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The complete communications committee roster and assistant newsletter editors can be found on the SPA website www.pedsanesthesia.org.

Editor’s Corner

We are now publishing four newsletters a year instead of three. This is the first of the increased newsletters. In the past we've always published one after each of the SPA meetings and decided to try and add a newsletter in the summer. Once again I need to thank all of my assistant editors for all their hard work in helping me get the newsletter out. I am consistently amazed at their willingness to contribute time, effort and articles to the newsletters as well as the quality of their work. I encourage anyone who is interested and thinks they may have a few hours to spare every few months to strongly consider joining the Communications Committee and becoming an Assistant Newsletter Editor. We always need new ideas and fresh perspectives. We want both the newsletters and the SPA website to reflect the needs and interests of the general membership, so the more input we get the better they will be.

This month we have a topic review for the Fellow's Corner by Manolo Montes, DO who is doing his Pediatric anesthesia fellowship in Michigan. The purpose of this Section is to allow fellows to review articles of interest (both recent or classic), ask questions, or discuss areas of interest to them. There are several other excellent topic reviews including one on thoracic epidurals (Dr. Lauro); EEG's; and Aprotonin use (Dr. Kussman). Dr. Mancuso has as always edited a fantastic Point/CounterPoint, and there are several good recent article reviews by Drs. Ahmed, Gooden and Khambatta.

Please let me know if there is anything else you would like to see covered and of course if you'd be willing to contribute: Agarwal.Rita@tchden.org

Rita Agarwal, MD, FAAP
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Do Anesthetic Agents Cause Harm to the Central Nervous System of the Human Newborn? Or Don’t Throw the Baby Out with the Sevoflurane

Thomas J. Mancuso, MD, FAAP

The possibility that various medications and other substances may harm the developing CNS has been rather widely discussed recently and subject to much scholarly work in animal models. Considering the great care with which any medication is given to pregnant women for fear of harming the developing fetus, questions about post-natal effects of medications seem quite appropriate. The CNS undergoes substantial and important development in post-natal life and therefore may be adversely affected by various medications, toxins or other environmental influences. For example, the deleterious effects of even low levels of lead in the blood on intellectual development of infants and toddlers and the substantial harm caused by higher lead levels is well known.

In this point-counterpoint review, although they consider the subject from slightly different perspectives, both authors take the view that I share. Based on the available clinical information as well as the results of investigations using animal models, I think that pediatric anesthesiologists must continue the careful monitoring and anesthetic care as it is currently practiced. We must also continue to carefully monitor our medical practices always aiming to improve care. At this point, however, I think that provision of anything other than complete, adequate general anesthesia would be a disservice to our patients.

Dr. McClain carefully summarizes much of the most recent and pertinent investigations on the effects of anesthetic agents on an animal model. While the data from investigators who have used the newborn rat pup model are of great interest, I am uncertain, as he is, of how precisely that model represents the situation in the OR with a newborn undergoing a surgical procedure with general anesthesia. However, I am certain, based on data described by Dr. Groeper, that NOT providing anesthesia to newborns undergoing surgery is harmful and contributes to poor outcome. Such a practice would also be considered both inhumane and unethical. In addition to the studies she described that indicate the importance of adequate anesthetic depth during surgical procedures for improved outcomes, we can look to the changes in the practice of neonatology for support. Neonatology has made great strides in the care of preterm newborns. Not only has mortality decreased greatly in younger and younger preterms, but so has morbidity. A large part of the improved outcome has come about because of growing awareness of the importance of decreasing the stress on the growing preterm newborn. Care is much more gentle, cares are grouped together, uncomfortable procedures are preceded with analgesics and/or sedation and the NICU is quieter. If the growth and development of these fragile infants is improved by measures such as those mentioned above, it is impossible for me to believe that surgery with inadequate anesthesia will lead to a better outcome than with adequate anesthesia.

Craig D. McClain, MD

One of the major issues facing the specialty of pediatric anesthesiology today is whether commonly used anesthetic agents may have deleterious effects on the developing brain. In animal models, accelerated apoptosis has been demonstrated as a result of exposure to various anesthetic agents during early neural development. A review of the animal data reveals numerous reports of neurodegenerative changes caused by exposure to volatile anesthetics, nitrous oxide, NMDA receptor antagonists, and alcohol; either individually or in combination.

In 1999 Ikonomidou, et al. reported that some commonly used drugs such as nitrous oxide and NMDA receptor antagonists can lead to increased apoptotic activity in immature neurons. Jevtic-Todorovic, et al. reported in 2003 that rat pups exposed to an anesthetic cocktail of nitrous oxide, isoflurane, and midazolam suffered diffuse

Kelly L. Groeper, MD

In the past 20 years, much has been learned about pain and stress in the neonate. We have come to accept that neonates do experience pain and suffer consequences from that experience of pain. Anesthesia is provided to newborns who undergo surgical procedures, as it to adults and older children. This is done both for humanitarian reasons and also to decrease the stress response to those surgical procedures or other painful, invasive interventions. The possibility that these anesthetic agents are harmful to the developing central nervous system has given rise to a debate about the appropriate use of these agents in the human newborn. However, the avoidance of anesthetic agents for surgical procedures in the newborn population has been shown to adversely affect outcome. We should not be tempted to discard the benefits of anesthesia for the undefined potential risks of anesthesia on the developing central nervous system.

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Should the Results of Animal Studies Change Clinical Anesthetic Care? Craig D. McClain, MD

Continued from page 3

Apoptotic neurodegeneration and persistent neurocognitive impairment. This 2003 study, and its implications, has generated lively discussion. Seven-day-old rats were exposed to midazolam (3, 6, or 9mg/kg), isoflurane (0.75%) and nitrous oxide (50, 75, or 150%) for six hours. Controls were exposed to a six-hour mock anesthetic. Groups then either underwent histopathology studies or were followed longer for behavioral studies. The authors demonstrated that animals exposed to their anesthetic cocktail suffered “widespread apoptotic neurodegeneration in the developing brain, deficits in hippocampal synaptic function, and persistent memory/learning impairments.”

Some commentators have advocated extrapolation of these results to humans. Anand and Soriano address several problems with the application of these findings to humans in their article in the August 2004 issue of Anesthesiology. Among the issues addressed, they discuss the relative duration of exposure between the rat pups and human neonates. While the rat pups were exposed to the anesthetic agents for six hours, this would correspond to an exposure time of several weeks in a human neonate. Obviously, this would be a rare occurrence, if it ever happened at all. Secondly, Jevtovic-Todorovic, et al. do not address the effects of malnutrition on the developing brain. There is a body of data showing a link between poor nutrition and an increased rate of learning disabilities. These rat pups were neither fed during the anesthetics nor given dextrose containing intravenous fluids. Clearly, this is a practice that many pediatric anesthesiologists would avoid. Thirdly, the Jevtovic-Todorovic group does not address the lack of continuous monitoring of hemodynamic and respiratory status in these rat pups under anesthesia. As clinical anesthesiologists, we would never dream of purposely deciding not to monitor the hemodynamic and respiratory status of a neonate or infant undergoing general anesthesia. Obviously, maintenance of physiologic homeostasis is of paramount concern in clinical anesthesia practice. Finally, there are well-described adverse consequences to withholding anesthesia or analgesia to babies undergoing surgery or painful procedures that are discussed in greater detail in other sources. Jevtovic-Todorovic and Olney have responded to these criticisms in an accompanying editorial to the Anand and Soriano article. This issue is further highlighted by the above authors in a letter and following reply in the April 2005 issue of Anesthesiology.

A recent abstract presented at the 2005 SPA Winter Meeting by Loepe, et al. looked at neonatal mice, pigs and rabbits exposed to midazolam, isoflurane, and nitrous oxide. These animals were monitored over the period of anesthesia. They found no accelerated neuronal cell death in contrast with the experiments of Jevtovic-Todorovic, et al. This study highlights the possibility that there may be differences across species in response to these drugs. One major criticism that has been directed at this work is the concern that the staining methods used may not be sensitive enough to detect neuronal death as compared to the Jevtovic-Todorovic paper.

The lay press has picked up on these ideas and the internet is bursting with warnings regarding possible long-term learning difficulties resulting from exposure to anesthetic agents as a neonate or infant. More and more parents are asking, “Will the anesthesia effect how smart my child will be?” How do we answer this? How will this affect our practice?

Anesthesia for neonates has evolved considerably over the past few decades. We have emerged from the days of keeping neonates still during surgery with pancuronium and oxygen to general anesthetics that attempt to blunt the stress response to surgery using narcotics, benzodiazepines, potent volatile agents, and other anesthetic drugs. We now recognize that there are unequivocally adverse consequences to human babies being subjected to painful stimuli without adequate anesthesia. It would be a tremendous disservice to our patients to take a thirty-year leap backward in the delivery of anesthetic care.

Obviously, the last thing any of us wants to do is cause harm to our patients. We cannot ignore the fact that these agents have been demonstrated to cause some degree of harm in the developing central nervous system of rats. However, we have no objective evidence that these agents result in neurocognitive deficits in developing humans.

How should we incorporate the data into the practice of pediatric anesthesiology? As Anand and Soriano have argued, simply extrapolating animal findings to humans carries many risks. Many of the surgical procedures performed on neonates are either urgent or emergent. Therefore it is unrealistic to simply put these procedures off until the patients are older. Similarly, performing these procedures without counteracting the stress of pain and surgery can also lead to adverse outcomes. There are differences across species as Loepe, et al. have shown. However, we cannot ignore the truth that there is compelling evidence to continue further investigations on the effects of these drugs on the developing nervous system. Questions regarding human neonates remain to be answered and further research needs to occur. At this time, it would be unwise for pediatric anesthesiologists to alter their current practice of providing safe general anesthesia using currently available agents for infants and neonates undergoing painful surgical procedures.

Would Clinical Outcomes be Improved with Lighter Anesthetic Techniques? Kelly L. Groeper, MD

Continued from page 3

As recently as the 1970s, some physicians were recommending little or no anesthesia for the treatment of newborns undergoing surgical procedures. This recommendation was likely based on the difficulty in maintaining a stable circulation in these patients during surgery itself and on the belief that the effects of anesthetic agents on cardiovascular performance would be detrimental to these patients. In addition, as mentioned above, newborns were thought to not experience or respond to painful stimuli. Objections to this approach led some to practitioners to look for safe alternatives. Fentanyl-air-oxygen was described as a safe technique for the ligation of patent ductus arteriosus (PDA) in preterm infants. Fentanyl and sufentanil-oxygen-pancuronium anesthesia was also determined to be safe and effective in infants undergoing cardiac surgery.

In 1987, Anand, et al. measured the stress response of neonates undergoing ligation of a patent ductus arteriosus (PDA). Half of the neonates received the standard anesthetic technique in use at that time consisting of muscle relaxation and intermittent nitrous oxide while the other infants received that anesthetic technique with the addition of fentanyl. Anand demonstrated an increased stress response in those neonates not receiving fentanyl. He found in these infants an increase in epinephrine levels and a prolonged and increased hyperglycemic response to surgery. A clinically unstable post-operative course was also observed in the non-fentanyl group compared to the fentanyl group. These findings led Anand to the hypothesis that prevention of this massive stress response may lead to improvement in clinical outcome. Full References Available Online
In 1992, Anand and Hickey reported stress attenuation in neonates undergoing cardiac surgery who were anesthetized using high dose opioids as compared to a similar group given anesthesia with morphine at a usual dose and halothane. These newborns undergoing cardiac surgery were randomized to receive one of the two anesthetic techniques. One half of the subjects received a high dose sufentanil technique followed by a sufentanil infusion for 24 hours post-operatively and the other subjects received a technique based on inhaled halothane with a usual dose of morphine followed by intermittent morphine and diazepam. The neonates receiving deep anesthesia with high dose sufentanil had decreased hormonal responses and had a decreased incidence of sepsis, metabolic acidosis, disseminated intravascular coagulation. Remarkably, fewer post-operative deaths were seen in the patients treated with high dose sufentanil when compared to the anesthetic group that received lighter anesthesia (morphine-halothane). Also, in the group of patients receiving the lighter anesthetic regimen with halothane, the survivors demonstrated a less extreme stress response when compared to the non-survivors.5

While these studies focus on the narcotic dosage and stress response, it should be noted that the majority of cardiac surgical procedures performed in newborns require a balanced anesthetic technique with narcotics, benzodiazepines, muscle relaxants and often, inhaled anesthetics. Which narcotic and in what dose, along with which additional anesthetic agents provide the most cardiovascular stability with the least amount of side effects is yet to be determined. A more recent study looking at dosing regimens of various narcotics with or without benzodiazepines, reports less of a decrease in the stress response than previous studies without any increase in mortality.6

It seems reasonable, in light of this data, to continue to use anesthetic agents in the newborn to blunt stress response to surgery in order to minimize the hormonal and metabolic effects of excessive stress response. Of course, ethical and humanitarian considerations compel the administration of analgesia and anesthetics to newborns undergoing surgery and other invasive painful procedures. With current medications, anesthetic techniques and monitoring, it is a very rare case indeed in which the provision of anesthesia will put a child or newborn at risk for harm due to cardiovascular instability. The data in animals is of note, and given the fragility of our newborn patients, we should not take lightly the possible side effects these agents may have on our patients, both in the peri-operative period and beyond. However, in view of the clearly demonstrated risks of inadequate anesthesia for newborns undergoing surgery, including increased morbidity and mortality, we should continue the current practice of providing safe, carefully monitored anesthesia to these newborns.

--- Full References Available Online ---

The three most valuable cards are the Egyptian God Cards. The one good thing about these cards is the improvement in Alexander’s reading skills! There are also Yu Gi Oh cartoons and toys that usually pitch Yu Gi or young Yu Gi and his friends against evil enemies. Hmmm...are we starting to see a pattern here?

Teen Titans is a cartoon about five super heroes - Robin (the leader); Raven, who is sort of goth looking and has weird dark powers; Star Fire, an alien from another planet who can shoot lasers from her eyes and fire balls from her hands; Beast Boy, who can change into any animal, and Cyborg, who is part teenager and part machine. Raven, and Star Fire can fly and Robin can ‘sort of’ fly. They are always waging battles against — evil enemies!!! They promote teamwork and friendship and of course the ubiquitous defeating evil enemies. The main evil enemies are Brother Blood and Slade. Some of the other cartoons that he enjoys are Spider Man, Shinzo (another trading card based confusing Japanese animé type cartoon) and Foster’s Home for Imaginary Friends (actually I really like the latter).

The most precious toys are Monster Trucks (there is nothing cuter than a 2 year old saying “monster truck”) and tractors, construction machines, monster trucks (there is nothing cuter than a 2 year old saying “monster truck”) and emergency vehicles are all particular favorites. Bubbles, songs and books also go over pretty well. Since most little ones this age will probably get a premed, the most important things to know are the tunes to Twinkle, Twinkle Little Star, the ABC song and The Wheels on the Bus!

I hope you have enjoyed this crash course in the mind and psyche of young boys. I encourage any of you who do have children and want to put photos of your kids in the newsletter to please share their passions (or at least interests and most recent crazes) with us, please contact me.
Fellow’s Corner

Congenital Long QT Syndrome

Long QT Syndrome (LQTS) is a cardiovascular disorder that causes syncope and sudden death from cardiac arrhythmias, typically polymorphic ventricular tachycardia (torsades de pointes) and ventricular fibrillation. The pathophysiology involves malfunction of calcium ion channels resulting from mutations in genes encoding critical channels of the heart (congenital LQTS). The acquired LQTS is different in that it is either drug induced e.g., procainamide, Amiodarone or caused by metabolic abnormalities e.g., magnesium deficiency.

There are two types of LQTS. The first was described by Jervell and Lang-Nielsen in 1957 as an autosomal recessive disorder associated with hearing loss. The second was described by Romano and Ward as an autosomal dominant disorder without congenital deafness.

There is significant morbidity and mortality secondary to cardiovascular compromise as a result of abnormal cardiac repolarization, QT prolongation and fatal arrhythmias. Anesthesiologists should have a high index of suspicion for patients with possible congenital LQTS.

Preoperative evaluation should include a history of abrupt syncope during exertion or auditory stimulation and a history of sudden death in the family. A preoperative EKG would manifest QT prolongation. However, up to 40% of patients with congenital LQTS will not be detected by EKG (called concealed LQTS). The Familllon test, developed in 1995, is a genetic test for congenital LQTS.

The prevalence has been estimated to be one in 5000 persons, presenting from birth to adulthood. Clinical features may range from a stable rhythm, albeit with QT prolongation, to the trademark dysrhythmia associated with congenital LQTS – Torsades de pointes. The patient with LQTS may present with a history of abrupt syncope triggered by situations associated with increased sympathetic nervous system output or drugs that prolong QT interval.

Treatment may include the use of beta blockade, implantable cardioverter defibrillator therapy, left cardiac sympathetic denervation and avoidance of drugs that prolong QT interval. Magnesium sulfate, which acts by stabilizing the membrane, is the current drug of choice.

The anesthetic plan should include minimizing the sympathetic response to any noxious stimuli and avoidance of precipitating factors of torsades de pointes. Preoperatively, patients should be kept in a quiet environment and premedication provided to avoid any stress response. Metabolic abnormalities should be avoided and QT interval monitored.

Finance Report

May 6, 2005

As the elected treasurer of the Society for Pediatric Anesthesia and chair of the finance committee, I am delighted to report on the financial health and well being of our organization. The society has been working very slowly and deliberately over the last two decades to grow our financial assets, primarily to lessen and ultimately eliminate our dependence on financial support from corporate sponsors to achieve our organizational goals (education, research, patient care). For example, in spite of the overall growth and success of both the annual and winter meetings, each meeting continues to generate costs in excess of revenue. However, through the generosity of the membership and the collective stewardship of the board of directors and officers over the years, it is very exciting to report that we have recently achieved a significant milestone, development of net assets in excess of one million dollars.

In anticipation of achieving this important goal, the finance committee and board have recognized that it is our best interest to manage these valuable assets very carefully. This is best done with the assistance of professional financial advisors. Hence, a request for proposals to financial asset management firms was circulated and the members of the finance committee have carefully reviewed proposals from six different firms over the last six months. In April, the committee unanimously recommended and the board of directors subsequently approved, the hiring of Independence Advisors, Inc. under the leadership of Charles (Chas) Boinske. Independence Advisors, Inc. comes with stellar recommendations from current clients and has offices in both Philadelphia and Detroit. The finance committee, with the assistance of these financial professionals, will continue to carefully monitor and grow our assets, while attempting to minimize risk. With our continued financial success, the society will ultimately be better equipped to provide useful educational and research products to the membership, thus leading to better care for the population of patients under our care.

I am indebted to the past and current members of the finance committee for their hours of hard work and dedication toward this important task. The current financial status of the organization is a tribute to their wisdom and commitment. I will close by thanking each of the current members of the committee: Nancy Glass, Frank Kern, Jay Przybylo, Peggy Seidman, Stephan Stayer, Michael Jon Williams, ex-officio – Frank McGowan, Joe Tobin. Anyone wishing to assist in these important tasks by joining the finance committee should contact me at lynn.martin@seattlechildrens.org.

Lynn D. Martin, MD, FAAP, FCCM
Treasurer and Chair, Finance Committee

ATTENTION RESIDENTS & FELLOWS

Congratulations to all of you whose residency or fellowship is about to end! Before the next phase of your career begins, we would like to ask that you take a moment to upgrade your membership with the Society. You will now have the option to choose a member category that will allow you a much greater role in the shaping of the SPA. As an SPA Active member, you will have voting privileges and the ability to serve on committees. Please contact the SPA Membership Coordinator, Joye Stewart at joye@societyhq.com for more details!
Electroencephalograms of Infants and Children During General Anesthesia


Reviewed by: Barry D. Kussman, MBCh, FFA(SA)

Review: These authors studied 53 neurologically normal infants and children, ranging in age from two days to 10 years. Following atropine premedication and tracheal intubation, the EEG was analyzed prior to and during the administration of 2% halothane. The EEG's, in comparison to those of adults, were classified into three types: infantile, transitional and adult type. The infantile type showed no remarkable changes i.e. no tendency to slowing, during halothane administration. It was entirely impossible to establish any criteria concerning the relationship between the depth of anesthesia and the EEG findings. This infantile type persisted up to 50 days of age. The transitional type showed some fast waves in the occipital lead with some tendency to form spindle bursts. The transitional type persisted from 50 days of age up to about six months of age. The adult type, appearing from about six months of age, showed the typical adult pattern with initial fast waves (20-25 Hz) dominant in the frontoparietal area superimposed on the basic activity. At light surgical depth spindle waves 12-14 Hz appeared in all leads.

Comment: The Joint Commission on Accreditation of Healthcare Organizations issued a Sentinel Event Alert (Issue 32, October 6, 2004) on reducing the risk and managing the impact of anesthesia awareness, and asking for assessment of the adequacy of current monitoring practices regarding anesthesia levels. Anesthetic agents produce dose-related effects on EEG amplitude and frequency, and devices using processed EEG parameters have been developed in an attempt to monitor depth of anesthesia.

Electroencephalographic activity has a close and consistent relationship to the maturational state of the brain, so that evolution of the brain is paralleled by a transformation of EEG patterns. Rapid changes occur in the preterm infant and neonate; slower changes occur during the first year of life, and full maturation of the EEG is reached in adolescence. Very few studies have been performed examining the effects of anesthetic agents on the pediatric EEG, particularly in children less than two years of age. This study highlights the different EEG patterns, particularly in infants (compared to adults), during halothane anesthesia. Maturation changes in the EEG and differing response to anesthetic agents can invalidate the measurements of an EEG device whose algorithm was developed using an adult database.

Sex Differences in Analgesia: A Randomized Trial of Mu Versus Kappa Opioid Agonists.

Miller PL, Ernst AA, UC Davis Department of Emergency Medicine, Southern Medical Journal 2004;97:35-41

Reviewed by: Zulfiqar Ahmed, MD

Review: The objective of the paper was to study the differences in the effects of opioids on opposite sexes. Prototypical mu-receptor agonist (morphine sulfate 2.5-5 mg) was compared with kappa agonist (butorphanol 0.5-1 mg). Ninety-four subjects were randomized into the two groups with moderate to severe traumatic injury: 52% of the patients were men and 48% were women and both the groups were similar in demographics (18-65 years of age, injury to upper and lower extremity and need for i.v. pain relief). Clinical effect was recorded by patient’s self-report of visual analog scale of pain. The primary end point stopped at 60 minutes and secondary endpoint was at 120 minutes of the initial injection. Appropriate exclusion criteria were applied like non acute injury, serious medical condition, multiple injuries to other body areas, altered sensorium, alcohol or drug abuse or inability to use visual analog scale for pain assessment. The results report that at 60 minutes, the women’s group responded better to butorphanol (p=.046) as compared to morphine and the men’s group reported better pain relief with morphine sulphate (p=.06).

Discussion: The above mentioned study was designed after similar reports in the animal model. The doses of morphine and butorphanol were approximately equianalgesic when check in micromedex. The implications to the pediatric anesthesia practice may be that a significant number of our patients have mature adult physiology and the above mentioned regimen may be applied to them while the implication on younger population is uncertain. The number of study subjects was described as convenience sample of the emergency population which may also be the reason for failure to reach statistical significance.

Anesthesia for Thymectomy in Children with Myasthenia Gravis.

Michelle C. White and Peter A. Stoddart. Pediatric Anesthesia 2004; 14: 625-635

Reviewed by: Hoshang J. Kambatta, MD

The authors have written an excellent review article on myasthenia gravis, an autoimmune disease with antibodies directed against acetylcholine receptors at the neuromuscular junction. The subject is introduced with three children who had thymectomy to control the disease. We have a special interest in the disease because of its interactions with various anesthetic agents. There is much written about the critical care and anesthetic management of the adult myasthenic patient, but not to nothing about the pediatric patient. It should be noted that besides children with autoimmune (or juvenile) myasthenia, there are two other forms: neonatal myasthenia, a transient condition caused by the passage of antibodies from myasthenic mothers across the placenta; and congenital myasthenia, a genetically inherited autosomal recessive disorder affecting the motor endplate. Neither of these two later conditions is associated with an abnormal thymus, so thymectomy is not indicated.

In the first case, a seven year old girl, presented with a three year history of predominantly ophthalmic myasthenia. She had a positive anticholinesterase test and positive acetylcholine receptor antibodies. She weighed 24 kg, with obvious ptosis, mild generalized weakness, and bulbar symptoms. Peak expiratory flow rate and forced expiratory volume were 83% and 73% of predicted respectively. She was on pyridostigmine 15 mg four times daily, prednisolone 20 mg twice daily, and azathiaprine 37 mg daily. Anesthesia was induced with propofol and alfentanyl and maintained with oxygen, nitrous oxide, isoflurane and intermittent fentanyl. Intubation was performed without muscle relaxant and she was mechanically ventilated. Thymectomy lasted 105 minutes and was performed through median sternotomy. The child was taken to the intensive care unit where the endotracheal tube was removed 90 minutes later following assessment of tidal volume and respiratory functions. Intravenous morphine was given for pain management. Over the next few days, pyridostigmine was titrated to clinical effect. She was discharged home five days later on pyridostigmine 15 mg twice daily, (half her preoperative dose), azathiaprine 27 mg daily, and with a plan to wean and then stop prednisolone.

Continued on page 8
In the second case, a 13-year-old girl, weight 50 kg was receiving a maximal dose of pyridostigmine and was able to tolerate, 60 mg three hourly. She had been followed for six months with ocular symptoms, and diagnosis was made with positive anticholinesterase test, positive acetylcholine receptor antibodies, and repetitive nerve stimulation. Her condition had deteriorated rapidly, with generalized weakness and marked bulbar symptoms. Peak expiratory flow rate and forced expiratory volume were 30 – 50% of that predicted. She required intravenous immunoglobulin to control her symptoms. Steroids were avoided because of planned thymectomy. Anesthesia was induced with propofol and fentanyl, and maintained with oxygen, nitrous oxide and isoflurane. Continuous neuromuscular monitoring of the ulnar nerve was carried out using a train of four monitors. Initially, a laryngeal mask airway was placed, which was later replaced with an endotracheal tube using 10 mg of atracurium. This enabled assessment and recording of her baseline neuromuscular function, and the depressant effect of both isoflurane and neuromuscular blockade. Spontaneous neuromuscular recovery, reaching a plateau, took 120 minutes after the administration of atracurium, thus demonstrating the prolonged action of this drug in myasthenia gravis. Following discontinuation of isoflurane, the neuromuscular depressant effects were also seen to wear off. A total of 150 minutes after induction, a half-dose of neostigmine, 1.25 mg, with glycopyrrolate 0.25 mg, was given. She was extubated in the operating room and transferred to the intensive care unit. Because of postoperative nausea and vomiting, she was unable to tolerate oral pyridostigmine, hence received intravenous neostigmine. She was discharged to floor after two days. Despite several adjustments to the dose of oral pyridostigmine, she remained very weak and was given intravenous immunoglobulin. She was discharged to home on postoperative day 13, on pyridostigmine 45 mg four times daily, a reduction of 200 mg compared with her preoperative dose.

The third case was a 14-year-old girl, weighing 67 kg, diagnosed with myasthenia 18 months previously, initially with only ocular symptoms. Within the last six months, she developed bulbar symptoms and proximal weakness. Thymectomy was planned but she developed respiratory infection, which led to cancellation of surgery. Respiratory infection precipitated a myasthenic crisis. She could not walk unaided or swallow any oral medication, and she required intravenous neostigmine and atropine every 60 – 90 minutes. She was given prednisolone 60 mg daily and a course of intravenous immunoglobulin without any improvement. Plasma exchange therapy was planned. A hemofiltration catheter was introduced under general endotracheal anesthesia. No muscle relaxant was used. After plasma exchange, she improved remarkably and was able to receive depolarizing phase I block is not reached, and phase II block will result in functional blockade by auto antibodies. Thus the threshold for causative crisis will worsen.

Myasthenia gravis is characterized by muscular weakness and fatigue after exertion. Ophthalmic features are common and children may initially present with strabismus, ophthalmoplegia, diplopia, and ptosis. However, children may present with ocular symptoms, generalized weakness or a combination. When respiratory muscles are affected requiring ventilatory support, the patient is said to be in myasthenic crisis. Infection, fever, surgical or emotional stress, and medication such as aminoglycosides or anticonvulsants may precipitate myasthenic crisis. Differential diagnosis of an acute or chronic weak child with myasthenia may be either myasthenic crisis or cholinergic crisis. Cholinergic crisis is caused by an excess of acetylcholine at the neuromuscular junction, and is caused by overtreatment with cholinesterase. The child may also present with cholinergic signs such as excessive secretions, diarrhea, abdominal pain, and blurred vision. Moreover, when intravenous edrophonium is given, cholinergic crisis will worsen.

Diagnosis is established by the standard pharmacological test. Administration of edrophonium, dose by child’s weight, (<10 kg 0.5 mg, 10-30 kg 1 mg, >30 kg 2 mg) which acts within 30 seconds, showing rapid improvement in muscle strength lasting 5 minutes. It is recommended that atropine and resuscitation equipment be readily available to treat any cholinergic side effects. Unfortunately, a negative response does not exclude myasthenia, but a positive response confirms it. Acetylcholine receptor antibodies are highly specific for myasthenia gravis, but seropositivity becomes more common with increasing age and duration of the disease. Electrophysiological studies such as repetitive nerve stimulation and single fiber electromyography are more definitive, but children may refuse these “needle tests”.

Anticholinesterases are the mainstay of treatment. Pyridostigmine is preferred over neostigmine. Corticosteroids are second line agents, but they may worsen effects of thymectomy, especially in adults. They may be withheld pending surgery, but if they are being used, the dose tends to be large, so additional steroids may be needed perioperatively. Other immunosuppressive agents such as azothiaprine, cyclophosphamide, and cyclosporine have been used, but serious side effects limit their use. Plasmapheresis and intravenous immunoglobulin are used when a patient is in crisis or to optimize neuromuscular function preoperatively. Plasmapheresis works by clearing the acetylcholine receptor antibodies from the circulation, whereas the mechanism of action of immunoglobulin is less clear, it may exert its effect by altering antibody production, binding of antibodies or prevention of interaction with neuromuscular junction. Plasmapheresis gives better results but with technical difficulties in obtaining venous access may limit its use in children. Therefore, immunoglobulin is used as the first line of treatment and plasmapheresis for the more recalcitrant patient. Finally, thymectomy is generally accepted as standard treatment, though there are no definitive studies to support it. The age at which thymectomy is performed is controversial. Early surgery increases the chance of remission. There is a theoretical concern of causing immunosuppression in young children, but it has never been reported. Most centers wait until the child is ten years old, but has been performed on children as young as two years.

With regards to anesthetic management, understanding of the response of muscle relaxants is imperative. Patients may appear “resistant” to succinylcholine. Adults may require twice the loading dose, and children may require three to four times the normal dose. For these patients, the usual dose cannot depolarize the motor endplate, due to the reduced number of receptors and their functional blockade by auto antibodies. Thus the threshold for causing depolarizing phase I block is not reached, and phase II block will occur. The picture may be further complicated by the preoperative use of anticholinesterase therapy, which inhibits the enzyme that breaks...
Anesthesia for the Child with an Upper Respiratory Tract Infection: Still a Dilemma?

**Reviewed by:** Cheryl K. Gooden, MD, FAAP

**Review:** This article takes an in-depth look at the effects of anesthesia in the presence of an upper respiratory tract infection (URI). In addition, the authors highlight the current trends, implications and anesthetic management associated with the child presenting with a URI. There is no doubt that for many of us in the pediatric anesthesia community, the issue of anesthesia and URIs is still considered to be one of the most controversial topics and promotes much discussion.

In the past fifty years or so, there have been a number of articles in the medical literature that have focused on the subject of anesthesia and URIs in pediatric patients. This review article refers to many of these earlier articles, and the underlying notion, that blanket cancellation of elective surgery in the presence of a URI is no longer the norm. As the authors, Tait and Malviya recommend, and many anesthesia providers may agree, that the child with severe URI symptoms have surgery postponed for at least 4 weeks. This time frame will vary, depending on the severity of symptoms.

There are several key issues in this article that deserve mention. First, it is imperative that the anesthesia provider have a good understanding of the risk factors that may lead to respiratory complications. These risk factors include: 1) a history of asthma 2) use of an endotracheal tube 3) copious secretions 4) nasal congestion 5) parental smoking 6) surgery of the airway and 7) history of prematurity. Second, to some extent, the decision to cancel surgery because of a URI, is becoming more of a selective process. This is in contrast, to the outright cancellation of surgery, in the presence of a URI. Third, the risk/benefit to the child with a URI receiving anesthesia is multifactorial. Finally, the article alludes to the future promise of additional treatments and management for the risks associated with anesthetizing the child with a URI. Of particular interest, is the use of recombinant human neutral endopeptidases to substitute for the natural forms lost during the viral infection.

**Comments:** The authors should be commended for their outstanding review article, on the issues of anesthesia and its impact on the child with a URI. This article provides some of the latest information with regards to pre-operative considerations and anesthetic management in the presence of a URI. The information presented is important to those of us who care for children.

**Forty Years of Clinical Aprotinin Use: A Review of 124 Hypersensitivity Reactions**

**Reviewed by:** Barry D. Kussman, MBCh, FFA(SA)

Aprotinin, by inhibiting fibrinolysis and preserving platelet function, has been shown to reduce blood loss and transfusion requirements in cardiac surgery, lung, and liver transplantsations, and hip replacement surgery. Aprotinin is a bovine protein and its anaphylactic potential is an important concern. The authors present a review of the 124 hypersensitivity reactions to aprotinin reported in the medical literature from 1963 to 2003, plus five of their own patients.

More than half of the classified reactions were life threatening and 9% were fatal. Greater than 80% of reactions occurred in patients with previous exposure to aprotinin, with most at reexposures within three to six months. Intravenous application had a greater risk of hypersensitivity than topical (fibrin sealants) application. Symptoms reported were cardiovascular (36.6%), cutaneous (27.2%), respiratory (17.4%), abdominal (7.6%), vegetative (5.8%), and neurologic (5.4%). The most frequently applied in vitro tests were measurement of aprotinin-specific IgE (positive in 27 of 46 reactions) and aprotinin-specific IgG (positive in 18 of 33 reactions). The incidence of specific serum-IgE is about 14% within the first three months postexposure, while serum-specific IgG is detectable in about 50% of patients having received one aprotinin treatment and may persist for several years. In the 20% of reactions in patients without prior aprotinin exposure, the pathophysiologic mechanism may be a direct drug action on the effector cells or a drug induced mediator release. Aprotinin was not capable of inducing a significant rise in a histamine release test. Of note, intravenous test doses, usually 10,000 KIU, have the potential to trigger acute reactions.

Based on these findings, a decision-making algorithm is recommended to reduce the risk of an aprotinin reaction. If there is a history of former exposure to aprotinin (documented or former operation with high bleeding risk), screening for aprotinin-specificantibodies should be performed. If positive, do not use aprotinin. If negative and exposure occurred within the prior six months, (i) do not use aprotinin if cardiopulmonary bypass is not planned or (ii) use with caution if cardiopulmonary bypass is planned and administer only when cannulation sites for bypass exposed. If negative antibody screen and exposure greater than six months prior or no history of aprotinin exposure, use aprotinin as per manufacturer’s guidelines.

**Comment:** Hypersensitivity reactions to aprotinin are rare, but serious events. Although an average anaphylactic risk on reexposure of 2.8% is quoted, adverse reactions tend to be under reported and without a denominator the true incidence remains unknown. The mean
age (45 ± 20 years) for which demographic data was available for this review needs to be taken into consideration when applying the findings to the pediatric population. Aprotinin is frequently used in neonatal cardiac surgery (including staged palliation), and the risk of a hypersensitivity reaction upon primary and re-exposure is unknown and may be not be the same as in adults. The recommendation by these authors that “aprotinin use should be avoided in all patients undergoing staged palliation of congenital heart disease requiring early reoperation” is not based on any presented data. Screening for serum-specific antibodies is certainly prudent, but may not be available in every institution and scheduling of surgery may not allow sufficient time for this to be done. The presence of serum-specific antibodies should probably preclude use of aprotinin (even considering a false positive), but in vitro testing is imperfect. False negatives may lull one into a ‘false’ sense of security as an anaphylactoid reaction may still occur. False positives may result in withholding a drug with beneficial antifibrinolytic, platelet-sparing and anti-inflammatory effects. The usual risk-benefit analysis needs to be considered, bearing in mind that re-exposure within three to six months places the patient at most risk. Ideally, aprotinin should be administered prior to skin incision. In patients undergoing repeat cardiac surgery where dissection may be long and difficult, or in those whose hemodynamic status is marginal, I agree with the recommendation to administer aprotinin only when the cannulation sites for cardiopulmonary bypass are exposed.

**Book Corner**

**Anesthesia for Congenital Heart Disease**


This is the first edition of this eagerly anticipated, recently published hardcover textbook on pediatric cardiac anesthesiology.

The text is divided into six sections: History, Education, and Science; Monitoring; Preoperative considerations; Management; Anesthesia for specific lesions; and Anesthesia outside the cardiac operating room. Twenty-seven chapters written by world-renowned pediatric cardiac anesthesiologists, from various children’s hospitals in North America, who are on the cutting edge in their clinical and research practices, are presented in a surprisingly clear and readable format. New material, heretofore never covered in a textbook of pediatric cardiac anesthesia, is provided. Topics covered include cardiac catheterization, laboratory anesthesia, cardiac intensive care, anesthesia for non-cardiac procedures and neurologic monitoring and outcome. Computers and technology, bleeding and coagulation, approach to the teenager and adult, approach to the premature newborn, the inflammatory response, regional anesthesia, cardiac magnetic resonance imaging, research teaching and administration are also discussed.

The chapters on the various congenital heart disease lesions consistently are all broken down into introduction, anatomy, pathophysiology, diagnosis, and surgical approach and anesthetic considerations. The section describing anesthetic management of specific lesions in the non-cardiac surgery and MRI chapter, provides particularly excellent short clear summations of anatomy and pathophysiology, issues in unrepaired patients, issues in palliated patients, issues in repaired patients and special anesthetic concerns. Figures are mostly black and white, and are clearly demarcated from textual material.

Overall, this is an excellent text, for pediatric anesthesiologists and pediatric cardiac anesthesiologists alike.

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**MARK YOUR CALENDAR!**

**Pediatric Anesthesia 2006**

February 16-19, 2006

Sanibel Harbour Resort & Spa
Fort Myers, FL

Abstract site opens: September 30, 2005
Abstract Deadline: December 5, 2005
www.pedsanesthesia.org

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**Breakfast Panel**

**American Academy of Pediatrics Section on Anesthesiology and Pain Medicine**

**New Orleans Hilton Riverside**

Wednesday, October 26, 2005
7:30 – 8:45 am

Tickets must be purchased through the ASA.

**Safety Concerns for Patients and Practitioners: How is it Changing the Practice of Pediatric Anesthesia?**

**Moderator:** Constance S. Houck, MD, FAAP

- **The Exploding Anesthesia Machine**
  - Joel B. Gunter, MD, FAAP

- **Safety Catheters and Needleless Systems**
  - Melissa Wheeler, MD, FAAP

- **JCAHO Regulations and Sentinel Events**
  - Randall M. Clark, MD, FAAP

**Tickets must be purchased through the ASA.**
Older children and teenagers have a more adult composition of the epidural space. For this reason, the caudal approach is no longer recommended. The patient in our stem case, may or may not cooperate with an awake epidural placement, and thus require the epidural catheter placed after the induction of general anesthesia. The lumbar route has been used with great success in all age group, where the catheter is usually placed after induction of general anesthesia. The patient is placed in the lateral decubitus position, with hips flexed. However once again either high doses of local anesthetic need to be used to achieve high enough sensory levels, or an attempt can be made to thread the catheter. Blanco et.al showed that only 22% of catheters placed at the lumbar space actually reached the desired thoracic level. On the other hand, the inability to use patient reports of pain or paresthesias dissuades many pediatric anesthesiologists from directly placing the catheter at the thoracic level, where the risk of spinal cord injury may be significant.6

The second controversial issue involves the use of confirmation for catheter placement. Some anesthesiologists place catheters blindly without radiological confirmation. However, radiological misplacement of catheters has been reported. In one case the catheter, one exited an intervertebral foramen in an infant and in another the catheter was found in the presacral space.12,16 Stylletted catheters may mitigate catheter malpositioning, albeit at the expense of a higher incidence of unintentional intravascular and subarachnoid penetration.12 In an anesthetized pediatric patient, whatever the age, the need for some sort of catheter confirmation is probably prudent This is because ease of catheter advancement alone is not a reliable sign of placement within the epidural space, nor is it possible to know where the tip of the catheter is. A retrospective review of 115 infants less than six months of age who had a thoracic epidural catheter placed by the caudal route revealed an incidence of thirty-two percent for catheter malpositioning.4 The gold standard confirmation device is epidurography.10,11 Radiographic contrast (Iohexol-Omnipaque-180) is administered and chest x-ray and abdominal x-rays identify and confirm catheter position.15 Many hospital operating rooms have a fluoroscopy machine that can be used for such a purpose. Other recent technological advancements for confirmation for catheter placement include ultrasound,13 nerve stimulation guidance,14 and electrocardiogram trace comparison.15 Many of these confirmatory methods have inherent limitations. Epidurography is invasive and fluoroscopy is time consuming and labor intensive. Epidural stimulation cannot be used in the presence of neuromuscular blockade.18 Ultrasound cannot neither visualize the epidural catheter in the epidural space in children greater than 6 months old, nor precisely identify the tip of the catheter.7 Electrocardiographic guidance may display subtle QRS changes in the high thoracic region and entail difficulty discriminating spinal levels when the epidural catheter tip is above the level of the heart.19

In answer to the anesthetic dilemma of postoperative pain management posed in the stem case, the literature doesn’t really help with the decision making process, which will ultimately depend on the anesthesiologist’s level of comfort with each of the possible techniques. If the child is cooperative an awake thoracic epidural can be attempted. The child and parents should both be active participants in this decision, and informed consent should be obtained from both. If there is trepidation about awake placement, the risks and benefits of anesthetized placement should be discussed. Induction of general anesthesia should proceed, after which either a lumbar epidural with an attempt to advance catheter the thoracic levels can be tried, or a the catheter can be placed directly at the thoracic level. In either case confirmation of catheter placement should be considered.

--- Full References Available Online ---
August 18-21: Townsville, Australia  
Society for Paediatric Anaesthesia in New Zealand and Australia (SPANZA) Meeting 2005: Joint Meeting with the Australian Society of Paediatric Surgeons  
Tel: +61 3 9698 7440, Fax: +61 3 9690 3944  
Information: Dr. Patrick Farrell, Secretary SPANZA  
Department of Anaesthesia, John Hunter Hospital  
Locked Bag 1, Hunter Region Mail Centre  
Newcastle NSW 2310 Australia  
Website: http://www.spanza.org.au

September 1-3: Cologne, Germany  
6th European Congress of Paediatric Anaesthesia  
Tel: +49 (0) 221 890752 64, Fax: +49 (0) 221 890754 94  
Information: Dr. Med. Josef Holzki, Abteilung für Anästhesie und Intensivmedizin Kinderkrankenhaus der Stadt Köln, Amsterdamer Strasse 59, 50735 Köln 60, Germany.  
Website: http://www.feapa-cologne2005.org

September 17-18: Boston, MA, USA  
Pediatric Sedation Outside of the Operating Room  
Tel: (617) 384-8600, Fax: (617) 384-8686  
Information: Harvard Medical School, Department of Continuing Education, P.O. Box 825, Boston, MA 02117-0825  
Website: http://www.cme.hms.harvard.edu/sedation

October 21: New Orleans, LA, USA  
Hilton New Orleans Riverside  
Society for Pediatric Anesthesia (SPA)  
19th Annual Meeting  
Tel: (804) 282-9780, Fax (804) 282-0090  
Information: Society for Pediatric Anesthesia  
P.O. Box 11086, Richmond, VA 23230-1086  
Website: http://www.pedsanesthesia.org

November 11-13: Toronto, ON, Canada  
Pediatric Anesthesia Conference  
Tel: (416) 813-7445, Fax: (416) 813-7543  
Information: The Hospital for Sick Children, University of Toronto, Toronto, Canada  
Website: http://www.sickkids.ca/anaesthesia

Footnote:  
Please forward all information concerning congresses relevant to Pediatric Anesthesia to: Helen V. Lauro, MD, FAAP, Department of Anesthesiology, Long Island College Hospital, 339 Hicks Street, Brooklyn, New York 11201.

February 16-19: Ft. Myers, Florida USA  
Sanibel Harbour Resort and Spa  
Society for Pediatric Anesthesia (SPA)/American Academy of Pediatrics (AAP)  
2006 Winter Meeting  
Tel: (804) 282-9780, Fax: (804) 282-0090  
Information: Society for Pediatric Anesthesia  
P.O. Box 11086, Richmond, VA 23230-1086  
Website: http://www.pedsanesthesia.org

June 25-29: Vancouver, Canada  
7th International Symposium on Pediatric Pain  
Tel: (604) 681-2153 Fax: (604) 681-1049  
Information: Conference Secretariat  
International Conferences Services Limited  
604-850 West Hastings Street  
Vancouver, BC, Canada, V6C 1E1  
Email: ispp2006@meet-ics.com

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POINT/COUNTERPOINT

Would Clinical Outcomes be Improved with Lighter Anesthetic Techniques?

References:

Should the Results of Animal Studies Change Clinical Anesthetic Care?

References:

**Topic Review**

**Pediatric Thoracic Epidural Catheter Insertion — To Insert Awake or Anesthetized; To Confirm or Not Confirm: Those are the Questions...**

By: Helen V. Lauro, MD, FAAP

**References:**