The 10 most frequently asked questions listed in order of frequency among responders

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Pediatric Anesthesia
22 (2012) 613–615

Anesthesia Effects on the Developing Brain

- Feasibility and pilot study of the Pediatric Anesthesia NeuroDevelopment Assessment (PANDA) project. Sun LS, Li Q, Biaggioni CJ, Byrne MW, Ing C, Miller TL, Bellegue PC, Han S, McGowan FX.
Volatile and Other Anesthetics

- Young rodents and other animals have shown apoptosis and cell death during critical periods of brain development
- It appears that a very fine balance between neuronal excitation and inhibition in the CNS is crucial, not only for neuronal survival, but for proper maturation and functioning
- Most anesthetics and sedatives increase inhibition

Of Mice and Men

- **Mice**
  - Brain Growth Spurt: first 1-2 weeks of life
  - Anesthetized for 5-6 hours
  - Many unmonitored
  - Pain and surgical stress are harmful

- **Humans**
  - Brain Growth Spurt: prenatal-24 months
  - Equivalent to several days-months
  - Monitored
  - Pain and surgical stress are harmful

3 Editorials in Anesthesiology

- **Anesthesia and Neurodevelopment in Children: time for an Answer?** Sun et al. Nov 2008.
  - Large new epidemiologic based study to examine effects of anesthesia exposure in children<3 under way
  - Siblings used as case controls, 1° outcome; global intelligence and specific domain measures etc in late childhood.

Volatile and Other Anesthetics

- Over-inhibition, just like over-excitation, may be toxic to a developing neuron
- The same agents that may cause over-inhibition of the neuronal system are also neuroprotective during both focal and global ischemia
- All volatile anesthetics, midazolam, propofol and ketamine have been implicated
- So far opioids seem to be OK
SMART TOTs

- Multidisciplinary team of researchers
  - IARS and FDA working in partnership
  - Drs. Roizen and Mehmet Oz
  - Sponsoring many ongoing trials investing both animal and human data
- Timing of exposure
- Duration of exposure
- Multiple exposure
- So far human results are mixed

Abstracts from IARS 2011

- LONG-TERM DIFFERENCES IN COGNITIVE AND LANGUAGE ABILITY AFTER EXPOSURE TO SURGERY AND ANESTHESIA IN INFANCY
  - AUTHORS: C. Ing, C. DiMaggio, A. Whitehouse, M. Hegarty, A. Davidson, L. Y. Sun
  - A history of anesthesia/surgery before age 3 was associated with an increased risk of clinical language impairment between 1.7 to 2.5 fold and abstract reasoning of 3.4 fold
  - Controlled for gender, birth weight, APGAR, race family income and paternal presence at home

Abstracts from SMART Tots 2011

- Creagh et al. Early exposure to anesthesia during cesarean delivery as a factor predisposing to autism spectrum disorder: a population based cohort study
  - Early exposure to anesthesia during cesarean delivery is not associated with the development of autism spectrum disorder
- Flick et al. Exposure to anesthesia and attention deficit hyperactivity disorder
  - Exposure to anesthesia is a significant risk factor for development of attention deficit hyperactivity disorder (ADHD) in children receiving multiple, but not single, anesthetics before age 2 y
Recent abstracts

- Flick et al-2 or more anesthetic exposures before age 5 may be associated with specific language and math difficulties-detailed records
- Sun et al-anesthetic prior to age 3 may have an association with learning problems-Medicaid records
- All concede the difficult in differentiating anesthetic effect from underlying medical condition and surgery

Should we wait to anesthetize infants and young children for elective procedures?

Elective procedures and anesthesia in children: pediatric surgeons enter the dialogue on neurotoxicity questions, surgical options, and parental concerns.
Byrne MW, Ascherman JA, Casade P, Cowles RA, Gallin FF, Maxwell LT.

Duration of exposure to cranial vault surgery: associations with neurodevelopment among children with single-suture craniosynostosis.
Naumann HL, Haberkem CM, Pietila KE, Bingfold CB, Starr JR, Kapp-Sinton KA, Hopper RA, Speltz ML.
Paediatr Anaesth. 2012 Apr 16.

Maternal anesthesia and fetal neurodevelopment.
Palaniyami A.

Cognitive and behavioral outcomes after early exposure to anesthesia and surgery.
Flick RP, Kasunic SK, Colligan RC, Wilder RT, Voigt RG, Olson MD, Sprung J, Weaver AL, Schneider DR, Warner DO.

Sevoflurane Anesthesia in Pregnant Mice Induces Neurotoxicity in Fetal and Offspring Mice.
Zhuang H, Dong Y, Xia Z, Crosby G, Calley DL, Zhang Y, Xie Z.
Anesthesiology. 2013 Jan 9.

Hays SR, Deshpande JK.

SmartTots: a public-private partnership between the United States Food and Drug Administration (FDA) and the International Anesthesia Research Society (IARS).
Ramnarayan R, Rosen M.
Paediatr Anaesth. 2012 Oct;22(10):969-72

Neurotoxicity and the Need for Anesthesia in the Newborn: Does the Emperor Have No Clothes?
“regardless of whether or not sevoflurane causes any clinically relevant toxicity, is it time to question the mantra that all babies need a hypnotic agent such as sevoflurane?”


Pre-op Anxiety

We don’t know
- Millions of children have been anesthetized over the years with few obvious problems
- Few procedures in the very young are truly elective
Fasting

- Parents' understanding of and compliance with fasting instruction for pediatric day case surgery.

Parents’ understanding of and compliance with fasting instruction for pediatric day case surgery.

During the fasting period, 4.9% would allow French fries, 22.3% toast/crackers, 17.5% cereal, 14.7% a sweet, 14.9% gum, and 12.6% tea with milk.

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Dexmedetomidine

- Potent α2 agonist, sedation and analgesia
- Being found to be very useful in children for a variety of conditions
  - MRI
  - Sleep endoscopy
  - Premedication
  - PICU sedation
  - Awake intubation
  - ?? Neuroprotective
Dexmedetomidine and OSA

- 2 studies looking at dex in patients undergoing T&A
  - 1ug/kg dex = 100ug/kg morphine
  - No adverse events
  - 2ug/kg bolus + 0.7ug/kg infusion of dex compared to fentanyl 1ug/kg
    - reduced opioid requirements, less emergence agitation, and fewer episodes of desaturation

Effects on Upper Airway

- 23 patients received low (1ug/kg) or high (3ug/kg) for MRI sedation
- Minimal changes in upper airway morphology with dex sedation detected on MRI

Intranasal Dexmedetomidine

- Yuen et. al in a series of studies have found 1 mug/kg intranasal dexmedetomidine to be effective in producing sedation in children at ~ 30 minutes, effects lasting for ~ 80 minutes.

Other Uses

- Decreases incidence of emergence agitation
- As an adjunct to decrease N&V
- Minimal effects on SSEP and MEP’s, therefore may be used for spine surgery

Other Uses

- Sleep endoscopy-used to simulate sleep for better evaluation of OSA
- Sole or in combination for MRI/CT scan sedation
- Electrocorticography, challenging medical conditions
- Awake craniotomies
- Sedation in multiple locations and for multiple procedures
Side Effects

- Bradycardia and occasionally arrest
- Depresses AV and SA node conduction
- Hypertension with rapid boluses
- Hypo or hypertension (with repeated boluses)
- May be neuroprotective or at least not destructive

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**Pain**

It is a common clinical problem to be presented with a pediatric patient with IV access for which there is doubt about the usability of the catheter. Vascular access is often bandaged, obscuring clinical assessment, children may not be capable of verbally communicating pain at injection sites, and a “twiddler's syndrome” has been described in which the child manipulates the catheter, causing it to migrate out of the vessel. Additionally, fluid leakage into surrounding tissue may initially go unnoticed owing to the distensibility of subcutaneous tissues in the very young.
Pernille Lykke Petersen, Pia Stjernholm, Viggo B. Kristiansen, Henrik Torup, Egon G. Hansen, Anja U. Mitchell, Ann Møller, Jacob Rosenberg, Jørgen B. Dahl, and Ole Mathiesen


TAP block after laparoscopic cholecystectomy may have some beneficial effect in reducing pain while coughing and on opioid requirements, but this effect is probably rather small.

Helena K. Hippard, Kalyani Govindan, Ellen M. Friedman, Marcelle Sulek, Carla Giannoni, Deidre Larrier, Charles G. Minard, and Mehernoor F. Watcha


One hundred seventy-one ASA physical status I and II children scheduled for BMT were randomized into 1 of 3 groups: group 1—nasal fentanyl 2 μg/kg with IV and IM saline placebo; group 2—IV morphine 0.1 mg/kg with nasal and IM placebo; or group 3—IM morphine 0.1 mg/kg with nasal and IV placebo

RESULTS: There were no significant differences in peak FLACC pain among the 3 groups

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Ketamine the old wonder drug
Ketamine has found many applications in pediatric anesthetic practice. Insights into the mechanism of action and the pharmacokinetics and pharmacodynamics of its isomers have led to a re-evaluation of this drug, expanding the range of applications in children. Ketamine is a remarkably versatile drug that can be administered through almost any route. It can also be used for different purposes.

0.3 mg/kg helps decrease pain on injection

Most studies show improvement in pain scores and or less opioid consumption in first 24 hours
No long term studies

Race and unequal burden of perioperative pain and opioid related adverse effects in children.
Results in adolescents are presented as results for a 70-kg person to allow comparison with adult parameters reported by others. Our study demonstrates that the PK of intranasal ketorolac in adolescents is similar to those reported in adults, assuming use of the same nasal administration device. Administration of ketorolac by the intranasal route resulted in a rapid increase in plasma concentration and may be a useful therapeutic alternative to IV injection in adolescents because plasma concentrations attained with the device are likely to be analgesic.

The Pharmacokinetics of Ketorolac After Single Postoperative Intranasal Administration in Adolescent Patients

Individual observed plasma ketorolac concentration profiles are shown for the 30-mg dose (upper panel) and the 15-mg dose (lower panel).

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Picture of the intranasal ketorolac delivery device.

©2012 by Lippincott Williams & Wilkins

The evolution of ketamine applications in children.
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Is ethnicity associated with morphine’s side effects in children?
Morphine pharmacokinetics, analgesic response, and side effects in children having tonsillectomy.
Race and unequal burden of perioperative pain and opioid related adverse effects in children.