Pediatric update: What are the little ones teaching us?

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OBJECTIVES

- By the end of this presentation, the learner will be able to:
  - Discuss the current literature on neurocognitive development and the effect of anesthesia on the developing brain
  - Debate techniques to reduce emergence delirium in children
  - Discuss the advantages and disadvantages in the use of uncuffed vs. cuffed endotracheal tubes in children under 8 years of age
  - Discuss the safety of ambulatory adenotonisllectomy
  - Discuss the advantages and disadvantages of pediatric regional anesthesia under general anesthesia.

What are the BIG unanswered questions in pediatric anesthesia???

- Neurocognitive outcomes after general anesthesia
- Medication choice in the time of drug shortages
- IV access in all patients?
- Pain management
- Obese pediatric patient management
- Emergence delirium
- Regional anesthesia
- Airway management: cuffed vs. uncuffed ett
- Ambulatory surgery cases: OP T&A
  - LMA vs. ETT

Neurocognitive outcomes under general anesthesia

- Millions of children exposed to anesthetics every year
- Safety concerns raised regarding risk of neuroapotosis after anesthetic
- Animal studies have shown NMDA antagonists (Ketamine, N2O) and GABA agonists (benzodiazepines, barbiturates, propofol, volatiles) induce neuroapoptosis with subsequent neurocognitive impairment
  - Most studies only done with Isoflurane

Recent history of pediatric neurocognition

- FDA (2007) Advisory Committee meeting to investigate the date on neurotoxicity and determine whether changes in anesthetic practice should be recommended
- Concerns from animal studies and the FDA's meeting resulted in sensational headlines and reports on potential 'brain damage' children may receive from anesthetic exposure

Center on the Developing Child
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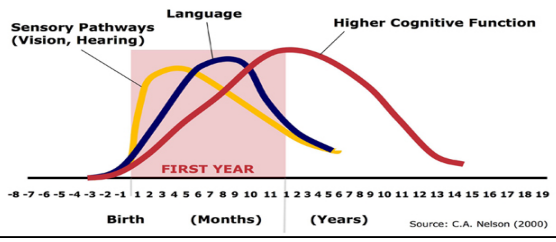
Human Brain Development

Neural Connections for Different Functions Develop Sequentially

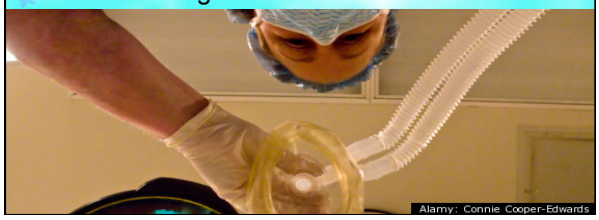


So what duration of anesthesia is safe?

- 2003: sentinel research by Jevtovic-Todorovic
  - Administered Versed, N2O, and Isoflurane to 7-day-old rats
  - Found after 6 hours, long-term potentiation (LTP) impaired
    - Form of synaptic plasticity→ electrophysiologic correlate of memory and learning

Anesthesia Before Age 3 May Be Linked to Learning Disabilities Later On

Huffington Post 10/5/2011



Developmental anesthetic neurotoxicity

- Cohort of children who had anesthetic before the age of 4 years
- Study showed those who had > 1 anesthetic and a cumulative duration of > 2 hours were at risk for learning disability
  - Subdivided groups into Physical Status I-II→ link persisted
  - Period of synaptogenesis peaks at 7 days postnatal but remains high up to 2 years
  - Measured IQ, memory, language skills, attention, visuospatial skills

Interventions for neuroprotection

- Alpha-2 agonists
  - Dexmedetomidine (1-25 mcg/kg)
  - Clonidine
    - Potent sedative/hypnotic qualities; Analgesic action
    - Potential organ-protective effects
    - Reduction in PONV
    - Reduction in delirium
    - Relative lack of respiratory side effects
- Xenon
- Melatonin
- Lithium
- Hypothermia

Recent studies

- 2011 study showed Sevoflurane < Isoflurane < Desflurane
  - Effects of neurotoxicity on immature brains
- Another recent study (2011) dispute these findings
  - Show similar neurotoxic profiles using equipotent doses of inhaled anesthetics in neonatal mice

Mechanism of anesthetic-induced neurotoxicity

- Previous speculation was abnormal neuronal inhibition from inhaled agents responsible for apoptosis
- Newer research suggests neuronal excitation in immature brains may be responsible
  - Based on anesthetic potency rather than inspired anesthetic concentration

Johns Hopkins Current Research Study

- Roger Johns, MD published in March 17, 2016 issue of Anesthesiology
- Findings: inhaled anesthetics bind to and interfere with certain proteins in excitatory neurons that are essential to transmit signals involved with anesthesia and pain perception via neuronal synapse formation

Johns Hopkins Current Research Study

Specific protein also involved with neuronal development→ connection with neurotoxicity reports and POCD in infants and neonates?

- Postsynaptic density protein-95 (PSD95)→ scaffolding protein helps assemble proteins needed for neurons to communicate
- Recent work found IA's bind to certain sites on PSD95 and prevent ability of excitatory neurons to transmit signals
- Could be preventing correct neuronal synapse development →long-term learning and memory deficits
- Protein mutations and dysfunctions already implicated in autism spectrum disorders and certain types of mental illness

Another theory…oxygen toxicity

- Reactive oxygen species (ROS) serve as cell signaling molecules for normal biologic processes
- Brain and lung target organs most prone to damage by ROS
- Immature neurons sensitive to oxygen toxicity
  - Oxidative stress→ neuroapoptosis
  - 40% oxygen did not demonstrate any increase in neuronal cell death
  - Duration plays a key role

Oxygen toxicity: Effects on neonates

- Intraventricular hemorrhage
- Retinopathy of prematurity (ROP)
  - Blindness due to overgrowth of blood vessels
- Bronchopulmonary dysplasia (BPD)
  - Due to epithelial and endothelial cell damage from ROS
  - Antioxidant enzymes, critical to lung function, may be inactivated by ROS
  - Antioxidant therapy theoretically could prevent brain damage, ROP and BPD but more studies needed
    - Vitamin E 100 mg/kg/day 4-6 weeks
    - Acetyl-L-carnitine (aLc)

Emergence Delirium (ED)

- Defined as mental disturbance from general anesthesia (GA) consisting of hallucinations, delusions, inconsolable crying and confusion manifested by moaning, restlessness, paranoid ideation, involuntary physical activity and thrashing about in bed
- Pain is not a major component
- Self-limiting→ 5-25 minutes
- Presents in ~ 20 – 30% of children receiving GA
- Higher risk of developing negative post-op behaviors and a PTSD state

Emergence Agitation (EA)

- State of mild restlessness and mental distress
- Can arise from various sources, including pain, physiological components, anxiety

Inhalational anesthetics

- Sevoflurane and Desflurane anesthetics have been implicated in pediatric emergence delirium
- Rapid emergence may create dissociative state
  - Awake child with altered cognitive perception excitation and agitation

Emergence delirium

- Sevoflurane and Desflurane has been shown to cause neuronal excitation in immature neurons as opposed to neuronal inhibition in mature neurons
- In recent studies, similar incidences of ED

Pediatric Anesthesia Emergence Delirium scale (PAED)

- Measures ED
  - Eye contact
  - Purposeful actions
  - Awareness of surroundings
  - Restlessness
  - Inconsolability
- Scores ≥10 demonstrate emergence delirium

Recent studies

- 25% of preschool children demonstrated ED during first 20 minutes after awakening from a GA
- Duration of ED significantly shorter with Desflurane
  - 5-10 minutes shorter
- Use of midazolam has not been shown to reduce incidence of ED
- Preop administration of melatonin 0.2 – 0.4 mg/kg reduced incidence of ED to 5.4%

Cuff or not to cuff; is THAT a question?

- During last 5 decades, uncuffed endotracheal tubes (ETTs) were recommended in children < 7- 8 years
- In recent decade, change in practice evolving
- Recent changes in clinical practice and design on ETT's explained

Uncuffed endotracheal tubes in children

- Traditional teaching for children < 8 – 10 years
- Rationale: cricoid cartilage narrowest part of the airway; choosing a predicted ETT that just fits ans seals makes cuff unnecessary
- Studies found ETT exchange rates as high as 30%
  - Large air leak→ unreliable ventilation and oxygenation, imprecise capnography, high gas flow consumption (> 2 L/min), environmental pollution, > risk of pulmonary aspiration
  - Oversized ETT→ laryngeal injury:
    - Post-op stridor, edema, subglottic stenosis

Cuffed endotracheal tubes in children

- Initially accepted mainly in PICU's for younger children not tolerating any change in tidal volume or airway pressure
  - Caused by change in head position or changes in level of sedation/muscle relaxation
  - Cons: higher costs, smaller internal diameters (IDs) required→ increased airway resistance WOB, potential for cuff hyperinflation, risk of laryngeal damage and post-op stridor

Cuffed endotracheal tubes in children

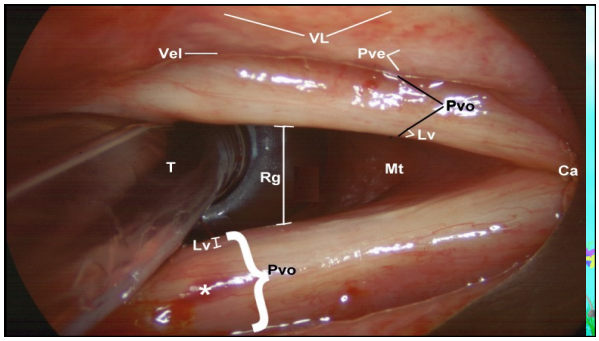
- Pros: smaller ID's not a real issue
  - Higher costs outweighed by savings in reduced need to exchange ETT's, lower anesthetic gas usage, reduced oxygen and air consumption
  - Reduced indirect costs from low environmental pollution

Pediatric endotracheal tube design

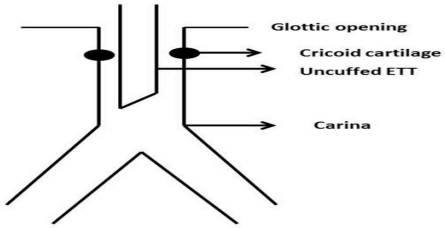
- Older ETT's had shortcomings in design
  - Inappropriate cuff diameter and position
  - Too long cuffs → endobronchial tube tip or intralaryngeal positioning
  - Absences or inaccurately positioned intubation depth marks
  - Differences in outer diameter sizes with identically sized ID's

Pediatric endotracheal tube design

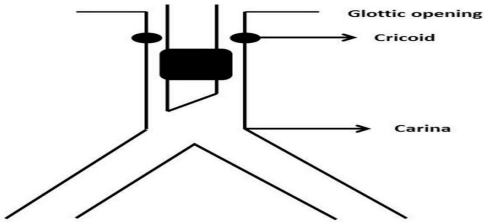
- 2004: new pediatric ETT became available with improved design and sealing properties (Kimberly-Clark)
  - Polyurethane cuff allows very short high volume, low pressure (HVLP) cuff
  - Murphy eye removed
  - Narrowed tube tip design for increased space around cuffed ETT in tracheal lumen
  - Automatic cuff pressure control mechanism
    - Cuff auto-inflation
    - Integrated pressure release valve

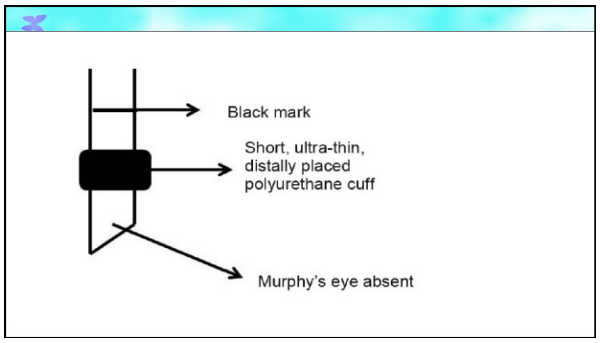


Ideal position of uncuffed ETT



Ideal position of cuffed ETT

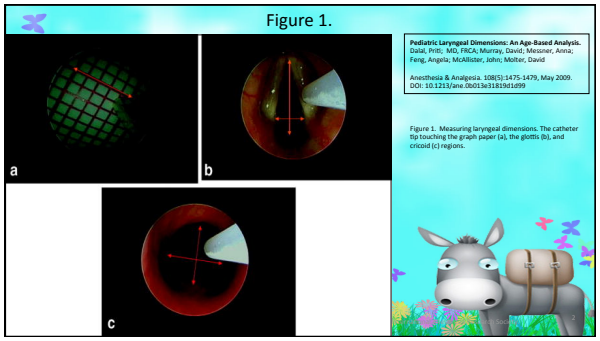




Pediatric airway anatomy

- Controversy still exists over shape of airway
- Some studies state not as circular as previously designed ETT's were developed for → more ellipsoid structure
- Others state more cylindrical (like adult) than funnel shaped
  - Does taper to funnel at level of glottis
  - Size the same at glottis and cricoid
- Glottis rather than cricoid narrowest position of pediatric airway
  - In anesthetized paralyzed children

Figure 1.



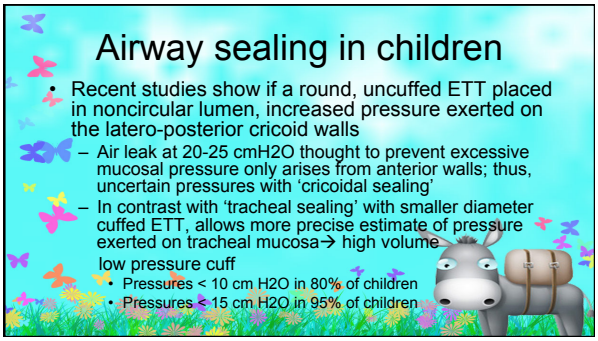
Pediatric Laryngeal Dimensions: An Age-Based Analysis.
Dalal, Priti; MD, FRCA; Murray, David; Messner, Anna; Feng, Angela; McAllister, John; Molter, David

Anesthesia & Analgesia. 108(5):1475-1479, May 2009.
DOI: 10.1213/ane.0b013e31819d1d99

Figure 1. Measuring laryngeal dimensions. The catheter tip touching the graph paper (a), the glottis (b), and cricoid (c) regions.

Airway sealing in children

- Recent studies show if a round, uncuffed ETT placed in noncircular lumen, increased pressure exerted on the latero-posterior cricoid walls
  - Air leak at 20-25 cmH2O thought to prevent excessive mucosal pressure only arises from anterior walls; thus, uncertain pressures with 'cricoidal sealing'
  - In contrast with 'tracheal sealing' with smaller diameter cuffed ETT, allows more precise estimate of pressure exerted on tracheal mucosa→ high volume low pressure cuff
    - Pressures < 10 cm H2O in 80% of children
    - Pressures < 15 cm H2O in 95% of children

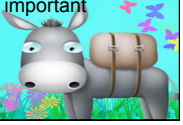


Formulas for ETT sizes

- Uncuffed
  - Modified Cole: ID (mm)=(age)/4 + 4
  - Morgan and Steward: ID(mm)= (16+age[yr])/4
- Cuffed
  - Motoyama: ID=(age)/4 + 3.5
  - Khine: ID= (age/4) + 3

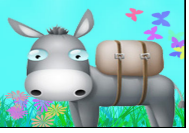
Recommendations for ETT's

- Cuffed ETT's recommended with I.D. ≥ 4.0 mm
- Preferred with patients at risk for:
  - Pulmonary aspiration
  - Low lung compliance (including laparoscopic and thoracoscopic procedures, bypass)
  - Precise ventilation and/or CO_2 control important
  - Severe burns
- Check cuff pressure



What age is safe for outpatient T&A's?

- Over past two decades, highly debated question
- 250,000 adenotonsillectomies performed per year
- 1996: Pediatric Otolaryngology Committee set guidelines recommending children < 3 be treated as inpatients
  - Biggest concern is risk of complications post-discharge
- Indication now: obstructive breathing (~80%) rather than infection
- Obstructive sleep apnea status crucial



Outpatient T&A's

- Complications
  - Hemorrhage: major complication
  - Dehydration: most common
    - Most common cause of all readmissions
  - Post-discharge nausea and vomiting
  - Fever
  - Reactive airway disease

Changes in surgical technique

- Transition from 'cold/classic' technique to 'hot/ bovie'
- Partial tonsillectomy using microdebrider or coblater
- Decreased incidence of primary hemorrhage and shorter recovery times

Intraoperative course

- Acetaminophen suppository 40 mg/kg
- Cefazolin 25 mg/kg (max 1 gm) IV
- Dexamethasone 0.5 mg/kg (max 10 mg) IV
- Odansetron 0.15 mg/kg (max 4 mg)
- Lactated Ringer's 30 ml/kg IV

LMA vs. ETT for T&A

- Evidence shows safety profile equal with both techniques
  - Pros and cons for both management techniques
  - Big concern is surgical visualization
- LMA advantages
  - Spontaneous respirations
  - Lower incidence of laryngospasm during emergence
  - Less postop hoarseness and coughing
  - Risk of aspiration non-significant

Recommendations

- Physical Status I and II only
- No diagnosis of severe obstructive sleep apnea
- Family resources caring for child at home
- Children 24 months, observe in PACU for 6 hours
- Children > 24 months can be scheduled for ambulatory surgery
- Discharge criteria:
  - Adequate postop fluid intake
  - Absence of need for supplemental oxygen
  - Stable vitals with no desaturations
  - Parental comfort with caring for child
- Nursing call to parents on POD # 1 (especially to assess for dehydration)

Does regional anesthesia under GA improve outcomes…and is it safe?

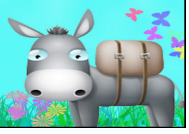
- Most pediatric regional anesthesia done under GA
- Why is there a difference in safety recommendations between children and adults?
- Research conducted by Pediatric Regional Anesthesia Network (PRAN)
  - Consortium of pediatric centers

Complications

- 15,000 blocks in cohort
- Low risk of complications
  - 1:1000
- Most detected at time of needle or catheter placement
  - Failed block
  - Inability to advance catheter
- No long-term sequelae

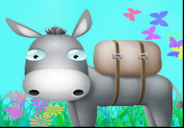
Use of localizing techniques

- Neuraxial blocks
  - None 86%
  - Epidurogram 8%
  - Nerve stimulator 3%
  - Fluroscopy 3%
  - Ultrasound 3%
- Lower extremity blocks
  - Ultrasound 64%
  - Nerve stimulator 63%
  - None 6%
  - Fluroscopy 2%



Ultrasound use

- Epidural puncture and dura visualized in 100% of children
- Epidural catheter visualized in epidural space in 97%
- Medication/saline injection visualized in 96%
- Improved quality, onset, duration and success rate compared to blind and nerve stimulator techniques



Recommendations from PRAN Registry regarding epidural anesthesia under GA

- Limit epinephrine dosing to test dose (0.5 mcg/kg)
- Prevent or promptly treat hypotension
- Consider severe hypotension due to subarachnoid placement unless proven otherwise
- Consider severe hypertension due to painful response to intraneural placement.
- Perform LOR with saline, not air
- Use nerve stimulation and/or ultrasound
  - Especially for thoracic placement

Recommendations from PRAN Registry regarding epidural anesthesia under GA

- Inject epidural loading doses slowly
- Use dilute local anesthetic solutions for intraop infusions
- Document degree of sensory and motor blockade in PACU/ICU
  - If block appears dense, stop infusion
  - If no regression at all over 3 hours, consider emergent MRI or neurosurgical consult
    - Remember to remove wire-wrapped epidural catheters before MRI

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