal paracetamol 30mg/kg PRN	CHEOPS: K lwr Rest (1.5vs2.5) & swallowing (3.5vs5) pain score at 6hrs: K Time to first analgesia: K 130 vs 84 mins Rescue in PACU: K 3/25 vs 9/25 Total paracetamol: lwr in K Oral intake: improved in K	PONV: ns diff No reported psychomimetic effects	1- non-validated pain tool; not clear which pain scores reported in results table; improvement in swallowing and oral intake
{Ozer, 2003 #42}	Observer blinded, randomised (?method)	T: tramadol 1mg/kg OR P: pethidine 1mg/kg	Bieri Faces Pain Scale (0-6) at 0, 10, 20, 45 mins in PACU Postop agitation: 1-3 (calm-	Pain scores higher in T grp at 0,10,20mins (approx 2.5 vs 4/6) Agitation: T>P but not significant	PONV: T 2/25; P 3/25	1- small sample size short follow up

	N=50 Age: 4-7yrs		hysterical)			
{Ewah, 2006 #27}	case cohort day stay tonsillectomy n=100 age: 2-14yrs	Protocol: PR diclofenac 1mg/kg; PR paracetamol 20mg/kg; IM codeine 1mg/kg; IV ondansetron 0.1mg/kg; dexamethasone 0.25mg/kg. Discharge meds: ibuprofen tds; paracet qds; codeine qds	Wong-Baker Faces (0-5) Rescue (score>2): oral ibuprofen 5mg/kg Q'airre telephone 3/7 after discharge (100% response rate)	Score 0-2: 88% before discharge Score 3-5: D1~18%; D2~20%; D3~16%	Vomiting: 0% before discharge; D1 7%; D2 3%	2+
{White, 2005 #31}	Cohort following guidelines n=37 Retrospective grp of previous practice n=34	Protocol: oral paracetamol 20mg/kg preop; fentanyl 1-2mcg/kg IV; diclofenac 1-2mg/kg PR Discharge meds: paracetamol 15mg/kg 4/24; ibuprofen & codeine PRN	Oucher (0-100) and nausea score (0-4) 4 hrly until discharge	After guidelines: Intraop morphine 0 vs 3/34; early analgesia 16% vs 41% Additional ibuprofen 70% at 7.5hrs, 59% at 14hrs	After guidelines: vomiting 5%	2- small sample sizes paracetamol alone insufficient analgesia postop

INTERVENTION: tonsillectomy + LA

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SEC OUTCOME	SIGN GRADE / COMMENTS
{Hollis, 2000 #18}	Meta-analysis Cochrane 6 trails	LA either injected before or after removal (5); spray after removal (1)	Pain score Supplemental analgesia	No significant difference	Small no. of trials and small sample sizes	1+
{Naja, 2005 #141}	DB RCT age 5-12 yrs n=90 (30/30/30)	GA: no injection; S: GA+ saline injection; LA: GA+ 1.5mls (1ml 2%lig, 0.5mls 0.5% bup, 3.7mcg fent, 6.7mcg clonidine ALL: fentanyl 3-4mcg/kg	VAS 0-10 at 0,6,12 hrs and daily for 10 days Pain at rest, with jaw opening, with eating Oral intake first 10 hrs; Time to solids; cumulated analgesia	VAS lower in LA grp for first 4 days; LA<GA at day 10 (0.48 vs 0.10) LA: incr oral intake; incr proportion leave hosp within 24hrs (93 vs 60 vs 41%) Decrease postop analgesic reqt	Ear pain: LA 20%, S 46%, GA 52% Parent – incr proportion satisfied (90 vs 37 vs 14%)	1+ Minor statistical changes in VAS after day 4 Saline injection alone increased surgical satisfaction and improved outcomes!
{Park, 2004 #10}	DB RCT (computer generated) N=130 Age: 2-12yrs	Postop injection in tonsillar fossa 3mls S: saline OR R: ropivacaine 0.5% with adrenaline All: PR paracetamol 30mg/kg; fentanyl 1mcg/kg; dexamethasone 1mg/kg (max 25mg)	Obj Pain Score in PACU for 180 mins Time to oral intake Analgesic use (rescue: fentanyl IV, later oral paracetamol and codeine Follow up q'airre (day 1,3,7,14)	Pain scores: no sign diff first 120 mins No sign diff: time to oral intake; rescue analgesia; time to normal activity postop	R: worse behaviour score (minimal diff); incr PONV (41% vs 19%; ns); incr neck pain (day 1-14)	1+ authors' question if adequate sample size or benefit masked by fentanyl
{Hung, 2002 #57}	DB RCT age 3-16 yrs n=99 (50/49) day case	S: saline B: bupivacaine soaked swabs in fossa after tonsil removed – no dose given ALL: diclofenac 1.5mg/kg	VAS Faces (1-6) at 1, 3, 6hrs; time to drink; time to eat; postop analgesia (paracet/codeine at home)	Decrease mean pain scores at 1,3,6hrs (eg.1.88±0.77 vs 3.12±1.88); decrease time to drink (104 vs 159mins); decrease time to solids (167 vs 194mins)	No diff in postop analgesic reqt Control: 2/49 admit for inadequate oral; 1/49 secondary haemorrhage	1+ statistical differences but relatively small ?clinical significance; groups too small for diff in side-effects
{Giannoni, 2001 #12}	DB RCT age 3-15yrs n=64 (21/21/22)	S:saline; R: ropivacaine 1% 0.15ml/kg; R+C: rop + clonidine 1mcg/kg peritonsillar injection pre-incision ALL: ibuprofen 15mg/kg + 1mcg/kg fentanyl	VAS (0-10) at rest and drinking at day 0, 1, 2, 3, 5, 10 Activity level (score 0-3) by parent Cumulative analgesia at day 3 and 5 (parac+codeine)	Additional analgesia in recovery: S 21/21, R 15/21, R+C 16/22 S: higher VAS in recovery – no diff at 24, 48 hrs – higher at day 3 and 5 VAS: no diff between R and R+C Cumulative analgesia: no diff at day 3, slight decr in R+C at day 5 (8 vs 11doses)	Ear pain: S 89%, R 63%, R+C 61% Earlier return to full activity: R+C 8.1 vs S 5.8 days No bleeding any grp	1- Mild improvement in recovery and at after day 3 VAS – same scale 0-10 for all ages VAS – lower for drinking than rest scores ?sensitivity
{Kaygusuz,	?blinded	B: 0.25% bupiv with adr 3-	VAS 0-5	VAS: All grps (~2.5) < P (4.3): ns	PONV: no difference	2-

2003 #142}	randomised (?method) n=80 Age: 6-14yrs	5mls pre-tonsillectomy D: 1mg/kg dex in tonsil L: 10% lignocaine spray qds P: saline spray qds	4hrly for 1st day, then day 1,3,7	diff b/w grps Day 3: L < P; ns diff b/w other grps	(8-10/20 each grp)	
{Somdas, 2004 #35}	Cohort N=30 Age: 5-15yrs	Bupivacaine 0.5% tonsillar fossa on right and saline on left All: metamizole in PACU, paracetamol later	No pain, more on left, more on right, equal pain both sides: 1,4,8,16,24hrs	Pain didn't change on left, decreased at 8,16 and 24hrs on bupi side		2- ?effect of LA injection only apparent after several hrs
{Akoglu, 2006 #156}	DB ?method of rand N=46 (16/15/15) Age: 2-12yrs	Peritonsillar fossa inj pre removal 3-5mls B: bupiv 0.25% R: ropiv 0.2% S: saline All: preop oral paracetamol 20mg/kg; fent 1mcg/kg	mCHEOPS (0-10) 15mins & 1,4,12,16,24hrs; score>5 fent 0.5mcg/kg or paracetamol 10mg/kg	LA groups: decr pain score from 1-24hrs; decr suppt analgesia; incr time to first rescue	No diff in nausea or otalgia	1-

INTERVENTION: strabismus or squint : LA / topical

AUTHOR	DESIGN (?RCT/?DB)	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY	SIGN GRADE / COMMENTS
{Steib, 2005 #109}	DB RCT Age: 2.5-6yrs N=40, 38 complete ?method of randomisation Surgery 35mins	Subtenon bupivacaine 0.5% vs saline before surgery by surgeon (2mls 2.5-4yrs; 3mls 4-6yrs) All: alfentanil 30mcg/kg + bolus 10mcg/kg if MAP increase 20% All: paracetamol 30mg/kg IV	CHEOPS pain scale (4-13) in recovery and every 30mins until discharge Rescue reqt: niflumic acid 20mg/kg PR score >6; nalbuphine 0.2mg/kg if high score persists	Intraop alfentanil*: 32.3±7.1 vs 43.8±11.5 Postop analgesic reqt for CHEOPS >6: NSAID* 12 vs 19 pts; nalbuphine* 0 vs 15 pts Decreased time in recovery*: 95±30 vs 145±47mins	Reduced OCR*: 4/35 vs 17/30 Reduced PONV*: nausea 0 vs 11; vomiting 1 vs 7 No block complications	1+ ? statistics incomplete pt numbers for pain scores – significant difference (9 vs 6) only at first and 30 minute time point (c/w titration of analgesia)
{Deb, 2001 #110}	Not blinded, ?method of randomisation Age: 5-14yrs N=50 (strabismus 15/25 and 17/25) Surgery 65 mins	Peribulbar block by anaesthetist (0.3mg/kg 2%lig 0.5%bup mix) vs pethidine (1mg/kg) All: pethidine 0.5mg/kg if HR or BP >20% increase	Modified CHEOPS (0-9) at 30mins, 2 & 6hrs Pain score : colour scale (no, mild, moderate, severe) + VAS 0-10 at 2, 6, 24hrs Analgesic reqt: request or VAS>5 ibuprofen 10mg/kg in first 24 hrs	Intraop analgesia*: 0/25 vs 6/25 Increased proportion pain free at 30mins, 2, 6 and 24hrs Postop analgesic reqt: 6/25 vs 19/25 Parent satisfied*: 18/25 vs 5/25	Reduced OCR*: 1/25 vs 15/25 Reduced PONV*: 5/25 vs 19/25; severe (>3 vomits) 2/25 vs 10/25 No block complications	2+ Statistically but not clinically significant differences in intraop BP and HR Not blinded and inadequate control grp CHEOPS modified by grp – not validated
{Sheard, 2004 #111}	Parents blinded Computer randomisation Age: 15yrs or younger (6±3yrs) N=111 (54/57) Surgery majority bilat	Subtenon lignocaine 1ml 2% lignocaine by surgeon at end All: codeine 1mg/kg PR, diclofenac 1mg/kg or paracetamol 20mg/kg PR if asthmatic; ondansetron 0.1mg/kg; amethocaine 1 drop 1% at end	Parental assessment of pain 30mins, 1,2,4hrs: Objective Pain scale (4-12) Suppt analgesia: oral ibuprofen or paracetamol; IM codeine if severe (not req)	Pain score: *at 30 mins 6 vs 4; *total score over 4hrs 18.5 vs 22 Suppt analgesia: ns 27/54 vs 23/57 (by nurses, not linked to pain score)	No block complications	1- no injection in control grp; parental assessment only; summed pain scores (not valid, all due to difference at 1st measure); incomplete data
{Chhabra, 2005 #112}	RCT (envelope) Postop assessor blinded	Peribulbar block (mix lig+bup by surgeon) vs fentanyl 2mcg/kg vs pethidine 1mg/kg	All India Pain Score at 2,6,24hrs Rescue: iv pethidine	Time to first analgesic*: 7.1±1.8 vs 4.7±2 vs 1.8 vs 2.6 Number requiring suppt: ns	PONV (block vs peth*) : 1 vs 4 vs 9 (if present	1- ? pain score method and not clear who

	Age: 3-15 yrs N=105 Surgery 40 mins	All: IM ketorolac 1mg/kg	0.5mg/kg or oral paracetamol 10mg/kg (which drug used not reported)		metoclopramide 0.15mg/kg) OCR: decreased by block (1 vs 8 vs 7)	assessed primary aim was PONV not pain

AUTHOR	DESIGN (?RCT/?DB)	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY	SIGN GRADE / COMMENTS
{Morton, 1997 #113}	Randomised (?method); ?blinded Age: 3-8yrs N=40 (18/17 analysed) Surgery 35 mins	2 drops oxybuprocaine 0.2% (shorter duration than amethocaine) vs diclofenac 0.1% after induction	Observer pain score (0-3) at wakening, 1,2,4,24 hrs Rescue: further eye drops; paracetamol 15mg/kg if pain persisted	Pain scores: 1 hr* 28% vs 71% no pain; other times similar Suppt analgesia: no differences (0-3 doses in 24 hrs)	PONV: ns differences OCR: no episodes in either group	1- ?adequate sensitivity; no opioids & low rate PONV Day case: duration approx 30 mins
{Kim, 2003 #114}	DB RCT Age: 2-7yrs N=51 (19/14/18) Anaesthesia time 60 mins	Amethocaine 0.5% vs ketorolac 0.5% vs saline: 2 drops at beginning and end of surgery All: dexamethasone 0.15mg/kg + perphenazine 35mcg/kg	CHEOPS every 5 mins in recovery Rescue: paracetamol 20mg/kg if pain score >6; codeine 1mg/kg second line (not req)	Pain scores: ns differences (mean 5 all groups) Analgesic requirement: ns (one dose paracetamol in 43%) Time to analgesic: ns (34 vs 57 minutes)	PONV: ns – rate low 2%' only recorded for first few hrs in hospital	1- ?adequate sensitivity authors question if CHEOPS adequate for ocular pain inadequately powered for time to first analgesic
{Bridge, 2000 #115}	DB RCT (?method of randomisation) Age: 4-12yrs N=30 (17/13) Surgery 25 mins	Ketorolac 0.5% vs saline: 6 drops at beginning and end All: paracetamol 20mg/kg preop	CHEOPS every 5 mins in recovery then Faces scale (Bieri 0-6) Rescue: morphine 20mcg/kg IV in recovery; codeine 0.5mg/kg oral later	Pain scores: ns Time to first analgesic: ns Rescue: ns; morphine 7/17 vs 6/13, codeine 11/17 vs 7/13, paracetamol at home 13/17 vs 9/13	PONV: rate low; 3/17 vs 4/13 (some 24 hr data incomplete)	1- ?adequate sensitivity authors question sensitivity/specificity of CHEOPS
{Snir, 2000 #116}	Randomised (odd/even) Single blind Age: 8 ± 6 yrs N=40 Surgery: majority bilat (no time)	Diclofenac 0.1% vs dexamethasone 0.1% immediately postop and regularly for 4 wks	Discomfort: 0-3 (none-severe) at 1 day, 1,2 and 4 wks	Discomfort: lower score with diclofenac at 2wks (0.2±0.3 vs 0.6±0.5)	Conjunctival chemosis and IOP better with diclofenac	1- statistical but not clinical significant difference in discomfort score : predominantly surgical outcome study
{Eltzschig, 2002 #117}	RCT (lottery randomisation) postop blinding only Age: 2-12yrs N=81	Remifentanil 1mcg/kg+ 0.1-0.2mcg/kg/min vs fentanyl 2mcg/kg+ 1mcg/kg every 45mins intraop All: PR paracetamol 10mg/kg	Objective Pain Score (0-10) at 15, 30, 45 and 60 mins postop Postop: score>3 PR paracetamol 10mg/kg, >5 oxybuprocaine drops	Higher pain scores for 30 mins with remi* (4.7 vs 2)	PONV: increased likelihood of early vomiting with fentanyl	1+ PONV primary aim

	Surgery 75 mins					

AUTHOR	DESIGN (?RCT/?DB)	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY	SIGN GRADE / COMMENTS
{Wennstrom, 2002 #118}	Open Randomised (?method) Age: 4-16 yrs N=50 Surgery 40 mins	PR diclofenac 1mg/kg at induction vs IV morphine 0.05mg/kg at end of surgery All: oral paracetamol 15mg/kg preop; fentanyl 2mcg/kg at induction	Wong Baker Faces (0-5) every 3rd hr Rescue: morphine 0.05mg/kg IV (score >2) + 6/24 paracetamol 15mg/kg	Pain scores: ns Suppt morphine: 5 vs 10pts	PONV*: 3/25 vs 18/25 Earlier discharge from PACU*: 240 vs 336 mins	2+
{Shende, 1999 #119}	Blinded observer postop Randomised (assignment list) Age: 2.5-15yrs N=52 Surgery 50mins	ketorolac 0.9mg/kg IV vs pethidine 0.5mg/kg	Objective Pain Score on arrival, 30 and 60 mins in PACU Rescue: paracetamol 20mg/kg oral	Pain scores: ns (all low, median 2) Suppt paracetamol: ns 10/26 vs 11/26	PONV*: 6/26 vs 19/26	1- pain scores low and only early assesst.
{Mendel, 1995 #120}	Randomised (?method) Nurse assessor blinded Age: 1-10yrs N=54 Surgery 30 mins	ketorolac 0.9mg/kg IV vs fentanyl 1mcg/kg vs saline	Objective Pain Scale (0-10) 20,40,60 mins then hourly Rescue: score >2 paracetamol 10-20mg/kg PR; >5 IV fentanyl 0.5mcg/kg (not req)	Pain scores: ns Suppt paracetamol: ns (13/18 vs 12/18 vs 14/18)	PONV*: 3/18 vs 13/18 vs 6/18	1- "pain scores low all groups" median 2-2.5 **full placebo group
{Kokki, 1999 #121}	DB RCT (?randomisation method) Age 1-12yrs N=59 Surgery 30 mins	ketoprofen 1mg/kg + 1mg/kg over 2hrs vs saline All: fentanyl 1mcg/kg	Maunuksela Pain score (0-10) 15 min intervals, VAS in older children Rescue: fentanyl 1mcg/kg score >3	Pain score*: lower only at 30min time point (correlation between observer and VAS reported scores) Suppt fentanyl: no. pts (21/30 vs 26/29) ns; no doses* (44 vs 62) Time to first analgesic: ns	PONV*: 5/30 vs 12/29 Incr PONV associated with postop fentanyl, not with no. muscles or technique (recession vs resection)	1+
{Mikawa, 1997 #122}	DB RCT (envelope method) Age: 2-11yrs N=90 Surgery 80mins	flurbiprofen 1mg/kg IV vs 0.5mg/kg vs saline	Objective Pain Scale on wakening then 30, 60, 90, 120mins, 3,4,5,6,8hrs Rescue: diclofenac PR 12.5 or 25mg if OPS>5	Highest OPS*: median lower with 1mg/kg, 4.5 vs 7.5 vs 7 Suppt diclofenac*: 15/30 vs 29/30 vs 28/30	PONV: ns 7/30 vs 9/30 vs 9/30	1+ Half-life 5.8hrs in adults Only max pain scores reported (?effect of time)

						**full placebo grp

INTERVENTION: vitreoretinal surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ 2^{o} OUTCOME & CONCLUSION	SIGN GRADE / COMMENTS
{Subramaniam, 2003 #138}	Case control; randomised (?method of rand) N=85 Age: 6-13yrs	Peribulbar block IV pethidine 1mg/kg	4 point VAS (0,1,2,3) at 2,4, 24 hrs CHEOPS in PACU Rescue: peth 0.5mg/kg	LA grp: lower pain score in PACU; higher proportion pain free at all time points; decreased supplemental analgesia	Decreased incidence oculocardiac reflex and decr PONV with LA	2+ "pre-emptive" in title but not adequate design
{Subramaniam, 2003 #139}	DB RCT (random number table) N=86 Age: 7-16yrs	Ketoprofen 2mg/kg Pethidine 1mg/kg	4 point VAS (0,1,2,3) at 2,4, 24 hrs Rescue: score 2: oral ibuprofen; score 3:peth 0.5mg/kg	No significant diffpain scores; no difference in rescue	PONV decr with NSAID	1-
{Deb, 2001 #110} **also in strabismus	Case control; randomised ?method N=50 Age: 5-14 Strabismus (32); vitreoretinal (18)	Peribulbar block Pethidine 1mg/kg	Coloured 10 point VAS at 2,4, 24 hrs CHEOPS at 30 mins in PACU Rescue: oral ibuprofen (VAS>5)	Intraop analgesia*: 0/25 vs 6/25 Increased proportion pain free at 30mins, 2, 6 and 24hrs Postop analgesic reqt: 6/25 vs 19/25 Parent satisfied*: 18/25 vs 5/25	Reduced OCR*: 1/25 vs 15/25 Reduced PONV*: 5/25 vs 19/25; severe (>3 vomits) 2/25 vs 10/25 No block complications	2+ Statistically but not clinically significant differences in intraop BP and HR Not blinded and inadequate control grp CHEOPS modified by grp – not validated

INTERVENTION: tympanomastoid surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ 2° OUTCOME & CONCLUSION	SIGN GRADE / COMMENTS
{Suresh, 2002 #123}	DB RCT (computer generated) N=40 Age: 2-18yrs cochlear implant (25), mastoidectomy (15)	Grt auricular nerve block 2ml 0.25%bupivacaine + saline IV Morphine 0.1mg/kg IV + saline block No other analgesia	Obj Pain Scale every 5 mins for 60mins in PACU, then every 30 mins for 6 hrs Rescue (OPS>6) morphine 50mcg/kg	No significant diff : trend higher pain score and increase rescue with LA Pain at home: no diff in number of analgesic doses (77% return q'aire)	PONV : treat ondansetron : increased in opioid grp	1- Power analysis based on PONV not analgesia; low numbers & high variability in pain scores (?sensitivity)
{Suresh, 2004 #124}	DB RCT N=40 Age: 2-18yrs cochlear implant (23), mastoidectomy (17)	BB: grt auric nerve block bupi 0.25% before incision and 1/24 before end of case SB: saline before incision, bupi 1/24 before end of case No other analgesia	OPS every 5 mins for 60 mins in PACU then hrly for 6hrs Rescure (OPS>6): morphine 50mcg/kg	No significant diff: OPS, amount of rescue in PACU or during admission, time to first analgesia	PONV: no diff	1- Aim to investigate pre-emptive effect
{Hasan, 2004 #128}	Retrospective case series N=144 Age: 11±3.7yrs 45% middle ear, 55% mastoid	Anaesthesia and analgesia not standardised : intraop fentanyl	Pain: Wong-Baker (<8yrs); VAS (>8yrs)	Mastoid: increased likelihood to need morphine in PACU and require admission. Higher risk of PONV and require admission: cholesteatoma, pain score >5, morphine reqt in PACU	36% discharged same day; 92% discharged within 23hrs	2-

INTERVENTION: dental procedures

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ 2^0 OUTCOME & CONCLUSION	SIGN GRADE / COMMENTS
{Purday, 1996 #102}	DB RCT (?method of rand.; observer only blind) N=120 (30 each grp) Age: 2-10yrs Day case dental restorations (~50% extractions)	Ketorolac 0.75, 1, 1.5mg/kg Morphine 0.1mg/kg	Objective Pain Score 15 & 30 mins after arrival in PACU Rescue: paracetamol 20mg/kg or codeine 1mg/kg if OPS>6	No diff in pain score at 15 or 30 mins No diff in rescue or paracetamol doses at home first 24hrs	Increased vomiting in morphine grp; no bleeding problems	1- Brief follow-up Scores low in all grps with wide range (?sufficient power)
{Littlejohn, 1996 #101}	DB RCT (?method of rand; observer only blind) N=60 (21/19/20) Age: mean 6yrs (minimum 2yrs) Day case extractions	IV nalbuphine 0.3mg/kg PR diclofenac 1-2mg/kg No analgesia	Objective Pain Scale (0-10) at 5,10,15,30,45 minutes after wakening Rescue paracetamol	No diff in pain scores, rescue or PONV		1- Very brief procedures : anaesth time <10mins Majority scores 0 (low sensitivity)
{Roelofse, 1999 #82}	DB RCT N=60 Age: 4-7yrs Extractions (mean 10)	Oral tramadol 1.5mg/kg Placebo 30 mins preop	Objective Pain Scale; Oucher faces scale Rescue paracetamol	Oucher: significantly lower at 60 and 120mins Rescue 19.4% vs 82.8%	Longer recovery with tramadol (48 vs 36mins; wide SD both grps)	1- (abstract only)
{Anand, 2005 #85}	Randomised: one side LA N=30 Age: 11.3±1.7yrs Extraction permanent molars	Intraligamental LA to one side of mouth	VAS; rate which side better	VAS not significantly different between LA and contralateral side; 63% pain better on LA side (85% boys, 47% girls)		2+ no control injection
{Andrzejowski, 2002 #97}	DB RCT (envelope; observer only blind) N=120 Age: 5-12yrs Extractions >5 teeth	Soaked swabs over exposed teeth sockets Bupivacaine 0.25% + adr Saline All: PR diclofenac ~1mg/kg	4 point pain scale (0=don't hurt to 3=hurt the most): include non-validated cartoon faces 15 and 30 mins following recovery	No diff in pain scores		1-

			Nurse observer score			
{Gazal, 2004 #87}	DB RCT (computer generated envelope) N=135 Age: 2-12yrs Extractions (mean 7)	Soaked swabs over exposed teeth sockets Bupivacaine 0.25% + adr Sterile water All: oral paracetamol 15mg/kg preop	5 point distress scale (0-4) [faces scale similar to wong-Baker] Preop, immediate postop and 15 mins	No diff in "distress" scores	Increased distress <6yrs compared with older children irrespective of treatment group	1- "decided to assess distress instead of pain because it can be difficult to measure pain in young children"
{Greengrass, 1998 #99}	DB RCT (envelope) N=24 Age: 7-15yrs Extractions	Pain after extractions (24 of 42) randomised to soaked swab on socket: Bupivacaine 0.25% + adr Saline	?method "asked whether had pain or not"	Reduction in pain at 10 minutes in 10/12 of bupivacaine grp		Abstract only available
{Atan, 2004 #90}	Cohort: morbidity after day stay GA dental treatment N=121 Age: 6-16 Restorations 30%; extractions 60%; surgical procedure 54%	All: PR analgesia diclofenac, codeine, paracetamol ± alfentanil (no details of dose) 92% : LA during procedure	Anxiety and pain (Objective Pain Score in PACU and verbal scales): preop, before discharge, 36, 72 and 148hrs postop	OPS: 50% no pain in PACU LA reduced pain (OR 0.39) At 36hrs: 28% moderate and 9% severe pain "Pain following dental GA was most prevalent and longlasting symptom of postoperative morbidity"	Increased pain associated with increased no. procedures.	2+

INTERVENTION: sub-umbilical surgery

h – inguinal hernia, o – orchidopexy, c – circumcision, hs – hypospadias, hc – hydrocoele, v – vur, p - phimosis

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Ivani et al., 2005)	RCTDB N=60 1-7yr h,o,c,hs	Caudal 1ml/kg 1. R0.2% 2. L0.2%	CHIPPS up to 24hrs Score>=4 paracet40mg/kg + codeine 1-2mg/kg	No difference pain scores Rescue analgesia Gp1(7) = Gp2 (6)	No difference motor block	1+
(Willschke et al., 2005)	RCT N=100 0-8yr h,o,hc	IL/IG NB L0.25% 1. Ultrasound 2. Traditional 0.3ml/kg	Intraop – haemodynamics OPS – duration of block Score>11 paracet 40mg/kg pr	Gp 1 - ↓ intraop fentanyl and more stable haemodynaics. Also ↓LA use – 0.19ml/kg Gp 1 - ↓ paracet use (6 vs 40%)	Gp1 ↓ time of surgery (ns)	1+
(Breschan et al., 2005)	RCT N=182 1-7yrs h,o	Caudal 1mg/kg 1. L0.2% 2. R0.2% 3. B0.2%	CHIPPS up to 24hrs Score>10 paracet 20-30mg/kg pr	No difference duration of analgesia, pain scores, analgesic use, No requiring no further analgesia (~1/3 in all gps)	No difference motor	1+
(Martindale et al., 2004)	RCTDB N=30 3mn-6yr h,o	Caudal B0.25% 1ml/kg 1. Plain 2. +S-Ket 0.5mg/kg (caud) 3. +S-Ket 0.5mg/kg IV Paracet 20mg/kg po premed + diclofenac 1mg/kg pr indn	mOPS up to 24hrs score>4 Rescue analgesia Time to 1st analgesia	Gp2 ↑ Time to 1st analgesia, ↓ analgesic use in 24hrs No difference pain scores	No difference sedation, PONV, mictn, motor	1+
(Leoni et al., 2004)	RCT n=82 0-8 YEARS MINOR ABDO AND UROLOGIC AL	28 – alfent 25mcg/kg iv. 24 - periph nerve blockade with ropivacaine 0.475% 1ml/kg. 30 – 12.5 mcg/kg alfent iv + periph nerve blockade with ropivacaine 0.475% 1ml/kg.	Intra op bp and pulse Post op FLACC obs tool + numerical scale done by nurses docs, parents and children	No difference intra or post op efficacy	No differences	1- no power calc. unequal groups suggests poor randomisation technique
(Ivani et al., 2003)	RCT N=60 1-7yr	Caudal 1ml/kg 1. L0.125% 2. L0.2%	Intraop haemodynamics CHIPPS upto 24hrs Score>=4 paracet 40mg/kg + codeine 1-	Time to 1st analgesia Gp2=Gp3>Gp1 No difference use rescue analgesia	No PONV Minimal motor block in all gps	1+

	h,o,hc,hs,p	3. L0.25%	2mg/kg			
(Weber and Wulf, 2003)	RCTDB N=30 1mn -9yrs h,o,c,hc	Caudal B0.125% 1ml/kg 1. Plain 2. +S-Ket 0.5mg/kg	Intraop – haemodynamics OPS upto 24hrs Score>3 Paracet 20mg/kg pr	No further analgesia Gp2>Gp1 (10 vs3)	No difference motor, Haemodynamics No psychomotor effects	1+
(Turan et al., 2003)	RCTDB N=44 1-6yr h,hs	Caudal R0.2% 0.5ml/kg 1. Plain 2. + Neo 2mcg/kg	Intraop – haemodynamics TPPPS up to 24hrs Score>3 paracet 20mg/kg pr Time to 1st analgesia	Gp2 - ↑ Time to 1st analgesia, ↓ pain scores at 6 & 12hrs, ↓ analgesic use, ↑pts requiring no analgesia (15 vs 4)	No difference PONV (low), sedation, motor	1+
(Suraserani vongse et al., 2003)	RCTB N=103 1-12yrs h,hc (2 exclusions analgesia for other reason)	Wound Infiltration vs IL/IG NB B0.5% 0.25ml/kg + Adr 5mcg/ml 1. Saline 20 – 60s pre closure 2. 20s pre closure 3. 60s pre closure 4. NB at induction	CHEOPS upto 24hrs Score>=7 fentanyl (hosp) paracet 10mg/kg (home)	Gp1 - ↑ pain scores, ↑ analgesic use, ↓ time to 1st analgesia No difference in other gps	PONV low in all gps 5pts in gp4 and 1pt in gp2 had temporary gait problems	1+
(Ivani et al., 2002b)	RCTB N=60 1-7yr h,o,c,hc	Caudal 1ml/kg 1. R0.2% 2. B0.25% 3. L0.25%	Intraop – haemodynamics OPS up to 24hrs Score>=5 paracet 10-15mg/kg + codeine 0.5-1mg/kg pr	5pts in each gp required rescue analgesia No difference time to 1st analgesia	↓ motor in 1st hr in gp1 No difference haemodynamics	1+
(Ivani et al., 2002a)	RCTB N=40 1-7yrs h,o	Caudal R0.2% 1ml/kg + Clon 2mcg/kg Vs IL/IG NB R0.2% 0.4ml/kg + Clon 2mcg/kg	Intraop – haemodynamics OPS upto 24hrs Score>=5 paracet/codeine pr	Rescue analgesia gp2>gp1 (70 vs 45%) Time to 1st analgesia Gp1 160min vs Gp2 265min (ns)	No difference sedation	1+
(Bosenberg et al., 2002)	RCTDB N=110 4-12yrs h,o,hc	Caudal 1ml/kg 1. R0.1% 2. R0.2% 3. R0.3%	Intraop – haemodynamics Faces + Observer 4pt scale up to 8hrs Score>3 or mod pain paracet 20-30mg/kg or tilidine 1mg/kg Time to 1st analgesia	No difference in time to 1st analgesia (3.3 vs 4.5 vs 4.2hrs) The higher the block the better the analgesia (ns) Pain scores and analgesic use ↑ Gp1 c.f. Gp3 In 1st 8hrs – 26pts in each gp needed paracet but dose↑ with ↓ Ropiv dose Tilidine use 18 vs 14 vs 11pts	Motor block: Gp3>Gp2>Gp1 No difference PONV (20-30%), mictn	1+
(Ivani et al., 2000)	RCTDB N=40 1-7yr h,o,c,hc	Caudal R0.2% 1ml/kg 1. Plain 2. +Clon 2mcg/kg	Intraop – haemodynamics OPS up to 24hrs Score>=5 paracet 10-15mg/kg + codeine 0.5-1mg/kg pr	Time to 1st analgesia ↑ Gp2 (225 vs 125 min) Analgesic use ↓ Gp2 (2 vs 9) 5pts Gp1 needed analgesia in 1st 3hrs (0 in Gp2)	No difference motor, sedation, haemodynamics No PONV	1+

(Kaabachi et al., 2005)	RCT N=98 1-12yr h,o	IL/IG NB B0.25% 0.3ml/kg 1. Plain 2. +Clon 1mcg/kg	CHEOPS 1-6yrs, VAS 6-12yrs upto 6hrs Score>6 or 50 paracet 15mg/kg iv Score 4-5 or 30-50 paracet 15mg/kg pr Parent questionnaire	No difference analgesic use, pain scores 3pts in each gp intraop fentanyl Over 6 days more pts in gp1 needed analgesia	No difference sedation scores	1-
(Passariello et al., 2004)	RCTDB N=44 1-5yrs h,o,hc	Caudal 1ml/kg 1. S-Ket 1mg/kg 2. S-Ket 1mg/kg + Clon 1mcg/kg	Introp – haemodynamics CHEOPS Score>=9 Paract 200mg/kg + codeine 5mg/kg	No difference – time to 1st analgesia (16 vs 20hrs), pain scores Rescue analgesia Gp1 > Gp2 (38 vs 18%)	No difference mictn, motor, haemodynamics No PONV,	1-
(Bano et al., 2004)	RCT N=60 1-8yrs ing + urogential	Caudal B0.25% 0.75ml/kg 1. Plain 2. +Midaz 50mcg/kg	Pain scoring(?) up to 24hrs Time to 1st analgesia Score>4 Diclofenac	↑ time to analgesia Gp2 (21.4 vs 9.9hrs)	↑ sedation in 1st hr in Gp2	1-
(Joshi et al., 2004)	RCTDB N=36 6mn-6yr h,o,hc	Caudal B0.125% 1ml/kg 1. Clon 2mcg/kg 2. Saline	Faces (hosp) – observational Mod/severe – fentanyl VAS (home) Rescue – paracet/codeine	No of patients needing fent > gp2 (9 vs 4) No difference time to 1st analgesia (3-4hrs) or analgesia at home	↑PONV gp2 (8 vs 2)	1-
(Khan et al., 2002)	RCTDB N=60 1-8yrs h,o Terminated at 30pts (10/gp) due to rate of PONV	Caudal B0.5% 2mg/kg 1ml/kg 1. Plain + IV saline 2. Plain + IV Buprenorphine 2.5mcg/kg 3. + buprenorphine 2.5mcg/kg + IV saline	Intraop – haemodynamics CHEOPS + VAS Score>4 or 30 – rescue analgesia Time to 1st analgesia	No further analgesics Gp3>Gp2>Gp1 (80 vs 50 vs 30%)	PONV Gp3>Gp2>Gp1 (80 vs 50 vs 20%)	1-
(Luz et al., 1999)	RCT N=36 6mn-6yr h,o,c	Caudal B0.18% 1.5ml/kg 1. + Clon 1mcg/kg 2. + Morphine 30mcg/kg	Intraop – haemodynamics OPS upto24hrs Score>3 paracet 100-200mg or nalbuphine 0.2mg/kg	No further analgesia Gp1 61% Vs Gp2 50% Remaining pts no difference in analgesic use (1-3doses) OPS No difference and low in both gps	No motor, mictn, haemodynamics problems PONV 5 vs 4pts	1-
(Bosenberg and Ratcliffe, 1998)	RCT N=88 2-10yrs h,o	1. IV Tramadol 1mg/kg 2. IV Tramadol 2mg/kg 3. IV Pethidine 1mg/kg 4. IV Saline	Intraop – haemodynamics 5pt verbal pain scale up to 6hrs Analgesic use	Pain scores Gp4>Gp3=Gp1>Gp2 Time to 1st analgesia: 218 vs 251 vs 223 vs 175min Pts needing rescue analgesia: 13 vs 9 vs 14 vs 15		1-

(Gulec et al., 1998)	RCT N=60 1-12yrs h,o,c,hs,hc	Caudal B0.125% 0.75ml/kg 1. Plain 2. + Midaz 50mcg/kg 3. + Morphine 50mcg/kg	Intraop – haemodynamics 5pt pain scale – Verbal >5yrs, observational < 5yrs Score>=3 paracet 50-100mg/kg/day	Time to 1st analgesia Gp2>Gp3>Gp1 (21 vs 14.5 vs 8.1hrs)	PONV: Gp1=Gp3>Gp2 (30,35 vs 15%) Sedation: Gp2=Gp3>Gp1 No difference mictn, motor	1-
(Anatol et al., 1997)	RCT N=183 5-12yr h,o,hc (15 exclusion lack of data or repeat procedure	B0.5% 0.4ml/kg 1. Infiltration 2. IL/IG NB 3. Combination	CHEOPS – up to discharge Score <=6 satisfactory, >=9 severe pain	No difference time to 1st analgesia, analgesic use (55-65%) Satisfactory pain – 78 vs 80 vs 81% Severe pain – 9.4 vs 8.4% vs5.9%	No difference PONV (~25%)	1-
(Ho et al., 1997)	RCT N=51 1-6yr h,o,c	Caudal B0.25% 0.6ml/kg + Adr 1:200,000 1. Pre surg 2. Post surg	Faces pain scale (observational) Analgesic use	No difference between the groups		1-
(Ivani et al., 1996)	RCT N=42 1-10yr h,o	Caudal Mepiv 1% 7mg/kg 1. + Saline1ml 2. + Clon 2mcg/kg	Broadman OPS	Time to 1st analgesia Gp2 >Gp1 (218 vs 143 min)	↑ sedation Gp2	1-
(Dalens et al., 2001)	Cohort study N=22 1-12yrs h,hc	IL/IG NB R0.5% 3mg/kg	OPS up to 6hrs Score>4 paract 30mg/kg or nalbuphine 0.2mg/kg	Pain < 4: 73% at 1hr, 86% at 2hr, 91% at 3-6hr Mod/severe pain in 3pts at 1-2hr 9/22 needed rescue analgesia	1pt PONV 1pt Fem NB	2- 5pts given alfentanil
(Lonnqvist et al., 2000)	Cohort study N=18 1-8yrs hs,o v	Caudal R0.2% 1ml/kg +paracet 100mg/kg/day	4pt pain scale upto 36hrs Time to 1st analgesia	90% pts good pain relief at all times Median time to 1st analgesia 12.6hrs	Vomiting 50% Pruritis 12% Motor block 0%	2-
(Ho and Keneally, 2000)	Case series N=90 1-13yrs h,o	Infiltration of IL/IG block – anaes dependent 2/3pts give paracet pr on indn	Pain scoring (?) in hosp Parent questionnaire at home Rescue paracet 15mg/kg or codeine 0.5 – 1mg/gk	More orchid patients required periop opioids and needed more paracetamol at home	PONV similar (20-30%)	3

INTERVENTION: Circumcision

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Allan *et al.* 2003)	Cochrane review 7 Studies 374pts 28dy – 16yr RCT	Caudal vs DNB (2) Caudal vs opioid (4) Caudal vs opioid + paracet (1)	Rescue Analgesia (3) VAS scores (6)	Caudal vs DNB – No difference Caudal vs opioid - ↓rescue analgesia in early postop	No diff PONV ↓PONV with caudal	1+ - small no of studies, no firm conclusions
(Weksler *et al.* 2005)	RCT N=100 3-8yrs	DNB B0.5% (+ aug) Vs Caudal B0.25% 1ml/kg	Intraop - haemodynamics Faces upto 2hrs Parent satisfaction + analgesia at home	No difference in any parameter	Caudal - ↑motor block and PONV	1+
(Choi *et al.* 2003)	RCTDB N=60 2-12yrs	EMLA 2-4g + Saline DNB Vs DNB B0.5% 0.2ml/kg + placebo cream	Intraop – haemodynamics Cheops upto 6hrs Rescue analgesia (25%↑ haemo or score >5) – fentanyl + paracetamol	No difference in rescue analgesia either intra or postop.	No adverse effects	1+
(Gauntlett 2003)	RCT N=60 1-10yrs	DNB B0.5% (+aug) Vs Caudal B0.15% 0.5ml/kg + Ketamine 0.5mg/kg	Parents OPS in hosp and at home Time to 1st analgesia (paracetamol)	No difference – time to 1st dose, no of doses and pain scores	↑ motor block and time to mict with caudal	1+
(Lee and Sanders 2000)	RCTDB N=32 18mn – 12yr	Caudal 1ml/kg R0.2% Vs R0.2% + ketamine 0.25mg/kg (+Fent 1mcg/kg at indn both gps)	Parent VAS Time to 1st dose (4 on VAS) No of analgesics (paracet)	R+K - ↑ time to 1st analgesia - ↓ no of paracet doses in 24hrs	No diff – sedation, motor block, micturition, PONV	1+
(McGowan *et al.* 1998)	RCT N=61 1-18yrs	1. DNB B0.5%0.3ml/kg 2. DNB + Diclofenac pr 2-2.5mg/kg 3. Diclofenac	CHEOPS upto 2hrs Questionnaire at home Rescue analgesia – morphine, paracet, lig gel	3 failed blocks Gp 3 ↑ pain score at 10min More paracetamol used (ns) Gp2 Less paracet over 2 days (ns) No difference – parental assessment	No difference bleeding /PONV	1+
(Matsota and Papageorgiou	RCT N=30	Subcutaneous RB L0.25% Vs	Intraop – haemodynamics 4pt pain scale for 24hrs	↑ Haemodynamic stability with RB ↑ post op analgesia with RB (ns)		1-

-Brousta 2004)	3-12yrs	Fent 2mcg/kg + paracet 30mg/kg	Time to 1st analgesia			
(Sharpe *et al.* 2001)	RCT N=74 1-9yrs	Caudal 0.5ml/kg 1. B0.25% 2. B0.25% + clonidine 1mcg/kg 3. B0.25% + clonidine 2mcg/kg	Intraop – haemodynamics Pain score (own) upto 4hrs, time to 1st analgesia, analgesic use	Trend toward ↑ time to 1st analgesia with↑ clonidine dose (ns) Low analgesic use and no difference	No difference sedation, micturiton, PONV (all low)	1-
(Holder *et al.* 1997)	RCT N=45 3-11yrs	RB B0.25% Vs DNB B0.5% 0.2ml/kg	OPS upto 1hr Rescue analgesia – morphine/paracetamol /diclofenac	RB – 3 oedamatous - ↑ pain scores - ↑ morphine/paracet use		1- random allocation of rescue analgesia
(Serour *et al.* 1996)	RCT N=250 6-17yrs	GA +DNB L2% + B0.5% 1ml/kg Vs DNB L2% + B0.5% 1ml/kg	Verbal Pain Score (own) Rescue analgesia	4pts in DNB needed GA GA group ↑ pain scores	GA - ↑ PONV and recovery time	1-
(Irwin and Cheng 1996)	RCT N=50 2-12yrs	Caudal Vs RB	Time to 1st analgesia	Caudal - ↑time to 1st analgesia 8% RB failure	Caudal - ↑ time to micturition No difference motor block	1-
(Taylor *et al.* 2003)	Open label N=22 5-24mn	Caudal L0.25% 0.8ml/kg	Intraop – haemodynamics Time to 1st analgesia – paracet 30mg/kg po/pr	All pts good intraop analgesia Time to 1st analgesia 7.9hrs	No adverse events	2+
(Soh *et al.* 2003)	Case series N=3009 1mn – 16yrs	DNB			9 complications Rate of 0.18% (excluding 2 drug errors)	3

INTERVENTION: Circumcision (neonates)

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Brady-Fryer *et al.* 2004)	Cochrane Review 35 Studies 1997 Newborns – term and preterm All RCT`s	DNB and/or RB (19 studies) EMLA/Lignocaine cream (12) Sucrose (9) Paracetamol (2) Environment manipulation (3) Either intervention vs placebo or intervention vs intervention All Awake	Haemodynamics Cry Pain scoring: NIPS, NFACS, PIPP + others Biochemistry	No study completely eliminated pain DNB, RB, EMLA, Lig > placebo DNB > RB > EMLA/Lig Sucrose, paracetamol, environment = placebo DNB – lower cortisol RB – oedema EMLA – results dependent on time of and success of aplication	No increased incidence of other side-effects with any procedure Using Mogen clamp ↓ duration of surgery	1++
(Lehr *et al.* 2005)	RCT N=54 Term, <1week	Lig 4% vs EMLA vs DNB All Awake	Haemodynaics baseline, drug application, procedure, recovery	HR – no difference RR – EMLA > Lig = DNB	2 EMLA, 1 Lig – local reaction	1-
(Taeusch *et al.* 2002)	RCT N=59 Term, neonate	DNB with lignocaine Mogen clamp Vs Plastibell All Awake	Length of procedure Behavioural score	Scores similar but: 70% DNB not fully effective 60% had “excessive” pain Plastibell procedure longer	Operators preferred Mogen Clamp	1-
(Taddio *et al.* 1998)	Review 3 Studies 138 Neonates RCT`s	EMLA vs Placebo (2 studies) EMLA vs DNB vs RB vs placebo All Awake	NFACS Haemodynamics Crying	DNB =RB > EMLA > placebo		1- (no stats)
(Russell and Chaseling 1996)	Case Review N=208 Neonates to 7 mn	EMLA preop All awake	Intraop behaviour Postop parent questionnaire	Little crying during procedure >90% settled rapidly postop, fed immediately, little pain at rest or on urinating	No serious complications	3

INTERVENTION……Hypospadias……. SEARCH DATE……...

COMPILED BY……G.Williams…… CHECKED BY…….

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Mahajan *et al.* 2004)	RCTDB N=80 2-8yrs	Caudal 0.5ml/kg B0.25% 1. Plain 2. + Neo 2mcg/kg 3. + Neo 3mcg/kg 4. +Neo 4mcg/kg	Intraop- Haemodynamics OPS – if >3 the rescue analgesia – Paracet Time to 1st Analgesia	↑ time to 1st analgesia and ↓ analgesic consumption in Gps 2, 3 and 4	No difference PONV, sedation, motor block, haemodynamics	1+
(De Negri *et al.* 2004)	RCTDB N=90 2-6yrs (9pts – failed block or change of surgery)	Epidural – intraop all pts R0.2% bolus → R0.125% infn Post op – infn 0.2mg/kg/hr 1. L0.125% 2. R0.125% 3. B0.125%	CHIPPS Score 4hly Score>4 rescue analgesia Time to 1st analgesia Analgesic consumption	No difference in pain scores, no rescue analgesia	No adverse effects	1+
(Gunes *et al.* 2004)	RCT N=134 1-3yrs	Caudal vs IV Tramadol 1. C 2mg/kg post surg 2. C 2mg/kg pre surg 3. IV 2mg/kg post surg 4. IV 2mg/kg pre surg	OPS (Broadman) upto 24hrs Rescue analgesia – IV pethidine 1mg/kg or paracet 20mg.kg po	Duration of analgesia 1=2 >3=4 IV Peth: 0 gps 1& 2 but 30/34 gps 3 & 4 OPS↓ gps 1 & 2 at 3hrs	PONV: gp 1 6% other gps 40%	1+
(Hansen *et al.* 2004)	RCTDB N=46 2-8yrs (2 exclusions – change surgery)	Caudal B0.25% 0.5ml/kg 1. + Clonidine 2mcg/kg C 2. + Clonidine 2mcg/kg IV Postop: P/NCA Morphine Bolus only (25ug/kg) and Paracet 20/kg 6hly po/pr	Intraop – haemodynamics Pain score – Obsevational (0-3) every 3hrs Score >1 – rescue morphine Time to 1st analgesia	No difference time to 1st analgesia, morphine use and pain scores (all low)	No difference sedation, PONV or motor block	1+
(Batra *et al.* 2003)	RCTDB N=120 2-8yrs	Caudal 0.5ml/kg + adr 1:200,000 1. Neo 10mcg/kg 2. Neo 20mcg/kg 3. Neo 30mcg/kg 4. Neo 40mcg/kg 5. Neo 50mcg/kg	Intraop – haemodynamics OPS score > 3 paracet 20 mg/kg po Time to 1st analgesia	Gp 1&6 No diff but sig ↓ duration analgesia ↑ duration of analgesia as dose ↑ (sin & ns) Gp 4 & 5 ↓analgeic consumption Gp 1 & 6 max analgesic use	Gp 4 & 5 ↑ PONV (upto 60%)	1+

		6. No Block				
(Abdulatif and El-Sanabary 2002)	RCT N=60 2-10yrs	Caudal 1. B0.25% 1ml/kg 2. B0.25% 1ml/kg + Neo 2mcg/kg 3. saline + Neo 2mcg/kg	Intraop – haemodynamics Pain score (0-10) – obs: score >4 paracet 15/kg Time to 1st analgesia	Intraop – gp 3 ↑RR, insp halothane Time to 1st analgesia ↑ gp 2 ↑ paracet usage gp 3 > gp 1 > gp 2	↑ PONV in gp 2 & 3 (~25%)	1+
(Ozbek *et al.* 2002)	RCTB N=109 1-9yrs	Caudal 0.5ml/kg 1 Alfentanil 20mcg/kg 2 Ketamine 0.5mg/kg 3 Alfentanil 20mcg/kg + Ketamine 0.5mg/kg	Intraop – haemodynamics CHEOPS upto 24hrs Score >= 7 paracet 15/kg po Time to 1st analgesia	Duration of analgesia 3=2>1 1st 6 hrs – no use of analgesics and no difference pain scores Post 6hrs – Patients needing analgesia gp1 65% gp2 34% and gp3 33%	PONV 4pts in each group No difference mictn, motor, haemodynaics No psychomotor effects	1+
(Prosser *et al.* 1997)	RCT N=90 13-53mns	Caudal 0.8ml/kg 1. B0.25% 2. Tramadol 2mg/kg 3. B0.25% + Tramadol 2mg/kg	Intraop – haemodynamics TPPPS – score >3 morphine 100mcg/kg or paracet 20mg/kg	↑ analgesic requirements and pain scores in gp 2	↑ PONV in gps 2 & 3 (ns)	1+
(Chhibber *et al.* 1997)	RCTB N=99 6mn-12yrs (2 exclusions – surgical)	DNB B0.5% 1. 0.5ml/kg post surg 2. 0.5ml/kg pre surg 3. 0.25ml/kg pre & post surg	mOPS (0-6) at 15 min, 3,12 and 24hrs Pain → paracet 15ml/kg	Pain scores; all times gp 3 < gp 1, at 3 & 12 hrs gp 3 < gp 2, at 15 min gp 2 < gp 1 ↓ paracet use in gp 3 after 3hrs		1+
(Kelleher *et al.* 1996)	RCT N=45 6mn-8yrs	Caudal B0.25% 0.5ml/kg 1. Plain 2. + diamorphine 30ug/kg	CHEOPS Time to 1st analgesia	↓ pain scores upto 30 min in gp 2 ↑ time to 1st analgesia in gp 2 (ns)	↑ PONV gp 2 (ns) ↑ time to mictn gp 2 (ns – most pts had catheter)	1+
(Ozyuvaci *et al.* 2004)	RCT N=60 3-12yrs	Caudal B0.25% 0.5ml/kg 1. + paracet 20-25mg/kg pr with C 2. C alone 3. + paracet 20-25mg/kg pr at end	CHEOPS upto 6hrs Time to 1st analgesia	No difference pain scores or time to 1st analgesia		1-
(De Mey *et al.* 2000)	RCTB N=60 8mn-13yrs	Caudal B0.25% 0.5ml/kg 1. Plain 2. + 1mck/kg clonidine 3. + 0.5mcg/kg sufentanil 4. + 0.5mcg/kg C + 0.25mcg/kg S	VAS if >5yrs CHEOPS if <5yrs 2hly upto 12hrs Score >40 or 6 paracet IV or PR	No difference pain scores or analgesic consumption	PONV – low in all groups	1-

INTERVENTION: Hypospadias repair

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Mahajan *et al.* 2004)	RCTDB N=80 2-8yrs	Caudal 0.5ml/kg B0.25% 1. Plain 2. + Neo 2mcg/kg 3. + Neo 3mcg/kg 4. +Neo 4mcg/kg	Intraop- Haemodynamics OPS – if >3 the rescue analgesia – Paracet Time to 1st Analgesia	↑ time to 1st analgesia and ↓ analgesic consumption in Gps 2, 3 and 4	No difference PONV, sedation, motor block, haemodynamics	1+
(De Negri *et al.* 2004)	RCTDB N=90 2-6yrs (9pts – failed block or change of surgery)	Epidural – intraop all pts R0.2% bolus → R0.125% infn Post op – infn 0.2mg/kg/hr 1. L0.125% 2. R0.125% 3. B0.125%	CHIPPS Score 4hly Score>4 rescue analgesia Time to 1st analgesia Analgesic consumption	No difference in pain scores, no rescue analgesia	No adverse effects	1+
(Gunes *et al.* 2004)	RCT N=134 1-3yrs	Caudal vs IV Tramadol 1. C 2mg/kg post surg 2. C 2mg/kg pre surg 3. IV 2mg/kg post surg 4. IV 2mg/kg pre surg	OPS (Broadman) upto 24hrs Rescue analgesia – IV pethidine 1mg/kg or paracet 20mg.kg po	Duration of analgesia 1=2 >3=4 IV Peth: 0 gps 1& 2 but 30/34 gps 3 & 4 OPS↓ gps 1 & 2 at 3hrs	PONV: gp 1 6% other gps 40%	1+
(Hansen *et al.* 2004)	RCTDB N=46 2-8yrs (2 exclusions – change surgery)	Caudal B0.25% 0.5ml/kg 1. + Clonidine 2mcg/kg C 2. + Clonidine 2mcg/kg IV Postop: P/NCA Morphine Bolus only (25ug/kg) and Paracet 20/kg 6hly po/pr	Intraop – haemodynamics Pain score – Obsevational (0-3) every 3hrs Score >1 – rescue morphine Time to 1st analgesia	No difference time to 1st analgesia, morphine use and pain scores (all low)	No difference sedation, PONV or motor block	1+
(Batra *et al.* 2003)	RCTDB N=120 2-8yrs	Caudal 0.5ml/kg + adr 1:200,000 1. Neo 10mcg/kg 2. Neo 20mcg/kg 3. Neo 30mcg/kg 4. Neo 40mcg/kg 5. Neo 50mcg/kg 6. No Block	Intraop – haemodynamics OPS score > 3 paracet 20 mg/kg po Time to 1st analgesia	Gp 1&6 No diff but sig ↓ duration analgesia ↑ duration of analgesia as dose ↑ (sin & ns) Gp 4 & 5 ↓analgeic consumption Gp 1 & 6 max analgesic use	Gp 4 & 5 ↑ PONV (upto 60%)	1+

(Abdulatif and El-Sanabary 2002)	RCT N=60 2-10yrs	Caudal 1. B0.25% 1ml/kg 2. B0.25% 1ml/kg + Neo 2mcg/kg 3. saline + Neo 2mcg/kg	Intraop – haemodynamics Pain score (0-10) – obs: score >4 paracet 15/kg Time to 1st analgesia	Intraop – gp 3 ↑RR, insp halothane Time to 1st analgesia ↑ gp 2 ↑ paracet usage gp 3 > gp 1 > gp 2	↑ PONV in gp 2 & 3 (~25%)	1+
(Ozbek *et al.* 2002)	RCTB N=109 1-9yrs	Caudal 0.5ml/kg 1 Alfentanil 20mcg/kg 2 Ketamine 0.5mg/kg 3 Alfentanil 20mcg/kg + Ketamine 0.5mg/kg	Intraop – haemodynamics CHEOPS upto 24hrs Score >= 7 paracet 15/kg po Time to 1st analgesia	Duration of analgesia 3=2>1 1st 6 hrs – no use of analgesics and no difference pain scores Post 6hrs – Patients needing analgesia gp1 65% gp2 34% and gp3 33%	PONV 4pts in each group No difference mictn, motor, haemodynaics No psychomotor effects	1+
(Prosser *et al.* 1997)	RCT N=90 13-53mns	Caudal 0.8ml/kg 1. B0.25% 2. Tramadol 2mg/kg 3. B0.25% + Tramadol 2mg/kg	Intraop – haemodynamics TPPPS – score >3 morphine 100mcg/kg or paracet 20mg/kg	↑ analgesic requirements and pain scores in gp 2	↑ PONV in gps 2 & 3 (ns)	1+
(Chhibber *et al.* 1997)	RCTB N=99 6mn-12yrs (2 exclusions – surgical)	DNB B0.5% 1. 0.5ml/kg post surg 2. 0.5ml/kg pre surg 3. 0.25ml/kg pre & post surg	mOPS (0-6) at 15 min, 3,12 and 24hrs Pain → paracet 15ml/kg	Pain scores; all times gp 3 < gp 1, at 3 & 12 hrs gp 3 < gp 2, at 15 min gp 2 < gp 1 ↓ paracet use in gp 3 after 3hrs		1+
(Kelleher *et al.* 1996)	RCT N=45 6mn-8yrs	Caudal B0.25% 0.5ml/kg 1. Plain 2. + diamorphine 30ug/kg	CHEOPS Time to 1st analgesia	↓ pain scores upto 30 min in gp 2 ↑ time to 1st analgesia in gp 2 (ns)	↑ PONV gp 2 (ns) ↑ time to mictn gp 2 (ns – most pts had catheter)	1+
(Ozyuvaci *et al.* 2004)	RCT N=60 3-12yrs	Caudal B0.25% 0.5ml/kg 1. + paracet 20-25mg/kg pr with C 2. C alone 3. + paracet 20-25mg/kg pr at end	CHEOPS upto 6hrs Time to 1st analgesia	No difference pain scores or time to 1st analgesia		1-
(De Mey *et al.* 2000)	RCTB N=60 8mn-13yrs	Caudal B0.25% 0.5ml/kg 1. Plain 2. + 1mck/kg clonidine 3. + 0.5mcg/kg sufentanil 4. + 0.5mcg/kg C + 0.25mcg/kg S	VAS if >5yrs CHEOPS if <5yrs 2hly upto 12hrs Score >40 or 6 paracet IV or PR	No difference pain scores or analgesic consumption	PONV – low in all groups	1-

INTERVENTION: Orchidopexy

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Verghese *et al.* 2002)	RCT N=50 1-6yrs	Caudal B 2mg/kg + NaHCO3 0.1ml + Adr 1:400,000 1. 0.8ml/kg 2. 1ml/kg	Intraop- haemodynamics Analgesic consumption	Response to cord traction Gp1 65% vs Gp2 30% 4 vs 2 pts needed rescue analgesia	No difference motor block	1+
(Findlow *et al.* 1997)	RCT N=40 2-7yrs (4 excluded – 2no surgery & 2 no follow up)	Caudal B0.25% 1ml/kg + ketamine 0.5mg/kg Vs IL/IG NB B0.25% 0.5ml/kg + Infiln B0.25% 0.5ml/kg (at end) Diclofenac 1-2mg/kg PR (both gps)	Parental OPS – 24hrs Score>4 – paracet 15mg/kg po Time to 1st analgesia and analgesic use	Time to 1st analgesia ↑Gp1 (10 v 3hrs) ↓ analgesic use Gp1 Gp 2 14 vs Gp 1 7 - Needing 2 or more analgesic doses	No difference sedation, motor, mictn, PONV (only 1 pt) No psychomotor effects	1+
(Semple *et al.* 1996)	RCT N=60 1-9yrs	Caudal B0.25% 1ml/kg 1. Ketamine 0.25mg/kg 2. Ketamine 0.5mg/kg 3. Ketamine 1mg/kg	Parental OPS for 24hrs Score>4 paracet 15mg/kg	↑Time to 1st analgesia with ↑ Ketamine – Gps 3 & 2 vs Gp 1 (sig) ↑ Analgesic requirement Gp1 vs Gp 3 (sig) and Gp 1 vs Gp 2 (ns) No difference pain scores up to 4hrs	No difference mictn, motor, sedation PONV ↑ with ↑ Ketanine but (ns) Gp 3 - 7pts short lived psychomotor effects	1+
(Somri *et al.* 2002)	RCT N=30 1-8yrs	Caudal B0.25% 1ml/kg Vs IL/IG NB B0.25% 0.5ml/kg + Infiln B0.25% 0.25ml/kg (at end)	CHEOPS upto 1hr Score >5 – fent 1mcg/kg or paracet 15mg/kg Stress Hormones	Gp 2 - ↑ pts needing fentanyl & more given (ns) No difference time to 1st analgesia and paracet use	↓Ad & Norad levels in caudal group post block insertion	1-
(Johnston *et al.* 1999)	RCT N=40 1-5yrs	Caudal 1ml/kg 1. B0.125% + 0.5mg/kg Ketamine 2. B0.25% + 0.5mg/kg Ketamine Diclofenac 1mg/kg PR at induction (both groups)	Parental OPS for 24hrs Score > 4 – paracet 15mg/kg po	Gp 2 ↑ time to 1st analgesia – 9.5 vs 8 hrs (sig) No difference in median No of paracetamol doses (=2)	No difference motor block, mictn, eye opening No psychomotor effects	1-

INTERVENTION: Inguinal Hernia

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
(Kumar *et al.* 2005)	RCTDB N=80 5-10yrs	Caudal B0.25% 1ml/kg 1. Plain 2. + Midaz 50mcg/kg 3. + Ketamine 0.5mg/kg 4. + Neo 2mcg/kg	Intraop – haemodynamiccs 5pt Verbal pain score for 24hrs Score>5 paracet 20mg/kg po Time to 1st analgesia	Time to 1st anangesia: Gp 2 = Gp4 > Gp3 >Gp1 (sig)	No difference PONV, sedation, neurological outcome, motor block 2pts with ketamine had hallucinations	1+
(Panjabi *et al.* 2004)	RCT N=60 6mn-10yrs	Caudal B0.25% 0.75ml/kg 1. + Ketamine 0.25mg/kg 2. + Ketamine 0.5mg/kg 3. + Ketamine 1mg/kg	Intraop – haemodynamics AIIMS pain scale up to 24hrs Score>4 peth IM 1mg/kg Time to 1st analgesia	Time to 1st anangesia: Gp 2 = Gp3 > Gp1 (sig) Supplementary analgesics – Gp1 90%, Gp 2 20% and Gp 3 0%	No difference sedation, motor block, mictn, PONV Behaviour effects Gp3 9, Gp2 1 and Gp1 0	1+
(Machotta *et al.* 2003)	RCT N=58 0-5yrs	Infiltration B0.5% 0.2ml/kg post surg Vs Caudal B0.25% 1ml/kg	OPS upto 24hrs Score>5 – piritramide 0.05mg/kg iv, paracet upto 100mg/kg/day	No difference use piritramide in recovery (11 vs 8) or paracet use on ward (10 vs 7) No difference pain scores at any time except 2hrs when lower with caudal		1+
(Memis *et al.* 2003)	RCTB N=45 1-5yrs (2 exclusions – analgesia for other reason)	Caudal B0.25% 0.5ml/kg 1. Plain 2. +Neo 1mcg/kg	Intraop – haemodynamics TPPPS score upto 24hrs Score>3 paracet 20mg/kg pr	No difference duration of block (15hrs – wide variation), those not needing any rescue (14 vs 15)	No difference PONV (1 vs 3), sedation, motor, haemodynamics	1+
(Baris *et al.* 2003)	RCTDB N=78 6mn-6yrs	Caudal B0.25% 0.75ml/kg 1. + fent 1mcg/kg 2. + midaz 50mcg/kg 3. plain	Intraop – haemodynamics CHEOPS for 24 hrs Score>5 paracet 20mg/kg pr	No difference pain scores (all low) or analgesic use (7 vs 8 vs 5)	No difference mictn, motor, PONV (low) or haemodynaics	1+

(Ozcengiz *et al.* 2001)	RCTDB N=120 4-10yrs (4 exclusions Unable to place block)	Caudal 0.5ml/kg 1. Tramadol 2mg/kg pre surg 2. Morphine 30mcg/kg pre surg 3. Morphine 30mcg/kg post surg	Intraop – haemodynamics OPS upto 24hrs Score>5 morph 0.1mg/kg IM	>90% pts in all gps – no further medication 8pts needed morphine (3 vs 3 vs 2)	No diff haemodynamics, PONV, sedation, puritis ↑ sevo use gp3	1+
(Koinig *et al.* 2000)	RCTDB N=42 1-7yrs	Caudal S-Ket 1mg/kg Vs IM S-Ket 1mg/kg	Intraop – haemodynamics OPS upto 24hrs Score>11 paracet 20mg/kg pr Time to 1st analgesia	Time to 1st analgesia - ↑ caudal Analgesic use 12/22 caudal vs 18/20 IM (sig) ↓pain scores caudal at 75 & 90min	No difference sedation, mictn, haemodynamics	1+
(Marhofer *et al.* 2000)	RCTDB N=49 3mn-6yr	Caudal 0.75ml/kg 1. B0.25% + Adr 1:200,000 2. S-Ket 0.5mg/kg 3. S-Ket 1mg/kg	Intraop- haemodynamics OPS up to 6hrs Score>11 paracet 30mg/kg/pr	Time to 1st analgesia Gp1 =Gp3 >Gp2 Analgesic use Gp1 30% = Gp3 33% < Gp2 72%	No difference haemodynamics, sedation, mictn	1+ But only 6hrs
(Gaitini *et al.* 2000)	RCTB N=60 1-8yrs	Caudal B0.25% 1ml/kg 1. Plain 2. + Fent 1mcg/kg	Intraop – haemodynamics CHEOPS upto 12hrs Score>5 fent1mcg/kg or paracet 15mg/kg po Time to 1st analgesia	No difference - time to 1st analgesia or pain scores (lower in gp2 but ns) Rescue analgesia – fent 5 vs 6, paracet 14 vs 12	No difference PONV (3vs4), sedation, catecholamine levels	1+
(Koinig *et al.* 1999)	RCTDB N=57 1.5-7yrs	Caudal 0.75ml/kg 1. B0.25% 2. R0.25% 3. R0.5%	Intraop- haemodynamics OPS up to 24hrs Score>11 paracet 20mg/kg pr Time to 1st analgesia	Time to 1st analgesia Gp3 > Gp1=Gp2 (large diff) Analgesic use Gp3 < Gp1=Gp2 Pain scores at 3,4hrs Gp3 < Gp1=Gp2	Time to mictn, standing ↑ Gp3	1+
(Kundra *et al.* 1998)	RCTDB N=60 9mn-12yr	Caudal B0.25% 0.66ml/kg + Morphine 0.02mg/kg 1. 15min pre incision 2. Post surgery	Intrao – phaemodynamics OPS up to 24hrs Score>=5 morphine 0.1mg/kg IM Analgesic use	OPS ↓ in Gp1 at all times (sig at 0.5, 4 & 8hrs) Time to 1st analgesia ↓ Gp1 Morphine use ↑ Gp2	No difference PONV	1+
(Klimscha *et al.* 1998)	RCTDB N=58 6mn-6yr	Caudal B0.25% 0.75ml/kg 1. Plain 2. +3.75mcg/kg Adr 3. +1mcg/kg Clon 4. +2mcg/kg Clon 5. Placebo	Intraop – haemodynamics OPS upto 24hrs Score>11 paracet 15mg/kg pr Time to 1st analgesia	In 1st 6hrs – Time to 1st analgesia: gp3=gp4 > gp1=gp2 > gp5 Analgesic use: all in gp5, gp3=gp4 < gp1=gp2 18hrs at home: Analgesic use: gp3=gp4 < gp1=gp2=gp5	No difference PONV, motor	1+

(Naja *et al.* 2005)	RCT N=50 5-12yr	GA/PVB – mixture Lig2% + Lig2% with Adr 1;200,000 + Fent + Clonidine Vs GA/Fentanyl	Intraop – haemodynamics VAS score – nurses then parents upto 48hrs Score>5 - tramadol, paracet if child/parent request	GA/PVB – stable haemodynamics intraop, lower pain scores	PVB – leave hosp earlier, ↑ surgeon and parent satisfaction	1-
(Sasaoka *et al.* 2005)	RCT N=100 6mn-10yr	Il/IG NB B0.25% 0.75ml/kg 1. Alone 2. + GenitoFem NB B0.25% 0.375ml/kg	Intraop – haemodynamics Pain score (?) upto 5hrs Rescue – Diclofenac 1mg/kg pr	↓ HR/BP on sac traction in Gp2 No difference pain scores and rescue analgesia		1-
(Sakellaris *et al.* 2004)	RCT N=45 6-10yrs	Infiltration R0.5% 0.25ml/kg 1. Pre surg 2. Post surg 3. No infiltration	OPS Paracet on demand Cortisol/prolactin levels	Time to pain score=0 ↓Gps 1 & 2	Gp 3 - ↑ postop cortisol and prolactin levels	1-
(Gunes *et al.* 2004)	RCTDB N=99 1-10yrs	Caudal 0.5ml/kg 1. R2mg/kg 2. R1mg/kg + Ketamine 0.25mg/kg 3. R1mg/kg + tramadol 1mg/kg	Introp – haemodynamics CHEOPS then parental assessment up to 24hrs Score>7 paracet 15/kg po Time to 1st analgesia	Time to 1st analgesia: Gp3 > Gp2 > Gp1 (ns 16-23hrs) Gp3 > Gp1 (sig) Analgesic use Gp1 = Gp2 (14, 11) > Gp3 (3)	PONV Gp1 (1) > Gp2 = Gp3 (7,8) No difference motor, haemodynamics, sedation	1-
(Tsuchiya *et al.* 2004)	RCTB N=30 1-8yrs	IL/IG NB 0.5ml/kg 1. R0.2% 2. B0.25% 3. Lig1%	FACES by parents at 2 & 6hrs Pain – paracet 50 – 100mg pr	Pain scores at 2 & 6hrs Gp3 > Gp1=Gp2 Analgesic use Gp1 1, Gp2 1, Gp3 3 (ns)	No PONV, motor	1-
(Schrock and Jones 2003)	RCTB N=54 1-6yr	Caudal B0.175% + Adr 1:200,000 1. 0.7ml/kg 2. 1ml/kg 3. 1.3ml/kg Paracet 30mg/kg PR indn (all gps)	CHEOPS in hosp, Parental VAS at home up to 24hrs Time to 1st analgesia Rescue analgesia – fent, oxycodone (hosp) paracet, codeine (home)	No difference Time to 1st analgesia (3.5-5hrs) CHEOPS no difference and low Recovery analgesia – 4 vs 3 vs 1 (ns) 36 pts analgesed at home – no diff between gps and no consistency with parental decision	No difference mictn, motor	1-
(Hager *et al.* 2002)	RCTB N=53 1-72mn	Caudal 0.75ml/kg 1. Ket 1mg/kg 2. Ket 1mg/kg + Clon 1mcg/kg 3. Ket 1mg/kg + Clon 2mcg/kg	Intraop – haemodynamics OPS up to 24 hrs Score>11 paracet 30mg/kg pr Time to 1st analgesia	Time to 1st analgesia – Gp2=Gp3>Gp1 Analgesic requirement – Gp2=Gp3 > Gp1 (16% vs 63%)	No difference mictn, haemodynamics No adverse effects	1-

(Lim *et al.* 2002)	RCT N=90 2-12yrs (5 exclusion Failure tech, poor anat, data lost)	IL/IG NB B0.25% 0.25ml/kg 1. Single shot 2. Double shot Post discharge paracet 10mg/kg po 6hourly (both gps)	Intraop – haemodynamics mCHEOPS up to 24hrs score4-5 paracet 15mg/kg po score 6 paracet + fent 1mcg/kg	Success rate 72% (both gps) No difference analgesic use 50% children pain in 24hr period		1-
(Senel *et al.* 2001)	RCT N=60 1-7yrs	Caudal 1ml/kg 1. B0.25% 2. B0.25% + Tramadol 1.5mg/kg 3. Tramadol 1.5mg/kg	Intraop – haemodynamics 3pt pain scale up to 24hrs Score>1 paracet 10mg/kg pr Time to 1st analgesia	Time to 1st analgesia gp2 (13.5hr) > gp1 (9.8) > gp3 (4.7) (sig) Gp3 - ↑ rescue analgesia + pain scores at 4 & 6hrs	No difference RR, sedation, PONV (low), mictn, motor	1-
(Hashizume *et al.* 2001)	RCT N=60 1-5yrs	Caudal 1mg/kg 1. Mepivacaine 1% 2. B0.25% 3. M 1% + B0.25% (50:50)	OPS up to 24hrs Score>3 paracet 20mg/kg pr	Low use of postop analgesia 4 vs 0 vs 0		1-
(Joshi *et al.* 1999)	RCT N=56 6mn-6yrs	Caudal 1ml/kg + Adr 1:200,00 1. B0.125% 2. B0.125% + Fent 1mcg/kg 3. B0.25% 4. B0.25% + Fent 1mcg/kg	OPS in recovery VAS at home by parent or child Rescue paracet/codeine	No difference pain scores, analgesics at home 21% pts received IV fent (?when and why) – more in Gp1		1-
(Splinter *et al.* 1997)	RCTB N=164 2-6yr	Infiltration + direct vision IL/IG NB B0.25% 0.2ml/kg (surgeon) 1. Caudal B0.2% 1ml/kg + Adr 1:200,000 2. Ketorolac IV 1mg/kg	mCHEOPS up to 24hrs score>5 morphine 50mck/kg or paracet 15/kg or codeine 1mg/kg	No difference pain scores in recovery ↓pain scores at home Gp2 Up to 2 hrs – paracet (59 vs 61) and codeine (56 vs 50) use no difference	PONV, motor and mictn all ↓Gp2	1-
(Dahl *et al.* 1996)	RCTDB N=50 2-10yr	Infiltration 1. B0.25% 1ml/kg pre + saline post 2. Saline pre + B0.25% 1ml/kg post Paracet 15-20mg/kg pr on admission to recovery (both gps)	OPS + questionnaire	↓score at 30min Gp1 No difference post op analgesia Postop opioids 54% vs 45%		1-
(Taylor *et al.* 2003)	Open label N=27 5-24mn	Caudal L0.25% 0.8ml/kg	Intraop – haemodynamics Time to 1st analgesia – paracet 30mg/kg po/pr	22/27 pts good intraop analgesia Time to 1st analgesia 7.34hrs	No adverse events	2+

(Kokki *et al*. 2000)	Open label N=190 6mn-10yrs	Spinal B0.5% 0.3-0.4mg/kg + IL?IG NB B at end of procudre + either ketoprofen 2mg/kg IV or Ibuprofen 10mg/kg pr or paracet 40mg/kg pr	Maunuksela pain scale Score>3 rest or >5 activity fent 1mcg/kg Parent questionnaire	183 successful – 2 GA, 7 sedation 28% fentanyl in recovery 83% pain at home (17%mod, 2%severe) 85% analgesia at home, median 4 doses	7% PONV 6% headache	2+
(Brindley *et al*. 2005) incarcerated hernia	Retrospective review N=12 2-17wk	Awake Cuadal B0.25% 1ml/kg		All successfully reduced	No adverse events	3

INTERVENTION: abdominal surgery

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Klamt, 2003 #1883}	RCT n=40 3-98 months MAJOR ABDO SURGERY	24hr epidural clonidine (1mcg/ml at rate of 0.2ml/kg/hour with pre bolus of 2mcg/kg) vs clonidine (1mcg/ml) and ropivacaine 0.1% at rate of 0.2ml/kg/hour both got ketoprofen 2mg/kg every 8 hours breakthrough got tramadol 1mg/kg	Unvalidated pain scale Tramadol requirement Sedation Resp and haemodynamic changes	No Difference: 77% (clon) and 59.3% (clon + ropiv) required no or one dose of tramadol. Both regimens ineffective for movement pain.	Clonidine alone (bolus + higher dose) caused more sedation. Hypotension following bolus in 2/20.	1- no power calc
{Cucchiaro , 2003 #1893}	RCT n=26 3-12 YEARS Major GI/urology	EPIDURAL rop + MOR or Clon. Ropivacaine 0.25% bolus (2.5 mg/kg) M (14) 0.08% Ropivacaine + 10mcg/ml morphine infusion C (12) 0.08% Ropivacaine+ 0.6mcg/ml clonidine	Pain (broadman/ VAS) Rescue Side effects	Vomiting and pruritus higher in M Pain sig higher in C group		1- power calc not based on hypothesis
{Kiffer, 2001 #2637}	RCT DB n=21 Mean age 12 Major abdominal and orthopaedic	Midaz pre med (rectal 0.3mg/kg) Epidural (n=11) 30mcg/kg MOR bolus injection Placebo (n=10) no puncture but dressing in same spot as epidural All had PCA morphine + iv proparacetamol	Pain (VAS)self report. Morphine consumption. Side effects.	VAS score and morphine requirements were smaller in epidural group (p=0.05) Pain scores satisfactory in both groups Opioid side effects similar in both	? no clinical difference between treatments	1+ (numbers required not achieved)
{Peters, 1999 #343}	RCT n=47 5-18 YEARS Major abdo or spinal surgery	PCA (Morphine) 15mcg/kg/hour + bolus of 15mcg/kg –lock out 10min CI (Morphine) 20 to 40 mcg/kg h	Analgesia (self reporting every 3 hours via VAS) Morphine needs Side effects	Morphine consumption SIG higher in PCA No difference in pain scores	No difference in side effects	1+ Multimodal technique not used. High incidence of moderate to severe pain scores.
{Chabas, 1998	RCT non blind Uro abdo surgery	Epidural morphine 50ug/kg IM morphine 100uk/gh 4-5 hrly	Pain (Andersen) FVC and FEV 1	No sig difference in groups	Significant improvement in	1- no power calc

#1909}	n=30 6-16 yrs		6 hours post op and every day for next 7 days		quality of analgesia and decrease morphine given in epidural group	
{Kart, 1997 #362}	DBRCT n=31 3months-6years	continuous epidural fentanyl and bupivacaine vs intermittent epidural administration of morphine		Bupiv+fentanyl superior to intermittent MOR		1
{Birmingham, 2003 #1114}	Case series lower-extremity bony orthopedic surgery (n = 42), pectus excavatum repair (n = 30), renal surgery (n = 20), laparotomy (n = 19), thoracotomy (n = 12), and a variety of other procedures (n = 9).	PCEA				
{Bosenberg, 1998 #316}	Case series	Epidural /Neonatal				
{Bozkurt, 1997 #861}	Case series	Epidural morphine				
{Ivani, 1999 #604}	DBRCT 28 infants, aged 1-12 months	major abdominal surgery 0.7 ml x kg(-1) bupivacaine 0.25% vs ropivacaine 0.2% via lumbar epidural block.	24hrs	No difference		
{Lerman, 2003 #1795}	DBRCT n=120 6 months to 12 yr	0.125% levobupivacaine; 0.0625% levobupivacaine; 1 µg/ml fentanyl; or 0.0625 levobupivacaine and 1 µg/ml fentanyl.	24 hrs			1+
{Bosenberg, 2003 #3009}	Case series n=45 0-1yr	bolus dose (0.9-2.0 mg.kg(-1) of ropivacaine 0.2%) followed by epidural infusion (0.2 mg.kg(-1).h(-1) for infants <180 days or 0.4 mg.kg(-1).h(-1) for infants >180 days).				2

{Moriarty, 1999 #595}	Case series n=272	72 children received an infusion of bupivacaine 0.125% + diamorphine 20 microg x ml-1, then 200 children received plain ropivacaine solutions.				
{Monitto, 2000 #1587}	Case series n=240 Mixed cases 74 abdominal surgery	Parent/Nurse NCA				
{van Dijk, 2002 #1676}	n=204 0-3yrs major abdominal or thoracic surgery	Continuous vs intermittent MOR				

INTERVENTION: Fundoplication

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Lejus 2001 *	Prospective evaluation of epidural over 6 years. n=348 (307 children 12 days to 18 years, median 72 months)	Bupivacaine (mean concentration 0.185%)and Fentanyl (5ug/kg/day). Different types of surgery including fundoplication.	Hourly pain scores (Krane et al) Global pain index	Combination provides safe analgesia	Urinary retention 17% N & V 14% Pruritus 0.6%	3 prospective but not analytical
Wilson 2001	Retrospective review Non random allocation n=104 (65 epidural, 39 infusion)	Epidural (bupivacaine/fentanyl mixture 0.125% at 0.4ml/kg/hr) v morphine infusion (10-40ug/kg/hr)	Hourly Pain measurements routinely performed. Need and duration of icu stay. Hospital stay M & M	Hospital stay greater for opioid group (13 v 8)	Mean duration of stay higher in opioid group. Patients in hospital more than 7 days higher in opioid group	3 case series
Dick 1998	Prospective non randomised (but blinded for data collection) n= 40 (20 open, 20 lap)	Assessment of morphine usage post op	Duration and amount of morphine given. Linear pain scale	Equal amounts of morphine given (0.432+/-0.28, o.427+/- 0.28 mg/kg) More morphine required day 1 for lap procedure (0.399 +/- 0.19 v 0.22 +/-0.11. p< 0.03) But shorter time in lap group 1.2+/-0.46, 2.7+/- 0.67 days p<0.02. Similar amounts of NSAID given		2- non randomised. no primary end point or calculation of power. Different surgeons performed open and lap procedures.
Brenn 1998	Prospective data acquisition. non-randomised 92 patients Mean age 107 months Orthopaedic and upper GI surgery	First 44 - bolus epidural morphine (caudal or lumbar) Subsequent 48 – post op continuos bupivicaine (0.2 – 0.5 ml/kg/hr 0.1%) and fentanyl (2mcg/ml)	CHEOPS used for analgesia. Incidence of complications. Comparison of di and quadroplegia	Vomiting seen more in diplegic group (p<0.01) Pruritus higher in diplegic group (p<0.0002) Neither of above related to mode of analgesia. Incidence of sedation higher in bolus group (p<0.01)	Bupivicaine and fentanyl better than opioid	3 non randomised

Rowney 2000	Retrospective review n=51 Laparoscopic Nissen Median age 6yrs (5 months – 20 yrs)	Multi modal technique Port infiltration with 0.25% bupiv + 1 in 200 000 adrenaline Intra op fentanyl (2mcg/kg/hr) +rectal NSAID (34 patients) and rectal para (36 patients). Morphine infusion (first 4 patients). IM morphine 100mcg/kg given at end of surgery (24 patients). IM codeine (1mg/kg) in 20 patients.	No formal pain scores or charting. Assessment by nurses and anaesthetists	No post op analgesia required in 34 patients after 24hrs. No post op analgesia required in 45 patients after 48hrs.		3 not analytical. no historical control.
Mcneely 1997	Retrospective review n=155 1 month to 19 years elective open fundoplication	bolus iv morphine n=91 (0.05 – 0.1mg/kg 1-2 hrly) v epidural n=72 (0.25% bupiv intra-op + fentanyl or morphine with 0.0625 – 0.125% bupiv	Post op course (analgesic efficacy, complications, hospital stay, cost) Pain via VAS or observational scale (Oucher)	Decrease complications in epidural group (decrease ventilation (P<0.01), shorter hospital stay (P<0.01), cheaper (P<0.01))		3 not analytical. only patients in epidural group managed by specific pain service

INTERVENTION: Appendicectomy

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Jensen, 2004 #3157}	DB RCT N = 68	B O.25% or 0.5% (>40kg<) or placebo 0.5 ml/kg sub cut	Morphine usage in first 24 hours	B 0.065mg/kg P 0.073mg/kg Ns	B group experienced longer pain relief (ns)	1+
{Yildiz, 2003 #3158}	RCT non blinded n= 40 (20 in each group) Age range 6 – 15	pethidine load (0.3 mg/kg then 150mcg/kg bolus iv. Pethidine load (0.3mg/kg then 75mcg/kg bolus + 15mcg/kg/hour background Lock out 20 mins in both	Pain Sedatiuon nausea in first 24 hours (4 point scale for each)	No difference between groups Background group had lower peth consumption in first 24 hours ($p<0.01$)	No significant side effects	1- no specific end point or power calculation
{Dix, 2003 #1727}	RCT non blinded n=75 Age 7-16 years	All had pca morphine + para +NSAID a) saline infusion b) Ketamine 500mcg/kg iv iv pre incision + saline infusion c) Ketamine 500mcg/kg iv iv pre incision + ket infusion 4mcg/kg/min postop	Primary - Morphine consumption at 24hrs Secondary - Rescue analgesia Side effects Satisfaction scores	No difference in morphine consumption in the groups Ket infusion required more doses of rescue and reported more side effects (hallucinations)		1+ envelope randomisation.
{Munro, 2002 #1119}	RDBT n=60 (53 completed) 5 – 13 years	Control (no intra or post op antiemetic) Ondansetron 0.1mg/kg (intra op + added to post op PCA) Droperidol 0/01mg/kg (intra op + added to post op PCA) All had morphine PCA (20mcg/kg bolus at 5 min lock out with background of 4mcg/kg/hour)	Pain (method not stated) Nausea Vomiting Sedation First 24 hours	No sig difference in PONV and sedation scores		1- unclear power calculation. low group numbers.
Wright	DBRCT	Wound infiltration	Post op pain assessed by	Significant decrease in pain in		1+

2001?? {Wright, 1993 #754}	n=60 (52 completed)	Either bupivicaine or placebo	child, recovery sister, ward sister Time to first narcotic injection	bupivicaine group		sample size seems low
{Morton, 1999 #2662}	RCT non blinded n=80 (20 in each group) 5-13 years	Pca morphine 20mcg/kg bolus then 4mcg/kg/hr background for 12 hrs. Morphine + diclo 1mg/kg 8hrly. Morphine + para 15-20mg/kg 6hrly. Morphine + diclo and para. All had wound infiltration with 0.25% bupiv 1mg/kg	Morphine consumption Analgesia (3 point pain score) 3 point nausea score 3 point sedation score	Morphine consumption reduced by diclo ($p<0.0033$ for MD and $p<00.28$ for MDP). Para not additive ($P<0.144$).	Analgesia effect significantly improved by diclo despite lower morphine consumption	1+ Equal in groups Duration of pca equal
{Ko, 1997 #3161}						
{Lohsiriwat, 2004 #3160}						
{Till, 1996 #683}		PCA		PCA effective		

INTERVENTION: Laparoscopy

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Borkar 2005	Randomisd non blinded n=50 3 – 13 years. laparoscopic procedures	1. caudal Bupivacaine 0.2% 1mg/kg 2. diclo supp 3mg/kg + Bupivacaine 0.5% port site infiltration at end of procedure	Hannallah objective PS 15,30,60,120 and 360 mins	Comparable pain scores at all times	12% G1 and 20% G2 required rescue (ns)	1- no power calc. no mention of randomisation method.
{Till, 1996 #683}						

INTERVENTION: Orthopaedics – lower limb surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Hiller 2006	DB RCT N=120 1-9 yrs (Soft tissue or orthopaedic) (11 exclusions from final analysis)	Gp1: Paracetamol 60mg/kg pr & 40mg/kg orally 8h post op Gp2: Ketoprofen 2mg/kg IV at induction & 8h post op Gp3: Both drugs	Morphine consumption OPS (0-9) for 24 h; Every 10 minutes for 2 hours, then hourly for 22 h Plasma drug concentrations at 4 hours N&V, anti-emetic use, retention pruritus	Cumulative morphine requirement less Gp3 by 30%. Difference SS Gp 1 vs Gp3 but not Gp2 vs Gp3 Mean time to 1st morphine Gp3> Gp1 & Gp2 OPS less in combination gp	Combination more effective in PACU, difference persisted in orthopaedic group for full 24 h No diff in adverse effects	1+
Goodarzi 1999	DB RCT N=90 3-19 years (fem osteotomy, VDO, tibial osteotomy, Ilizarov & talectomy)	Comparison of epidural opiates: Morphine 10mcg/kg/h vs Fentanyl 1mcg/kg/h vs Hydromorphone 1mcg/kg/h	VAS (1-5) Side effects Hourly for 30 hrs	No difference in pain scores Resp dep: M>F=HM Somnolence: M>F=HM N&V: M>F>HM U.retention: M>F>HM	Epidural hydromorphone fewer side effects & comparable analgesic efficacy	1+
Duflo 2006	DB,RCT N=33 7-15 yrs (large bone osteotomy, arthrotomy, cyst, tumour resection)	Fascia iliaca compartment block or sciatic nerve popliteal block. Bolus 0.2% ropivacaine, 0.5ml/kg PCRA 0.1ml/kg bolus, 30 min lockout + 0.02ml/kg/h background vs CRA 0.1ml/kg/h	VAS 4 hrly for 48 hrs Demand to delivery ratio Quality of awakening Satisfaction Plasma ropivacaine levels at 24 & 48 hrs	Mean VAS in 1st 24 h: 1.1 PCRA, 1 CRA Mean VAS in 2nd 24h: 0.8 PCRA, 0.9 CRA Supplemental analgesia: 3 PCRA, 9 CRA No diff in satisfaction or quality of awakening Ropi plasma levels: significantly lower in PCRA gp	3 exclusions Potentially lower systemic toxicity Dec cost	1+

Lovstad 2001	DB RCT N=42	1. Sevo, epi with fentanyl vs, 2. sevo epi no fentanyl vs 3.propofol, epi no fentanyl 1: 0.1% bupivacaine, fentanyl 2mcg/ml, epinephrine 2mcg/ml 2 & 3: 0.15% bupivacaine, epinephrine 2mcg/ml	Verbal pain scale (0-4) PONV (0-3) Pruritus At 0h & 4 hrly for	Plain bupivacaine gps needed 55-75% larger bupivacaine doses & 10/26 needed IV opiates. No diff in pain scores Fentanyl: 7/16 nausea, 2/16 vomited		1+
Castillo-Zamora 2005	DB RCT N=45 (Hip surgery)	Comparison of three doses of epidural morphine: 11.2, 15 & 20 mcg/kg	Pain Side effects	12-14 hrs analgesia in all groups	PONV: 46.7%, 60% & 86.7%, with incr morphine	1+
Bai 2004	RCT Unblinded N=91 1-14 yrs (lower limb surgery due to CP, polio, hip dysplasia)	PCEA lidocaine 5mg/h, 2.5mg bolus, 8 min lockout vs NCA fentanyl 1mcg/kg/h background	Parent VAS & Objective Pain Score 0-10 at 0, 6 & 24 hrs Side effects	OPS lower in epi group ($p<0.05$) PVAS lower in epi group ($p<0.05$)	PONV: 16% epi group, 30% fentanyl group (not signif)	1+ (? Validity of parent VAS & OPS)
Reinoso-Barbera 2002	DB, RCT N=30 2-16 yrs (Vertebral arthrodesis, bone graft, amputation, osteotomy)	Epidural fentanyl (1mcg/ml) + lidocaine 0.4% @ 0.1-0.35ml/kg/h vs epidural morphine 20mcg/kg 8 hrly All received IV metamizol	> 6yrs old VAS 0-10 < 6yrs old LLANTO 0-10 (validated Spanish OPS) ? frequency & duration Plasma lidocaine levels	Pain score < 4 95% of time on FL group & 87% of time in M group Statistical but not clinical significance	Plasma lidocaine levels not toxic No diff in SEs	1-
Dadure 2006	Randomised Unblinded N=54 (club foot repair, ankle & foot osteotomy)	Continuous epidural block (CEB) vs Continuous popliteal nerve block (CPNB) Bolus 0.5 – 1ml/kg of equal volume mixture 0.25% bupivacaine & 1% lidocaine – both groups Ropivacaine 0.2% infusion at 0.1ml/kg/h for CPNB & 0.2ml/kg/h for CEB	Pain on movement VAS (0-10) or CHIPPS at 1 hr & then 6hrly for 48 hrs	No difference in pain scores or rescue analgesia Satisfaction 100% in CPNB, 86% in CEB	Increase adverse effects in CEB gp: Technical problems, urinary retention, PONV	1-

Antok 2003	RCT Unblinded N=48 7-12 yrs (osteotomy, arthrotomy, tumour)	PCEA vs CEA 0.2% ropivacaine All received ketoprofen & propacetamol	VAS 0-10, 4 hrly For 48 hrs	No difference in VAS PCEA gp received 50% ropi dose compared with CEA gp (p<0.001)	No difference in SEs	1-
Tran 2005	RCT Unblinded N=36 12-19 yrs (ACL surgery)	Fem-Sci NB with 0.125% bupivacaine & clonidine2mcg/kg (FSNB) vs intra-articular bupivacaine 0.25%, clonidine1mcg/kg & morphine 5mg (IA) All received PCA morphine	VAS 0-10 at 0, 1, 4, 8, 12 ,16 & 18 hrs Intra-op fentanyl Morphine usage Time to 1st morphine SEs	FSNB: Dec intra-op fent (p=0.04) Dec morphine usage (p=0.03) Longer duration of analgesia (p=0.0001) Dec VAS (p=0.01)	2 pts excluded from FSNB gp – failed block IA : 50% PONV FSNB: 11% PONV	1-
Kiffer 2001	DB, RCT N=21 6-15 yrs	Epidural morphine 30mcg/kg vs control All received PCA morphine & IV propacetamol	VAS hrly for 24 hrs Morphine consumption Side effects	VAS & morphine requirements significantly less in epi morphine group	No difference in incidence of side effects	1-
Paut 2004	DB RCT N=6 5-15 yrs (femoral surgery)	Fascia iliaca compartment block 0.7ml/kg 0.5% ropivacaine (4 pts) vs 0.7ml/kg 0.275% ropivacaine (2 pts)	Plasma levels of ropivacaine	3/4 pts receiving higher concentration had a Cmax that exceeded the maximum recommended level	All had satisfactory analgesia	1-
Gouda 2003	N=36 1-=24mts (Club foot)	Comparison of IVRA with ropivacaine0.1% vs IVRA with lidocaine0.3% vs control	Time to first analgesia OPS	T to 1st analgesia = 52, 44 & 10min, ropi, lido, control		1-
Eberson 1999	Case control N=64 6m-18 yrs (Long bone osteotomy & CTEV)	Ketorolac 1mg/kg loading dose, 0.5mg/kg 6h for 24 hrs + breakthrough IV morphine Controls (N=37) IV morphine 0.1mg/kg 3 hrly prn	Morphine usage GI complications Length of stay Bleeding complications	K gp: 2.29 morphine doses Controls 10.02 morphine doses (p<0.05)	No bleeding complications GI effects: K: 4%, controls 32% (p<0.05) Length of stay: K: 3.63 days Controls: 4.74 days	2+
Herrera 2004	Cohort study N=35 (Femoral nailing)	Intra-operative haematoma block 1-2ml/kg of 0.5% or 0.25% bupivacaine vs control all received 0.1mg/kg morphine	"Narcotic equivalent dose" Time to 1st opiate 12 hrs	Time to 1st opiate inc by 5 hrs (p=0.08) Narcotic equivalent requirement in haematoma block gp: 0.05Eq/kg & 0.12Eq/kg at 6 & 12 hrs	No adverse effects	2-

				In controls: 0.09Eq/kg & 0.13Eq/kg (not ss)		
Black 2003	Retrospective Case control N=92 (Club foot surgery)	Caudal vs no caudal	Opiate usage for 8hrs	No diff		2- Abstract only
Tobias 1999	Case series N=20 6m-12 yrs (foot & ankle surgery)	Popliteal fossa block 0.75ml/kg of 0.2% ropivacaine	OPS (0-10) 30 min, 60 min& 2hrly for 12 hrs Analgesic use	12 hrs analgesia 19/20 no other analgesia for 8 hrs 8/20 no other analgesia for 12 hrs	Unsuccessful in 1 pt No adverse effects	3
Dadure 2004	Case series N=15 1-14 yrs (Femoral shaft & hip surgery)	Continuous psoas compartment block, 0.2% ropivacaine	VAS & CHIPPS at 1, 6, 12, 18, 24, 30, 36 & 48 hrs	Median pain score 1 at 1 hr 0 thereafter	No adverse effects	3
Brenn 1998	Case control N=92 4 – 13 yrs (CP pts, orthopaedic & Nissen fundo)	Bolus epidural morphine vs CEA bupivacaine & fentanyl		91/92 excellent analgesia	6.5% XS sedation in bolus group	Abstract only
Lejus 2001	Prospective case series N= 348 12 days – 18 yrs (orthopaedic 80% & general)	CEA Fentanyl 0.2mcg/kg/h With Bupivacaine <20kg 5mg/kg/day 21-40kg 4.2mg/kg/day >40kg 3.2 mg/kg/day	0-5 pain score (Krane) hrly for 43 hrs Side effects	86% of all pain scores <3 2.5% pain scores = 5	PONV in 14% Pruritus 2/348 No seizures, hypotension or respiratory depression	3 Low efficacy in club foot
DeVera 2006	Retrospective case series N=1809 2m-20 yrs	1011 lower extremity blocks 646 upper extremity blocks 579 neuraxial blocks	Complications	2 self limiting complications following PNB		3
Lovstad 1997	Case series N=100 4-14 yrs (femoral osteotomy)	Epidural 0.1% bupivacaine, fentanyl 2mcg/ml, epinephrine 2mcg/ml Rectal paracetamol	Verbal pain score 0-4 Side effects	99% 0 or low pain score at rest for 80% of time 80% 0 or low pain score for 80% of time on movement	63% PONV 49% pruritus	3 (Abstract only)

Vas 2005	Case series N=160 4m-12 yrs (Foot surgery, tendon transfers, tibial osteotomy)	Continuous Sciatic block 0.25% bupivacaine, 0.75ml/kg bolus followed by 0.3mg/kg/h bupivacaine	CHEOPS 6 hrly for 72 hrs	Pain score 1-4 86% 5-6 13%, 7 <1%	Block failed in 9	3
Duflo 2004	Case series N=27 4-17 yrs (Lower limb surgery)	Patient controlled regional analgesia. Fascia iliaca block or sciatic nerve popliteal block 0.2 % ropivacaine, 0.5ml/kg bolus PCRA: 0.2% ropi 0.02ml/kg/h, 0.1ml/kg bolus, 30 min lockout Paracetamol & Ketoprofen	VAS or CHEOPS for 48 hrs Demand to delivery ratio	Mean VAS 1.09 Mean CHEOPS 4.75 2 pts req additional analgesia	2/27 motor block 1/27 catheter removed because of leak No serious complications	3
Paut 2001	Case series N=20 1-16 yrs (Knee & thigh surgery & fractured femur)	FIC block Bolus 0.25% bupivacaine 0.62ml/kg Infusion 0.135mg/kg/h	Plasma levels at 24 & 48 hrs VAS (0-100) or CHEOPS 4 hrly for 48 hrs Block efficacy	Plasma bupivacaine levels within the safe range	No severe side effects	3
Manion 2005	Case series N=14 5-11yrs (pelvic & femoral surgery)	Lumbar plexus block 0.5ml/kg of 0.5% bupivacaine + 1mcg/kg clonidine	Pain score? which For 72 hrs	Effective analgesia	No complications	3 Abstract only

INTERVENTION: Upper limb surgery (Orthopaedic & Plastic surgery)

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Iwata 2000	DB, RCT N=26 2-11 years	Fentanyl brachial plexus block vs saline Axillary approach	Time to onset of pain	Time to onset of pain in fentanyl group 809 minutes, 199 in controls		1- FT not seen
Thornton 2003	DB, RCT N=35	Axillary block with 0.2% ropivacaine 0.5ml/kg vs 0.25% bupivacaine 0.5ml/kg	FLACC at 0,3,6,12 & 24hrs Time to 1st opioid analgesia	No difference		1+
Fleischmann 2003	Prospective, randomised N=40 1-10 years	Axillary (ABP) vs Lateral infraclavicular (LVIBP) Both groups: 0.5ml/kg of 0.5% ropivacaine	Sensory & Motor blockade	Sensory (quality & distribution) & motor blockade more effective in LVIBP	No major complications in either group LVIBP less painful	1-
Pande 2000	Prospective case series N=200 5-12 years	Supraclavicular brachial plexus block for upper extremity trauma	Ability to perform procedure	Satisfactory block	No pneumothorax	3
Carre 2000	DB, RCT N=70 4-15 years	Single injection (S) vs multiple fractionated doses (M) for axillary block	Motor & sensory block	No benefit to fractionated doses (easier diffusion of LA in perineural space cf adults)		1+
Fisher 1999	N= 185 patients, 250 procedures Case series 5 mts – 17 yrs	Axillary block with 0.25% bupivacaine 0.5-0.6ml/kg	Intra-operative & postop analgesia	54% no further intra-operative analgesia Block failed in 6%	No complications	3
De Jose Maria 2004	Case series N=55 5-17 yrs	Vertical infraclavicular block with 0.5ml/kg of 0.5% ropivacaine	Number of attempts, response to surgery, VAS, complication & duration of block	1st or 2nd attempt 85% 3rd or 4th attempt15% 98% effective for surgery VAS <3 all patients Mean sensory block 8.45 hrs Mean motor block 6.52 hrs	No pneumothorax or puncture of major vessel 2 pts Horner's	3
Altintas	N=49	Axillary block with 0.8ml/kg of	Isoflurane	No difference in pain scores in 1st 8		1+

2000	1-11 yrs	0.25% bupivacaine Performed pre-surgery or post surgery	requirements Faces 2, 4, 6, 8, 10 & 24 hrs Analgesic requirements for 24 hrs	hours. 8 in pre-group & 20 in post group did not require analgesia in the 24 hr study period		

INTERVENTION: Spinal Surgery

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Gall 2001	DB, RCT N=30 9-19yrs	All: PCA morphine Intrathecal morphine 0, 2 or 5 mcg/kg	Time to 1st morphine Morphine consumption VAS (0-100) at rest & on movement For 24 hours	Time to 1st morphine: 5>2>0 mcg/kg VAS at rest: 5=2>0 mcg/kg VAS on movement no difference	Dec intra-op bleeding with 5mcg/kg	1+
O'Hara 2004	DB, RCT N=31	All: PCA morphine Epidural: bupivacaine: 0, 0.1% or 0.0625% Both bupivacaine solutions contained 5mcg/ml fentanyl (mid-thoracic epidural)	VAS, morphine usage, 4 hourly for 96 hours Time to oral intake, ambulation & discharge	No difference		1-
Blumenthal 2006	RCT N=30 11-17yrs (Anterior surgery)	Double epidural catheter 0.3% ropivacaine(E) vs Continuous IV morphine 50mcg/kg/h (M) (All received TCI remi until 1st post-op morning = T0) All received rofecoxib & IV paracetamol	VAS(0-100) at rest (6hrly) & on movement (24, 48 & 72h) Rescue analgesia Motor block PONV & pruritus (6 hrly), Bowel function (12hrly) Patient satisfaction	E group: significantly less pain at rest & on movement, less rescue morphine, improved bowel activity & higher patient satisfaction	Motor block – transient in 2 patients. No hypotension Less PONV & pruritus No neurologic complications	1-
Blumenthal 2005	Prospective, randomised, unblinded N=30 12-22yrs	Continuous IV morphine vs double epidural catheters 0.3% ropivacaine (All received TCI remi until 1st post-op morning = T0)	VAS (0-100) at rest & on movement Rescue analgesia PONV, pruritus 6 hrly from T0 – T72h, bowel	Epi group: VAS lower at rest except at 12, 60 & 72 hours. VAS lower on movement at 24, 48 & 72 hours	Epi group: Less pruritus & PONV Bowel function better	1-

			function 12 hrly			
Cassady 2000	Prospective, RCT, unblinded N=33 11-18yrs	Thoracic epidural bupivacaine + fentanyl vs PCA morphine	VAS, time to resumption of bowel sounds, liquid intake, and side effects	No difference in pain score	Earlier resumption of bowel sounds in epi group – but no diff in time to oral intake	1-
Goodarzi 1998	Prospective Randomised 10-16y N=80	Intrathecal morphine 20mcg/kg + 50mcg sufentanil vs IV sufentanil	"descriptive scale" 0-10	IT group "pain relief for 14.5hrs" IV group required PCA morphine	IT group decreased blood loss IT group: respiratory depression in 1st hour but not thereafter	1- No mention of pain scores in results
Sucato 2005	Retrospective Case Series N=613	Epidural 0.1% bupivacaine + hydromorphone vs PCA morphine	Faces (0-5) At 2,4, 6, 8,12, 24, 36 & 48h	Epidural group had significantly better pain scores on average & at each time point. Range of pain scores & average max score less in the epi group	Epi group had inc pruritus, PONV & respiratory depression	2++
Vitale 2003	Retrospective review of complications of ketorolac use N=208	Ketorolac (60 pts) vs no NSAID (148 pts)	Post-op bleeding & bone fusion	No difference		2+
LaMontagne 2003	RCT Unblinded 11-14 yrs	Coping instruction vs concrete objective information vs combination All had PCA	VAS 0-10 Day 2-4	Coping strategy gp reported less pain		2
Shaw 1996	Case series N=71 (30 retrospective & 41 prospective) 7-19 yrs	Epidural 0.0625% - 0.125% bupivacaine with fentanyl, morphine or hydromorphone (61pts)		Did not compromise neurological assessment 64 effective analgesia		3
Lowry 2001	Prospective review N=10 (anterior fusion)	Epidural fentanyl 1mcg/kg + hydromorphone 5 mcg/kg at end of surgery. Post-op 0.1% ropivacaine + hydromorphone 10mcg/ml @ 0.2ml/kg/h	VAS 0-10 For 5 days	Mean of median pain scores: 2.1 Mean maximum pain score: 4.1	3/10 pruritus 1/10 drowsiness	3
Tobias 2001	Case series N=14 5-17 yrs	Double epidural Fentanyl + hydromorphone at end of surgery	VAS 0-10 & objective pain score 0-10.	Mean of median pain score: 1.5, 1.6, 1.4, 1.1, 0.9 Mean of maximum pain score: 3.5, 4,	No adverse effects	3

		Post-op ropivacaine + hydromorphone	2-4hrly for 5 days	3.1,2.4, 2.2.		
Ekatodramis 2002	Prospective case series N=23 12-19 yrs Anterior surgery	Double epidural 0.0625% bupivacaine, fentanyl 2mcg/ml & clonidine 3mcg/ml	VAS 6 hrly for 48 hrs	VAS 0 at rest in all patients VAS 30 on movement in 17%	Pruritus 0 N&V 17%	3
Turner 2000	Case series N=14	Epidural bupivacaine 0.1% bupivacaine + 5mcg/ml fentanyl	VAS Placement checked radiologically	Correct placement associated with "effective analgesia"		3
Arms 1998	Case series N=12 10-18yrs	Epidural 0.0625% - 0.125% bupivacaine + morphine	Faces 0-10	Effective analgesia	Pruritus 7/12	3
Goodarzi 1996	Case series N=10 15-18yrs	IT morphine 20mcg/kg + 50mcg/kg sufentanil	Effect on SSEPs	No effect on SSEPs		3

INTERVENTION: Plastic surgery of head and neck (Cleft lip & palate & otoplasty)

AUTHOR	DESIGN	TREATMENT	OUTCOME MEASURE	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
Bremerich 2001	DB RCT N=80 1-20 months Cleft palate	Rectal paracetamol: 10, 20 & 40mg/kg vs placebo	Paracetamol plasma level CHIPPS (0-10) Opioid administration	Plasma levels sub therapeutic No difference in opioid use		1+
Prabhu 1999	DB RCT N=30 4-20 months Cleft lip	Infra-orbital nerve block vs peri-incisional local infiltration 0.125% bupivacaine	Pain **relief** score (Attia) 0-20 At 0,1,2,4, 8 & 24 hrs	Statistically significant better pain relief up to 8 hrs post-op with IOB. IOB less rescue analgesia	Not recorded	1+
Cregg 1996	Single blind randomised N=43 3-15 yrs Otoplasty	Gp A local infiltration with 1% lidocaine with epi 0.4ml/kg Gp B regional nerve blockade with bupivacaine 0.5% 0.4ml/kg	Pain score (0-10) At 0, 30,60,90,120,180, 240, 360 & 480 min Time to 1st supplemental analgesia	No differences in pain scores, supplemental analgesia or PONV Time to 1st supplemental analgesia 8.6h gp A, 10.5 gp B	Haemostasis better in lidocaine with epi gp	1-
Dawson 1996	Single blind, randomised N=34 Mean age 11 yrs Alveolar cleft bone graft	All received PCA morphine 0.015mg/kg 8 min lockout 18 received ketorolac 1mg/kg loading dose followed by 0.5mg/kg 6h	Morphine usage Time to mobilisation & discharge	No difference in morphine usage No difference in time to mobilisation or discharge	Effect on bleeding not studied	1-
Eipe 2006	Case series N=20 Cleft lip	Infra-orbital nerve block	Time to 1st analgesia	6-24 hrs analgesia		3
Sylaidis 1998	Case series N=20 6m-9y Cleft palate	Diclofenac 1mg/kg 12 hrly & Paracetamol	Risk of post-op haemorrhage	Effective analgesia No further opiates required	Early discharge Not associated with increased bleeding	3

.

INTERVENTION: Neurosurgery

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Tobias, 1997 #1944}	Case control n=24 13m-10.5 yr	Intrathecal morphine 20mcg/kg vs No treatment (retrospective cohort)	Time to first postoperative analgesia Total dose paracetamol and Nalbuphine 24hr VAS (>5yr) or Unvalidated behavioural scale	Significant delay in TTA (p,0.0001) Significant reduction in total doses postoperative analgesia Scores not reported	PONV, pruritis, urinary retention, respiratory depression (no difference)	2-
{Monitto, 2000 #1587}	Case series n=240 Mixed cases 0-6 yr (2.3±1.7 sd) 12 neurosurgery	Parent/ Nurse controlled analgesia with fentanyl (10 cases) or hydopmorphone (2 cases)	Duration of treatment Daily morphine dose Max daily pain scores ('objective pain score' or self report)	Duration of treatment 4 (3-5) days. Neurosurgery patients 4 (3-5). Morphine use ± 30mcg.kg.hr on ist 2 days decreasing thereafter. At least 80% pain scores, 3/10 on 1st 2 days.	Naloxone for resp. depression 9/250 No significant risk factor (including age) identified.	3

INTERVENTION: Cardiac surgery/ sternotomy

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Finkel et al., 2002, Paediatr Anaesth, 12, 327-31}	RCT not blind 14, 2x7 7mths-7.5 yrs	Intrathecal Morphine 10mcg/kg + hyperbaric tetracacine 0.5% or tretracaine followed by Hypobaric Morphine/saline	Pain score Duration of analgesia 1hrly/12hrs	No difference in scores/duration	PONV decreased in hypobaric group	1- small size unblinded
{Pirat et al., 2002, Anesth Analg, 95, 1207-14}	RCT 30, 3*10 6months-6years	IV fentanyl IT fentanyl IV+IT fentanyl	COMFORT CHEOPS Analgesia in CICU Cortisol Glucose, insulin ,lactate 24hrs.	No difference in pain scores or Time to 1st analgesia	PONV Time to extubation(TTE) No diff PONV TTE IT+IV<IT=IV	1- Small size Randomisation not described Blinding'observer unaware'
{Gupta et al., 2004, J Cardiothorac Vasc Anesth, 18, 454-7}	RCT 70, 2x35 2.5months-14.5ys	IV ketorolac 0.5mg/kg (max 15mg) Commenced 6 hours after admission to CICU. Sig. bleeding in 1st 6 hrs excluded	Bleeding 48hrs	No difference, ketorolac didn't increase bleeding	TTE, Morphine requirement, pericardial effusion. Length of hospitalisation Creatinine. No difference	1+ no pain scores, no difference in analgesic requirements.
{Suominen et al., 2004, Acta Anaesthesiol Scand, 48, 875-82}	RCT 71, 35+36	IT Morphine 20mcg/kg vs Intravenous morphine	Analgesic consumption. Time to 1st analgesia. (TTFA) 24hrs	Morphine consumption (0.03) TTFA 8.7 vs 12.3hrs (0.003)	PONV Itching Respiratory Depression No difference 0.65	1+ Closed envelope randomisation. IT group significantly younger.
{Hammer et al., 2005, Anesth Analg, 100,	RCT 37, 17+18 3months-6years	IT Tetracaine0.5% +Morphine 7mck/kg vs No treatment Remi-based GA technique	Pain score FLACC/Wong Baker	Pain scores lower in IT group for 8 (0.046) and 24(0.05) hours.	Vomiting Respiratory depression	1- Randomisation not described

1283-8}			Analgesic consumption-PCA fentanyl 5+ days	Fentanyl consumption lower at 8(0.003) and 24(0.004) hours.	Itching All no difference.	Observer blinded
{Chu, 2006 #2822}	RCT 40 3.5yrs (±2.5)	IV Tramadol vs IV morphine NCA	CHEOPS Sedation scote TT Awakening TT1st NCA bolus TTTExtubation Vital signs	No difference in pain score Time to awakening shorter with tramadol	PONV Resp depression ICU stay No difference	
{Shayevitz et al.,1996 J Cardiothoracic Vasc Anesth}	Case control (retrospective casenote review) 54, 27=27 5-6 years old (0.3-19)	IV opioid, IVO, Fentanyl (6 mcg/kg/min) vs Lumbar epidural morphine LEM (3-4 mcg/kg/min)	'Global pain rating' using observer VAS Supp opioid medication Time to extubation Transfer from ICU Resumption normal diet. Discharge LOS. 5 +days	"Global pain rating" less day 1 for LEM Supplementary analgesic use less for late extubated LEM No differences for non-pain outcomes in early extubated. Shorter ICU stay, time to normal diet for late extubated	PONV Itch No difference	2- ~47 sets of records examined in each group and 27 selected according to pre-set criteria. Use of 'opioid equivalents' LEM may be useful for selected populations.
{Leyvi et al., 2005 J Cardiothoracic Vasc Anesth}	Rectrospective cohort study 3 cohorts ASD 34, VSD 37, TOF 46	Caudal Morphine 70-110mcg/kg + Bupiv 0.25% 1ml/kg vs IV Opioid	PICU/ hospital stay	No differences detected	FLACC and Morphine consumption in mixed subgroup (25 pts). No difference	2- risk of bias, small number in pain analysis
{Hammer et al.,2000, Anesth Analg 90, 1020-4}	Retrospective case series. 50, 25 SAB and 25 TEB Ages ~3-5ys	SAB tetracaine + Morphine TEB bupivacaine 1.25mg/kg+ hydromorphone	Vital signs Hypercarbia PONV Wong-Baker (>3yr) Unspecified behavioural pain scale (<3yr)	Vital signs, no difference. SAB more Analgesia and sedation than TEB. PONV no difference but SAB received prophylactic ondansetron.		3 (9 cases also in Petersen et al 2000)
{Petersen et al., 2000, Anesth Analg 90.1014-9}	Retrospective case series. 220 (76 non-sternotomy)	SAB Tetracaine +Morphine TEB Bupivacaine or Lidocaine+ Morphine or hydromorphone Caudal Bupivacaine + morphine	OPS (<3yr) Wong Baker (>3yr) VAS>7yr Analgesia	TEB Pain score <5 for 48hr in patients with catheters 51/55 No cath, variable time to 1st analgesia	PONV 86/220 Itching 21/220 Urinary Retention 16/220 (most	3 (9 cases also in Hammer et al 2000)

			requirement	7-13hrs.	catheterised!) Resp depress 4/220 Infection 0 Haematoma 0	

INTERVENTION: Thoracotomy

AUTHOR	DESIGN (?RCT/?DB) (Ages) (n=…)	TREATMENT	OUTCOME MEASURE (include evaluation times)	RESULT & CONCLUSION	SIDE-EFFECT/ SECONDARY OUTCOME & CONCLUSION	EVIDENCE GRADE / COMMENTS
{Bozkurt, 2004 #1879}	RCT (not blind) Ages 2-14 yrs n=32 (16 x2)	Thoracic epidural morphine 100mcg/k vs IV morphine infusion 20mck/kg/hr (LD 50mcg/kg)	Pain (24hr; 1, 4, 8, 12, 24 (Wong Faces) Sedation Compications Plasma Cortisol Plasma Glucose Insulin Se Morphine	Pain scores similar at 1 4 8 12 hrs Epi>systemic 24hr Rescue 5/16 epi 1/16 IV morphine Conclusion no difference	Sedation no diff PONV Epi4/16 IV 2/16	1- I think that IV is superior.
{Matsota, 2001 #1834}	RCT Ages 5-12 n=20 (2x10)	Direct vision Intercostal Bupivacaine (3mg/kg) vs IV single dose pethidine (1mg/kg)	Duration (time to first analgesia) Side effects	Longer duration with ICB	No side effects	1-
{Lynn, 2003 #2853}	Cohort study. Comparison of cyanotic and acyanotic infants n=20 (2x10) 0-90 days	Continuous infusion of morphine to target plasma concentration of 30ng/ml	Modified infant pain scale	Effective analgesia in both groups	Age more important than presence of cyanosis for morphine clearance CO2 response curves similar in both groups	2- ?validity of pain score
{Lynn, 2000 #929}	RCT Infants 42-165 days N=83 Mixed surgery, 5 thoracotomy	Continuous or intermittent (bolus) morphine All received paracetamol	Modified infant pain scale	Infusion more effective at reducing pain scores ($p<0.001$) but higher dose with infusion.		1- low number of thoracotomy patients limits transferability of findings ?validity of pain score
{van Dijk, 2002 #1676}	DB RCT Comparison of IV infusion and bolus N=181 (30 thoracotomy)	Efficacy of 10mcg/kg CI vs 30mck/kg bolus 3 hourly. Following 100mcg/kg loading dose.	COMFORT VAS	60% if patients in both groups effective analgesia. Age and dose related differences. 10mcg/kg ineffective in 30% of patients. This dose more effective in neonates.		1- not stated which groups thoracotomy patients distributed.

	Ages 0+3years					
{Cheung, 1997 #951}	Prospective observational study/ case series. Ages: 1.5 weeks Range 0.1-20.4 Newborn to 5 months n=22	Continuous Paravertebral Direct vision catheter placement after surgery. GA with Fentanyl 2mcg/kg. 1.25mg/kg bupivacaine + Epi LD, followed by 0.25mg/kg/hr (fixed rate) All patients received paracetamol	CRIES pain score for 48hr (modified) 'Rescue' IV morophine Serum bupivacaine	18/22 median mean pain score 0.29 (0.00-1.63) 86% satisfactory analgesia. 3 patents rescue morphine. Serum bupivacaine > 3mcg/ml in 3 patients (30, 42, 48hr) No observed toxicity	2/22 leakage of infusate 2/22 accidental disconnection	3 No formal measurement of clinical toxicity
{Downs, 1997 #2864}	Prospective observational study/ case series Ages 1-9 years n=9	Exprapleural Intercostal block (/ paravertebral), direct vision. Bupivacaine LD 0.25-0.5% 0.28±0.1ml/kg) , infusion 0.21±0.09ml/kg/hr Bupivacaine infusion 72±15hr Morphine infusion 48hr	Bupivacaine dose Posoperative morphine requirements (continuous infusion or PCA)	Mean dose bupivaciane 0.28±0.08 mg/kg/hr Morphine < 0.03mg/kg/hr	No PONV No Resp depression	3 Abstract only
{Gibson, 1999 #2860}	Retrospective case control. Ant. spinal fusions and thoracic surgery n=13	Retropleural intercostal catheter Bupivacaine 0.25-0.125% at 0.5ml/hr (n=7)+ IV morphine IV morphine only controls (n=6)	Total morphine use	Morphine 0.544mg/kg/day vs 0.204mg/kg/day P=0.001		2- no pain scores or discussion of quality of analgesia
{Higgins, 1999 #1133}	Retrospective Audit/ Case series Strenotomy and Thoracotomy patients n=114	Administration of prescribed regular analgesia Use of faces pain scale in older than 39 months	Total drugs administered Frequency of pain evaluation	Thoracotomy patients < 24 months old least analgesia Sternotomy patients .36 months most analgesia Pre-dose Scale 35%, post dose 15% Conclusion: analgesia poorly managed		3
{Karmakar, 1996 #952}	Case series Infants 5.3weeks (2d-5months) n=20	Paravertebral block Bupivacaine 1.25mg/kg LD followed by 0.5mg/kg/hr	CRIES Rescue morphine infusion Serum bupivacaine	18/20 (90%) pain score 0.46 (0.0-1.4) Maximum bupivacaine 2.0 cg/ml	1 Patient ipsilateral Horners syndrome.	3

			24hr.	(SD 0.63).		
{Semsroth, 1996 #753}	Case series n=20 9 infants < 15kg 11 children >15kg	Intrapleural bupivacaine LD 0.625mg/kg+Epi, followed by 1.25mg/kg/hr	Pain Score Infusion rate adjustment Supplementary opioid	Intrapleural bupvacaine is effective for infants and children	No Cardiorespiratory complications	3 Abstract only
{Shah, 1997 #2863}	Case series Age 9.8yrs (2-16) n=15	Paravertebral block 9 Pre-emptive 6 Postoperative	Faces Pain Score VAS Rescue morphine requirements	No differences in alalgesia Paravertebral block is effective	No complicationswolf	3 Abstract only
{Ioscovich, 2004 #2623}	Case series 10-15years old n=7 (6 thoracotomy, 1 sternotomy)	Intrathecal morphine 80-100microgm in 2ml saline. All patients received IV paracetamol 1-2 g or dypirone 500mg 6hrly	VAS 2hrly Sedation score Rescue analgesia 24hrs	VAS <3 No additional opioids in 1st 24hrs	PONV 1/7	3
{Kokki, 2006 #2842}	Case series 10m-12yrs n=10	Interpleural bupivacaine +epi 2mg/kg, then 1mg/kg 2hrly for pin score > 4 IV oxycodone 0.1mg/kg if pain score not reduced by bupivacine All received 10mg/kg rectal Ibuprofen 6hrly	Pain score: VAS Total bupivaciane doses Total oxycodone doses	All received 3-10 (6.1 SD 2.3) doses bupivacaine. All children received 3-10 doses oxycodone (6 SD 3.6)	Interpleural bupivacaine = ibuprofen isufficient for thoracotomy pain	3
{Lin, 1999 #2859}	Retrospective case series 7months-27months N=27	1. Single injection caudal bupivacaine 1mg/kg + epi (n=6) 2. Single injection caudal bupivacaine 1mg/kg+epi, +PF Morphine 50-100microgm/kg (n=11) 3. LD Bupiv 0.5-0.75mg/kg+PF Morphine 10+30microgm/kg then 0.1%bupivacaine+morphine 10microgm/ml at 0.25-0.3ml/kg/hr (n=10)	Supplementary postoperative opioid	Continuous infusion (Gp3) no postoperative opioid supplements (p=<0.05)	Duration of anaesthesia Gp3>Gp2 (p0.05) Length of ICU stay: Gp 3 , Gp2 (p<0.05) POEmesis: Gp 2> Gp 3 (p=0.05) Time to oral intake Gp3<Gp2 (p<0.05) Length of hospital stay	2- Unvalidated pain score (0-10)

					Gp3 < Gp1 (p<0.05)	
{Karmakar, 1997 #2899}	Case report N=1 11 months old	Bilateral paravertebral catheters	Pain score Supplementary analgesia Serum Bupivacaine	Satisfactory pain scores No supplementary analgesia Bupivacaine levels below toxic.		3
{Birmingham, 2003 #1114}	Case series	PCEA				3
{Monitto, 2000 #1587}	Case series n=240 Mixed cases 74 abdominal surgery	Parent/Nurse NCA				
{Lejus, 2001 #1266}	Prospective evaluation of epidural over 6 years. n=348 (307 children 12 days to 18 years, median 72 months)	Bupivacaine (mean concentration 0.185%)and Fentanyl (5ug/kg/day). Different types of surgery including fundoplication (9).	Hourly pain scores (Krane et al) Global pain index	Combination provides safe/ effective analgesia	Urinary retention 17% N & V 14% Pruritus 0.6%	3 prospective but not analytical
{Peters, 1999 #343}	RCT n=47 5-18 YEARS Major abdo or spinal surgery	PCA (Morphine) 15mcg/kg/hour + bolus of 15mcg/kg –lock out 10min CI (Morphine) 20 to 40 mcg/kg h	Analgesia (self reporting every 3 hours via VAS) Morphine needs Side effects	Morphine consumption SIG higher in PCA No difference in pain scores	No difference in side effects	1+ Multimodal technique not used. High incidence of moderate to severe pain scores.
{Moriarty, 1999 #595}	Case series/ unmatched cohort study n=272 (n=29 thoracic)	72 children received an infusion of bupivacaine 0.125% + diamorphine 20 microg x ml-1, then 200 children received plain ropivacaine solutions. PRN diclofenac (or codeine)+ paracetamol.	Pain score (‘5 point faces score’ validity not stated) Sedation score ‘Nausea score’ Pruritis	Both methods satisfactory analgesia (±20%incidence of moderate pain: pain scores < 3).	Difference in side effects for PONV and pruritis (significance not reported)	3 Thoracic sub-group not specifically identified/reported