Official Newsletter of the

SPA | Society for Pediatric Anesthesia

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THE ANNUAL MEETING

By Randall C. Wetzel, M.D.

The plans are well underway for the Society for Pediatric Anesthesia Annual Meeting to be held on Friday, October 13, 1989 in New Orleans. The Board of Directors, Dr. Crone and Dr. Maze have organized an exciting program that will certainly be of interest to practitioners of pediatric anesthesia across the country.

The morning symposium will center on advances in our understanding of cardiopulmonary support and resuscitation. Dr. Russ Raphaely (of the Children's Hospital of Philadelphia) will give an overview of the outcomes of CPR in children and an historical perspective. Dr. Richard Traystman from the Department of Anesthesiology at the Johns Hopkins Hospital will discuss the physiologic basis and consequences of CPR. This will be followed by Dr. Charles Schleien, also from Johns Hopkins, discussing metabolism during CPR, and the effects of CPR on cerebral blood flow. These two investigators have extensive experimental and clinical experience with models of pediatric resuscitation. This morning session should provide a thorough up-to-the-minute review of pediatric CPR. Following coffee, Dr. Charles Rice, from the University of Washington, will discuss one of the leading etiologic factors in ischemic injury, that of leukocyte activation. He will focus on the role of activated leukocytes in ischemic injury. He, along with Dr. Jeff Morray, also of the University of Washington, will discuss therapeutic approaches, as well as clinical recommendations for CPR in children.

This exciting morning session will be followed by luncheon. If it is as well planned as in past years, the gastronomic desires of members of the Society can be expected to be well satisfied.

After lunch, Dr. David Steward of the University of British Columbia has kindly consented to lead a panel consisting of Drs. Lynn Broadman from Children's Hospital in Washington, DC, Gene Betts from the Children's Hospital of Philadelphia, Jerry Lerman from the Hospital for Sick Children in Toronto, and Frederic Berry of the University of Virginia, to discuss current issues regarding preoperative fasting and postoperative vomiting, a controversy in pediatric anesthesia. The second controversy panel will be moderated by Fritz Berry and will concern transfusion therapy. Drs. Mark Rockoff from Children's Hospital in Boston, Peter Rothstein from Columbia University, Eric Furman from Cook-Fort Worth Children's Medical Center, Ramez Salem from the Illinois Masonic Medical Center and Charlie Cote from Massachusetts General Hospital will discuss multiple aspects of transfusion therapy for children

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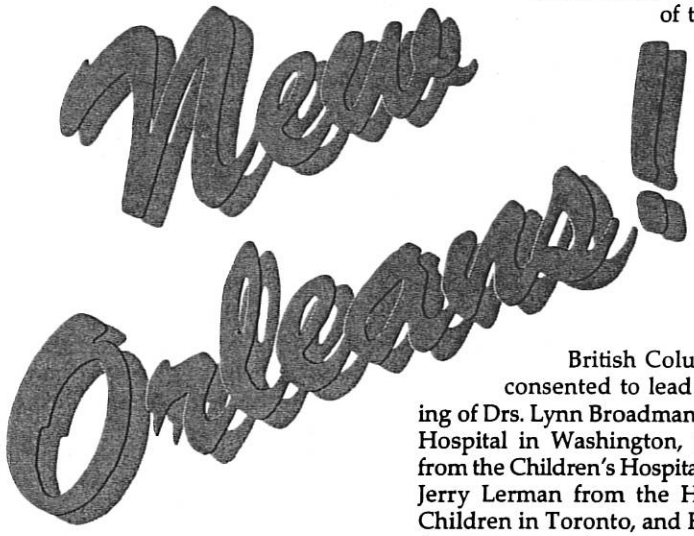

Contents:

Dues and Costs

The cost of the second meeting (guest speaker costs, meeting place expenses, and food) was underwritten by membership dues. We hope to continue this policy of using membership dues and corporate donations to pay for the annual meetings in the future. Indeed, we believe that the dues structure of the organization is such that members will get "their money's worth."

Please note that a new fiscal year has started and members should send their dues of $100 with an application form. Interested physicians can apply for membership by mailing the enclosed application form with $100 to:

THE SOCIETY FOR
PEDIATRIC ANESTHESIA
515 Busse Highway
Park Ridge, IL 60068

Help Wanted Future Projects

The Officers and Board of Directors are interested in the continuing involvement of the Society's membership. Members interested in running for office or participating in the newsletter are encouraged to write to us at the SPA office in Park Ridge. We hope to expand the newsletter next year and include features such as literature review and debates on controversial subjects.

The Newsletter

Publication of the Newsletter and its contents continues to evolve. Departments include "Ask the Experts", "Literature Review", and a "Calendar of Meetings". Volunteers to help with the Newsletter, or who may have suggestions should notify one of the Editors:

Randall Wetzel, M.D.
The Johns Hopkins Hospital
(301) 955-7612

Roger Moore, M.D.
Deborah Heart and Lung Center
(609) 893-6611

ASK THE EXPERTS

By Roger Moore, M.D.

Do you have a burning question? Do you lie awake nights wondering about the proper pediatric anesthesia management of a specific problem? Find relief in the "Ask the Experts" column. Send any and all questions to the Society for Pediatric Anesthesia Newsletter and we will solicit in-depth answers from some of the most knowledgeable physicians in that field.

Thank you.

Question:

Is there anything that can be done to reduce the risk of professional liability?

WILLIAM M. GILD, M.D., J.D.
Assistant Professor of Anesthesiology
Hahnemann Medical College and Hospital

Answer:

Malpractice litigation remains a source of concern to all of us, not only because of the time and money spent insuring and defending against it, but also because of the implications and inferences drawn against the physician named in a lawsuit. "No smoke without fire" might seem a cruel judgment for those named, but I suspect no small amount of self doubt and guilt accompany the years of processing a malpractice claim succeeding the initial notice of a suit.

During a career, 31.5 percent of anesthesiologists will be sued (1987 data from AMA Socioeconomic Characteristics of Medical Practice), as compared with 37.0 percent of all physicians in this country. The average professional liability premium paid by anesthesiologists in 1987 was $22,900, as compared to $15,000 for all other specialties. Comparing the above data, it seems clear that while we are sued, as a group, slightly less frequently than others, our premiums (and thus, what the industry calls loss experience) are greater. There exist several reasons for this; brain damage emanating from an anoxic or hypoxic event is an expensive "event" for obvious reasons; we rarely, if ever, establish long-term rapport with our patients, thus contributing to the disaffection element in the relationship; and our medical management is usually facilitatory, rather than therapeutic. Each of these factors are true for both the adult and the pediatric anesthesiologist.

Liability in pediatric anesthesia is a special concern for a number of reasons. These reasons include the increased relative risk in the pediatric age-group and the "risk" to the pediatric anesthesiologist in terms of the likelihood of malpractice suit. The two need not necessarily be related.

Are children at greater risk? I know of no studies addressing that question specifically. There are many variables other than age, which make drawing conclusions difficult. One might argue that children undergoing surgery are generally healthier than adults, but physiologic and pharmacodynamic/kinetic variables expose the child to greater risk. Small errors in dosage formulation have far greater implications in the child (particularly the small child). A smaller functional residual capacity of the lungs and, in the case of infants, non-compliant cardiac ventricles, reduce the margin of safety preserving oxygenation and cardiac output.

Preliminary findings from the American Society of Anesthesiologists' (ASA) Closed Claims Study (performed by the ASA Committee on Professional Liability) indicate that inadequate ventilation, as a cause of injury, is more common among children than adults. Outcome in the cases was universally poor (25 deaths, five severely brain damaged survivors - out of 111 pediatric claims). While closed claims studies cannot generate incidence data, the above preliminary data suggest (Geiduschek, JM, et al personal communication) that use of pulse oximetry may play a role in preventing these types of mishaps in the future, especially in view of the fact that the heralding signs of the impending event (a cardiac arrest in 30 of the 31 patients who were inadequately ventilated) were a combination of hypotension, bradycardia or cyanosis (n=23), apnea (n=2) or asystole (n=6). Pulse oximetry and/or capnography may have prevented complications in all but one of these cases.

The second issue, concerning the legal risk inherent in the practice of pediatric anesthesiology, is even more complex. Aside from the child with complex congenital cardiac malformations, children undergoing anesthesia are, I suspect, generally healthier than their adult counterparts, and thus not expected to sustain injuries from the anesthetic itself. This perception (usually on the part of parents) may generate an increased willingness to sue for untoward outcomes whether negligence is involved or not. Furthermore, in cases of permanent brain damage following hypoxic episodes, the life expectancy would be significantly longer (and thus cost of settlement higher) than in the case of a damaged adult whose age and premorbid condition would limit the cost of settlement. Lastly, the Statute of Limitations,

the period between the occurrence of an event and when a lawsuit can be filed, is potentially much longer in children than adults. Generally, a suit must be filed within two years of discovery of injury, but in the case of children, the statute begins to "toll" only at the attainment of the age of legal majority. The implications of this extended period are obvious and significant (for obstetricians too). Reserve funds mandated by state insurance law must take this into account, thus adding to the overall cost of doing business by the insurance company, and, by extension, the practitioner.

Pediatric anesthesia is a specialty holding rich rewards for the practitioner, but also the potential for increased risk in terms of technical and physiologic problems and for litigation due to the malpractice situation unique to the pediatric age range. Improved training, greater understanding of pharmacology and physiology and the concentration of pediatric anesthesia in institutions geared to the young patient will improve safety generally. However, information emanating from the American Society of Anesthesiologists' Closed Claim Study indicates that possibly the single most important controllable positive intervention is the routine use of pulse oximetry and capnography - both of which are noninvasive and economically sensible.

Question:

How much fentanyl should we give to provide anesthesia for a neonate undergoing surgery?

DENNIS M. FISHER, M.D.
Associate Professor of Anesthesia
and Pediatrics
University of California, San Francisco

Answer:

Since Robinson and Gregory's description in 1981 of fentanyl anesthesia for premature infants undergoing PDA ligation [1], narcotics have become popular anesthetics for neonates. However, the clinical practices regarding narcotic administration to neonates vary widely. I will briefly review reasons for the popularity of narcotics in neonatal anesthesia and the factors influencing the choice of drug and dosage.

The anesthetized neonate often becomes hypotensive as a result of its smaller cardiovascular reserve, preoperative diuretics and fluid restriction (particularly prior to PDA ligation), and incorrect data regarding anesthetic requirements (e.g., neonatal halothane MAC was believed to be 1.1 percent while more recent reports place the value close to 0.9 percent [2]. In this context, the practice of paralyzing, but not anesthetizing, neonates became popular. The landmark work of Anand et al. [3] showed that paralysis without anesthesia produced a marked stress response and a worse outcome. As a result, paralysis alone is now considered inappropriate.

Why narcotics? One answer is that these drugs have minimal hemodynamic effects, even in the high-risk premature infant. For example, Robinson and Gregory observed no hypotension in neonates given fentanyl, 30-50 ug/kg, pancuronium, and a fluid bolus, in contrast to a high incidence of hypotension in a similar group anesthetized with halothane. Recently, Yaster et al. [4] reported that fentanyl doses as high as 3000 ug/kg minimally affected lamb's hemodynamics. Thus, the major advantage of narcotic anesthetics in the neonate is that, with concomitant administration of a vagolytic drug (e.g., pancuronium or atropine) and a fluid bolus, hypotension is rare.

Which narcotic? Any answer lies more with tradition than science. Morphine has a bad reputation in neonatal anesthesia because it is a potent respiratory depressant [5] (morphine, 0.05 mg/kg, depressed neonate's ventilation more than adult's while meperidine, 0.5 mg/kg, affected ventilation minimally). These findings probably result from the increased permeability of the immature blood-brain barrier to water-soluble morphine [6]. In contrast, meperidine's (and probably fentanyl's) lipid solubility permit it to cross the blood-brain barrier freely. As a result, central nervous system concentrations probably change minimally with age. Beyond these data and studies which demonstrate that fentanyl blunts pulmonary hemodynamic reactivity in neonates with congenital heart disease, [7] there has been little evaluation of narcotics in neonates. As a result, there is little basis to recommend one drug over another. However, we do have more clinical experience with fentanyl.

The final question is how much narcotic? Published recommendations vary widely. For example, Robinson and Gregory noted that following fentanyl, 30-50 ug/kg, "within an hour of surgery, all infants were awake and breathing spontaneously." Similarly, Collins et al. noted that "a bolus of 30 ug kg^{-1} of fentanyl in preterm infants may not be adequate to cover the increased stimulus of skin closure after closure of a PDA." [8] In contrast, Yaster [9] reported that a smaller fentanyl dose, 12.5 ug/kg, provided 90 minutes of anesthesia.

The discrepancy between these observations may result, at least partly, from pharmacokinetic differences among patients. For example, in full-term neonates, clearance is decreased when abdominal surgery is being performed. [10] This probably occurs because increased intra-abdominal pressure decreases hepatic blood flow [11] (fentanyl is metabolized by the liver), resulting in decreased fentanyl clearance). Fentanyl clearance also increases markedly during the first month of life, [12] probably a result of maturing hepatic function (increasing activity of cytochrome P-450) and increasing hepatic blood flow (as the ductus venosus closes). The relative contribution of these and other factors (such as inhaled anesthetics, hypoxia, hypo- or hypercapnea) on hepatic blood flow and fentanyl metabolism is not known; we can only observe that patients studied by Yaster were younger than those of Robinson and Gregory and Collins et al. In addition, patients in the latter two studies had surgery unlikely to decrease hepatic blood flow; in contrast, some of Yaster's patients had abdominal surgery, which might decrease their metabolism of fentanyl and, hence, anesthetic requirements.

These observations suggest that neonatal dose requirements for fentanyl vary with postnatal age and the type of surgery. The role of other factors in altering narcotic requirements remains to be determined.

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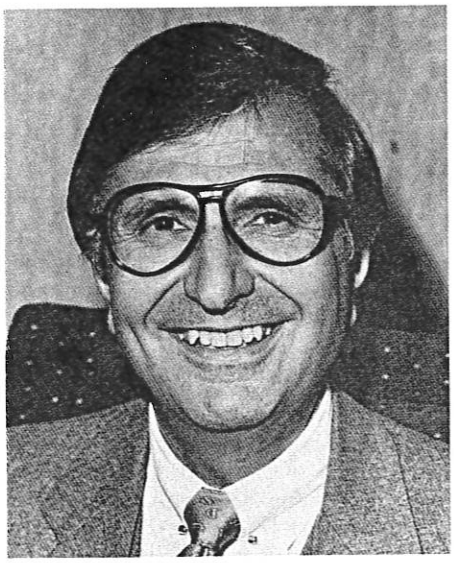
THE ANNUAL MEETING

(Continued from page 1)

and provide us with current views regarding transfusion in children.

The afternoon session will be moderated by Aubrey Maze and will be an overview of the pain management techniques in children. This rapidly evolving field in pediatrics has had many changes and the question "How do you do it in children?" will be addressed by Navil Sethna of the Children's Hospital of Boston, Elliott Crane of the Children's Hospital Medical Center in Seattle, Myron Yaster of The Johns Hopkins Hospital, Will McIlvaine of the Children's Hospital in Denver and Don Tyler of the Children's Hospital in Seattle.



Russell C. Raphaely, M.D. will discuss CPR in children during the morning symposium

The business meeting will follow these exciting sessions. After the business meeting, a wine and cheese reception will be the start of a well rounded evening.

This well-organized and comprehensive program of key issues in pediatric anesthesia promises to provide something for all the practitioners of anesthesia in children. □

SOCIETY FOR PEDIATRIC ANESTHESIA

ANNUAL MEETING

October 13, 1989

New Orleans, Louisiana

7:15 - 8:15	Registration and Continental Breakfast
8:15 - 8:30	Introduction: Robert K. Crone, M.D. and Aubrey Maze, M.D.

MORNING SYMPOSIUM

CPR: Advances in our Understanding of Cardiopulmonary Support and the Sequelae of Hypoxic Ischemic Injury.

8:30 - 9:00	Outcome of CPR in Children: An Historical Perspective. Russel Raphaely, M.D., Professor, University of Pennsylvania
9:00 - 9:50	The Physiologic Basis and Consequences of CPR. Richard Traystman, M.D., Professor, The Johns Hopkins University
9:50 - 10:30	Cerebral Blood Flow and Metabolism During CPR. Charles Schleien, M.D., Assistant Professor, The Johns Hopkins Unive...
10:30 - 11:15	The Role of the White Blood Cell in Ischemic Injury: Possible Approaches to Therapy. Charles Rice, M.D., Professor, University of Washington
11:15 - 11:45	CPR — Clinical Recommendations for the Pediatric Patient. Jeffrey Morray, M.D., Associate Professor, University of Washington
11:45 - 12:15	Panel Discussion
12:15 - 1:30	LUNCHEON

AFTERNOON SYMPOSIUM

1:30 - 2:30	**Controversies in Pediatric Anesthesia — I**
	Pre-Op Fasting — Post-Op Vomiting David Steward, M.D.
10 minutes:	Metaclopromide — Is it an effective antiemetic? Lynn Broadman, M.D., Children's Hospital, Washington, DC
10 minutes:	Droperidol — Does it work? Gene Betts, M.D., Children's Hospital of Philadelphia
10 minutes:	Pre-Operative Fasting — Does it matter? Jerrold Lehrman, M.D., Hospital for Sick Children, Toronto
10 minutes:	Do you need p.o. fluids before discharge from day surgery? Frederic Berry, M.D., University of Virginia
20 minutes:	Panel Discussion

AFTERNOON SYMPOSIUM

(Continued)

2:30 - 3:45 p.m. Controversies in Pediatric Anesthesia — II

Transfusion Therapy
Frederic Berry, M.D., Moderator

10 minutes: When to transfuse: How low do you go?
Mark Rockoff, M.D., The Children's Hospital, Boston

10 minutes: Radiating Blood Products for Newborns — Is it necessary?
Peter Rothstein, M.D., Columbia University

10 minutes: Hemodilution — Is it worth it?
Eric Furman, M.D., Cook-Fort Worth Children's Medical Center

10 minutes: Hypotensive Anesthesia — Does it help?
Ramez Salem, M.D., Illinois Masonic Medical Center

10 minutes: Fresh Frozen Plasma — Is it necessary?
Charles Cote, M.D., Massachusetts General Hospital

25 minutes: Panel Discussion

3:45 - 4:00 p.m. BREAK

4:00 - 5:00 Pain Management Techniques — How Do You do it in Children?
Aubrey Maze, M.B., Moderator

10 minutes: Spinal Anesthesia
Navil Sethna, M.D., The Children's Hospital of Boston

10 minutes: Caudal Anesthesia
Elliot Krane, M.D., Children's Hospital and Medical Center, Seattle

10 minutes: Use of Nerve Stimulator for Brachial Plexus Blocks
Myron Yaster, M.D., The Johns Hopkins University

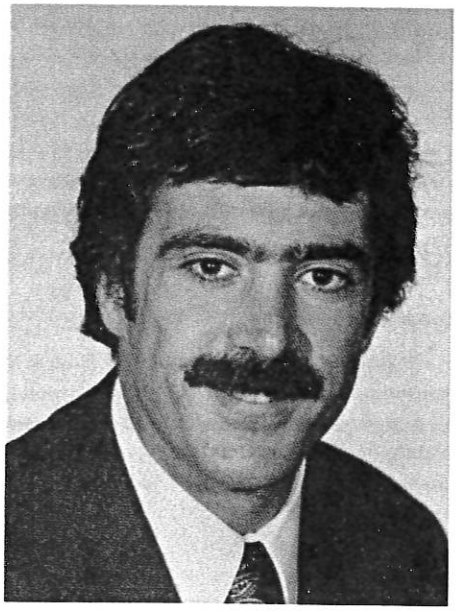
10 minutes: Intrapleural Analgesia
Will McIlvaine, M.D., The Children's Hospital, Denver

10 minutes: PCA in Children
Don Tyler, M.D., Children's Hospital and Medical Center, Seattle

10 minutes: Questions and Answers

5:00 - 5:30 p.m. BUSINESS MEETING

5:30 - 6:30 p.m. WINE AND CHEESE RECEPTION



"CPR—Clinical Recommendations for the Pediatric Patient"
will be presented by
Jeffrey Morray, M.D. during the
SPA Annual Meeting.

SPA MEMBERSHIP

It is not too late to become a member of the Society for Pediatric Anesthesia and attend the annual meeting. Over 700 physicians with an interest in pediatric anesthesia are now Society members. The Society also extends membership to fellows and residents who are in approved programs, with a letter of interest drafted by the resident or fellow and cosigned by the residency program director, certifying enrollment.

Your membership and participation in SPA will enable the Society to continue bringing you the annual meeting and a quarterly Newsletter, plus your support will allow SPA to expand its programs to bring new information and technology to your attention on a timely basis. If you have not renewed your SPA membership in 1989, please do so and encourage your friends and colleagues to take an interest in the Society for all anesthesiologists who are concerned with the care of children. □

"Ask The Experts"

(Continued from page 3)

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Question:

What are the advantages of rectal midazolam over other rectal or oral agents used as premedicants to ease separation anxiety?

ANNE E. DICKISON, M.D.
Director of Pediatric Anesthesia
Assistant Professor
Departments of Anesthesiology
and Pediatrics
University of New Mexico
Albuquerque, New Mexico

Answer:

Few young children will separate graciously from parents to enter an area where masked strangers apply monitors, masks, needles or physical restraints. To reduce the stress of this separation scenario — traumatic for all concerned — a variety of techniques and pharmaceuticals have been tried.

Parental presence during induction of anesthesia is an option often precluded by the logistics of the operating room. Even in the presence of a reassuring parent, a significant fraction of children will still object strenuously to masks, needles and restraints.

Oral premedication has been used extensively. In order to achieve its pacifying effect at the time of separation, however, it must be administered 45-90 minutes prior to induction. Nicolson [1] reports that in over 40,000 pediatric patients who had received the oral premedication consisting of meperidine/diazepam/atropine or meperidine/pentobarbital/atropine, only a small percentage became too sleepy to ambulate, and the use of oral premedication was very well received by all concerned. Disadvantages of oral premedication, besides the necessary interval between administration and effect, include rejection of the medicine by the child by physical resistance, spitting it out, or excitement-induced emesis, potential for synergistic sedation with intra-operative agents, and the occasional hyperactive or dysphoric response to the premedicant.

Rectal administration offers an expedient, relatively acceptable route of premedication, though the child greater than three to four years of age has been educated to modesty and protection from strangers of that part of the body, and will usually object to the instillation. Drugs administered in this fashion have rapid systemic absorption and effect. In general, venous drainage from the lower ⅔ of the rectum is systemic, and from the upper ⅓ of the rectum is portal. Anastomoses between the drainage veins plus variations in individual anatomy and pressure gradients will affect the percentage of systemic versus portal plasma concentrations. Drugs with high first-pass hepatic clearance characteristics should achieve greater bioactivity if they bypass the portal circulation. By nature of their pKa and liposolubity (characteristics which also enhance passage of the drug into the nervous system), most anesthetic or sedative-hypnotic agents have the potential for rectal administration with improved absorption and bioavailability as compared to the oral route.

Barbiturates have enjoyed the status of being the most widely used rectal premedicant-induction agents. [2, 3, 4, 5] Administration of 25 mg/kg methohexital results in roughly 85 percent of patients falling asleep in 15 minutes. Side effects include respiratory depression, apnea or upper airway obstruction in 3-4 percent, laryngospasm in < 1 percent, hiccoughs in 2-10 percent, and occasional sequelae of histamine release, circulatory depression, emesis, dysphoria, or paradoxical hyperactivity. The most commonly encountered complication is mucosal irritation with resultant rapid expulsion of the drug onto the parents' clothing.

With a failure rate of 10-15 percent (impaired absorption, defecation, hyperactivity), the search for the ideal rectal induction agent goes on. In the last year, [6] rectal midazolam has gained increasing attention and popularity. As clinical usage is much less extensive than with rectal methohexital, statistical comparisons of the incidence of side effects are not yet available. However, preliminary reports are quite encouraging.

The clinical appearance of a pediatric patient given rectal midazolam is one of tranquility rather than sedation. The child often becomes quite suggestible. Parents, instructed that about 75 percent of patients will get the giggles and the other 25 percent will look drunk and then go to sleep, will look forward to the results of the drug administration with decreased anxiety and even a sense of entertainment. Separation becomes quite atraumatic, and the child will often comply in a docile manner to the application of monitors and masks. Though there is individual variation, many children will not even fuss with painful procedures like IV starts, LPs, or cast applications. Sedation can be augmented with nitrous oxide; in this situation, the child will usually remain asleep until the nitrous oxide is removed at the end of the procedure, and will then rouse immediately and completely. This sedative combination of rectal midazolam and nitrous oxide is an excellent adjunct to regional anesthesia in pediatrics, and seems to provide surgeons with good operating conditions while still avoiding the patient risks of exposure to potent volatile anesthetics or the respiratory depressant affects of narcotics.

Doses of midazolam administered per rectum range from 0.3 to 5 mg/kg with an average of 0.5 to 1.0 mg/kg. At Children's Hospital of New Mexico, we are using 1 mg/kg for children up to 10 kg, and 10 mg midazolam diluted to 20 ml volume with normal saline for children weighing more than 10 kg. Euphoric effects are usually noted in two to three minutes, willingness to separate from parents in five minutes, and the onset of sedation in 10 minutes. In more than 400 premedicant-inductions here there has yet to be upper airway obstruction, apnea, larynogspasm or a hyperactive response. If intraoperative narcotics and other sedative drugs are avoided or minimized; prolonged wake-ups have not been observed. Defecation of doses has not been observed at all, unlike the 10-15 percent incidence of defecation seen in 10 percent methohexital. Post-op nausea and vomiting is seen in 2-5 percent of the recipients of rectal midazolam.

In summary, rectal midazolam seems to achieve ease of separation and acceptance of operating room conditions without the complicating risks of airway compromise, respiratory depression, hiccoughs, emesis, and hyperactivity that have been observed with rectal methohexital.

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Question:

With all the new muscle relaxant drugs now available is there any use for the old fashioned relaxants in modern pediatric anesthesia practice?

D. RYAN COOK, M.D.
Professor of Anesthesiology
and Pharmacology
University of Pittsburgh School of Medicine
Director, Department of Anesthesiology
Children's Hospital of Pennsylvania

Answer:

A modern cartoon (drawn by Dr. Goudsouzian) depicts traditional long-acting relaxants attending the burial of succinylcholine and wondering who will be buried next. Because of the many side effects of succinylcholine and because of the availability of intermediate-acting relaxants and the development of short-acting relaxants, many have suggested that succinylcholine be eliminated from elective use in pediatric anesthesia. One now wonders whether traditional long-acting relaxants have a role in pediatric anesthesia. Whose burial will be next?

Non depolarizing relaxants can be given as a bolus to facilitate endotracheal intubation, to facilitate control of ventilation during surgical procedures or during mechanical ventilation, and to provide surgical relaxation. The majority of pediatric surgical procedures are less than one hour's duration. Thus, in many cases a so-called intubating dose of atracurium or vecuronium and a top-up dose of intermediate relaxant will prove suitable. These drugs diminish the need for pharmacological antagonism and increase the reliability of such antagonism. For longer surgical cases most clinicians prefer long-acting relaxants rather than giving frequent repetitive doses or infusions of short or intermediate duration relaxants. Metocurine, d-tubocurarine, pancuronium, and gallamine are the traditional old hands and high dose vecuronium, doxacurium, and pipecuronium are the new actors. In selecting one nondepolarizing relaxant over another for use in infants and children, one should consider the onset time, duration of effect, nonneuromuscular blocking side effects (including cardiovascular side effects), routes of elimination (renal, hepatic, or spontaneous) and cost. In addition, one should consider how the age or pathologic condition of the patient may influence the kinetics of the relaxant. The nonneuromuscular-blocking properties of the nondepolarizing relaxants are primarily cardiovascular effects; related to the magnitude of histamine release, ganglionic blockade, and vagolysis. In addition, the cardiovascular effects appear to be age-related.

In infants and children minimal cardiovascular effects are seen following atracurium, metocurine, and vecuronium at several multiples of the ED95. In adults atracurium at three times the ED95 causes slightly less histamine release than two times the ED95 of metocurine and less than half as much histamine release as once the ED95 of d-tubocurarine. Vecuronium (at any multiple of ED95) is not associated with histamine release. Infants and children appear to be less susceptible than adults to histamine release following relaxants. In a small series of infants five times the ED95 of atracurium did not elicit flushing or alter heart rate or blood pressure. Local signs of histamine release after direct intravenous injection of atracurium in infants and children have been described; rarely, flushing with mild hypotension is seen at high multiples of the ED95. At high doses d-tubocurarine may cause hypotension and histamine release in children.

Keon and Downes compared changes in heart rate, changes in blood pressure, and differences in intubating conditions in infants (average, 5.6 months) "anesthetized" with nitrous oxide-oxygen following either d-tubocurarine (0.6 mg/kg) or pancuronium (0.1 mg/kg) (unpublished data). None had received premedication. In both groups there were modest increases in pulse rate, but transient episodes of bradycardia occurred during intubation in some infants in both groups. No infant given pancuronium developed significant hypotension or hypertension (greater than 10 percent change from control levels). In contrast, 25 percent of infants given d-tubocurarine experienced decreases in blood pressure greater than 10 percent from controls (range, 11-26 percent).

In children anesthetized with halothane and nitrous oxide we noted that in one instance the ED95 of gallamine increased the heart rate by 42 beats/min and in another the ED95 of pancuronium increased the heart rate by 19 beats/min. Both drugs increased mean arterial pressure under these conditions by about 10 torr. At two times the ED95 further increases in heart rate were seen with pancuronium, but not with gallamine. In contrast, gallamine or pancuronium minimally affected the heart rate in infants. Unless the heart rate had slowed from halothane, neither gallamine nor pancuronium showed any vagolytic effects. Occasionally, however, gallamine or pancuronium significantly increased the heart rate. Since the infant and child often responds with bradycardia to a variety of stimuli (potent inhalation agents, hypoxia, intubation), the "potential" vagolytic effects of pancuronium and gallamine may be "wanted" side effects.

The combination of high-dose fentanyl or sulfentanil and pancuronium usually produces a dull, boring anesthetic. The use of "clean" neuromuscular blocking agents with "dirty" narcotics, however, may produce profound bradycardia. We have frequently seen profound bradycardia in children given low doses of fentanyl, sulfentanil, or alfentanil in combination with atracurium or vecuronium; alternatively, these patients become bradycardic during the intubation. For shorter surgical procedures atropine in appropriate doses can minimize the likelihood of bradycardia; for longer surgical procedures pancuronium or gallamine might be reasonable alternatives. Purists suggest that it would be preferable to give clean long-acting relaxants and atropine. This is a costly, contentious solution. On the other hand, in children in whom blood pressure control is an issue (Harrington rod procedures, coartectomies) we have found d-tubocurarine, metocurine, and high-dose vecuronium to be useful adjuncts; doxacurium and pipecuronium will be useful as well.

Marketing campaigns, useful cardiovascular profiles, and cost will determine the survivors. The bell is tolling for gallamine, d-tubocurarine, and metocurine. Gallamine and d-tubocurarine have few clinical advocates and lack unique profiles. Metocurine's cardiovascular profile is probably indistinguishable in children from vecuronium, doxacurium, or pipecuronium but it has no marketing push. Therefore, one suspects that metocurine will slide into oblivion. Pancuronium has useful side effects and low cost and will survive. The role of new drugs in pediatric anesthesia will be largely defined in the future by awareness of age-related drug interactions. Relaxants with minimal or no cardiovascular side effects may be hazardous in infants or small children since potent inhaled agents or narcotics may produce profound bradycardia. □

LITERATURE REVIEW

By James Viney, M.D. and Randall C. Wetzel, M.D.

The following literature reviews have been selected from various issues of *Anaesthesia, Anesthesiology,* the *British Journal of Anaesthesia,* the *Journal of Pediatrics* and the *New England Journal of Medicine.*

Malignant Hyperthermia: Experience in the Prospective Management of Eight Children

Dubrow TJ., Wackym PA, Abdul-Rasool IH, Moore TC: *J Pediatr Surg* 24:163-166, 1989.

These authors report their experience with the prospective management of eight children with caffeine contracture test proven malignant hyperthermia. The management of their patients prospectively followed standard anesthetic guidelines, using a clean machine, barbiturates, opiates, tranquilizers, non-depolarizing muscle relaxants, and nitrous oxide. The patients ranged in age from 5-14 years and had surgical procedures that lasted for up to seven hours. The patients were all monitored in a routine fashion and none of them developed signs of malignant hyperthermia. Of particular note is that dantrolene prophylaxis, either orally or intravenously, was not given.

I mention this article so that we may be familiar with what our surgical collegues are reading. In this leading pediatric surgery journal, dantrolene preoperatively is not recommended. There certainly remains some controversy, and for those of us who like a belt and suspenders approach to medicine, avoidance of trigger agents with preoperative dantrolene still remains the method of choice. However, the complications of dantrolene, which include muscle weakness with potential for impaired respiration, perhaps can be avoided. Despite the successful treatment of 8 children with malignant hyperthermia without the use of dantrolene, dantrolene must be instantly available to be given as early as possible if the patient exhibits symptoms and signs of malignant hyperthermia.

Brain damage by nonatal hypoglycaemia

Lancet 1:882, 1989.

This editorial serves as a nice review of the implications of neonatal hypoglycemia, and reminds the anesthesiologist of the need to continually monitor blood glucose levels intraoperatively. This editorial reviews two articles - the first by Lucas et al, published in the BMJ (297:1304-1308, 1988) where 661 infants with birth weights less than 1850 grams had 6 hourly blood glucose determinations for the first three days, and subsequently less frequently for as long as a month. There were several interesting findings. Symptoms did not predict hypoglycemia, rather they occurred coincidently with it. Infants who had plasma glucose levels less than 45 mg percent had a significant correlation with developmental retardation. Recurrent episodes had a more significant effect on development. Symptoms did not appear to predict outcome. This was correlated with another study by Koh et al (Arch Dis Child 63:1353-1358, 1988) looking at somatosensory and brain stem evoked potentials. The conclusion of this study was that neurophysiologic abnormalities were detectable in a large percentage of patients with blood glucose below 45 mg percent. These children were also asymptomatic.

In the past we have been concerned about hypoglycemia in symptomatic children. This has been a specific worry for anesthesiologists as the symptoms of hypoglycemia (altered level of consciousness, sweating, tachycardia) are difficult to observe intraoperatively. It turns out that it doesn't matter. Hypoglycemia, whether accompanied by symptoms or not, appears to be associated with acute neurophysiologic changes which are highly correlated with subsequent developmental retardation. These reports seem to confirm that the lowest acceptable level of glucose in preterm and small for gestational weight babies is 45 mg percent, and levels in excess of 50 mg percent should be maintained. Anesthesiologists should assure that they make no contribution, intra- or postoperatively, to the serious consequences of neonatal hypoglycemia.

Noninvasive assessment of cardiac output by impedance cardiography in the newborn canine

Gotshall RW and Miles DS: *Crit Care Med* 17:63-65, 1989.

These authors compared cardiac output determined by impedance cardiography and thermodilution in seven canine pups, six to seven days of age, weighing between 0.66 and 0.86 kg. Their method of determining stroke volume by impedence cardiography applied a previously described formula and an impedence cardiograph with four electrode placement to determine the stroke volume. Their results demonstrated a remarkably good correlation (r=.96) ove the range of flows from 100-400 ml/min/kg; with however, some increasing variance at higher flows. These authors conclude that impedence cardiography may be clinically useful to monitor cardiac output in neonates.

For years now, the promise of noninvasive continuous monitoring of stroke volume and therefore cardiac output by impedence cardiography, has tantalized the clinician. It has been difficult, although not previously unreported, to apply this technique to infants. This report shows promise that noninvasive cardiac output determination in small patients (less than 1 kg) may indeed by possible. I have several reservations with this study. The first is that there is strikingly little difference between the two determinations. I find this somewhat surprising because the variability of thermodilution cardiac output in infant animals this size is quite large. The fact that the variability for impedence cardiography would be in the same direction, and of the same magnitude as to give such good correlation, is somewhat difficult to believe. These results may be achieved in an electrically neutral atmosphere (unlike our operating rooms) with meticulous attention to technical details, however they may be difficult to reproduce clinically. We all eagerly await perfection of any technique o noninvasive cardiac output monitoring; however, as of yet, the implications of this potential modality of monitoring in clinical practice are unknown.

A multicenter randomized, placebo-controlled trial of surfactant therapy for respiratory distress syndrome.

Horbar JD, Soll RF, Sutherland JM, et al: *N Engl J Med* 320:959-965, 1989.

This large multicenter trial compared 78 infants treated with a single dose of surfactant given prophylactically at birth with 81 placebo treated matched infants. All infants were between 750 and 1750 grams. Only those infants that demonstrated clinical criteria for RDS were treated. All treatment was before 8 hours of life. The authors report that it was possible to ventilate treated children with RDS at lower mean airway pressures and lower FiO_2s, and that they had higher arterial alveolar oxygen ratios than the placebo treated controls. Additionally, the incidence of pneumothorax was 10 in 78 in the treated group, and 30 in 81 in the nontreated group, a striking, significant difference. However, the ultimate clinical outcome of treated versus untreated patients did not differ. The incidence of bronchopulmonary dysplasis, necrotizing enterocolitis, and periventricular hemorrhage, as well as clinical outcomes by 28 days of age did not differ between

groups. The mortality was identical at 17% in both groups.

Comment: For those of us who have been watching the development of surfactant therapy for infantile respiratory distress syndrome (hyaline membrane disease HMD), this report is disturbing. Apparently treatment of premature infants with known RDS does not ultimately affect the clinical outcome, nor the incidence of serious complications (other than pneumothorax) despite an initial improvement in ventilatory function. There are multiple trials going on at this time, including the prophylactic treatment of all infants who are prematurely born and below a certain birth weight (usually 1700 grams). The preliminary results from some of these trials are more encouraging. One other interesting point - if correction of the underlying disorder with surfactant allows decreased airway pressures and FiO_2, but does not decrease the incidence of complications, hitherto thought to be related to mechanical ventilation in neonates, such as periventricular hemorrhage and BPD, perhaps other etiologic factors need to be considered for these complications.

Continuous intravenous phenylephrine infusion for treatment of hypoxemic spells in tetralogy of Fallot.

Shaddy RE, Viney J, Judd VE, McGough EC: *J Pediatr* 114:468-470, 1989.

This report details the use of phenylephrine in four children between seven days and three and a half years of age who developed hypercyanotic spells that were resistant to other medical therapy, or were about to undergo surgical repair. All children immediately responded with reversal of their hypoxemia. The dose of phenylephrine which was used was a 5 mcg/kg bolus followed by continuous infusion of from 0.1-3 mcg/kg/min of phenylephrine.

Treatment of tet spells can be facilitated by lowering pulmonary vascular resistance (oxygen, morphine, beta blockade) or elevating systemic vascular resistance (knee-chest position, peripheral vasoconstriction). Although elevating, SVR has been an option for treating tet spells for many years - there are few reports of its use in the literature. This article serves as a nice reminder that a bolus of 5 mcg/kg may rapidly reverse a tet spell and a continuous infusion may be used to prevent it. Frequently, immediately preoperatively, the use of narcotics with increased respiratory depression and propranolol with the fear of cardiac depression are worrisome options. A titratable, rapidly reversible agent which will increase blood pressure to enhance oxygenation and reverse the right-to-left shunting in tetralogy seems a physiologically reasonable approach. These authors demonstrate that it works. Indeed, it even worked in some patients after failure of the routine therapy with either beta blockade or morphine and knee-chest position. Perhaps, as the authors suggest, the routine availability of a continuous infusion of phenylephrine for children with tetralogy in the perioperative period, is indicated.

Long-term Pulmonary Sequelae of Meconium Aspiration Syndrome

Swaminathan, Quinn, Stabile, Bader, Platzker and keens: *J Pediatr* 114:356-361, 1989.

This group looked at pulmonary function in 11 survivors of meconium aspiration syndrome now at an average of eight years. Compared to nine age matched controls the study group had mild airway obstruction, hyperinflation and increased closing volumes. Four of the 11 had exercise induced bronchospasm. They were able to achieve normal maximal oxygen consumption in response to exercise. These problems are similar to, but milder than the problems found in ex-prematures with BPD, centering on small airway disease and hyperreactivity. Premature or not, a newborn's developing airway can be permanently affected by respiratory insults and their necessary therapy. Careful attention to the neonatal history may provide useful information for effective patient mangement.

Percutaneous Femoral Venous Catheterizations: A Prospective Study of Complications

Stenzel, Green, Fuhrman, Carlson and Marchessault: *J Pediatr* 114:411-415, 1989.

Dr. Stenzel et al retrospectively looked at 395 central lines placed in pediatric ICU patients. Forty-one percent were placed femorally and the average duration of catheter use was nine days. Foley catheters were only used if necessary for urine output monitoring (what percentage had these in place is not stated). There was no statistical difference in incidence of infectious or noninfectious complications between femoral and non-femoral catheters. The majority of other catheters were placed in the right internal jugular vein. This study suggests the neck and groin are both acceptable places for central line placement with due consideration to patient selection and operator experience. This article is one of several exonerating femoral catheter placement.

The Hemostatic Effect of Transfusing Fresh Whole Blood Versus Platelet Concentrates After Cardiac Operations

Mohr, Martinowitz, Lavee, Amroch, Ramot and Goor: *J Cardiovasc Surg* 96:530-534, 1988.

These investigators compared hemostasis in 27 adult patients who were randomly assigned to receive ten units of platelets of one unit of fresh whole blood after the termination of CPB. No patients had to return to the OR due to excessive bleeding. After CPB, platelet count, bleeding time, thromboxane formation and platelet aggregation was abnormal in both groups. One unit of whole blood increased platelet count equally to five units of platelets. Platelet aggregation in response to collagen and epinephrine was better after one unit of whole blood than ten units of platelets. Neither regime improved aggregation to ristocetin or ADP. Thromboxane formation was greater after fresh blood compared to ten units of platelets. The bleeding time was better than getting six units of platelets. The total blood loss was similar between the groups. After CPB there are quantitative and qualitative deficiencies in the blotting cascade and platelets. This study suggests that fresh whole blood is equal to or superior to component therapy to address these problems, at a lesser price and exposure to fewer total number of units of blood products, thereby reducing risk of mismatch and infection. Fresh autologous blood may not be practical for the small patients who may require CPB. Our experience with fresh whole blood in neonates post-bypass is almost magical in its effect on hemostasis compared to component therapy. Whether this is due to evanescent plasma factors or better platelet preservation or some other explanation is unknown. One reminder, in the small child, the use of fresh whole blood requires the concomitant use of calcium to counteract the citrate load.

Isoflurane attenuates baroreflex control of heart rate in human neonates.

Murat, Lapeyre and Saint-Maurice: *Anesthesiology* 70:395-400, 1989.

These investigators examined the effects of isoflurane on the pressor and depressor responses of 8 neonates in a surgical intensive care unit. They found:

(1) isoflurane (1 MAC) decreased systolic BP by 30 percent in the unstimulated neonate with no increase in heart rate.

2) the newborn baroreflex responses slopes are lower than adult values with marked interpatient variability,

3) the depression of baroreflex responses in neonates is marked and greater than that seen in adults.

The implication is that neonates may not be able to compensate for hypovolemia when anesthetized with isoflurane. I guess we must continue to pay attention to the blood and fluid needs of our patients and not rely on an anesthetic agent to keep us out of trouble, once again proving there is no such thing as a free lunch.

(Continued on page 10)

"Literature Review"

(Continued from page 9)

Pulse Oximetry

Tremper and Barker: *Anesthesiology* 70:98-108, 1989.

Doctors Barker and Tremper have written a useful review of the physics, efficacy and pitfalls in pulse oximetry. If you're not currently using it on every patient, perhaps you should think again about this extremely valuable monitor.

Physiologic Dead Space, Venous Admixture and the Arterial to End-tidal Carbon Dioxide Difference in Infants and Children Undergoing Cardiac Surgery

Burrows: F: *Anesthesiology* 70:219-255, 1989.

Dr. Borrows looked at 41 infants and children undergoing median sternotomies for cardiac surgery in the two to ten year range. Nine patients had normal anatomy and were having surgery for arrhythmias. Nine had acyanotic heart disease and nine had cyanotic heart disease. The patients were anesthetized with fentanyl and pavulon and no leaks around their endotracheal tubes at less than 34 cm H_20. $PaCO_2$ was controlled to values between 30 and 40. They measured $PaCO_2$, PET CO_2 and calculated Vd/Vt and Qs/Qt. The children with normal anatomy and acyanotic heart disease had good correlation between $PaCO_2$ and PET CO_2. Cyanotic children with either decreased or normal to increased pulmonary blood flow had poor correlation. The increased difference between the $PaCO_2$ and PET CO_2 in the cyanotic children correlated with the greater Vd/Vt and the increased Qs/Qt in these children. The increased Vd/Vt was the most important variable. The PET CO_2 was not even a reliable trend monitor in the cyanotic children as the Qs/Qt was variable intraoperatively. (I would like to see data looking at Qs/Qt, Vd/Vt and delta PCO_2 in children having thoracotomies before and after lung retraction. My clinical experience is that the PET CO_2 is unreliable as a trend monitor particularly in small babies with the lungs retracted, with or without heart disease.)

Pediatric Regional Anesthesia

Yaster and Maxwell: *Anesthesiology* 70:324-338, 1989.

Doctors Yaster and Maxwell have presented a nice overview of regional anesthesia in children, when to consider it, how to do it and potential problems. They discuss caudal, spinal, epidural, axillary, penile, femoral and groin blocks. Their diagrams are easily understood as are their recommended doses. A nice article for those of us who like simple formulas and big pictures.

Abnormalities of Diaphragmatic Muscle in Neonates with Ventilated Lungs

Knisley, Leal and Singer: *J Pediatr* 113:1074-1077, 1988.

This is a postmortem study looking at 13 infants who received uninterrupted ventilatory support for 12 days or more and had no neuromuscular blockade. Their muscle samples were compared to infants who had been ventilated for less than seven days and to the same patients control samples of non-respiratory muscle. The pathology was consistent with disuse atrophy, denervation atrophy or failure of normal growth in the diaphragmatic muscles compared to controls. This study certainly has implications concerning the weaning of ventilation and the amount of added respiratory work the chronically ventilated neonate might be expected to perform. Intraoperatively, if extubation is planned, cautious monitoring and care with neuromuscular blockade is suggested.

Caudal Anesthesia in Pediatric Surgery: Success Rate and Adverse effects in 750 Consecutive Patients

Bernard Dalens and Abdou Hasnaoui: *Anesth Analg* 68:83-89, 1989.

Doctors Dalens and Hasnaoui have shared their experience in 750 consecutive patients given caudal anesthesia for hernia repair, orchiopexy, circumcision, rectal procedures and some miscellaneous operations. All patients had an I.V. started and were given atropine and valium. Ninety-four percent were performed after general anesthesia was induced, and most were continued with a light general anesthetic post block. Seventy percent were successful on the first try and an additional 26 percent succeed after two to four tries. They recommended using a 23 gauge 25 mm short bevel caudal needle as they had significantly less problems (mostly vascular penetration) with this needle. One ml/kg of anesthetic seemed to give the best results with 85 percent having an appropriate block and only 1 percent having an excessive block and 8 percent having an inadequate block. The most common adverse effect was vomiting in 17 percent of patients. They didn't find a good formula to express the extent of anesthesia and found 1.25 ml/kg to be too much in 30 percent of their patients. They found that light general anesthesia was associated with ventilatory problems in 12 percent of patients, but that patients who were awake might not be able to tolerate the operation psychologically. If one looked at just those under seven years of age (with the highest success rate) and assumed all patients' blocks were performed with short beveled needles (with the lowest rate of complications) and that 1 ml/kg is the optimum dose, then the failure rate was 1.2 percent, another 1 percent had an excessive block and 8 percent had an inadequate block making a total of about 10 percent with some difficulty with the block. In addition, 12 percent needed intubation and ventilatory assistance for hypercapnia (I assume the excessive block group might have been represented in this group). There was no mortality or major morbidity or serious hypotension due to the blocks. The technique was well accepted by parents and patients, but as can be seen from the above problems, it is not something that can be put on "autopilot". If the incidence of mortality in ASA Class I or II children having these types of operations is in the range of 1 in 35,000 to 1 in 60,000 then we will need a very large series to assess relative risks of general versus regional anesthesia.

Caudal Epidural Morphine for Control of Pain Following Open Heart Surgery in Children

Rosen and Rosen: *Anesthesiology* 70:418-421, 1989.

Doctors Rosen and Rosen studied 32 children post open heart surgery who were planned to be extubated at or near the end of the case. They compared .075 mg/kg sterile preservative free MS in saline injected caudally at the end of the case to no caudal injection. ACT's were to within 10 percent of baseline prior to injection. Five ml was used if the dose was less than one ml and 19 ml was used if the dose was greater than one mg. The study group required significantly less supplemental MS in the first 24 hours post op with some not requiring any supplements for 12 hours. The study group had lower pain scores for that time period. There were no cases of respiratory depression or pruritus in the study group, there were 4/16 cases of mild nausea in the study group, and 1/16 in the control. They all had foleys so urinary retention couldn't be evaluated.

The variety of ways to provide post op pain control is certainly increasing. One can use local infiltration of anesthetics, nerve blocks, epidural, caudal or axillary nerve blocks, IM or IV boluses or constant infusions with or without patient control of narcotics or agonist/antagonists or caudal, epidural or subarachnoid narcotics (and agonist/antagonists are being examined in Canada in this respect, but are not available yet in the USA for study). How best to keep nerves or narcotic pain sites blocked but not respiratory, vomiting or psychosis sites occupied is still not clear. Maybe we need multinstitutional study to decide which patients are best served (least pain and side effects and risks) with which techniques? □

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