Double standards in anesthesia

Key words: Anesthesiologist, negligence, standard of care.

Studies cannot distinguish between the quality of care provided by nurse anesthetists and the quality of care provided by anesthesiologists. In fact, the quality of anesthesia care in this country is remarkably high. Yet, malpractice attorneys, surgeons, and others sometimes recommend increased supervision of CRNAs or restrictions on CRNA practice. The AANA, of course, responds with facts showing that these actions will not make anesthesia any safer but will make it more expensive. One thread that many of these episodes have in common is that they begin with an anesthesia accident, sometimes one that involved a CRNA.

Although anesthesia today is very safe, it is not totally safe. Unfortunately, accidents happen, and given the nature of anesthesia, when they happen, they often have disastrous results. People read of an anesthetic disaster and ask, “How can we avoid that?” If the administrator is a nurse anesthetist (and since nurse anesthetists administer 65% of the anesthetics, then two out of three times it is), the uninformed will suggest that the nurse anesthetist be supervised by or replaced with an anesthesiologist. But this “solution” ignores the fact that studies show that anesthesia administered by an anesthesiologist is no safer than anesthesia administered by a CRNA. Nonetheless, the same arguments continue to be made and the same people, either out of ignorance or to promote their own purposes, continue to make the same arguments.

While I would hope to see an absence of error in anesthesia administered by CRNAs, I know that this cannot and will not happen. Anesthetists, both CRNAs and anesthesiologists, are human. Anesthesia requires great effort, concentration, and organization, and occasionally there are lapses. That is the nature of anesthesia (and human life in general). What is upsetting is that when a CRNA makes an error, the automatic response is anesthesiologist supervision or replacement. When an anesthesiologist makes an error, there is no similar or corresponding outcry.

Anesthesiologists are human and make errors too. They suffer from the same problems as CRNAs. They lose concentration in the alternating boredom and terror of the operating room. They become confused. They do things they should know they should not, and they neglect to do things they should know they should. Does this make anesthesiologists, as a class, bad practitioners? Should anesthesiologists be forced to practice only with experienced CRNAs? Of course not, but surgeons, malpractice attorneys, administrators, and critics must recognize that while any anesthesia mishap is a tragedy and should have been avoided, mistakes are made by all anesthetists.

I have always known that I could easily find mistakes by anesthesiologists every bit as embar-
rassing as those committed by CRNAs. However, I did not look for them because I knew the irrelevance of finding an occasional error by an anesthesiologist. Even when the rate of anesthesia error is reduced to less than 1 in every 250,000 administrations, there are still millions and millions of anesthetics administered each year. Therefore, there will still be some sizable number of anesthetic incidents, no matter how safe anesthesia becomes.

Having seen restrictions imposed on nurse anesthetist practice because of a rare and unfortunate error by a CRNA, I feel it necessary to point out that anesthesiologists can also make anesthesia errors. The following mistakes were made by anesthesiologists. They are drawn from cases which have appeared in appellate decisions in the last year. Because I understand how irrelevant these errors are, I will not embarrass particular practitioners or institutions, and I will make these reports anonymous. The AANA, however, has the list of the actual cases from which these facts are taken. In none of the cases was a CRNA involved, in any way, with the patient’s care. Yet, avoidable accidents happened. In some of these cases, surgeons and hospitals were sued along with the negligent anesthesiologist.

Spinal cord injury caused by excessive attempts to intubate

The patient was severely injured in a car accident. Paramedics administered first aid and immobilized the patient by placing him in a cervical collar and securing him to a rigid board. The paramedics then transported him to a trauma center. The patient had suffered, among other things, closed head trauma, a fractured scapula, a torn right brachial plexus, and a cervical spine injury. Although the patient could no longer move his right arm because of the torn brachial plexus, the patient had some voluntary movement of the left arm, pain reflexes in his legs, and rectal tone, an indication he was not paralyzed below the waist.

Because of the patient’s closed head injury, the surgeon called for an anesthesiologist to establish an airway in order to reduce the swelling of the patient’s brain by means of hyperventilation. The anesthesiologist responded and was informed of the patient’s condition by the surgeon. Thereafter, the anesthesiologist made five attempts to establish an airway by inserting a tube through the patient’s nasal passage. When these attempts failed, the anesthesiologist made five unsuccessful attempts at oral intubation using a laryngoscope. Following these attempts by the anesthesiologist and one further unsuccessful attempt by the surgeon, the surgeon established a surgical airway by making an incision in the patient’s windpipe and inserting a tube. The following day, it was discovered that the patient had suffered a spinal cord injury rendering him a quadriplegic.

After a jury award in favor of the patient, the anesthesiologist appealed claiming he should have received a directed verdict because there was not sufficient evidence to establish the requisite causal connection between his acts and the patient’s injuries.

The Appellate Court affirmed the award against the anesthesiologist. The plaintiff's expert had testified to the standard of care for physicians attempting to intubate a patient with a known or suspected cervical spine injury in a situation where establishing an airway was not “urgent.” The patient’s expert stated that, in his opinion, the anesthesiologist violated this standard of care by inappropriately and excessively attempting to intubate the patient orally. According to the patient’s expert, one attempt at oral intubation without moving the patient would have been acceptable, but multiple attempts using a laryngoscope was a violation of the standard of care because such a procedure inevitably causes movement of the patient’s head and neck.

As for causation, the patient’s expert stated that his review of the medical records indicated the patient did not become a quadriplegic because of the motor vehicle accident. The patient’s expert specifically testified that it was his opinion, to a reasonable degree of medical certainty, that the injury to the patient’s spinal cord occurred during the oral intubation attempts, and that this injury resulted in quadriplegia and eventual death. Further, the patient’s expert testified that, in his opinion, had the anesthesiologist not made multiple attempts at oral intubation, the patient would have walked out of the hospital within two or three weeks.

Lack of anesthesiologist availability

Plaintiff was experiencing labor symptoms and was admitted to a hospital in a suburb of a major East Coast city. Periodic examinations of the plaintiff suggested fetal distress. The attending nurse called the obstetrician. Within 5 minutes of receiving the nurse’s call, the obstetrician appeared. By 8:56 p.m., the obstetrician had ordered the plaintiff to be moved to a “labor room.” In the next 10 minutes, the obstetrician attempted to deliver the baby vaginally. By 9:07 p.m., the obstetrician called for cesarean section surgery and gave orders to call anesthesia and two additional surgeons, as well as to prepare the “delivery room” for surgery. The plaintiff was placed in the “delivery room” for preparation while the obstetrician pre-
pared for surgery. By the time the patient and doctor were prepared, no anesthesiologist had appeared.

Initially, the obstetrician decided to wait for the anesthesiologist, but after a while, he began the operation using local anesthesia. This decision required him to cut into the plaintiff while she was fully conscious, and required him to anesthetize each progressive layer of the abdomen before each incision. The baby was born at 9:34 p.m. Approximately 7 minutes later, an anesthesiologist arrived and administered an anesthetic to permit the doctors to complete the operation on the plaintiff.

The baby was born with complications. Testimony indicated that she had suffered from oxygen deprivation while in utero. As a consequence, she suffers from a seizure disorder and has a reduced mental capacity which borders on mental retardation.

The baby and her parents brought suit against the obstetrician, the anesthesiologist, the hospital, and the anesthesiologist corporation, asserting a number of claims including, but not limited to, negligence and negligent infliction of emotional distress. After a lengthy trial, the jury returned a verdict absolving the obstetrician and the anesthesiologist group of all liability. The jury awarded the plaintiff $2,500 on her claim against the hospital but failed to reach a final verdict on the baby's claim against the hospital. Upon consideration of post-trial motions, the trial court granted a new trial against the hospital only.

Plaintiffs appealed, and the Appellate Court ordered a new trial against the anesthesiologist group as well, because the trial court had not permitted the plaintiff to assert its claims fully. While this case does not involve an anesthesia mistake, the Appellate Court agreed with the plaintiff that it was negligence for the anesthesiologist group to fail to show up. Note that, in the view of the jury, the obstetrician was not responsible for the failure of the anesthesiologist group to show up but he was, nonetheless, sued.

Negligent insertion of anesthesia needle into patient's eye

The plaintiff instituted this action against an anesthesiologist and an ophthalmologist group (yet another case where surgeons were sued when working with anesthesiologists). The patient was having vision difficulties in his left eye and sought treatment from an ophthalmologist. It was agreed that the patient would have laser surgery. The anesthetic was supposed to be inserted into the tissue surrounding the eyeball, but in performing the anesthetic procedure the anesthesiologist inserted the needle directly into the eyeball itself and injected the anesthetic into the patient's eye. It caused extensive permanent damage including tearing and detachment of the retina and substantial impairment of the patient's vision.

The plaintiff's lawsuit was based on assault and battery for an alleged nonconsensual anesthetic procedure, negligence, res ipsa loquitur, and negligence based on medical malpractice.

Negligently administered spinal

During labor, the plaintiff received an epidural anesthetic administered by an anesthesiologist. The anesthesiologist first attempted to insert a catheter into the plaintiff's upper spinal cord near her neck but was unsuccessful. The anesthesiologist then administered the anesthetic by inserting the catheter into the plaintiff's spine in her lower back. Soon after delivering a healthy baby, the plaintiff began experiencing headaches, sensitivity to light and loud noises, and numbness in her back.

The plaintiff brought suit against the hospital which convinced the trial court that the anesthesiologist was an independent contractor for whom the hospital was not responsible and that the patient had failed to show that her injuries were caused by the spinal. The Court of Appeals sent the case back to the trial court for trial.

The plaintiff's expert stated that, in his opinion, the anesthesiologist's care fell below the standard of care required by physicians administering an epidural. Another expert stated that "Plaintiff's symptoms of low back pain and headaches are consistent with the loss of spinal fluid which accompanied the insertion of the epidural in the cervical region of the plaintiff's back." The Appellate Court held that this was sufficient testimony, if believed by a jury, to support a verdict of malpractice on the part of the anesthesiologist. Whether or not the hospital will be liable will depend on whether the jury believes the hospital allowed people to think that the anesthesiologist was its apparent agent.

Permitting oxygen too close to a hot surgical instrument

During the removal of a cyst, the plaintiff suffered burns on the face, left ear, and shoulders because an instrument being used during her surgery ignited the oxygen being administered to the anesthetized plaintiff. The patient sued the hospital and the surgeon. The case is primarily concerned with the effects of legal maneuvering as the patient dismissed the surgeon and then attempted to sue him again. While the plaintiff consistently
Drug abuse

A State Medical Board filed a petition for an order to enforce a subpoena issued to a hospital for peer review records concerning a physician who was the subject of an investigation regarding an apparent drug problem. The Superior Court granted the petition and ordered the hospital to comply with the subpoena. The Court of Appeals affirmed. The hospital sought further review. The State Supreme Court granted review and held that the investigative subpoena issued by the State Medical Board as part of its inquiry into the conduct of a physician with an apparent drug problem was not "discovery" within the meaning of a statute providing that records of a hospital peer review committee are not "subject to discovery."

In the spring of 1992, several nurses at a hospital observed an anesthesiologist on the medical staff behaving, while on duty, as if he were under the influence of narcotic drugs. The first incident took place one evening in March 1992. The anesthesiologist was on call when a patient required emergency surgery. As the anesthesiologist was interviewing the patient, a nurse observed that his speech was slurred. In discussing the case with him before surgery, she saw that his attention and comprehension were impaired. Nonetheless, the anesthesiologist administered a general anesthetic. Following the surgery, the nurse reported the anesthesiologist's abnormal behavior to her supervisor.

The second incident occurred in late May 1992. A patient was awaiting surgery, but the anesthesiologist could not be found. After being paged several times he arrived and began interviewing the patient. A nurse observed that his speech was even more slurred than during the first incident. She promptly called her supervisor and expressed her "grave concern" about his condition. Thereafter the patient was taken into the operating room and the anesthesiologist administered sedation intravenously.

On another day that month a nurse was trying to take a patient into a bathroom but found the door locked. A visitor told her that someone had been in the bathroom for a long time. She unlocked the door and found the anesthesiologist asleep in the room. He did not respond to his name, and the nurse had to shake him several times. When he awoke, he was disoriented and unsteady; in the nurse's opinion, he "did not behave like someone who had simply fallen asleep." She told him that he was needed in surgery; he responded "OK," and went off to the operating room. She then reported the incident to her supervisor. Later that day, another nurse remarked that the anesthesiologist's behavior in the recovery room had been "strange" and he had had to lay his head on a desk.

Approximately 6 weeks thereafter, a nurse noticed that the anesthesiologist's handwriting was shaky on several occasions and again reported it. She also saw that the anesthesiologist had made an entry in a record—possibly a patient's chart—stating that he had broken an ampule of fentanyl during a procedure.

At some point during this period, the Medical Executive Committee—a peer review committee—began to investigate the matter. The anesthesiologist appeared before the committee and admitted he had been injecting himself with fentanyl, which he had taken from the hospital's narcotics supplies.

Based on these facts, the State Supreme Court ruled that the State Medical Board was entitled to enforce its subpoena to examine the hospital's peer review records.

Conclusion

The episodes described above are not particularly shocking or outrageous. They do not imply that anesthesiologists are bad practitioners and in fact, for the most part, they do not even suggest that the anesthesiologists mentioned in these cases are even bad practitioners. What they do make clear is that anesthesia is a difficult process. While education and dedication have made it very safe, practitioners cannot lose concentration. When they make an occasional human error, it can have disastrous consequences.

Of course, the most important thing it shows is that anesthesiologists are human. While nurse anesthetists cannot and should not deny that anesthesia can have disastrous consequences, anesthesiologists are also human and suffer the same consequences with the same frequency.

Both anesthesia providers, CRNAs and anesthesiologists, must recognize that despite their best efforts, they are human and accidents will happen. We should resolve to dedicate ourselves to identify and eliminate those errors which can be avoided. But using an occasional and isolated error as an excuse to change the way anesthesia care is delivered is a cynical game which only the foolish will play.
Rapid onset and short duration make Nesacaine-MPF the logical epidural anesthetic for outpatient procedures.
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- 60-minute or less duration.

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No disodium EDTA dihydrate.
No preservatives, period.
Available in 2% and 3% 20-mL single-dose vials.

CONTRAINdications
Nesacaine and Nesacaine-MPF Injections are contraindicated in patients hypersensitive (allergic) to drugs of the PABA ester group. Lumber and caudal epidural anesthesia should be used with extreme caution in persons with the following conditions: existing neurological disease, spinal deformities, septicaemia, and severe hypertension.

Local anesthetics should only be employed by clinicians who are well versed in diagnosis and management of dose-related toxicity and other acute emergencies which might arise from the block to be employed, and then only after ensuring the immediate availability of oxygen, other resuscitative drugs, cardiopulmonary resuscitative equipment, and the personnel resources needed for proper management of toxic reactions and related emergencies. (See also ADVERSE REACTIONS AND PRECAUTIONS.)

In properly managed cases of dose-related toxicity, underventilation from any cause and/or altered sensitivity may lead to the development of cardiac arrest and, possibly, death. Nesacaine (chloroprocaine HCl) Injection USP contains methylparaben and should not be used for lumbar or caudal epidural anesthesia because safety of this antimicrobial preservative has not been established with regard to intrathecal injection, other intravascular or unintentional. Nesacaine-MPF Injection contains no preservative, discount unused injection remaining in vial after initial use. Nitroglycerin must not be used in the presence of ergot type vasoconstrictive drugs, since a severe persistent hyperperfusion may occur.

To avoid intravascular injection, aspiration should be performed before the anesthetic solution is injected. The needle must be repositioned until no blood return can be elicited. However, the absence of blood in the syringe does not guarantee that intravascular injection has been avoided.

Mixtures of local anesthetics are sometimes employed to compensate for the slower onset of one drug and the shorter duration of action of the second drug. Experiments in primates suggest that toxicity is probably additive when mixtures of local anesthetics are employed, but some experiments in rodents suggest synergism. Caution regarding toxic equivalence should be exercised when mixtures of local anesthetics are employed.

PRECAUTIONS

General
The safety and effective use of chloroprocaine depend on proper dosage, correct technique, adequate precautions and readiness for emergencies. Reuse of equipment, oxygen and other resuscitative drugs should be available for immediate use. (See WARNINGS and ADVERSE REACTIONS.) The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Injections should be made slowly, with frequent aspirations before and during the injection to avoid intravascular injection. Syringes should also be prepared and used briefly before and during each supplemental injection in continuous (intermittent) catheter techniques. During the administration of epidural anesthesia, it is recommended that a test dose be administered (3 mL of 0.5% or 5 mL of 2% Nesacaine-MPF Injection) initially and that the patient be monitored for central nervous system toxicity and cardiovascular toxicity, as well as for signs of unintended intrathecal administration, before proceeding. When clinical conditions permit, consideration should be given to employing a chloroprocaine solution that contains epinephrine for the test dose because the circulating changes characteristic of epinephrine may also serve as a warning sign of unintended intrathecal injection. An intravascular injection is still possible even if aspirations for blood are negative. With the use of continuous catheter techniques, it is recommended that a fraction of each supplemental dose be administered as a test dose in order to verify proper location of the catheter.

Injection of repeated doses of local anesthetics may cause significant increases in plasma levels with each repeated dose due to slow accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the physical condition of the patient, including, but not limited to, age, weight, electrolyte and acid-base changes associated with the prolongation of A-V conduction produced by the liver, chloroprocaine should be used cautiously in patients with hepatic disease. Local anesthetic injections containing a vasoconstrictor should be used cautiously and in carefully circumscribed quantities in areas of the body supplied by end arteries or having otherwise compromised blood supply. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result. Since suture-type local anesthetics are hydrolyzed by plasma cholinesterase produced by the liver, chloroprocaine should be used cautiously in patients with hepatic disease.

Local anesthetics should also be used with caution in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these drugs. Use in Ophthalmic Surgery: When local anesthetic injections are employed for retrobulbar block, lack of corneal sensation should not be relied upon to determine whether or not the patient is ready for surgery. This is because complete lack of corneal sensation usually precedes clinically acceptable external ocular muscle akinesia.

Information for Patients
When appropriate, patients should be informed in advance that they may experience temporary loss of sensation and motor activity, usually in the lower half of the body, following proper administration of epidural anesthesia.

Clinically Significant Drug Interactions
The administration of local anesthetic solutions containing epinephrine or norepinephrine to patients receiving monamine oxidase inhibitors, tricyclic antidepressants or phenothiazines may produce severe prolonged hypertension or hypotension. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

CONGENITAL HYPERPLASIA OF THE ADRENAL CORTEX"

Carcinogenesis, Mutagenesis, and Impairment of Fertility
Long-term studies in animals to evaluate carcinogenic potential and reproductive toxicity have not been conducted.

Pregnancy: Category C
Animal reproduction studies have not been conducted with chloroprocaine. It is also not known whether chloroprocaine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Chloroprocaine should be given to a pregnant woman only if clearly needed.

Labor and Delivery
The use of some local anesthetics for paracervical block in early pregnancy (as anesthesia for abortion) suggests that systemic absorption under these circumstances may be rapid. The recommended maximum dose of each drug should not be exceeded.
Injection should be made slowly and with frequent aspiration. Allow a 5-minute interval between sides. There are no data concerning use of chloroprocaine for obstetrical paracervical block when trauma of pregnancy is present or when fetal distress or prematurity is anticipated in advance of the block; such use, therefore, is not recommended.

The following information should be considered by clinicians who select chloroprocaine for obstetrical paracervical block anesthesia:

1. Fetal bradycardia (generally a heart rate of less than 120 per minute for more than 2 minutes) has been noted by electronic monitoring in about 5 to 10 percent of the cases (various studies) where initial total doses of 125 mg to 400 mg of chloroprocaine were employed. The incidence of bradycardia, within this dose range, might not be dose related.

2. Fetal acids have not been demonstrated by blood gas monitoring around the time of bradycardia or afterwards. These data are limited and generally restricted to nonevent cases where fetal distress or prematurity was not anticipated in advance of the block.

3. No intact chloroprocaine and only trace quantities of a hydrolysis product, 2-chloro-4-aminobenzoic acid, have been demonstrated in umbilical cord arterial or venous plasma following properly administered paracervical block with chloroprocaine.

4. The role of drug factors and non-drug factors associated with fetal bradycardia following paracervical block are unexplained at this time.

**Nursing Mothers**

If it is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when chloroprocaine is administered to a nursing woman.

**Pediatric Use**

Guidelines for the administration of Nesacaine and Nesacaine-MPF Injections to children are presented in DOSAGE AND ADMINISTRATION.

**ADVERSE REACTIONS**

Systemic: The most commonly encountered acute adverse experiences that demand immediate countermeasures are related to the central nervous system and the cardiovascular system. These adverse experiences are generally dose related and may result from rapid absorption from the injection site, diminished tolerance, or from untoward intrathecal injection of the local anesthetic solution. In addition to systemic dose-related toxicity, unintentional subarachnoid injection of drug during the intended performance of caudal or lumbar epidural block or nerve blocks near the vertebral column (especially in the head and neck region) may result in underventilation or apnea ("Total Spinal"). Factors influencing plasma protein binding, such as acidosis, systemic diseases that alter protein production, or competition of other drugs for protein binding sites, may diminish individual tolerance. Plasma cholinesterase deficiency may also account for diminished tolerance to type I local anesthetics.

**Central Nervous System Reactions:** These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness, lassitude, blurred vision or tremors may occur, possibly proceeding to convulsions. However, excitement may be transient or absent, with depression being the first manifestation of an adverse reaction. This may quickly be followed by drowsiness merging into unconsciousness and respiratory arrest.

The incidence of convulsions associated with the use of local anesthetics varies with the procedure used and the total dose administered. In a survey of studies of epidural anesthesia, overt toxicity progressing to convulsions occurred in approximately 0.1 percent of local anesthetic administrations.

**Cardiovascular System Reactions:** High doses, or unintended intravascular injection, may lead to high plasma levels and related depression of the myocardium, hypotension, bradycardia, ventricular arrhythmias, and, possibly, cardiac arrest. Allergic: Allergic type reactions are rare and may occur as a result of sensitivity to the local anesthetic or to other formulation ingredients, such as the antimicrobial preservative methylparaben, contained in multiple dose vials. These reactions are characterized by signs such as urticaria, pruritus, erythema, angioneurotic edema (including laryngeal edema), tachycardia, sneezing, nausea, vomiting, dizziness, syncope, excessive sweating, elevated temperature, and possibly anaphylactoid type symptoms (including severe hypotension). Cross sensitivity among members of the ester-type local anesthetic group has been reported. The usefulness of screening for sensitivity has not been definitely established.

**Neurologic:** In the practice of caudal or lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter may occur (see PRECAUTIONS). Subsequent adverse observations may depend partially on the nature of the drug administered intrathecally. These observations may include spinal block of varying magnitude (including total spinal block), hypotension secondary to spinal block, loss of bladder and bowel control, loss of pain sensation and sexual function. Anarchocinesis, persistent motor, sensory and/or autonomic (sphincter control) deficit of some lower spinal segments with slow recovery (several months) or incomplete recovery have been reported in rare instances. (See DOSAGE AND ADMINISTRATION discussion of Caudal and Lumbar Epidural Block.) Backache and headache have also been noted following lumbar epidural or caudal block.

**DOSAGE AND ADMINISTRATION**

Chloroprocaine may be administered as a single injection or continuously through an indwelling catheter. As with all local anesthetics, the dose administered varies with the anesthetic procedure, the vascularity of the tissues, the depth of anesthesia and degree of muscle relaxation required, the duration of anesthesia desired, and the size and physical condition of the patient and the rate of systemic absorption from a nerve block.

1. Use an adequate test dose (3 mL of Nesacaine-MPF 3% Injection or 5 mL of Nesacaine-MPF 2% Injection) prior to induction of complete block. This test dose should be repeated if the patient is moved in such a fashion as to have displaced the epidural catheter. Allow adequate time for onset of anesthesia following administration of each test dose.

2. Avoid the rapid injection of a large volume of local anesthetic injection through the catheter. Consider fractional doses, when feasible.

3. In the event of the known injection of a large volume of local anesthetic injection into the subarachnoid space, after suitable resuscitation if the catheter is in place, consider attempting the recovery of drug by draining a moderate amount of cerebrospinal fluid (such as 10 mL) through the epidural catheter.

As a guide for some routine procedures, suggested doses are given below:

**Anesthetic Procedure**

<table>
<thead>
<tr>
<th>Location</th>
<th>Solution Concentration</th>
<th>Volume (mL)</th>
<th>Total Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>1.5%</td>
<td>3</td>
<td>50</td>
</tr>
<tr>
<td>Intraoral</td>
<td>1.5%</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Digital (without epinephrine)</td>
<td>2%</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Perianal (see also PRECAUTIONS)</td>
<td>2%</td>
<td>1</td>
<td>20</td>
</tr>
</tbody>
</table>

2. Caudal and Lumbar Epidural Block: NESACaine-MPF INJECTION. For caudal anesthesia, the initial dose is 15 to 25 mL of a 2% or 3% solution. Repeated doses may be given at 40 to 60 minute intervals.

For lumbar epidural anesthesia, 2 to 2.5 mL per segment of a 2% or 3% solution can be used. The usual total volume of Nesacaine-MPF Injection is from 15 to 25 mL. Repeated doses 2 to 6 mL, less than the original dose may be given at 40 to 60 minute intervals.

The above dosages are recommended as a guide for use in the average adult. Maximum dosages of all local anesthetics must be individualized after evaluating the size and physical condition of the patient and the rate of systemic absorption from a particular injection site.

**Pediatric Dosage:**

It is difficult to recommend a maximum dose of any drug for children, since this varies as a function of age and weight. For children over 3 years of age who have a normal lean body mass and normal body development, the maximum dose is determined by the child's age and weight and should not exceed 11 mg/kg (5 mg/lb). For example, in a child of 5 years weighing 50 lbs (23 kg), the dose of chloroprocaine HCl without epinephrine would be 250 mg. Concentrations of 0.5–1.0% are suggested for infants and 1.0–1.5% for neonates for nerve block in order to guard against systemic toxicity. The lowest effective concentration and lowest effective dose should be used at all times. Some of the lower concentrations for use in infants and smaller children are not available in pre-packaged containers; it will be necessary to dissolve available concentrations with the amount of 0.9% sodium chloride injection necessary to obtain the required final concentration of chloroprocaine injection.

**Preparation of Epinephrine Injections:** To prepare 1.250,000 epinephrine-chloroprocaine HCl injection, add 0.1 mL of a 1:1000 EpiPhrine Injection (USP) to 30 mL of Nesacaine-MPF Injection. Subsequent epinephrine-chloroprocaine injection is compatible with calcium salts and their carbonates, soap, silver salts, iodine and iodides.

Pediatric drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever injection and container permit. As with other anesthetics having a free aromatic amino group, Nesacaine and Nesacaine-MPF Injections are slightly photosensitive and may become discolored after prolonged exposure to light. It is recommended that these vials be stored in the original outer containers, protected from direct sunlight. Discolored solution should not be administered. If exposed to low temperatures, Nesacaine and Nesacaine-MPF Injections may deposit crystals of chloroprocaine HCl which will redissolve with shaking when returned to room temperature. The product should not be used if it contains undissolved (i.e., particulate) material.

**Nesacaine-MPF (chloroprocaine HCl injection, USP)**

Rapid onset. Rapid recovery.
Letters
(continued from page 104)

ing Center in Chicago. After speaking with CRNAs from all over the country, I realized that many of them were seeing problems of hypotension on induction of general anesthesia in patients taking Redux® or fenfluramine/phentermine (fen/phen) combination. I stated that very little information regarding these medications appears in the literature and after reviewing the drug pharmacology noted that a relationship may exist between the drug's potential catecholamine-depleting effects and persistent hypotension on induction of anesthesia.

I have a background in trauma anesthesia providing coverage in a level I trauma center. I began to question myself and others about the potential effects of Redux or fen/phen on the trauma victim. If an individual taking Redux or fen/phen is involved in an accident and is potentially catecholamine depleted, what effect will that have on patient outcome or survival from the time of the traumatic event to the arrival of the first medical responder capable of treating the patient with appropriate vasopressors? I have not cared for a trauma patient on any of the antiobesity medications, but I think the question is important.

It is reported that the number of prescriptions for Redux has increased dramatically in just a short period of time. As a concerned anesthetist, I encourage all healthcare providers to remain vigilant and informed regarding these medications.*

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*Note: In March 1997, the Food and Drug Administration Medical Products Reporting Program (MedWatch) issued an alert concerning Pondimin® C-IV (fenfluramine tablets) indicating that its use with phentermine (fen/phen) is not approved. It was also noted that potent anesthetic agents should be administered with caution in patients taking Pondimin. For more information, contact MedWatch at 1-880-934-5556.

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Rapid, nonspecific esterase metabolism
- Non-organ-dependent elimination
- Consistent offset of action regardless of gender, age, weight, or renal/hepatic status
- Metabolism unaffected in patients with pseudocholinesterase deficiency

No accumulation means predictable offset of action within 5 to 10 minutes
- No opioid accumulation regardless of dose or duration of infusion
- Rapid clearance
- No change in context-sensitive half-time, even with prolonged administration
- Clinically inactive metabolite

No accumulation, unlike other opioids.

Time Required for a 50% Decrease in the Effect-Site Opioid Concentration of Fentanyl Analgeses

Adapted from Egan et al.1

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.
Esterase metabolism provides an opioid with rapid onset and offset.

<table>
<thead>
<tr>
<th>Pharmacokinetics</th>
<th>ULTIVA</th>
<th>Alfentanil</th>
<th>Fentanyl</th>
<th>Sufentanil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset—blood-brain equilibration (mean)</td>
<td>1 min²</td>
<td>1 min²</td>
<td>6.6 min³</td>
<td>6.2 min³</td>
</tr>
<tr>
<td>Offset—context-sensitive half-time * (mean)</td>
<td>3 min¹</td>
<td>50-55 min¹</td>
<td>&gt;100 min¹</td>
<td>30 min¹²</td>
</tr>
<tr>
<td>Non-organ-dependent metabolism</td>
<td>Yes</td>
<td>No¹</td>
<td>No⁵</td>
<td>No⁵</td>
</tr>
<tr>
<td>Nonspecific esterase metabolism</td>
<td>Yes</td>
<td>No¹</td>
<td>No⁵</td>
<td>No⁵</td>
</tr>
</tbody>
</table>

*The time required for drug concentrations in blood or at effect-site to decrease by 50%. Based on 3-hour infusion duration.

¹Increases with increased duration of infusion due to accumulation.

ULTIVA® (REMIFENTANIL HCl) FOR INJECTION

Rapid clearance and lack of accumulation result in rapid offset of analgesic effects (5 to 10 minutes) following discontinuation of ULTIVA; therefore, when postoperative pain is anticipated, adequate postoperative analgesia should be established before discontinuation.
ULTIVA™
(REMIFENANIL HCl)
FOR INJECTION

Optimizes intraoperative analgesia without delaying recovery

Rapid onset for profound analgesia during intubation
- Onset of action achieved in approximately 1 minute
- Fewer responses to intubation versus other opioids
- Reduces dose requirements of propofol or thiopental for loss of consciousness

Hypotension occurred in 5% of patients receiving ULTIVA compared to 2% of patients receiving alfentanil or fentanyl.

The flexibility to administer higher opioid doses—for superior control of intraoperative stress responses
- Ability to use higher relative doses (ED$_{20}$) of ULTIVA permits optimal analgesia without prolonging recovery*
- Rapidly titratable to desired depth of anesthesia/analgesia for precise control of intraoperative stress
- Can be titrated to preempt occurrence of major stressful events
- Allows decreased use of propofol, isoflurane, and thiopental by up to 75%†

*The higher relative doses of ULTIVA (ED$_{20}$) resulted in a higher frequency of hypotension (16%) compared to ED$_{50}$ doses of other opioids (5%).
†Subhypnotic doses should be avoided.

Consistently reduces responses to skin incision, signs of light anesthesia, and responses to skin closure in various anesthetic techniques.

<table>
<thead>
<tr>
<th>Outpatient Laparoscopic Surgery</th>
<th>Inpatient Major Abdominal Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Response to Skin Incision</strong></td>
<td><strong>Response to Skin Incision</strong></td>
</tr>
<tr>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>69%</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Signs of Light Anesthesia</strong></td>
<td><strong>Signs of Light Anesthesia</strong></td>
</tr>
<tr>
<td>34%</td>
<td>48%</td>
</tr>
<tr>
<td><strong>Concurrent Hypotension</strong></td>
<td><strong>Concurrent Hypotension</strong></td>
</tr>
<tr>
<td>34%</td>
<td>87%</td>
</tr>
<tr>
<td><strong>Response to Skin Closure</strong></td>
<td><strong>Response to Skin Closure</strong></td>
</tr>
<tr>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>34%</td>
<td>11%</td>
</tr>
</tbody>
</table>

ULTIVA 0.4 mcg/kg/min (n=35)  Alfentanil 1 mcg/kg/min (n=35)  Fentanyl 1.5-3 mcg/kg bolus (n=97)

**ULTRA  ALFENTANIL  FENTANYL**

While not all doses of ULTIVA were equipotent to the comparator opioid (ED$_{20}$ versus ED$_{50}$), all comparator agents were administered in accordance with their recommended dosing guidelines.
Fast recovery, well-suited for outpatient procedures

- Recovery from opioid effects within 5 to 10 minutes
- No cases of recurrent respiratory depression*

Rapid clearance even after prolonged administration.

Rapid recovery of respiratory drive.

Within 5 to 10 minutes after the discontinuation of ULTIVA, no residual analgesic activity will be present; therefore, when postoperative pain is anticipated, adequate postoperative analgesia should be established before discontinuation.

Failure to adequately clear the IV tubing to remove residual ULTIVA has been associated with the appearance of respiratory depression, apnea, and muscle rigidity upon the administration of additional fluids or medications through the same IV tubing.

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.
Rapid response to titration that meets specific monitored anesthesia care needs

Unique esterase metabolism means precision and titratability during monitored anesthesia care procedures

- Provides patient comfort and analgesia during placement of local or regional anesthetic block
- Optimizes analgesia without oversedation
- Highly titratable to maintain adequate respiration

Single dose of ULTIVA effective in control of pain.

<table>
<thead>
<tr>
<th>% Patients With No or Mild Pain to an Ophthalmic Block(^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmic regional block</td>
</tr>
<tr>
<td>No Pain 77%</td>
</tr>
<tr>
<td>Mild Pain 19%</td>
</tr>
<tr>
<td>ULTIVA 1 mcg/kg over 30 seconds (n=26)</td>
</tr>
</tbody>
</table>

\(^*\)Ophthalmic block was placed 90 seconds after administration of ULTIVA. The incidence of nausea, respiratory depression, and muscle rigidity was 12%, 4%, and 7%, respectively.

ULTIVA effectively provides patient comfort.

<table>
<thead>
<tr>
<th>% Patients With No Treated Discomfort Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopedic, urological, gynecological, lower abdominal procedures requiring subarachnoid, epidural, or peripheral block</td>
</tr>
<tr>
<td>97%</td>
</tr>
<tr>
<td>ULTIVA 0.5 mcg/kg bolus; 0.1 mcg/kg/min (n=61)</td>
</tr>
</tbody>
</table>

The incidence of nausea was 26%.

In monitored anesthesia care, when patients are breathing spontaneously rather than on a ventilator, it is not recommended that bolus doses of ULTIVA be administered simultaneously with a continuous infusion of ULTIVA because of a high incidence of apnea and muscle rigidity.

It is strongly recommended that supplemental oxygen be supplied whenever ULTIVA is administered.

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.
**Adverse events typical of μ-opioids**

Well tolerated without the effects of opioid accumulation during general anesthesia or monitored anesthesia care

- Widespread use with experience in over 2,800 surgical patients
- Opioid-related adverse events may occur rapidly, however, dissipation occurs within minutes of rate reduction or discontinuation of ULTIVA
- No cases of recurrent respiratory depression
- Less need for naloxone postoperatively compared to fentanyl or alfentanil* (respiratory depression after discontinuation: 2% ULTIVA, 4% fentanyl/alfentanil; P<0.05)

**General anesthesia: Adverse Events ≥5%**

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>ULTIVA (n=921)</th>
<th>Alfentanil/Fentanyl (n=466)</th>
<th>ULTIVA (n=929)</th>
<th>Alfentanil/Fentanyl (n=466)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>&lt;1%</td>
<td>0%</td>
<td>36%</td>
<td>43%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>19%</td>
<td>6%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>16%</td>
<td>20%</td>
</tr>
<tr>
<td>Muscle rigidity</td>
<td>11%*</td>
<td>8%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>7%</td>
<td>5%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Shivering</td>
<td>&lt;1%</td>
<td>0%</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Fever</td>
<td>&lt;1%</td>
<td>0%</td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

WHILE NOT ALL DOSES OF ULTIVA WERE EQUIPOTENT TO THE COMPARATOR OPIOID, ALL COMPARATOR AGENTS WERE ADMINISTERED IN ACCORDANCE WITH THEIR RECOMMENDED DOSING GUIDELINES.

*Included in the muscle rigidity, incidence is chest wall rigidity (5%).

**Monitored anesthesia care: Adverse Events ≥5%**

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>ULTIVA (n=159)</th>
<th>ULTIVA + 2 mg midazolam (n=103)</th>
<th>Propofol (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>44%</td>
<td>18%</td>
<td>32%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>22%</td>
<td>5%</td>
<td>21%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>18%</td>
<td>16%</td>
<td>0%</td>
</tr>
<tr>
<td>Headache</td>
<td>18%</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Shivering</td>
<td>5%</td>
<td>&lt;1%</td>
<td>2%</td>
</tr>
<tr>
<td>Sweating</td>
<td>6%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5%</td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

In monitored anesthesia care, it is not recommended that bolus doses of ULTIVA be used simultaneously with a continuous infusion because of a high incidence of apnea and muscle rigidity.
OPSIOD POWER
WITHOUT OPIOID ACCUMULATION

FROM HERE

TO RECOVERY

- The first nonspecific esterase-metabolized opioid
- Rapid onset of action (approximately 1 minute)
- Superior control of intraoperative stress responses*
- Rapid response to titration
- Rapid, predictable recovery from opioid effects within 5 to 10 minutes
- Consistent offset regardless of gender, age, weight, or renal/hepatic status

A comprehensive educational program is available. Contact your Glaxo Wellcome Representative for more information.

- For additional information call:
  1-888-4-ULTIVA (1-888-485-8482) for automated information;
  1-800-334-0089 for a Glaxo Wellcome Drug Information Specialist
  (8:30 AM to 5:00 PM Mon-Fri; emergency access 24 hours a day)

ULTIVA®
(REMIFENTANIL HCl)
FOR INJECTION

PRECISE CONTROL, PREDICTABLE RECOVERY

*The higher relative doses (ED50) of ULTIVA administered resulted in fewer responses to intraoperative stress compared to fentanyl and alfentanil (approximately ED50). The doses of ULTIVA used to achieve this profile resulted in a higher frequency of hypotension (16%) versus the other opioids (5%).

Rapid clearance and lack of accumulation result in rapid offset of analgesic effects (5 to 10 minutes) following discontinuation of ULTIVA; therefore, when postoperative pain is anticipated, adequate postoperative analgesia should be established before discontinuation.

References:
6. Data on file, Glaxo Wellcome Inc.

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.

GlaxoWellcome
Glaxo Wellcome Inc.
Research Triangle Park, NC 27709
### TABLE 1: Adverse Events Reported in ≥1% of Patients in General Anesthesia Studies at the Recommended Doses of ULTIVA®

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Total (n = 92)</th>
<th>Male (n = 48)</th>
<th>Female (n = 44)</th>
<th>Male (n = 30)</th>
<th>Female (n = 30)</th>
<th>Male (n = 20)</th>
<th>Female (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>23 (25%)</td>
<td>10 (21%)</td>
<td>13 (29%)</td>
<td>7 (23%)</td>
<td>6 (20%)</td>
<td>6 (30%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (11%)</td>
<td>6 (13%)</td>
<td>4 (9%)</td>
<td>5 (17%)</td>
<td>5 (17%)</td>
<td>3 (15%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Methemoglobinemia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>16 (18%)</td>
<td>8 (17%)</td>
<td>8 (19%)</td>
<td>4 (13%)</td>
<td>6 (20%)</td>
<td>6 (30%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>10 (11%)</td>
<td>5 (11%)</td>
<td>5 (12%)</td>
<td>5 (17%)</td>
<td>5 (17%)</td>
<td>4 (20%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>16 (18%)</td>
<td>8 (17%)</td>
<td>8 (19%)</td>
<td>4 (13%)</td>
<td>6 (20%)</td>
<td>6 (30%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*See Table 7 in full prescribing information for recommended doses. Not all doses of ULTIVA were evaluated to the comparator opioid. Administration of ULTIVA in excess of the recommended dose (i.e., doses ≥1 and up to 20 mg/kg) resulted in a higher incidence of some adverse events: nausea (22%), hypotension (2%), hyperglycemia (4%), and tachycardia (4%).

**Included in the study of the total number of adverse events:

- The overall incidence of hyperglycemia is 1% if administered concurrently or after a hypoglycemic injection.
- The incidence of hypotension is higher, whereas the incidence of nausea and vomiting is lower.

### TABLE 2: Incidence (%) of Most Common Adverse Events by Gender in General Anesthesia Studies at the Recommended Doses of ULTIVA®

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Overall (n = 92)</th>
<th>Male (n = 48)</th>
<th>Female (n = 44)</th>
<th>Male (n = 30)</th>
<th>Female (n = 30)</th>
<th>Male (n = 20)</th>
<th>Female (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>23 (25%)</td>
<td>10 (21%)</td>
<td>13 (29%)</td>
<td>7 (23%)</td>
<td>6 (20%)</td>
<td>6 (30%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (11%)</td>
<td>6 (13%)</td>
<td>4 (9%)</td>
<td>5 (17%)</td>
<td>5 (17%)</td>
<td>3 (15%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*See Table 7 in full prescribing information for recommended doses. Not all doses of ULTIVA were evaluated to the comparator opioid. The frequencies of adverse events from the clinical studies of the recommended doses of ULTIVA (remifentanil hydrochloride) for injection in monitored anesthesia care are given in Table 3.

### TABLE 3: Adverse Events Reported in ≥2% of Patients in Monitored Anesthesia Care Studies at the Recommended Doses of ULTIVA®

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Overall (n = 92)</th>
<th>Male (n = 48)</th>
<th>Female (n = 44)</th>
<th>Male (n = 30)</th>
<th>Female (n = 30)</th>
<th>Male (n = 20)</th>
<th>Female (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>23 (25%)</td>
<td>10 (21%)</td>
<td>13 (29%)</td>
<td>7 (23%)</td>
<td>6 (20%)</td>
<td>6 (30%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (11%)</td>
<td>6 (13%)</td>
<td>4 (9%)</td>
<td>5 (17%)</td>
<td>5 (17%)</td>
<td>3 (15%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*See Table 7 in full prescribing information for recommended doses. Administration of ULTIVA in excess of the recommended infusion rate (i.e., starting doses >1 mg/kg/min) resulted in a higher incidence of some adverse events: nausea (66%), sleep (8%), and muscle rigidity (5%).

**With higher medication doses, higher incidences of respiratory depression and apnea were observed.

Other adverse events are less commonly reported adverse clinical events from all controlled general anesthesia and monitored anesthesia care studies are presented below.

Event frequencies are calculated as the number of patients who were administered ULTIVA (remifentanil hydrochloride) for induction and were reanalyzed as part of the total number of patients in ULTIVA in all controlled studies including cardiac and neurosurgical studies (i.e., 1,883 general anesthesia, i.e., 60% monitored anesthesia care).

Incidence Less than 1%:

- Respiratory depression, abdominal distension, decreased renal function, gastrointestinal reflex, dysphonia, diahrhea, fever, nasal.
- Cardiovascular: vasodilation, vasoconstriction, arrhythmias, blood pressure, tachycardia, blood pooling.

**Miscellaneous muscle stiffness, miscellaneous chest pain.

**Respiratory: cough, dyspnea, bronchospasm, laryngospasm, hoarse, stridor, nasal congestion, pharyngitis, pleural effusion, dyspnea(p), paresthesia, tachypnea, trigger, wheeze, stridor, urticaria.

**Body in a Whole decreased body temperature, osteoporosis, delayed recovery from neuromuscular block.

Skin rash, urticaria.

Uncommon side effects: dyskinesia, dyskinesia, seizure, incontinence.

Infusion Site Reaction: erythema, pruritus, rash.

**Metabolism and Nutrition: abnormal liver function, hyperglycemia, electrolyte disorders, increased CK level.

**Ocular: conjunctivitis, lacrimation, lacrimation, photophobia, keratoconjunctivitis.

**Drug Abuse and Dependence: ULTIVA is a Schedule II controlled substance that can produce drug dependency of the morphine type and has the potential for being abused.

**Dosage and Administration:** Please see full prescribing information for driving and administration guidelines.
Changes in the health care industry have brought many new challenges to CRNAs and we want to make sure you have the right insurance products to meet those challenges. Anesthesia Professional Liability Services, (A+) now has policies for virtually every practice setting including:

+ Students
+ Hospital-Employed CRNAs
+ Physician-Employed CRNAs
+ Self-Employed CRNAs
+ Part Time CRNAs
+ Locum Tenens CRNAs
+ CRNA Groups
+ MD/CRNA Groups
+ Staffing Agencies
+ Professional Liability Services

A+ will continue to offer Claims-Made coverage through St. Paul. In addition, we will now be offering Occurrence form coverage through TIG Insurance Company (formerly Transamerica Insurance Group) which has a Best's rating of “A” (Excellent). The Occurrence form coverage through TIG is available exclusively through A+.

A+ has more products and coverages for CRNAs than any other source. Some of the highlights of our new products include:

+ Occurrence form coverage for all practice settings
+ Discounted rates for Part Time CRNAs
+ Discounted rates for Employed CRNAs
+ Discounted rates for New Graduates
+ Practice Interruption Discount
+ Defense Coverage for Disciplinary Actions
+ Loss of Earnings Due to Court Appearances

If you have questions about your professional liability coverage, call A+.

Professional liability for CRNAs is our specialty. It’s all we do!

A+ is a wholly-owned subsidiary of the AANA.
When you support A+, you’re also supporting the AANA.

1-800-343-1368
Anesthesia Professional Liability Services
222 S. Prospect Avenue
Park Ridge, IL 60068
Versatile
The compact Eagle® 3000 monitor offers flexibility by combining vital signs and EtCO₂.

Innovative
A bright EL display and menu selection with Trim Knob® control makes it ideal for monitoring from subacute to intensive care areas.

Powerful
Features you'd expect in more expensive monitors:
- Simultaneous multi-lead ECG and ST analysis
- Ethernet LAN ready
- EtCO₂ for both intubated and non-intubated care
- Marquette and Nellcor SpO₂ probe compatible

For more information, call 1-800-917-6000, ext. 5419.