

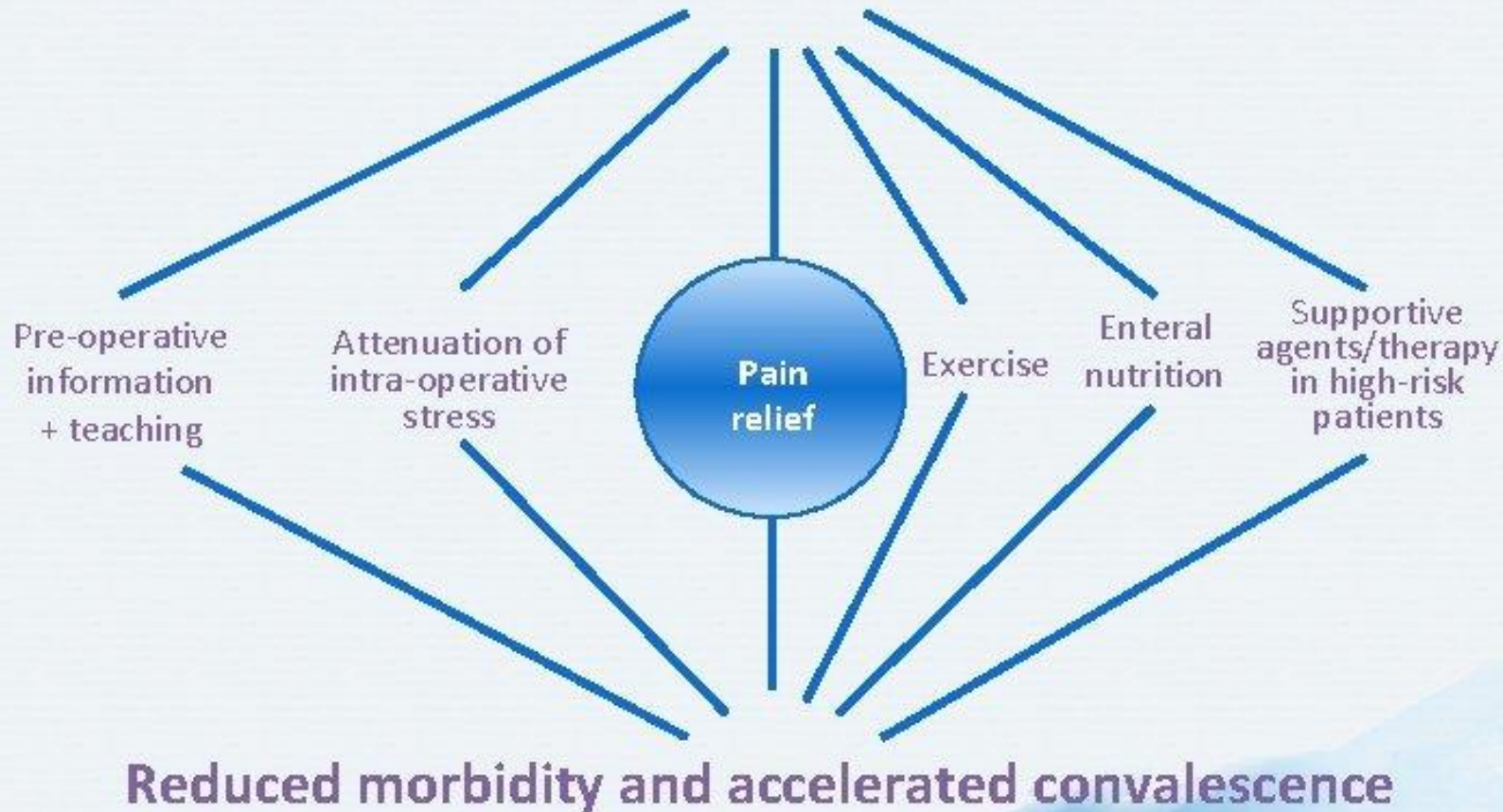
# pain in infants, children and adolescents

*topics and aims*

**why it matters**  
**developmental pharmacology**  
**aspects specific to neonates and infants**

Karel Allegaert, neonatology/clinical pharmacology  
[karel.allegaert@uzleuven.be](mailto:karel.allegaert@uzleuven.be) or [k.allegaert@erasmusmc.nl](mailto:k.allegaert@erasmusmc.nl)

# Controlling Post-operative Physiology



Kehlet H. *Br J Anaesth* 1997; 78(5):606-17.

ORIGINAL ARTICLE

## The severity of analgesia requirements after orchidopexy

David W. Stewart<sup>1,2</sup>,

1 University of Melbourne, M

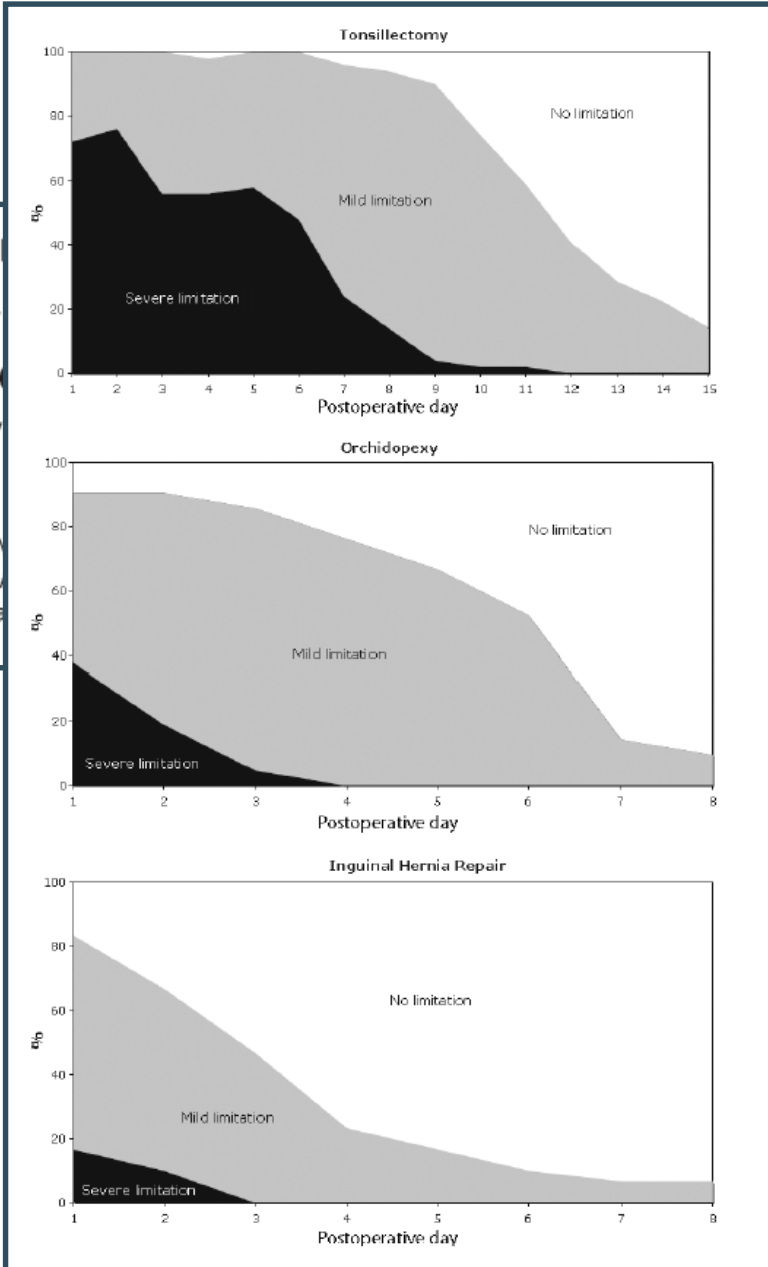
2 Department of Paediatric A

3 Murdoch Children's Resea

## Pain and analgesia requirements after orchidopexy and tonsillectomy

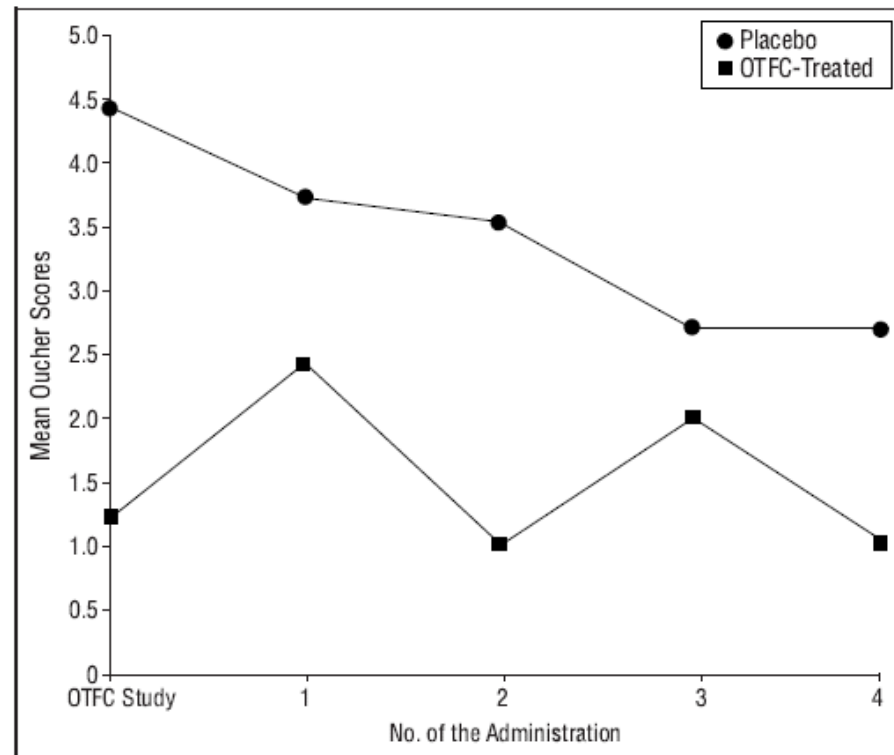
Chalkiadis<sup>1,2,3</sup>

ic., Australia



# Consequences of Inadequate Analgesia During Painful Procedures in Children

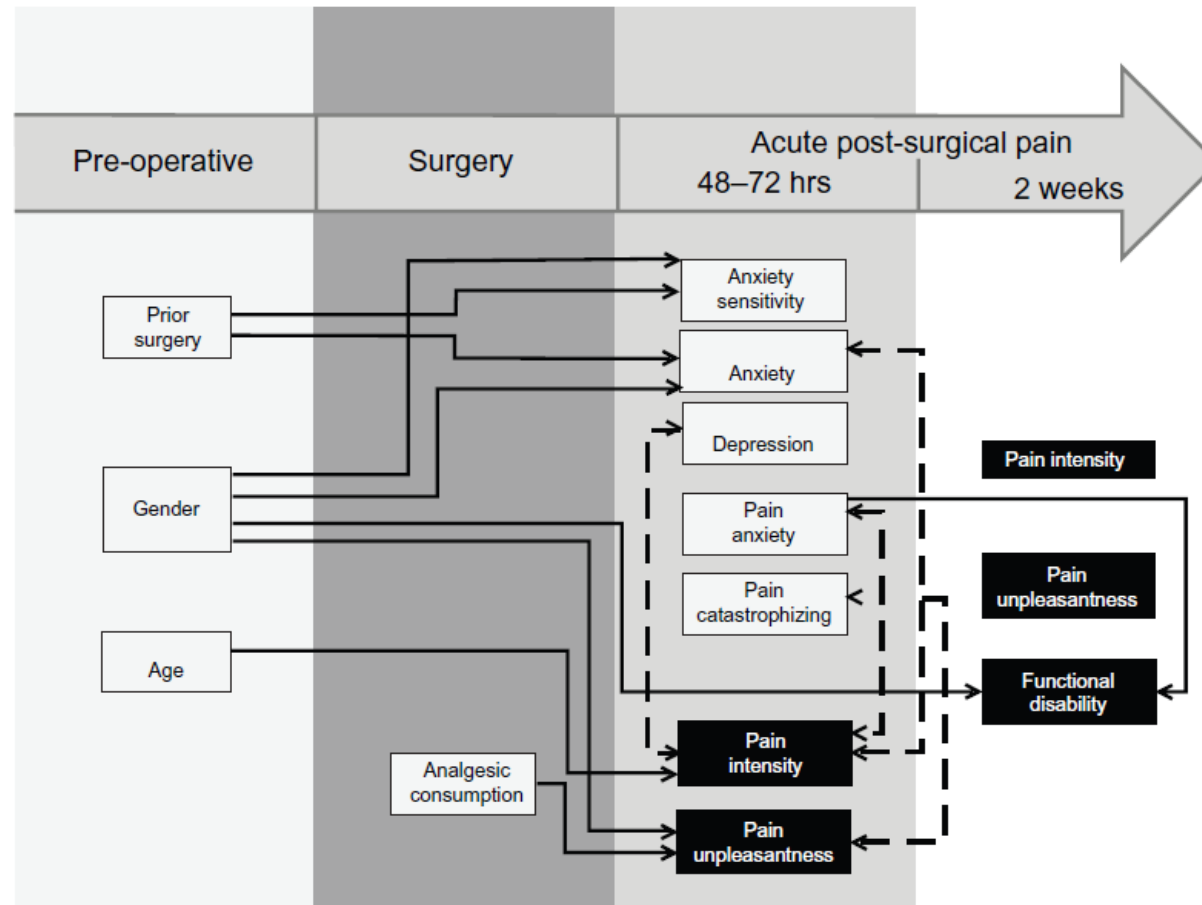
Steven J. Weisman, MD; Bruce Bernstein, PhD; Neil L. Schechter, MD



**Figure 2.** Mean Oucher scale scores for children 8 years old or younger. OTFC indicates oral transmucosal fentanyl citrate was administered for pain.

**Editor's Note:** This provocative little study should make us stop and think about any painful procedure and the long-lasting effects of inadequate analgesia. Once smitten, twice spurned—or something like that.

Catherine D. DeAngelis, MD



**Figure 1** Summary of results showing that children who were surgery-naïve had higher levels of anxiety sensitivity and general anxiety compared with children who had undergone surgery in the past.

**Notes:** Girls reported higher levels of anxiety sensitivity, general anxiety, and pain unpleasantness 48–72 hours after surgery, as well as functional disability 2 weeks after discharge compared with boys. Age, depression, general anxiety, and pain anxiety scores were significantly associated with pain intensity, while analgesic consumption and pain catastrophizing were significantly associated with pain unpleasantness 48–72 hours after surgery. Levels of pain anxiety 48–72 hours after surgery predicted levels of functional disability 2 weeks after discharge from hospital. Plain one-sided arrows represent predictors of pain outcomes. Long-dashed, double-sided arrows represent correlates of pain outcomes. Short-dashed arrows represent predictors of changes in pain and functional disability over time. Black boxes represent pain and functional disability outcomes. Gray boxes represent predictors and correlates.

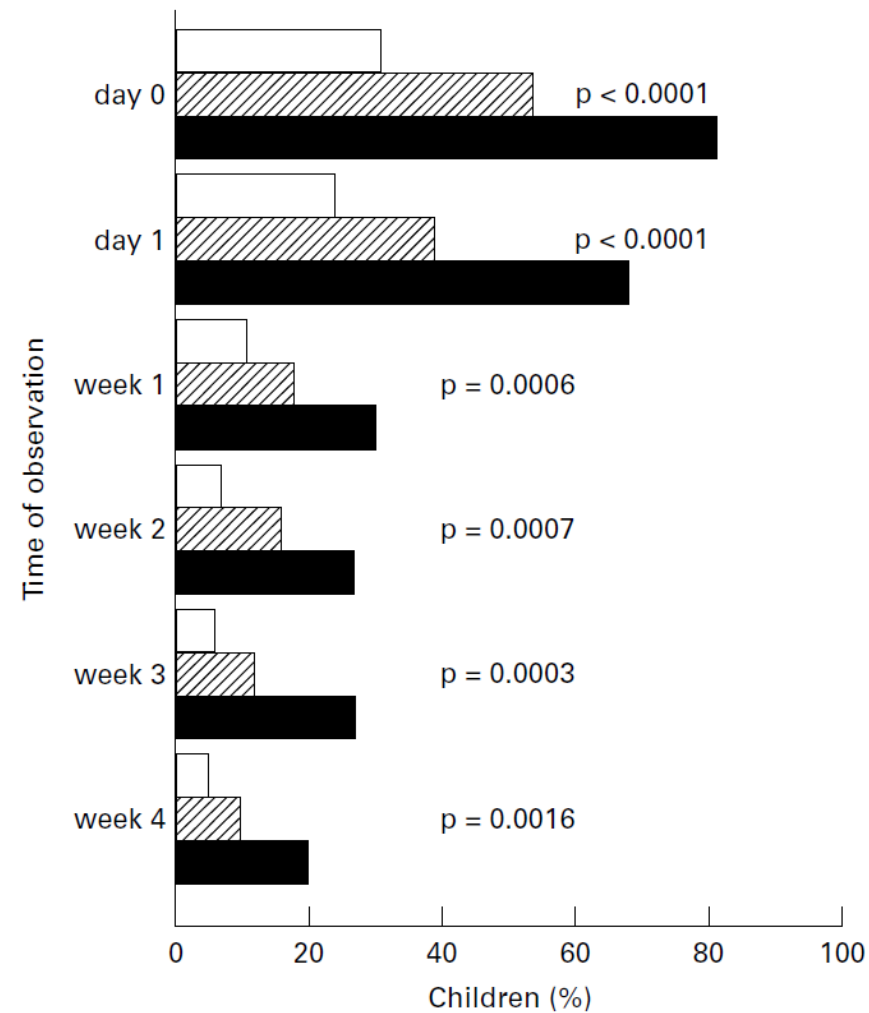
# Behavioural changes in children following day-case surgery: a 4-week follow-up of 551 children

L. H. Kotiniemi,<sup>1</sup> P. T. Ryhänen<sup>1</sup> and I. K. Moilanen<sup>2</sup>

*1 Department of Anaesthesiology and 2 Department of Child Psychiatry, University of Oulu, Kajaanintie 52 A, FIN-90220 Oulu, Finland*

## Summary

The purpose of this prospective multicentre survey was to evaluate the occurrence and the type of changes in children's behaviour during the first 4 weeks following the day of surgery, and to assess the significance of some patient-related factors on the incidence. Pre- and postoperative questionnaires were completed by the parents of 551 children aged 4 months to 13.4 years in five hospitals incorporating nine operative units in Northern Finland. The overall incidence of problematical behavioural changes was 47% and that of beneficial changes 17%. Problematical changes were most common in the 1.0 to 2.9 year olds and the incidence decreased significantly from 46% on the day of the operation to 9% 4 weeks later ( $p < 0.0001$ ). Predictors by multiple logistic regression analysis were age, mild pain at home following surgery, severe pain and a previous bad experience of health care which had adversely affected the attitude of the child towards doctors or nurses. Hospital influenced playing was a significant factor 3 and 4 weeks after the operation. By the 4th week, beneficial and problematical changes were equally common (9%). Gender, previous operations and experience of repeated paracenteses (for treatment of middle ear infection) did not have a significant effect on the incidence. Pain on the day of the operation predicted the occurrence of behavioural problems up to the 4th week, 2–4 weeks longer than the duration of pain itself. The results emphasise the importance of effective prevention of postoperative pain as well as the importance of avoiding unpleasant experiences in all contacts children have with health care. Playing could perhaps be used to help children cope with a short hospital experience.



**Figure 3** The effect of pain at home on the day of the operation (none □, mild ▨ or severe ■ as evaluated by the parents) on the occurrence of problematic behavioural changes in 551 children at different observation times. The p values refer to significance within each of the observation times.



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## Health

## CHILDREN'S HEALTH

## Pain in babies may cause later harm



Photodisc file

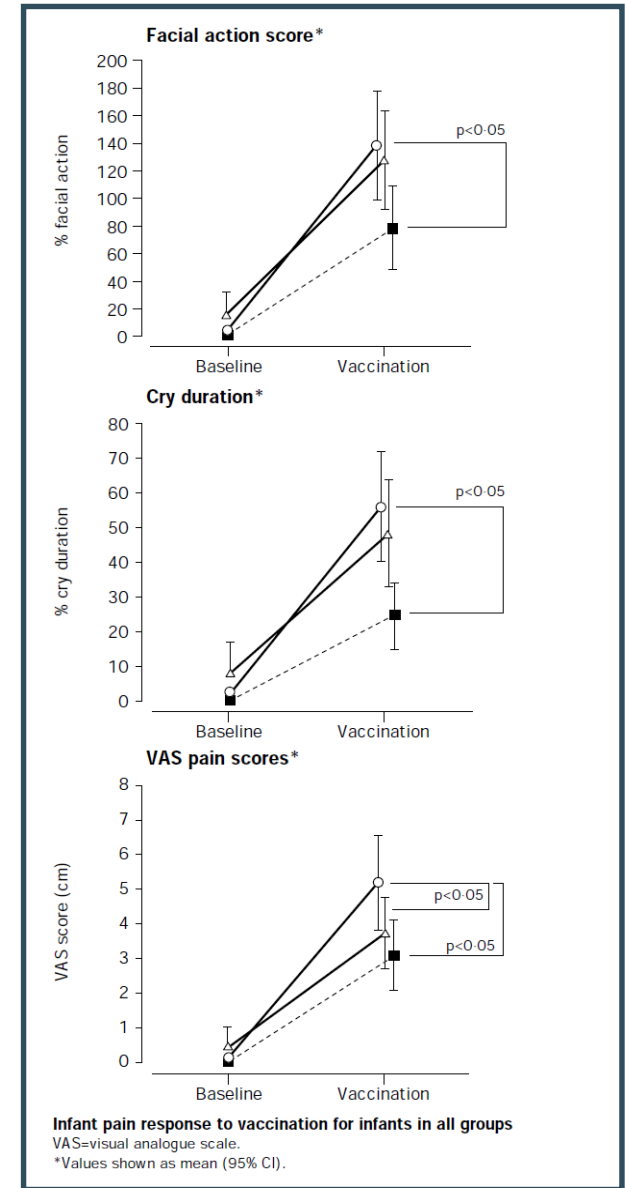
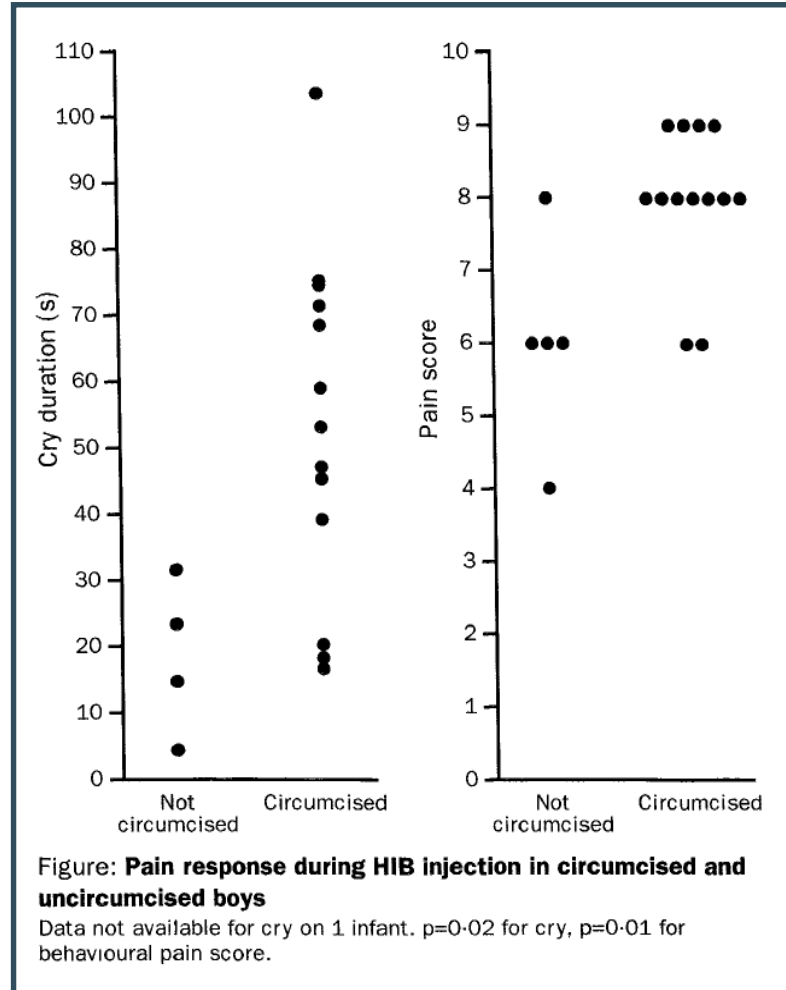
Study in newborn rats suggests early trauma rewires nervous system

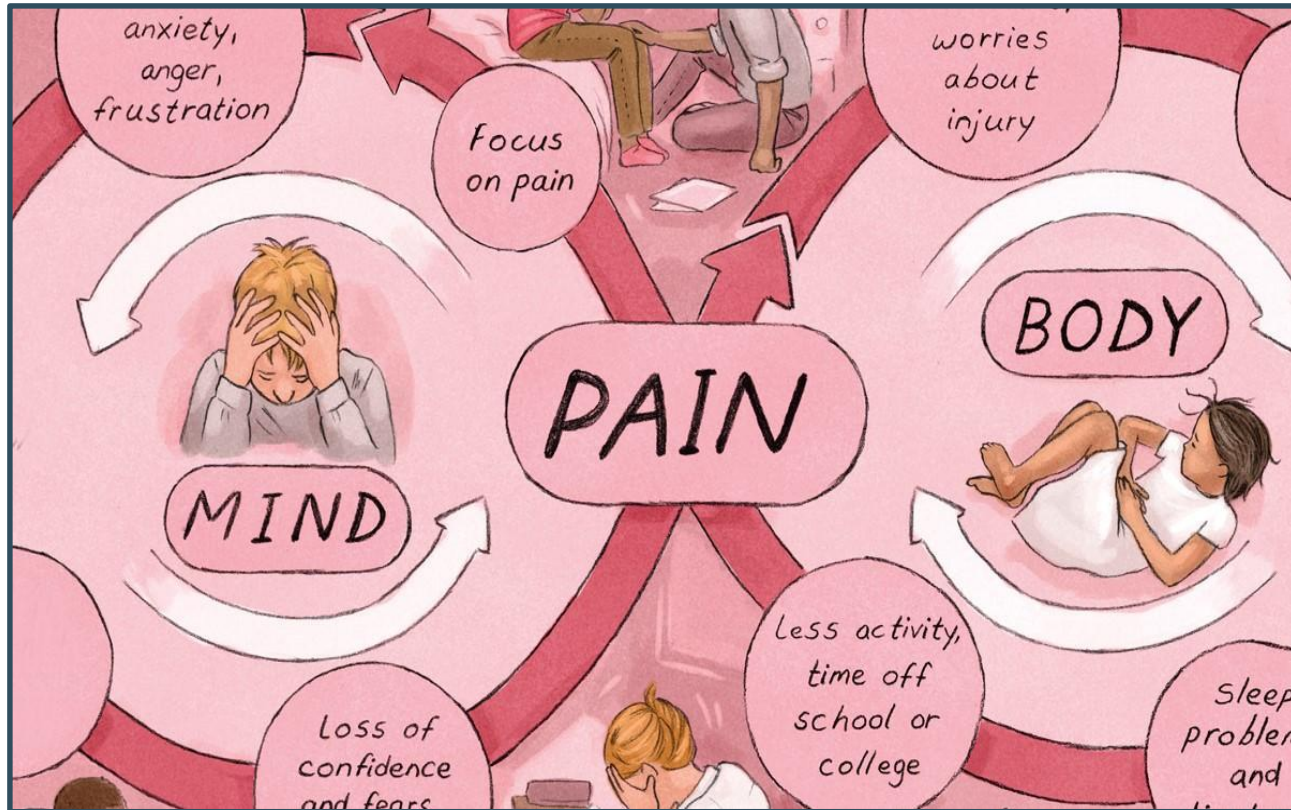
Debate has been raging in the medical community over how newborns experience pain and the impact later on.

REUTERS

July 27 — Newborns who have painful, but often life-saving, medical procedures in the early weeks of life may have a lower pain threshold in later years, according to a new animal study released Thursday.







beyond ethics

targets obviously differ

*age specific*

approaches are similar, but  
different in their applications

*pharmacology*

*physiotherapy*

*psychology*

dose



concentration



effect

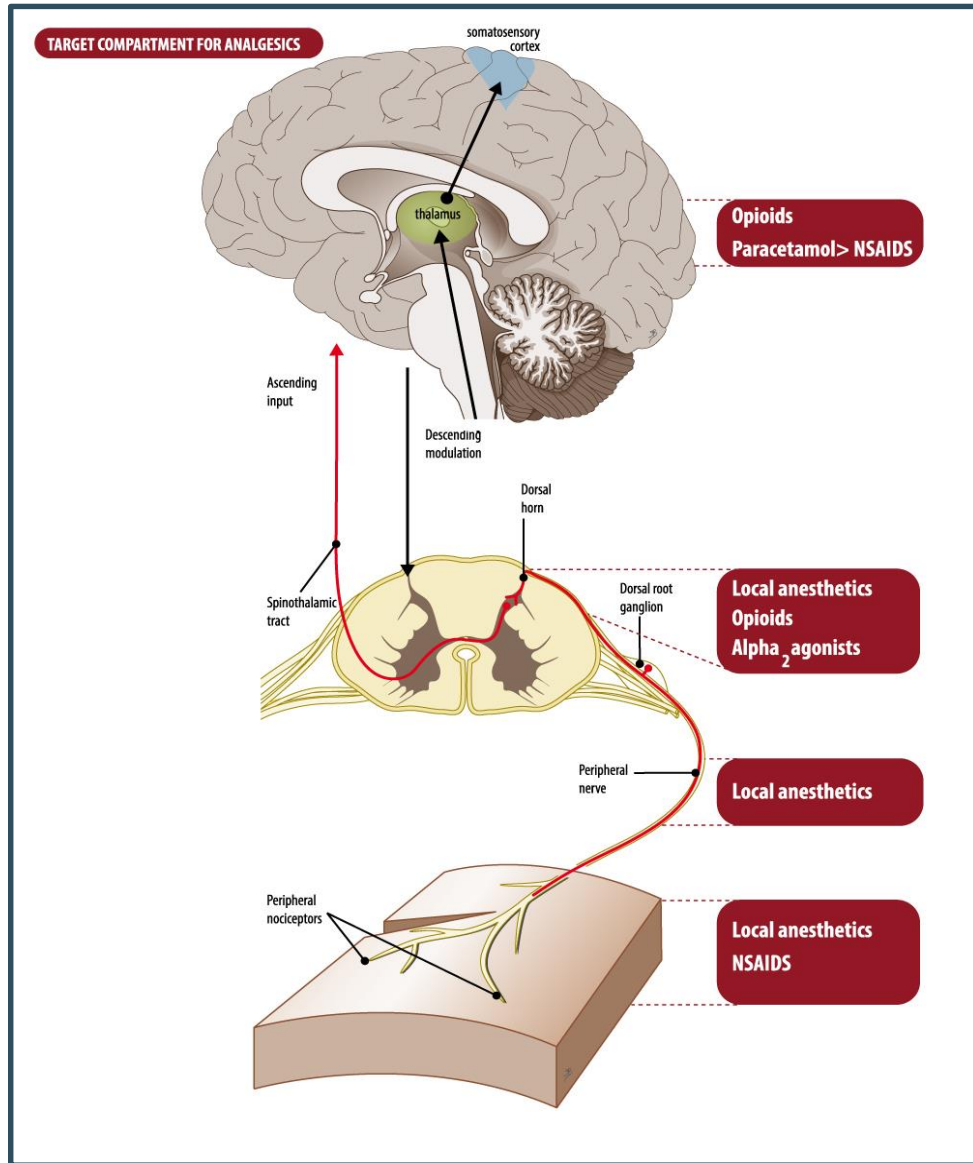
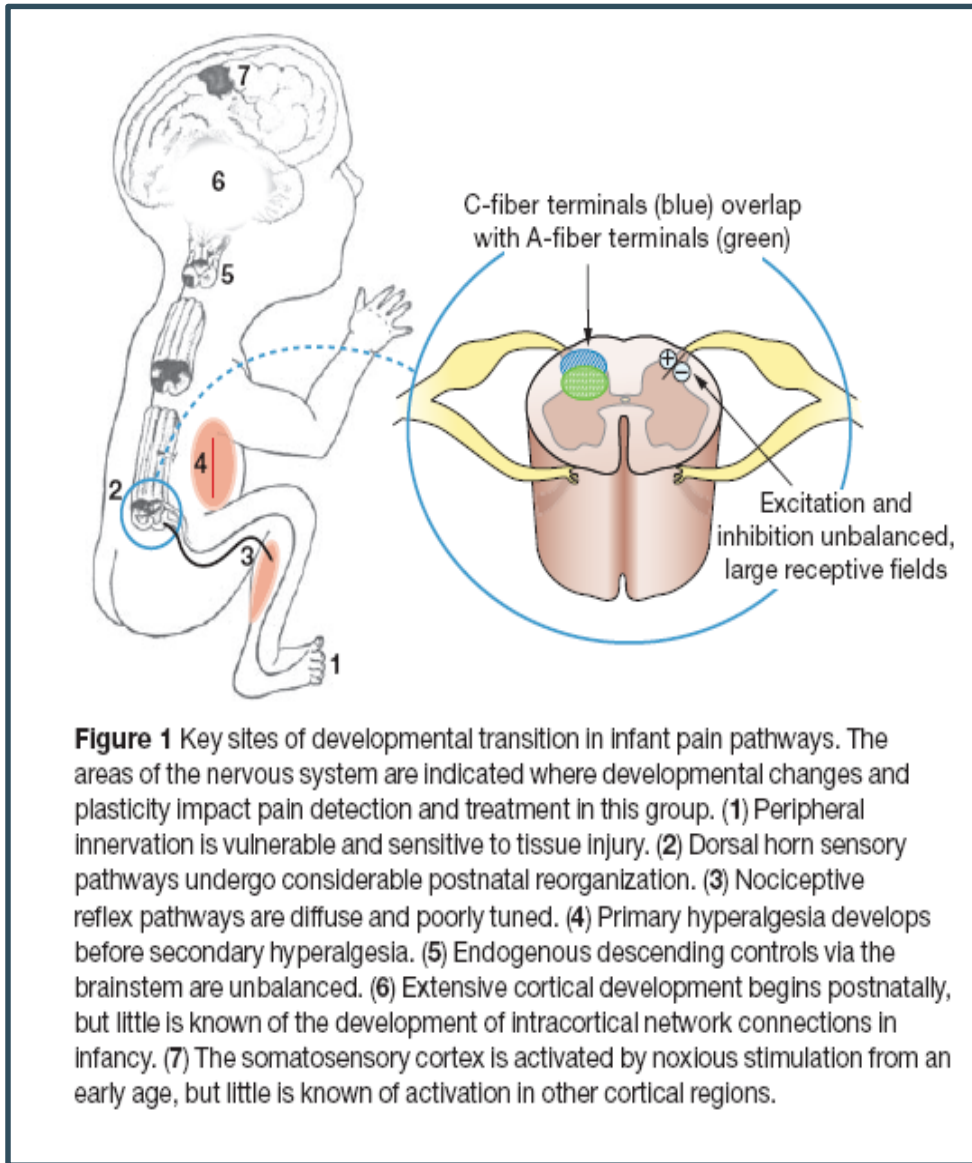
*Pharmacokinetics*

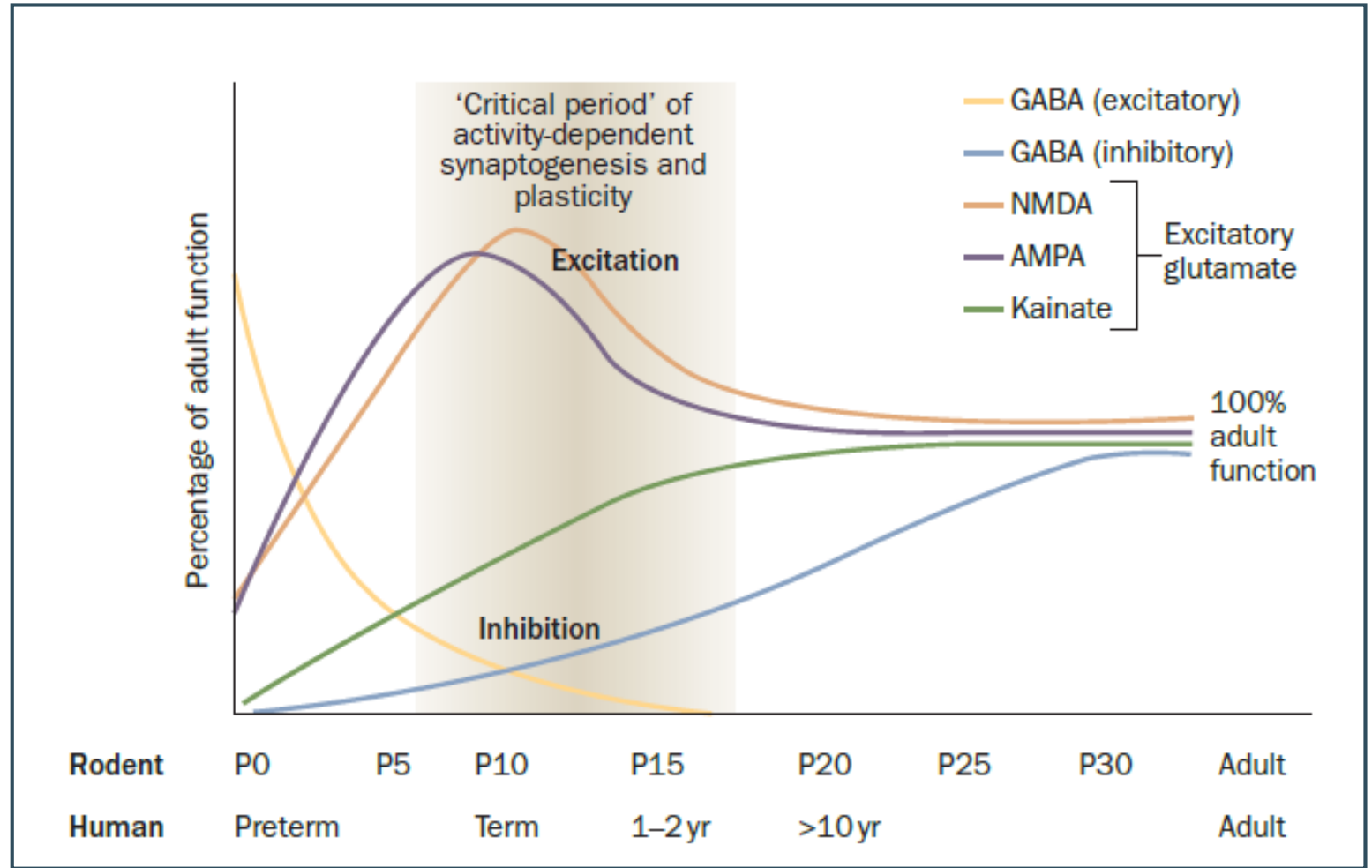
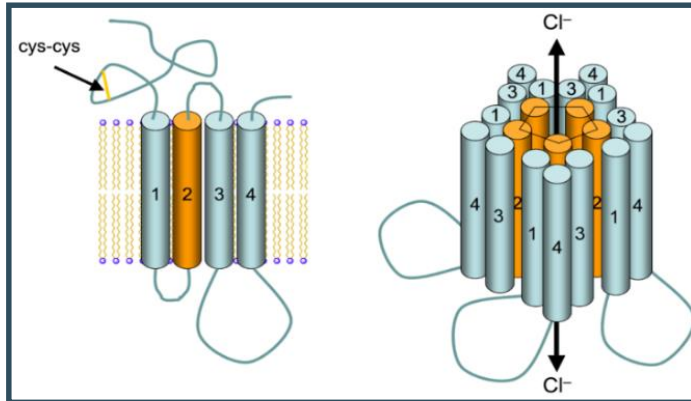
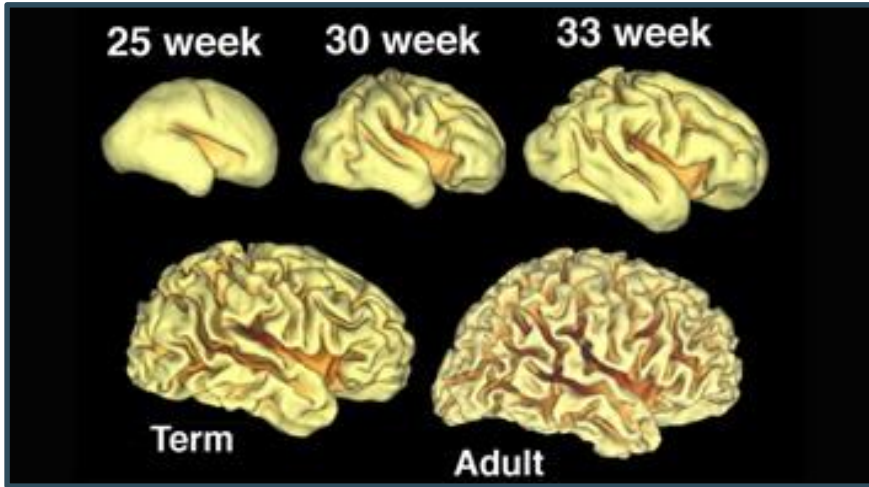
*A*bsorption  
*D*istribution  
*M*etabolism  
*E*limination

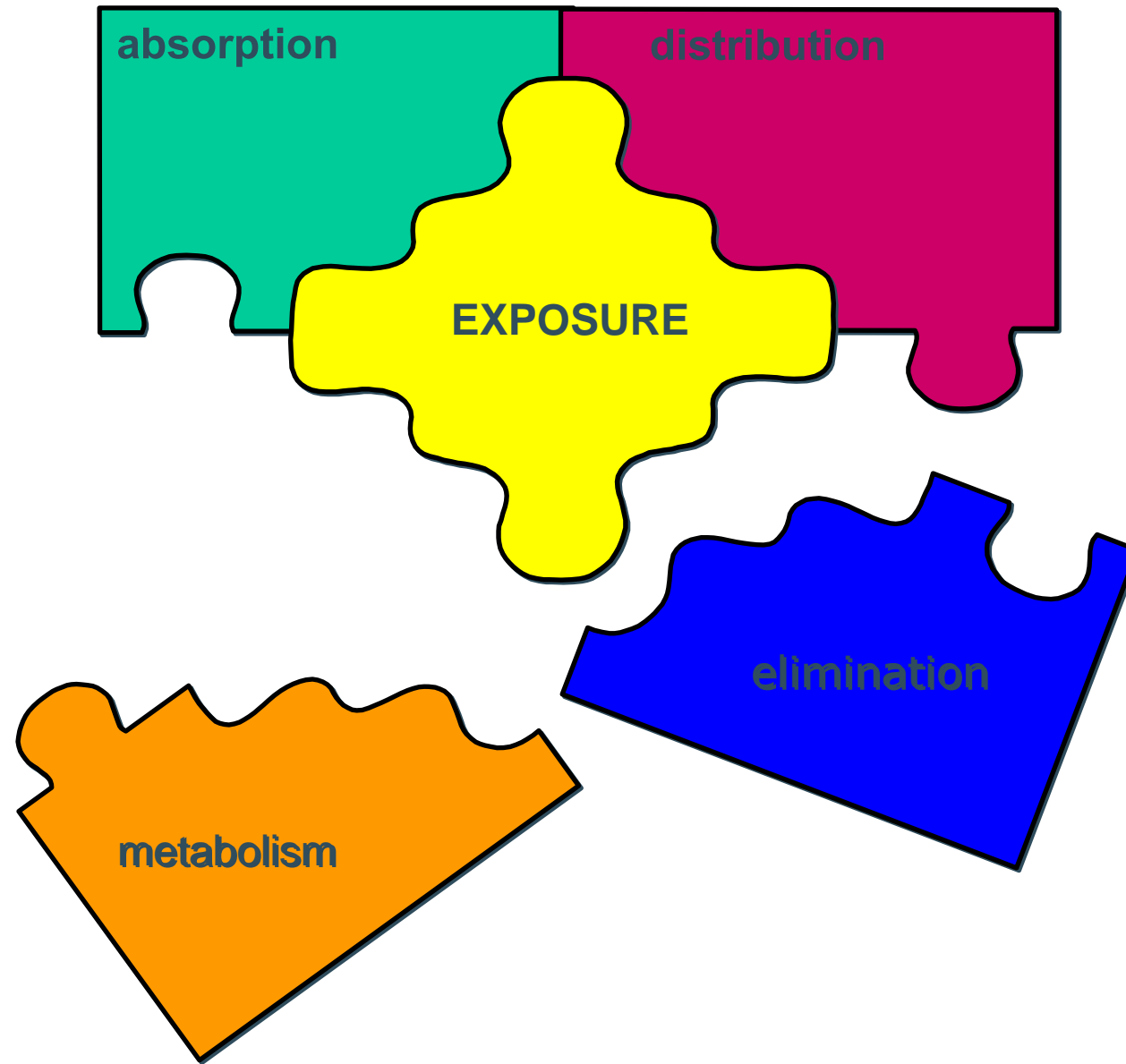
*Pharmacodynamics*

*concentration-effect*  
maturational differences

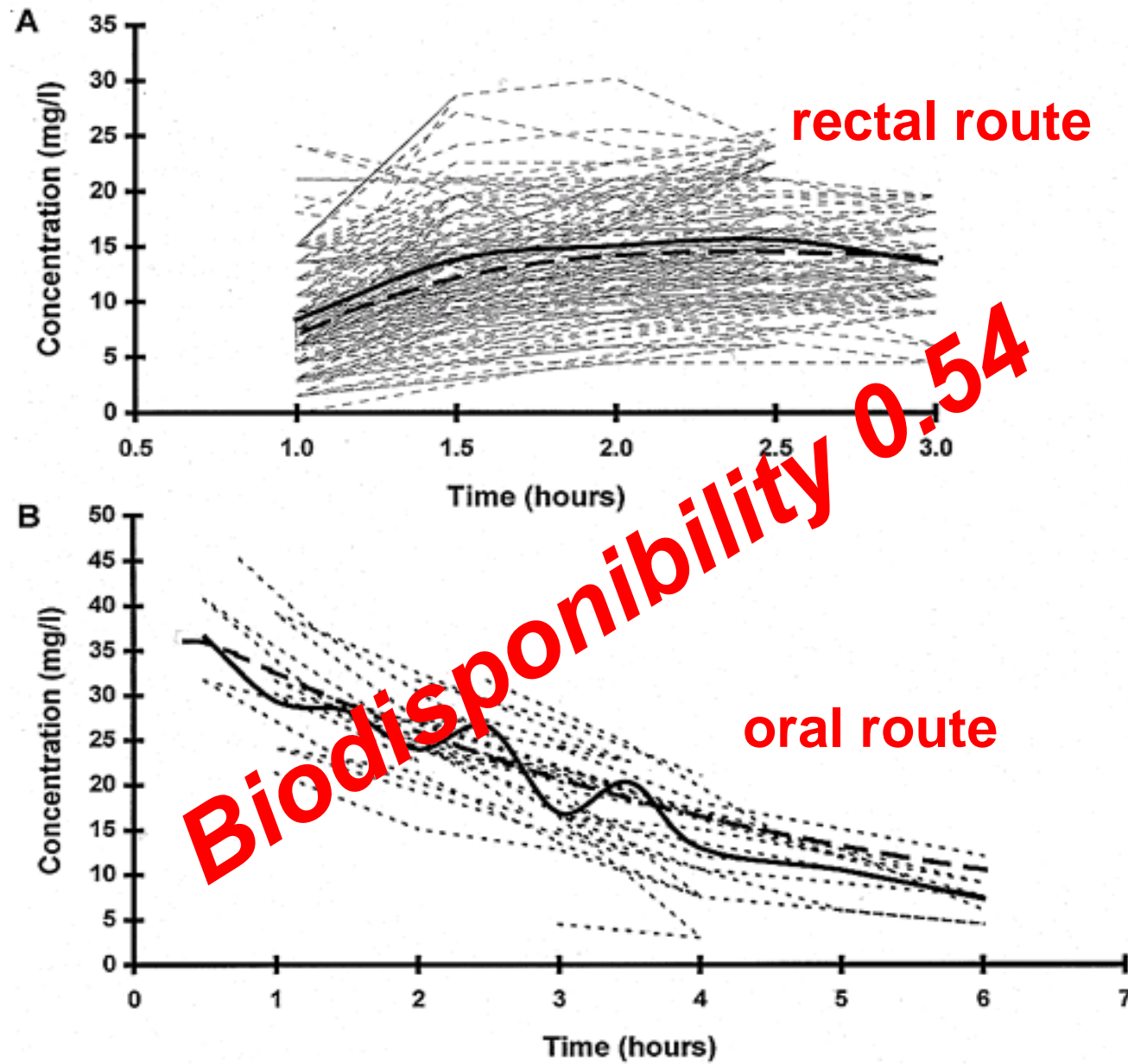








basic PK pattern, **applied to paracetamol** PK throughout childhood



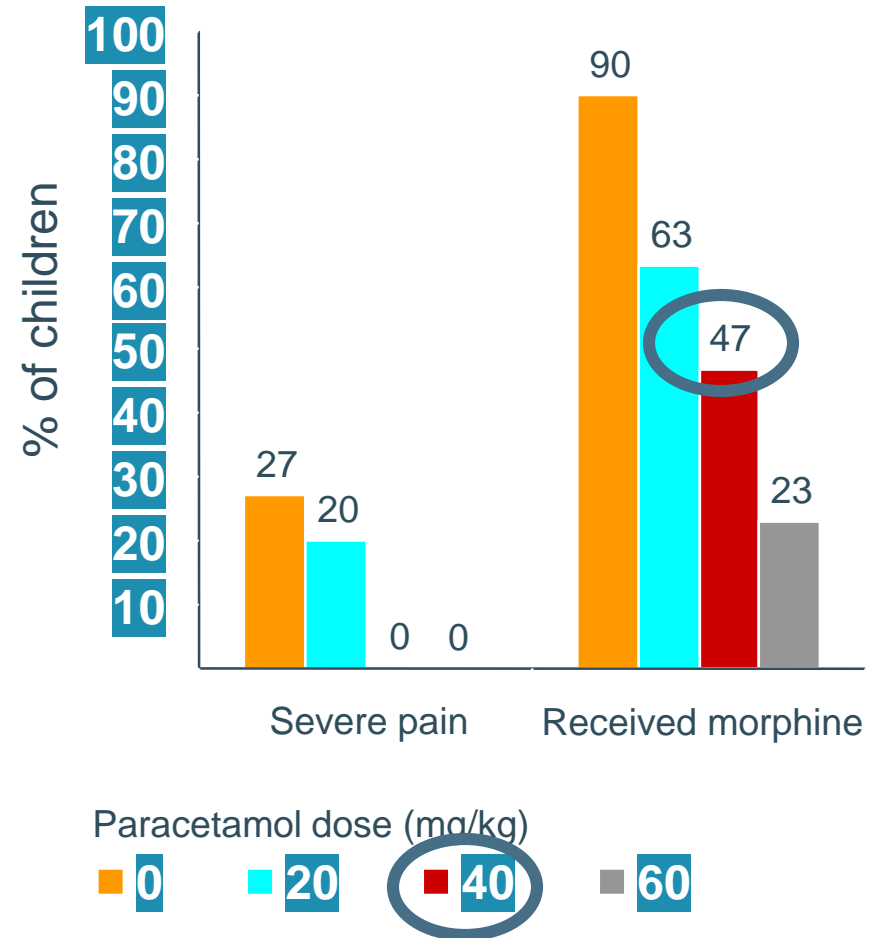
*rectal paracetamol is effective, but...*

Minor surgery

hernia repair, adenoidectomy  
or excision of nevus

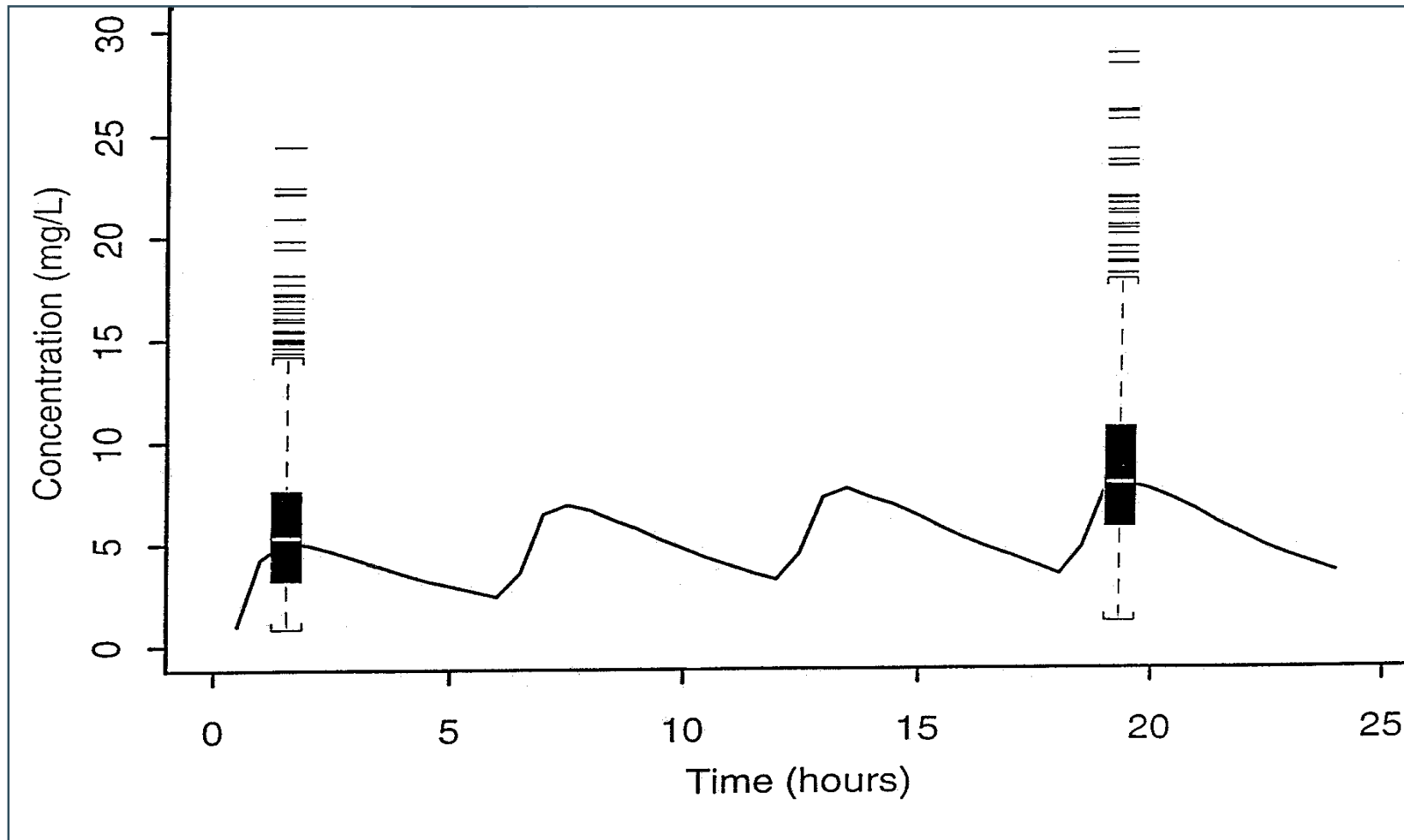
Single rectal dose of 40–60  
mg/kg paracetamol has a  
morphine sparing effect

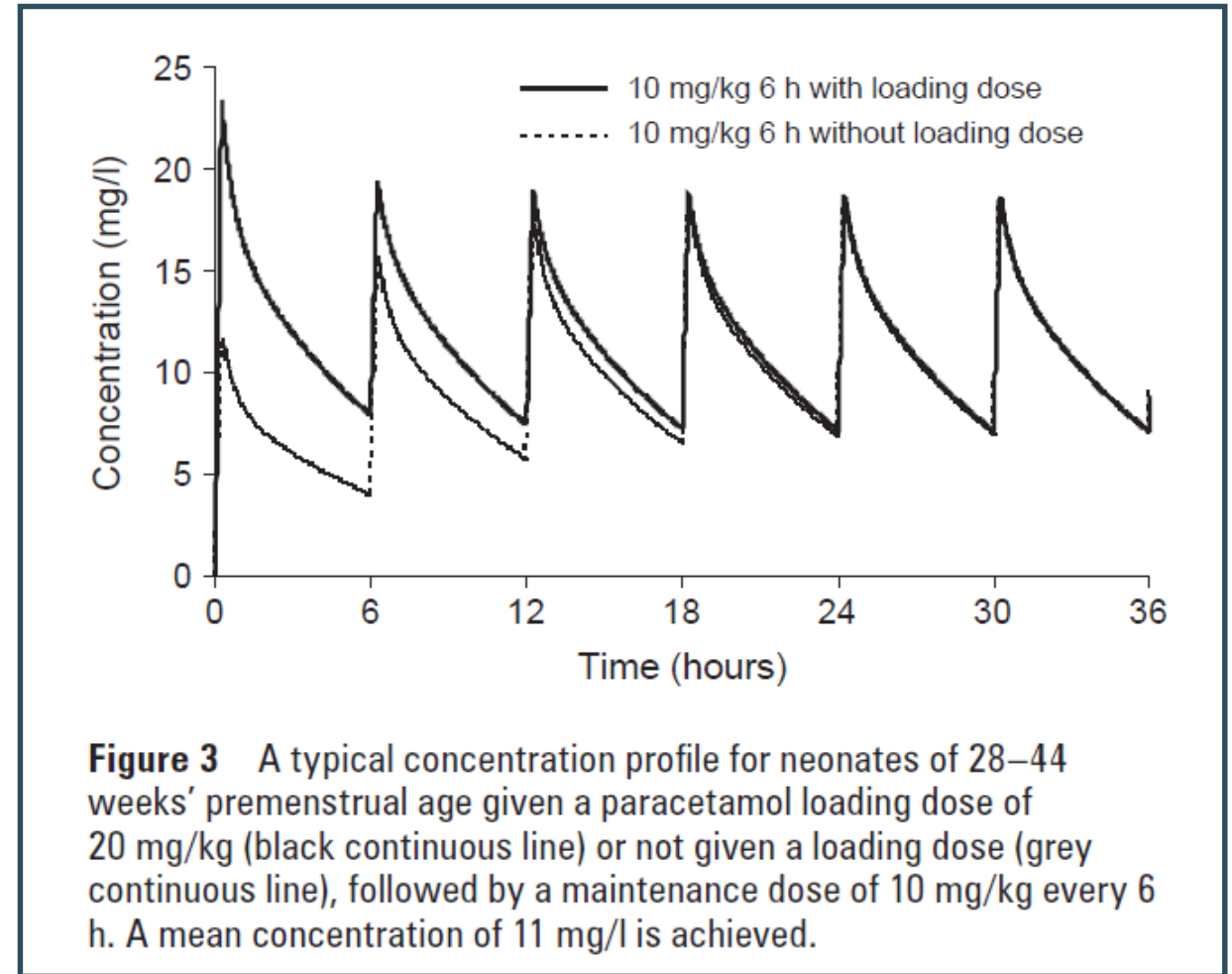
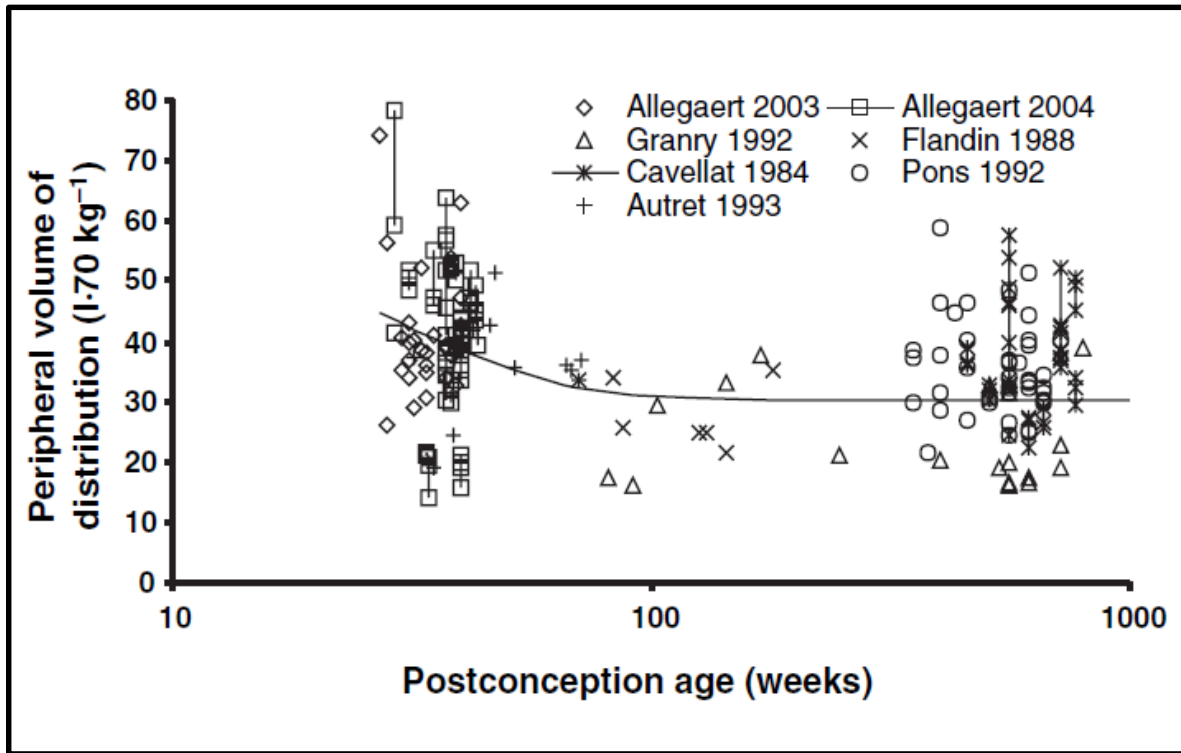
decreased morphine  
requirement can reduce PONV





*rectal paracetamol is effective, but...*





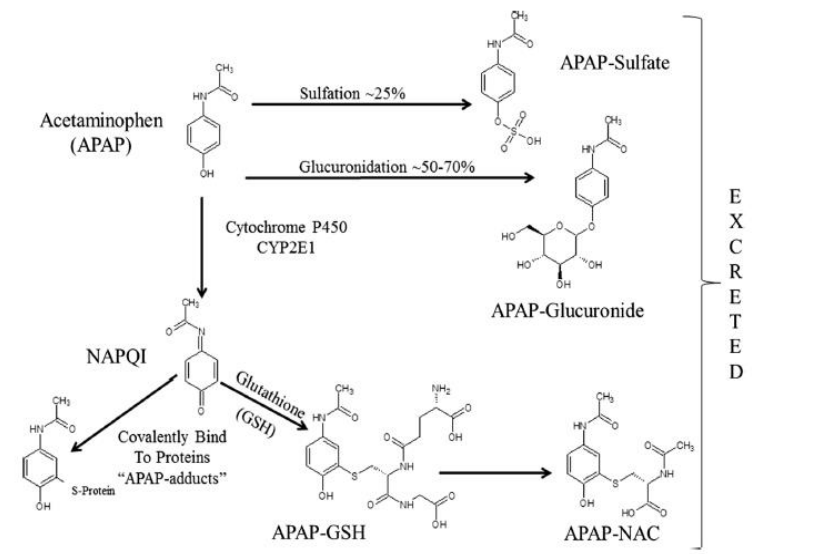
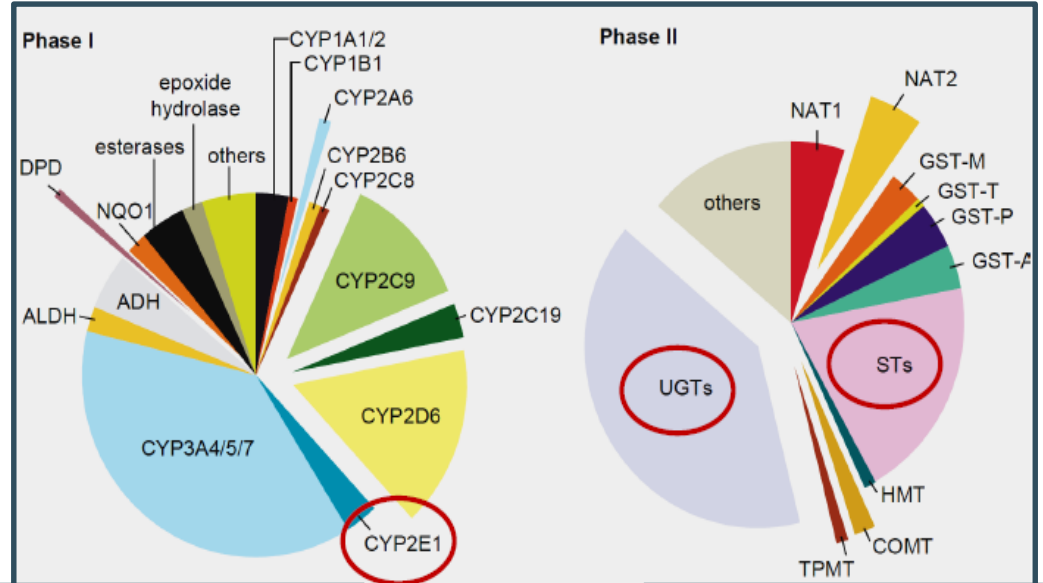
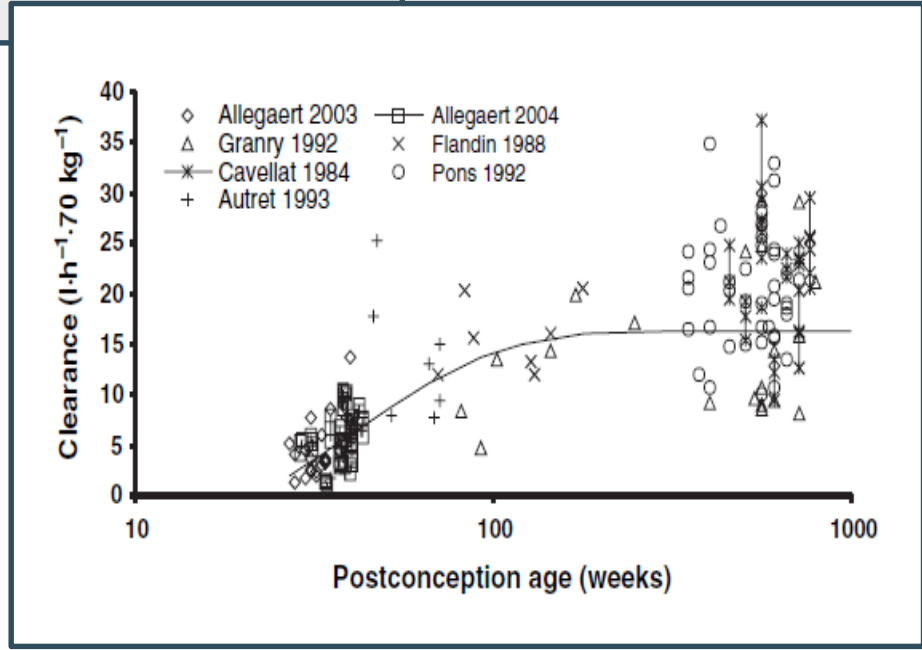


Fig. 1 Cartoon depicting acetaminophen phase II metabolism to APAP-sulfate and APAP-glucuronide. APAP is metabolized by CYP2E1 to NAPQI which can be subsequently metabolized to APAP-GSH with the addition of GSH and then metabolized to APAP-NAC





*Drug choice ?*

in search of synergisms  
clinical path –  
multidisciplinary

## Combination of drugs

160 children (1-6 yr) operated on adenoidectomy  
paracetamol 40 mg/kg (rectal route) and/or ibuprofen 15 mg/kg  
(rectal route) at induction

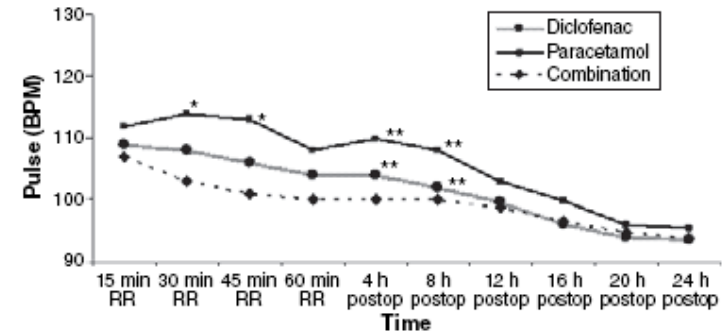
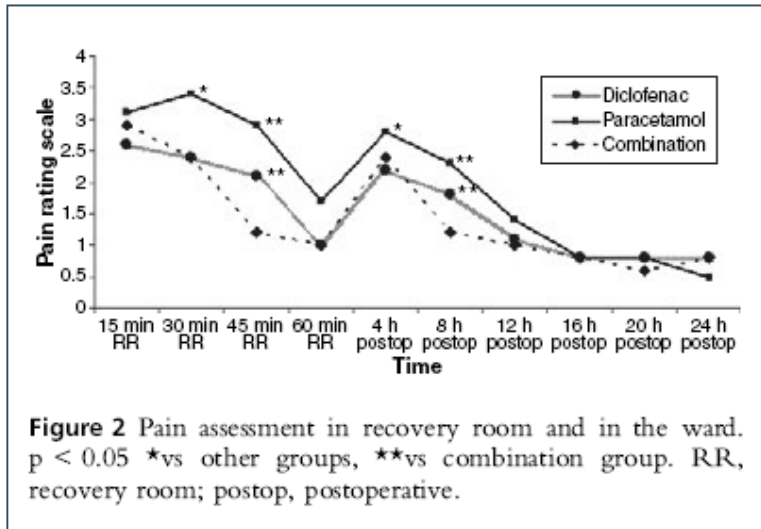
	control n=38	paracetamol n=40	ibuprofen n=41	paracetamol +ibuprofen n=40	
Time to 1st analgesic (min)	10 ± 5	11 ± 11	12 ± 7	13 ± 8	ns
pethidine (mg/kg)	1.0 ± 0.4	0.9 ± 0.4	0.8 ± 0.4	0.8 ± 0.4	ns
Discharge time(min)	124 ± 42	124 ± 36	104 ± 37	133 ± 53	ns
Rescue analgesic at home	77%	74%	76%	49%*	P<0.05

## Pre-operative analgesia with rectal diclofenac and/or paracetamol in children undergoing inguinal hernia repair

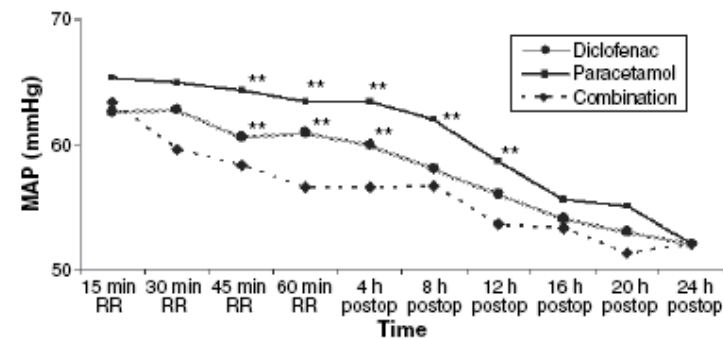
W. Riad<sup>1</sup> and A. Moussa<sup>2</sup>

N = 108 inguinal

paracetamol, 40 mg/kg and/or  
diclofenac, 1 mg/kg  
rectal

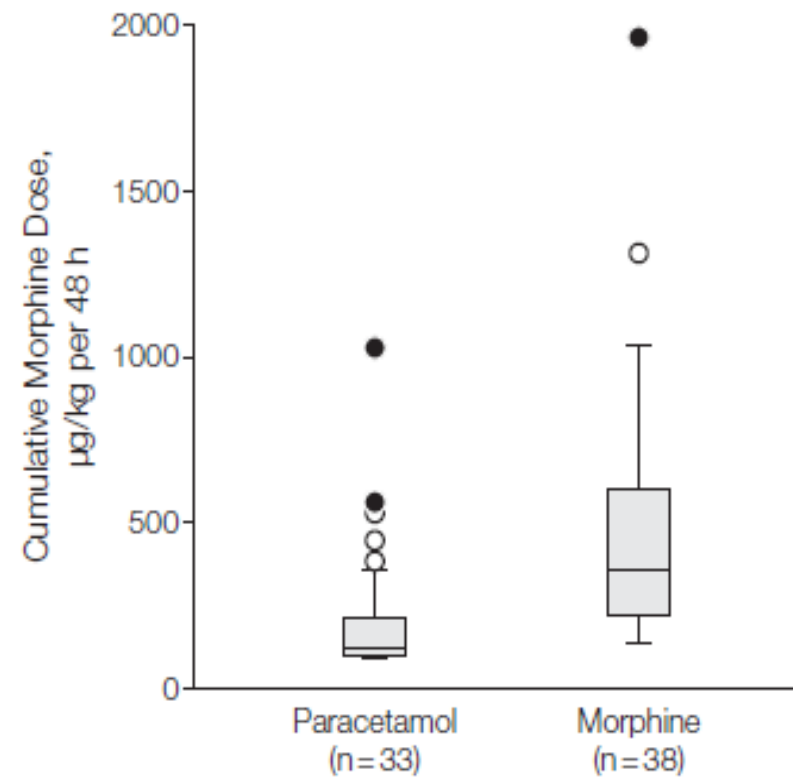


**Figure 3** Pulse measurement in recovery room and in the ward.  $p < 0.05$  \*vs other groups, \*\*vs combination group. RR, recovery room; postop, postoperative.



**Figure 4** Mean arterial pressure (MAP) in recovery room and in the ward.  $p < 0.05$  \*vs other groups, \*\*vs combination group. RR, recovery room; postop, postoperative.

**Figure 2.** Cumulative Morphine Dose for Morphine and Paracetamol Study Groups Over 48 Postoperative Hours

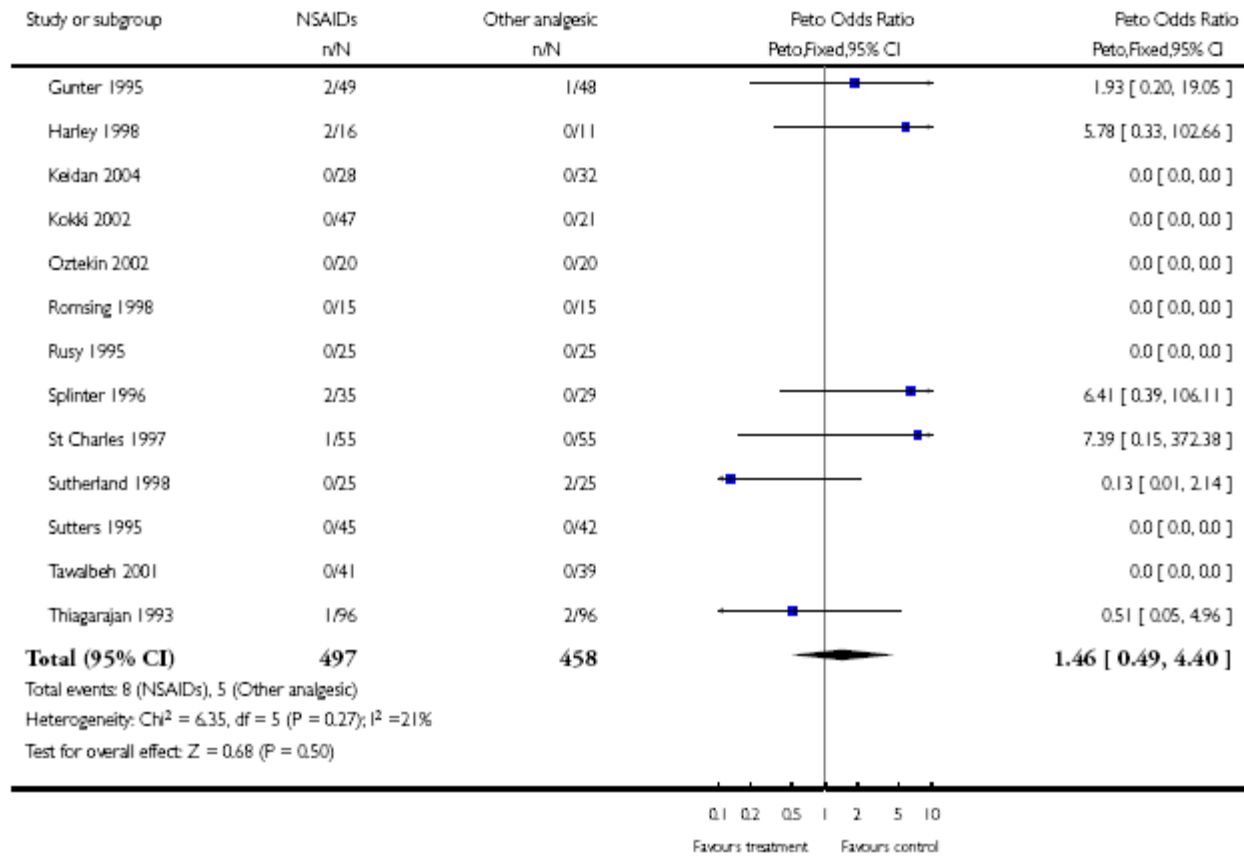


### Analysis 1.1. Comparison 1 nonsteroidal vs other analgesic, Outcome 1 Bleeding requiring surgical intervention.

Review: Non-steroidal anti-inflammatory drugs and perioperative bleeding in paediatric tonsillectomy

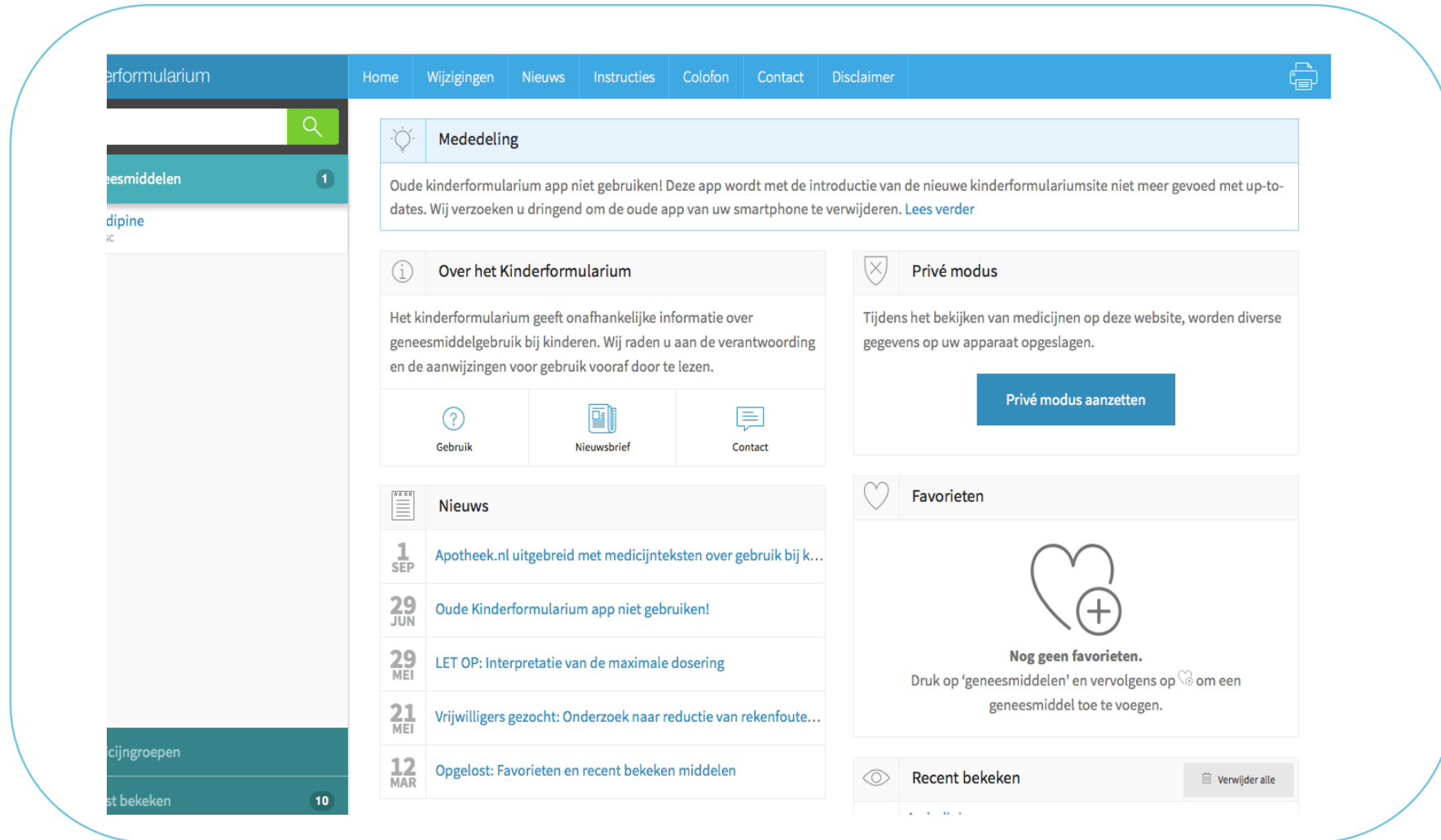
Comparison: 1 nonsteroidal vs other analgesic

Outcome: 1 Bleeding requiring surgical intervention









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Over het Kinderformularium

Het kinderformularium geeft onafhankelijke informatie over geneesmiddelgebruik bij kinderen. Wij raden u aan de verantwoording en de aanwijzingen voor gebruik vooraf door te lezen.

Gebruik Nieuwsbrief Contact

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- 29 JUN Oude Kinderformularium app niet gebruiken!
- 29 MEI LET OP: Interpretatie van de maximale dosering
- 21 MEI Vrijwilligers gezocht: Onderzoek naar reductie van rekenfoute...
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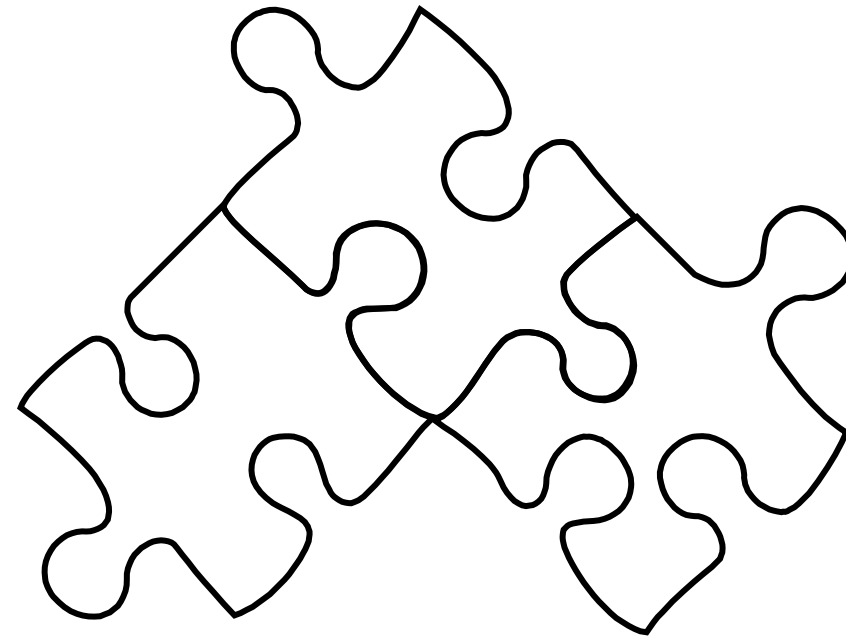
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# *the puzzle of neonatal pain*

treatment

assessment



prevention

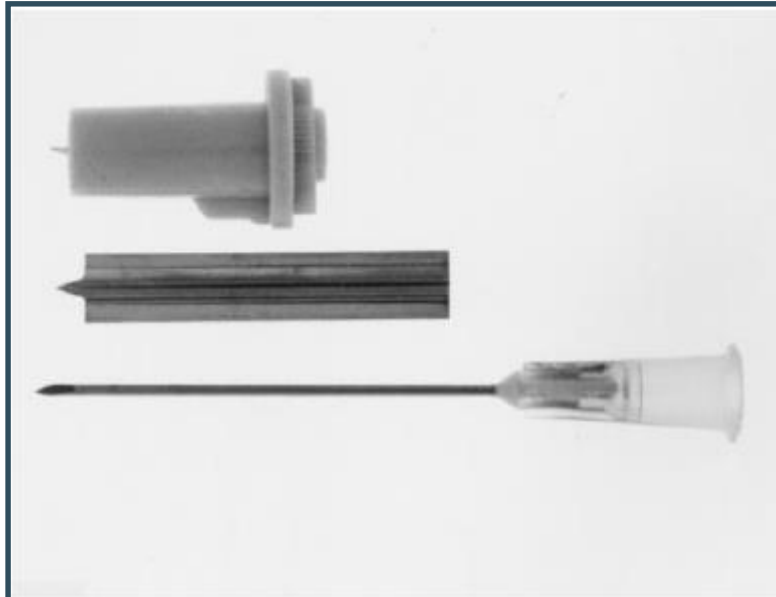
## *prevention matters*



## *prevention matters*

### Venipuncture Is More Effective and Less Painful Than Heel Lancing for Blood Tests in Neonates

Björn A. Larsson, MD\*; Gunnilla Tannfeldt, RN\*; Hugo Lagercrantz, MD, PhD†; and Gunnar L. Olsson, MD, PhD\*



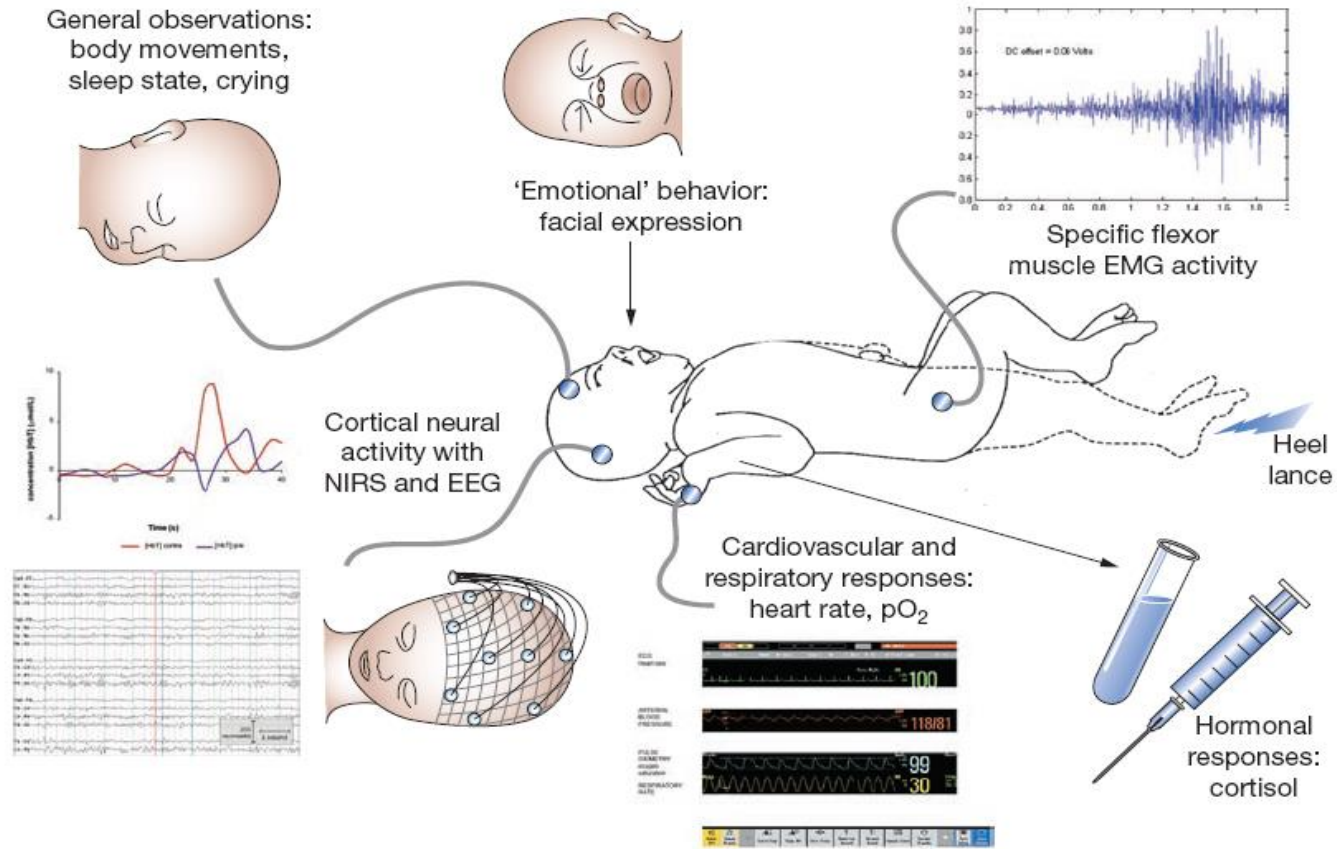
**Fig 1.** Three devices used for the PKU test. From the top: the CCS Minilancet used in the SL group, the Microlance used in the LL group, and the Microlance needle (0.9 × 40 mm) used in the VP group.

## assessment tools

PIPP-R [27, 28]	Premature infant pain profile, procedural pain score. Gestational age, behavioral state, heart rate, saturation, brow bulge, eye squeeze, nasolabial furrow
AN [29]	Douleur Aiguë du Nouveau-né. Procedural pain score. Facial expression, limb movement, vocalizations, and attempts to vocalization
MBPS [30]	Modified Behavioral Pain Scale. Procedural pain score. Facial expression, cry, and body movements
COMFORT [31]	Prolonged pain, including postoperative pain. Alertness, calmness/agitation, respiratory response, crying (only in non-ventilated cases, physical movement, muscle tone, facial tension (initially behavioral and physiologic measures)
COMFORT-neo [32]	Prolonged pain, adapted from the COMFORT score. Similar to the comfort score, 7 behavioral items are scored, but muscular tone is scored based on observations (clenched toes/fists), while “no movement” was converted to “no or minor movement” to adapt for specific characteristics of neonates. One of the behavioral items is either crying (in non-ventilated cases), or respiratory response (in ventilated cases)

CRIS [33]	Crying, requires increased oxygen, increased vital signs, expression, sleeplessness. Prolonged pain, including postoperative pain
FLACC [34]	Face, legs, activity, cry, consolability. Prolonged pain, including postoperative pain
N-PASS [35]	Neonatal pain, agitation, sedation scale. Procedural and prolonged pain, including ventilated or postoperative. Indicators assessed are crying/irritability, behavior state, facial expression, extremities (tone) and vital signs (heart rate, respiratory rate, blood pressure, oxygen saturation)
NIPS [36]	Neonatal Infant Pain Scale. Facial expression, cry, breathing patterns, arm movements, leg movements, and state of arousal
EDIN [37]	Echelle de la Douleur inconfort Nouveau-Né. Facial activity, body movements, quality of sleep, quality of contact with nurses, consolability
NFCS [38]	Neonatal Facial Coding Scale. Brow bulge, eye squeeze, nasolabial furrow, open lips, stretch mouth (vertical and horizontal), lip purse, taut tongue, chin quiver
BPSN [39]	Bernese Pain Scale for Neonates. Respiratory pattern, heart rate, oxygen saturation, alertness, duration of cry, time to calm, skin color, brow bulge with eye squeeze, posture

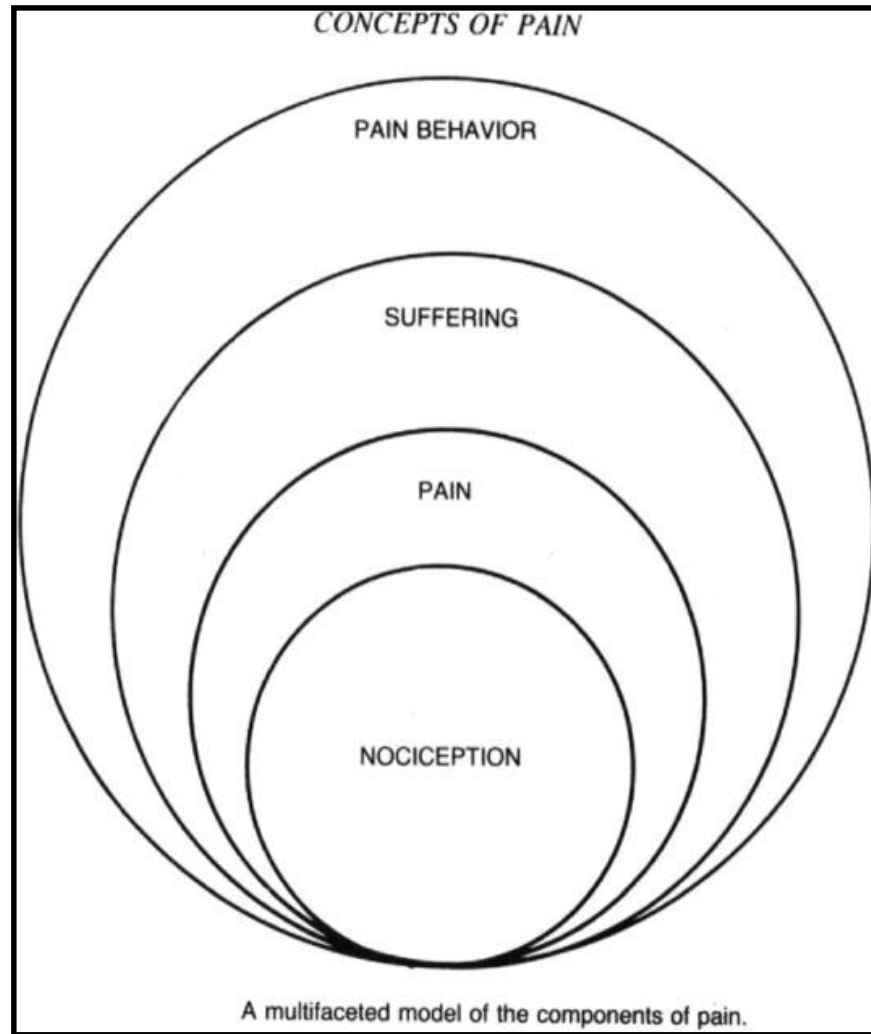
# assessment tools



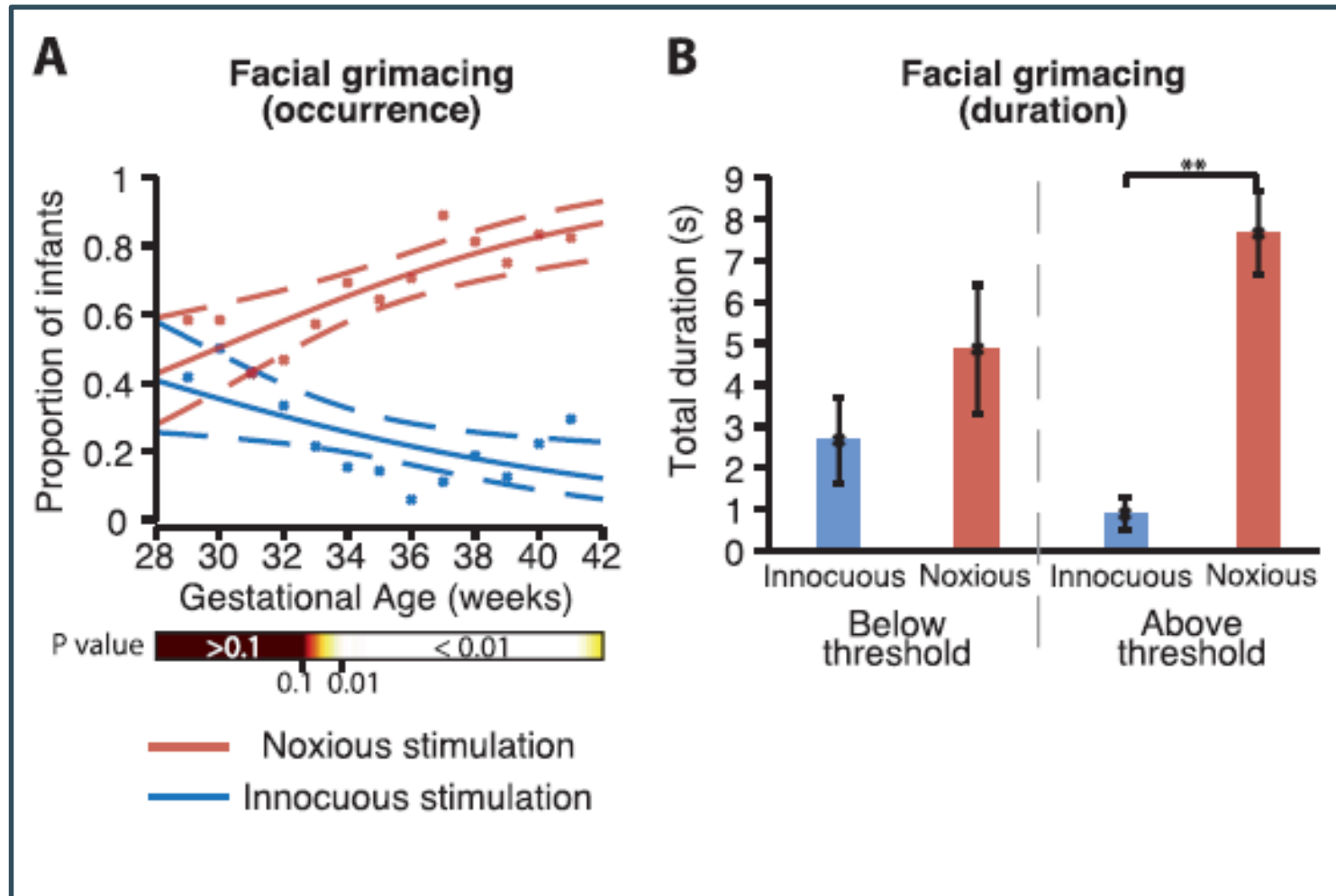
**Figure 2** Methods of assessing infant pain. In the absence of language, infant pain is assessed by a number of different physiological methods. Some of these methods are integrated into current clinical pain assessment tools. The neurophysiological techniques EMG, EEG and NIRS are not used for routine pain assessment but are increasingly being used in research studies of infant pain. Abbreviations: EMG, electromyogram; NIRS, near-infrared spectroscopy; pO<sub>2</sub>, partial pressure of oxygen.



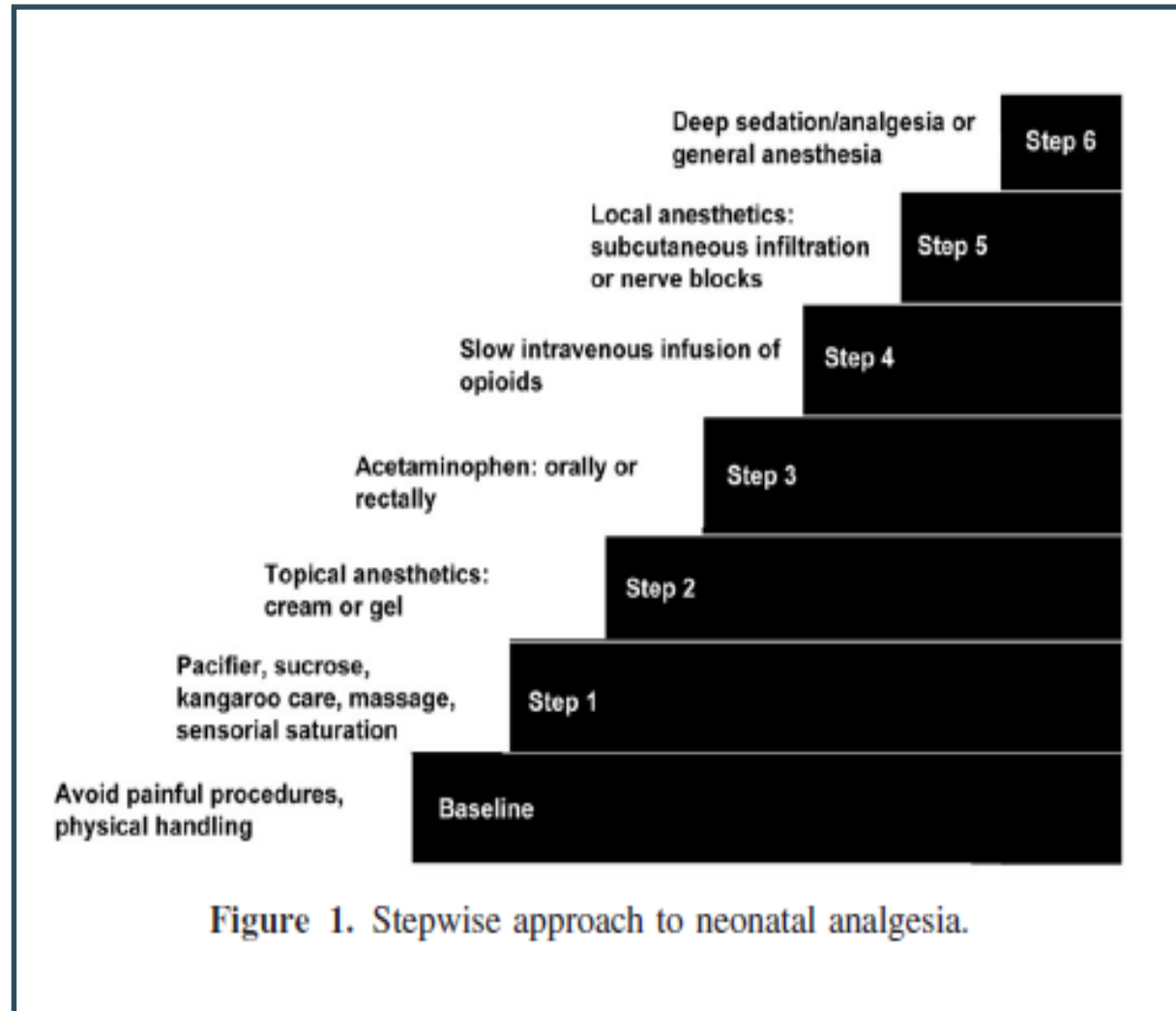
# assessment tools



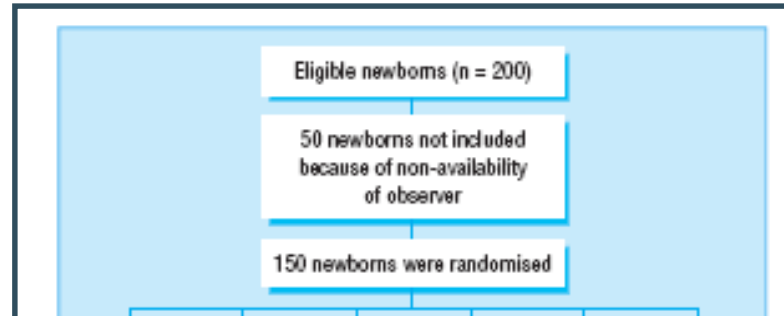
## assessment tools



# *pharmacological treatment*



# pharmacological treatment



Acta Pædiatr 86: 787–8. 1997

## INVITED COMMENTARY

### Calming minds or killing pain in newborn infants?

S Lindahl

*Department of Anaesthesiology and Intensive Care, Karolinska Hospital and Institute, Stockholm, Sweden*

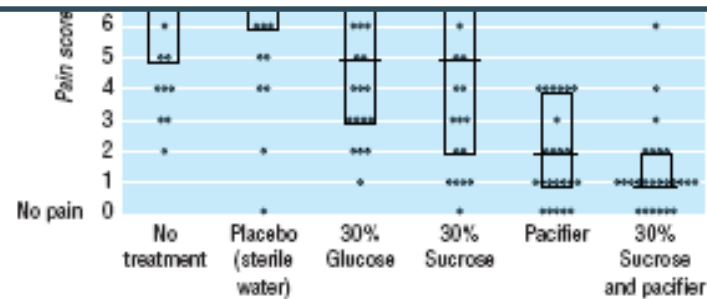


Fig 2 Pain evaluation with DAN scale (0 to 10) during venepuncture in 150 newborns randomised to six equal sized groups, with values for individual infants, median values, and interquartile ranges (for 30% sucrose and pacifier lower quartile coincides with median value)

# pharmacological treatment



## The 3 P's of Helping your Baby during Vaccinations A Parent's Guide: Babies up to 1 year old



Vaccine injections can be painful and stressful for babies and parents, but you can really make a difference.

For your baby's next vaccine injection, plan with your health care provider to:

- 1) Apply topical anaesthetics to numb the skin – these are medicines you can buy at a pharmacy without a prescription.
- 2) Give your baby sugar water for comfort – make sugar water at home or at the clinic by mixing 1 teaspoon of sugar with 2 teaspoons of water.
- 3) Distract your baby – choose an age-appropriate item to bring.

Read the 3 P's of vaccination pain management below and combine these strategies to improve pain relief.

For more information and a video, visit the **SickKids** (The Hospital for Sick Children, Toronto, Canada) website: [www.aboutkidshealth.ca/pain-free-injections](http://www.aboutkidshealth.ca/pain-free-injections).

### STEP 1: PHARMACOLOGICAL (PAIN MEDICINE)



#### Apply topical anaesthetics

#### TOPICAL ANAESTHETICS

- Available products: lidocaine (Maxilene™), tetracaine (Anestop™), lidocaine-prilocaine (EMLA™).
- Apply to either the upper outer part of the leg (infants less than 1 year), or upper arm (infants 1 year old), 30 to 60 minutes before injection – check product instructions.
- If 2 or more injections are planned, apply to both legs or arms.

- May cause temporary reddening or whitening of skin – this is normal. If there is a rash, talk to your doctor – it could be an allergic reaction.
- Avoid acetaminophen (Tylenol™), ibuprofen (Advil™), ice and cold sprays before injection – they have not been proven to reduce injection pain. After injection, acetaminophen or ibuprofen may be used to relieve fever or discomfort.

#### SUGAR WATER



#### Give sugar water

- Give your baby sugar water to drink right before the injection.

### STEP 2: PHYSICAL (BODY POSITION AND ACTIVITY)



#### Hold upright

#### HOLD

- Hold your baby close during injection – in a hug or on your lap. This feels good and helps your baby stay still.
- Avoid holding your baby too tightly – this can increase pain and distress.

#### BREASTFEED

- Start breastfeeding your baby before injection and continue during and after injection.
- If 1 injection is planned, position your baby to expose 1 leg; expose both legs for 2 or more injections.
- If the baby cannot be breastfed, offer a bottle or pacifier starting before injection and continue during and after injection.



#### Breastfeed

### STEP 3: PSYCHOLOGICAL (THOUGHTS AND BEHAVIOURS)



#### Deep breaths

#### BREATHE DEEPLY

- Stay calm and use your normal speaking voice. This helps your baby stay calm – babies look to their parents for how to act and feel.
- If you are nervous, take a few slow, deep breaths to calm yourself before and during injection – breathe so your stomach expands, not your chest. You can do this while holding your baby.

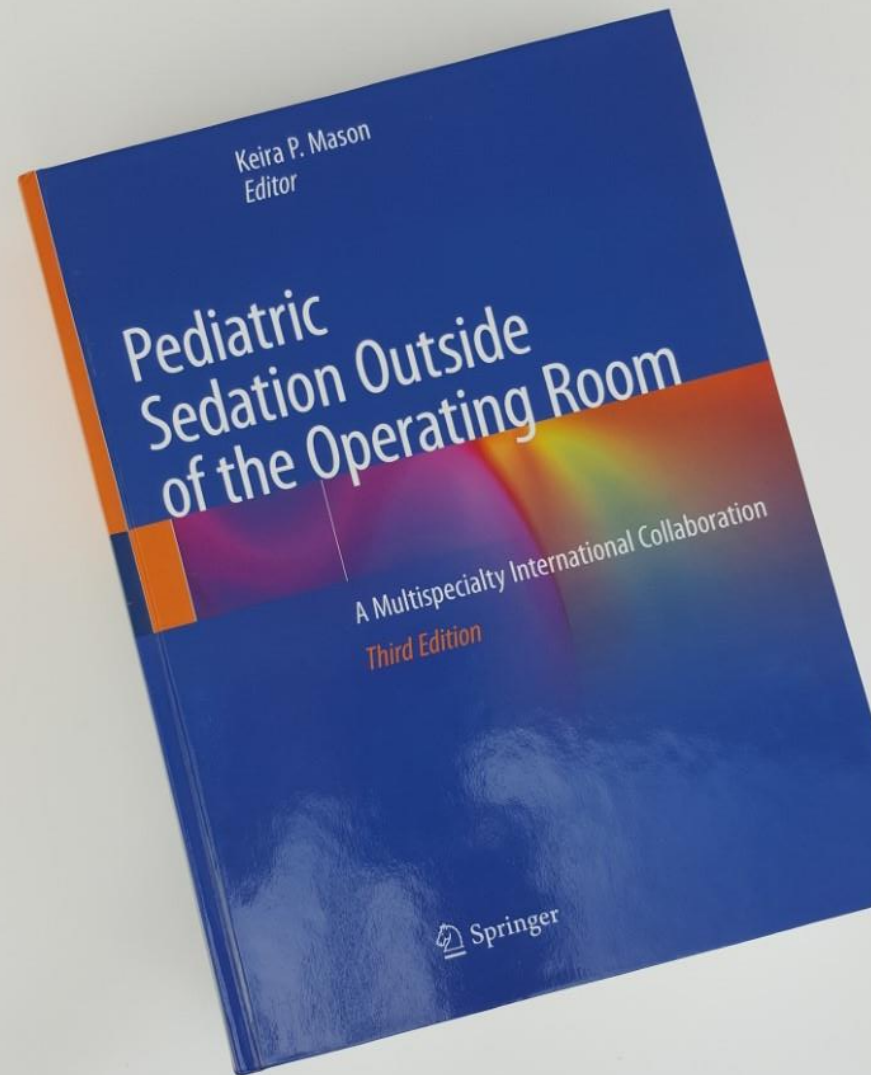
#### DISTRACT

- Help keep your baby's attention away from the injection.
- Distractions you can use: rocking, cuddling, singing, talking, sucking (breastfeeding or pacifier). Distract with objects or toys (bubbles, pop-up books, rattles) when your baby is calm enough to do so; otherwise, distress can be increased.



#### Distract

These are scientifically proven ways of reducing pain in babies during vaccine injections. Think about what worked and plan ahead to make the next vaccination less painful.



Keira P. Mason  
Editor

# Pediatric Sedation Outside of the Operating Room

A Multispecialty International Collaboration  
*Third Edition*

 Springer

## references, pdfs provided

Keira P. Mason (editor), 3rd edition. Springer

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chapter 42: principles of clinical pharmacology, applied to analgesics in children.