Anesthesiology

Cover: "Full Left," cardboard, vinyl, acrylic paint, by Linden Sheldon, a Providence artist. (e-mail: dochaus@hotmail.com)

Medicine & Health
RHODE ISLAND

PUBLICATION OF THE RHODE ISLAND MEDICAL SOCIETY

✑ COMMENTARIES ✑

Looking Good, Feeling Bad, The Marilyn Monroe Syndrome

I have been in the habit of telling my patients how well they look when they do, in fact, look well. I don't tell a fib unless I'm asked to. "Don't I look good?" "Yes, of course you do." Only to patients whom I know well do I say, "You don't look so well today, what's going on?" In these patients I trust my instinct that they appreciate my honesty and my encouraging them to share their problems with me so that we may team up to try to deal with them.

Many patients, especially those with progressive incurable conditions, try to please their doctor who might, in the patient's mind, abandon them. Some patients feel they've failed the doctor rather than vice versa if they worsen or complain. I hope that I can disarm them with my blunt honesty and get them to honestly share their difficulties.

I've been impressed, though, with the occasional response to, "you look great!" with, "If you only knew. . ." And the rare response, "It pains me so much to have people come up to me and tell me how wonderful I look when I feel so rotten inside. It really galls me." A large percentage of my patients have Parkinson's disease and a fair number of others have similar progressive, incurable conditions. I've recently taken a small poll, asking patients how they feel when people tell them they look well. What I discovered was not terribly surprising but reflects, I believe, one aspect of the patient's condition that we, as treating physicians, often don't perceive.

Most patients love it when their friends and relatives tell them they look well. This makes them more positive in their own outlook, as if, despite having their disorder, they're not only compensating, but actually making some progress. For many this buttresses an already positive outlook. For others, who desperately want to "do well," this puts them on a firmer foundation for thinking their life might not be so bad. They do not have the inner strength to maintain a positive outlook on their own and, like most people, require an occasional outside boost.

The patients who are upset by positive comments tend to be depressed. They tend to want to share their suffering with the

world. They interpret the compliment as a denial, a refusal by outsiders to acknowledge their illness and disability. They interpret it as a put-down, as if being told, "It's not so bad. You have no reason to complain." Of course some patients are upset that the compliment is a pro forma statement of no import, like saying, "Hello," or "How're you doing?" in a setting when you don't expect to get a response other than, "OK". It is a statement of social convention, meant only for politeness. These patients would prefer that a "You're looking well" kind of statement should follow or precede an inquiry. "I hope you're feeling as well as you look. Are you?," but then the inquiring person must be prepared to listen to the answer. While politeness dictates an "I'm doing well, thank you," that may not be the answer, especially from someone with pent up frustration.

Social conventions call for different interactions between doctor and patient in the office, of course, than between two friends or acquaintances in a social setting. And the interaction between a doctor and a non-patient in a social setting often puts the doctor in a role of presumed patient advocate by a person frustrated or angry at "not being heard."

When I ask old people how they feel, I

always recall the response old Jewish women used to give in the 1950s during the early days of Israel, "Oy, Nasser (then leader of Egypt) should only feel so good." Undoubtedly 15-20 years earlier it would have been Hitler and just outside of Israel the response may well substitute "Ariel Sharon." This is yet a different response. It's a clever, humorous, hence self-mocking, response not much different than, "things could be worse."

For my patients who I know don't like to receive compliments I say, "How are you doing?" For the ones I'm unsure of I may say, "I hope you feel as well as you look," and for most I'll say, "You're looking well today" or something similar. The incurable and progressive nature of PD and the related disorders makes patients often view their appointments with me as a test, with a grade attached. I think that at the end of the day the patient or caregiver reports back to the rest of the family that their doctor said, "He looks great,"(an A); "He's doing pretty well" (B); "He's holding his own," (C); "He's not doing badly considering" (How long he's had the disease or how old he is) (D); "The doctor can't do much more" (F). I always point out that I can only parrot back what the patient told me during the evaluation. Yet the words from the doctor's mouth

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In memoriam: Richard Carleton

DICK CARLETON, a long-time member of the editorial board of *Medicine & Health/ Rhode Island*, was the chief of medicine when I began working at Memorial Hospital 5 years ago. He retired, quite gracefully, as chief of medicine and chief of cardiology, but remained in the background as an "eminence grise." He was an honest, direct, smart, unassuming man who was a born leader. He led by example and helped improve the public health significantly, due to his untiring efforts to promote understanding of cardiac risk factors in the general community as well as among physicians and health professionals. I am unsure if he took more pride in his sailing accomplishments or his medical and intellectual. During his terminal illness he expressed great satisfaction and pride in his recent supervision of a national "opti" (small sailboat) competition in Barrington. The fact that he was dying with his illness didn't seem to put a crimp into his participation or even his enjoyment of the event. He seemed to me to have achieved a wonderful balance in his life, again providing a wonderful role model for others.

– Joseph H. Friedman, MD

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may have a major impact. A positive outlook carries a better prognosis for all medical problems.

When patients don't like compliments, are they depressed or cynical? Their attitude may be part of their problem but "fixing" it may be no easier than curing their disease. We must, however, be sensitive to this outlook and address it, if possible, as one of the many factors contributing to the disease burden.

– **Joseph H. Friedman, MD**

The Coldness That Does Not Abate

The Bible was not intended as a source of clinical information. But there are Scriptural passages where, in a few terse words, an accurate medical portrayal is nonetheless provided. Consider the opening words of 1 Kings: "King David was now old, advanced in years; and though they covered him with bedclothes, he never felt warm." David was now seventy years of age and had lived a contentious life of victory and defeat, glory and ignominy, and had suffered grievous losses including the death of his son, Absalom.

In a few unembellished words, this passage depicts a disorder common to the elderly: a diminishing capacity to maintain body heat and a greater vulnerability to core heat-loss when exposed to the cold. This phenomenon, called hypothermia, can at times be more than a discomforture; it can be life-threatening.

Hypothermia is often thought of as a disorder encountered in sailors who have survived ocean water immersion for extended intervals; or young cross-country skiers lost for days in some snow-covered terrain. Hypothermia, in reality, is substantially more common amongst the very elderly.

The control of internal body temperature [thermoregulation] is achieved principally through a number of involuntary, systemic measures, such as shivering [which generates more heat], and diversion of the blood flow toward the periphery of the body [which loses heat through vasodilation] or away from the periphery of the body [which conserves heat through vasoconstriction]. These mechanisms are under central nervous system control and they tend to function less well, and less promptly, in the elderly person.

Hypothermia is defined as a core body temperature lower than 95° Fahrenheit. Core temperatures below this threshold produce a number of systemic changes. The earliest symptoms include unusual fatigue, increased weakness, some slurred speech and minor confusion. The victim's skin feels cold, the pulse is unduly slowed and irregular. There is an inappropriate reduction in shivering. Cardiac rate and output fall. Breathing becomes significantly slowed and the skin appears somewhat purple [cyanosis]. There may be substantial fluid leakage from the cells into the tissue spaces with some swelling of the limbs. Kidney function is altered and even the many body enzymes begin to malfunction, causing damage to organs such as the pancreas. Terminally, the voluntary muscles become more rigid, the pupils of the eyes dilate, reflexes are diminished or abolished and coma supervenes.

Hypothermia, obviously, occurs more commonly in the winter months. And a random, winter-time check of the ambulatory elderly in this country showed that about 10% have body temperatures which are at the borderline of hypothermia. In England, for example, 3.6% of all hospital admissions in persons 65 years or older were hypothermic.

As with virtually all illnesses, hypothermia is not randomly distributed. Persons with certain predisposing factors are at substantially greater risk. These factors include: First, elderliness; then, those who are underweight; those whose thyroid function is below normal [hypothyroidism]; those with lowered blood sugar; those who have not eaten for days or are chronically malnourished; those made immobile by stroke, incapacitating arthritis, or, especially, by drugs. [Alcoholism is one of the leading causes of hypothermia through dilating peripheral blood vessels, thus causing increased heat-loss; in addition, it has a sedative effect, thus making the person insensitive to the ambient cold.] Other predisposing drugs include sedatives such as the barbiturates. Increasingly, those elderly who are confused or demented [such as those with Alzheimer's disease] are especially vulnerable to exposure leading to hypothermia. Other predisposing factors include head injury and systemic infection.

The elderly, particularly those with one or more of these risk factors, may often declare: "I never feel warm enough even when I wear two sweaters and am in a warm room." But they will not fall prey to clinical hypothermia unless they are unnecessarily exposed to cold weather for prolonged intervals as with elderly persons who are demented or homeless people benumbed by alcohol.

Durng a two-decade interval [1979-1998] there have been 13,970 persons dying of hypothermia in the Untied States, particularly the northern states. About half of these recorded deaths [6,857] occurred in persons 65 years of age or older. The overall national rate of hypothermia deaths has diminished from about 1,000 deaths per year in 1981 to fewer than 500 deaths in 1998. In terms of age, the highest rates were noted in those 85 years or age or older. Elderly males were about three times more likely to die of hypothermia than females of similar age.

Most public health officials agree that these data represent a substantial under-reporting of hypothermia deaths. First, because hypothermia leaves virtually no identifying evidence after death; and even at post-mortem examination there will be little that represents incontrovertible proof of hypothermia. Second, because many hospitals do not use low-reporting thermometers in their emergency rooms; and low body temprature in stuporous admissions may therefore go undetected.

The conventional fever thermometer is designed to detect elevations rather than depressions in body temperature. Indeed, the calibrated mercury column will not go down unless the thermometer is vigorously shaken; and even then it rarely goes below 95° Fahrenheit. The usual home thermometer, therefore, is of little value in detecting hypothermia.

Two typical stories of environmental hypothermia:

* In December, an 89 year-old woman, with a history of wandering, was found to be missing from the nursing home where she had been living. The outdoor temperature that night was 23°F. After a search she was found partially immersed in a neighboring pond and rushed to a hospital, where she died.

* In January, a 51 year-old man was found dead behind a dumpster. The temperature on that day had been 25°F. Toxicological examination of the victim's blood indicated a significant amount of alcohol as well as traces of various opiate drugs. Needle tracks and drug paraphernalia were also found.

In the Presidential election of last year, both major candidates indicated that this nation was wealthy enough so that no child should be left behind. Perhaps our wealth is also sufficient to insure that no adult - demented or not, chemically addicted or not - should be abandoned to the elements.

– **Stanley M. Aronson, MD, MPH**

Anesthesiology: Patient Care, Innovation and Safety

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Richard A. Browning, MD

Modern anesthesia practice began about 1940, approximately 100 years after its first public demonstration. This coincided with the transformation of medicine in general from an art to a discipline based on scientific inquiry. The discovery of antibiotics, in particular, made possible a vast array of surgeries previously deemed too risky. In fact, prior to the advent of inhalational anesthesia in 1846 patients often approached all but the most superficial of surgeries as an event characterized by pain, infection and death. The surgeon could only offer combinations of oral opium and alcohol and a reputation of speedy handiwork. Pain was an inevitable consequence of surgery, and the ability to endure pain was often looked upon as an ennobling or purifying experience.

In the 1940s and 50s new therapies for disease management and introduction of numerous pharmacologic agents led to an explosion of medical knowledge and opportunity that have persisted to the present time. The development of intravenous agents and safe, reliable techniques to deliver them gave pioneering anesthesiologists the opportunity to broaden the scope of care for the surgical patient. Investigation of cardiac and respiratory physiology was vigorously pursued and numerous physicians sought training in this developing medical specialty.

Early in the evolution of the specialty, these new scientist-physicians began to critically evaluate the safety of their craft. In 1953 the benchmark for overall anesthesia-related deaths was established at 1:1,560. While this represented an improvement over previous eras, it was still an unacceptably high mortality rate, especially for elective surgical procedures.

Further investigation by anesthesiologists in concert with basic science departments brought steady gains in our understanding of pharmacology and pharmacokinetics of anesthetic agents. Additionally, the understanding of our patient's physiologic response to medications and surgical stimulation became more refined. Application of this knowledge allowed technology and monitors from the laboratory to be applied in the clinical arena. This led to the routine use of electrocardiography, quantification of blood pressure by automated means, arterial blood gas analysis and mechanical ventilation. Innovations that are now routine throughout the hospital found their earliest applications in the operating room before being adopted by the modern post-anesthesia recovery room and ICU.

By the 1970s the risk of anesthesia related mortality had improved to about 1:25,000. A marked improvement from the previous two decades but still not at the level many anesthesiologists felt was attainable. The 1980s saw further action on the patient safety front by anesthesiologists. The Anesthesia Patient Safety Foundation was established and the American Society of Anesthesiologists undertook the ASA Closed Claims Study. The latter process started the development of numerous practice policies and guidelines designed to demonstrate a series of best practices. These activities, coupled with significant increases in trained anesthesiologists, new monitoring applications (pulse oximeter, end-tidal CO2 and anesthetic gas analysis), and pharmacologic advances have helped drive the anesthetic related mortality to somewhere between 1:150,000 to 1:250,000 in U.S. hospitals.

The remarkable improvement in patient safety has resulted in numerous requests to extend anesthesia care beyond the traditional confines of the operating room. Anesthesiologists as well as other trained providers have been called upon to administer sedatives, analgesics and general anesthetics throughout the hospital campus and even in office settings. While many of these settings are appropriate they do present obstacles to safe care not found in the traditional operating room environment. The challenge that must be met is to assure that the safety record established in the operating room is maintained in alternative procedural environments.

This issue of *Medicine & Health/ Rhode Island* is fortunate to have contributions from several regionally and nationally known anesthesiologists who, through their work, are continuing a tradition of innovation and improved patient care. Doctor Andrew Triebwasser has written an article on sedation and analgesia for procedures performed outside the operating room for non-anesthesiologists, an area of increasing concern as more procedures are performed in an uncentralized location. Doctor George Buczko has written a piece covering sedation challenges for the ICU patient, while Dr. Frederick Burgess has made contributions on the subject of pain management. Doctors Sung-Hee Lee and Yusef Barcohanna, from Women & Infants Hospital, have an update on analgesia and anesthesia for the obstetric patient. Additionally, Dr. Arthur Bert and Dr. Andrew Maslow discuss the current state of transesophageal echocardiography for non-cardiac surgical patients.

It has been a privilege for me to work with these authors and the *Medicine & Health/Rhode Island* staff to demonstrate both the diversity of current anesthesia practice and the high level of local expertise.

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Sedation and Analgesia by Non-Anesthesiologists

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Andrew Triebwasser, MD, and Richard A. Browning, MD

INTRODUCTION AND HISTORICAL BACKGROUND

The past decade has seen a dramatic increase in the use of sedatives, analgesics, and general anesthetic agents for patients outside the traditional operating room setting, often by non-anesthesiologists. Benefits of sedation and analgesia include allowing the patient to undergo unpleasant or distressing procedures without anxiety or pain and expediting procedures in which lack of movement is crucial (e.g. many diagnostic procedures in children). The risks include: i. *oversedation* - leading to hypoventilation, apnea, airway obstruction, and generalized cardiorespiratory compromise that, if not immediately reversed, might result in hypoxic brain damage, cardiac arrest, or death; ii. *undersedation* - leading to pain, psychological distress, or actual patient injury due to uncontrolled movement. This complex endeavor has attracted significant attention from anesthesiologists, pediatricians, radiologists, emergency room physicians, and every other procedural oriented specialty. The **Joint Commission on Accreditation of Healthcare Organizations (JCAHO)** has also given it special attention. Reports of complications[1] and the failure of non-anesthesiologists to adhere to uniform standards[2] have been prime motivational forces in the development of practice guidelines.

The first significant guidelines were proffered in 1992 by the **American Academy of Pediatrics (AAP) Committee on Drugs (COD)**.[3] In its completed form, these pediatric guidelines serve as a template for the development of local policies and individual practice regarding patient evaluation and selection, definition of "conscious" sedation, monitoring, drug selection, equipment, fasting intervals, record keeping and post-procedure surveillance and discharge criteria.

An additional motivating force for the establishment of uniform standards of care for sedation was the 1995 JCAHO standard, which states:

"patients with the same health status and condition receive a comparable level of quality of surgical and anesthesia care throughout the hospital." (Sec MS.4.9)[4]

The JCAHO also determined that deep sedation should be equated with general anesthesia:

"The standards.. apply.. for patients who receive general, spinal, or other major regional anesthesia..and..in any setting, receive for *any purpose*, by *any route*..sedation (with or without analgesia) for which there is *reasonable expectation* that in the manner used, the sedation/analgesia will result in the loss of protective reflexes for a *significant percentage* of patients." (Sec 1)

Obviously, the application of these criteria for a given institution requires medical staff to specifically define the terms "a reasonable expectation" and "a significant percentage of patients". The director of Anesthesiology must establish broad standards of care within a hospital for all patients undergoing sedation for non-operating room procedures. To assist in this endeavor, the **American Society of Anesthesiologists (ASA)** Task Force on Analgesia and Sedation by Non-Anesthesiologists has adopted guidelines that allow standards to become more uniform across institutional lines.[5] These guidelines are the first to be developed in the rigorous manner recommended by the United States Department of Health and Human Services, in which connections between interventions and outcome are supported or refuted by meta-analysis of published data and/or consensus opinion of a panel of experts.

GENERAL GUIDELINES OF SEDATION

I. Definition of Terms (Appendix 1)

It is important to note that "conscious" sedation describes the state which allows cooperative, minimally depressed (and usually amnestic) patients the ability to tolerate uncomfortable procedures while maintaining the ability to respond to gentle voice or touch. Cardiorespiratory stability is implied. Sleepy patients who will not respond purposefully to physical or verbal stimuli (but may withdraw from pain) are sedated to a greater degree. In pediatric patients, the oxymoron term "conscious sedation" is, at best, imprecise; it has been replaced in the ASA guidelines by the more specific term "sedation and analgesia".

Appendix 1.

AAP COD: continuum of sedation

SEDATION	AROUSAL	REFLEXES
conscious	voice touch	intact
deep	pain	±lost
general	none	lost

Appendix 2.

ASA physical status (ASA PS) Classification

ASA I	normally healthy
ASA II	mild systemic disease
ASA III	severe systemic disease
ASA IV	life-threatening disease
ASA V	moribund
E	emergency

II. Patient Preparation

The COD advocates utilization of ASA Physical Status Classification (Appendix 2) to gauge concurrent systemic illness that might impact on the risks associated with sedation. In general, only ASA class I and II patients are considered suitable candidates for sedation/analgesia by non-anesthesiologists. The clinician administering sedation should be familiar with relevant aspects of the patient's history, including current medications, drug allergies, and previous experiences with sedation. Practitioners must be taught to assess patients for potential organ system abnormalities which might

lead to problems with sedation, including: a history of congenital heart, gastroesophageal reflux, asthma, seizures or intracranial hypertension to name just a few. Additionally, anatomic airway abnormalities must be recognized. Predictors of airway difficulty include stridor, snoring or sleep apnea, dysmorphic facial features (especially micrognathia), short neck, limited cervical extension, small mouth opening, and macroglossia.

Preprocedure preparation should include adequate patient and family counseling, with informed consent. Children, in particular, may benefit from learning about the planned procedure, proposed sedation, and additional coping mechanisms that can be utilized.

Fasting prior to the procedure should allow for adequate gastric emptying. Current recommendations at Rhode Island Hospital are to withhold solids and milk products for 6 hours prior to the procedure, with clear fluids permitted up to 2 hours before the procedure. It should be noted that certain patient conditions might delay gastric emptying; these include obesity, pain and stress, and concurrent use of opioids.

III. Guidelines for the Procedure

In addition to patient preparation, the COD guidelines emphasize such aspects of sedation as monitoring, emergency plans (including on-site equipment, skill of personnel and back-up emergency services), documentation before, during, and after the procedure, and post-sedation monitoring and discharge criteria. In particular, it should be noted, pulse oximetry is regarded as a cornerstone of monitoring for all patients both during and after the procedure.

Like the AAP COD, JCAHO guidelines emphasize the need for uniform standards of care for all patients, regardless of intended depth of sedation. Levels of sedation are viewed as a continuum, with patients slipping easily and unpredictably from conscious sedation to deep sedation and general anesthesia. Deep sedation and general anesthesia are indistinguishable, since each might result in loss of protective airway reflexes. Unlike the AAP, however, the JCAHO has distinguished between conscious sedation (responsive but slurred speech) achieved by titration of intravenous agents and light sedation (anxiolysis in an awake patient) achieved predominantly through oral sedatives (CAMH Update 4. November 1997). Unlike conscious sedation, light sedation does not require continuous monitoring. In any case, institutional guidelines must be in place to define qualified monitoring personnel and to credential practitioners for both the performance of procedures and the prescription of sedative-analgesic medication.

Patients continue to be at risk for complications after the procedure is completed due to delayed drug absorption, prolonged effects of certain pharmacologic agents, and/or decreased procedural stimulation. Appropriate monitoring during the recovery period and suitable discharge criteria (such as those found in Appen-

Appendix 3: Pharmacology of Sedation and Analgesia		
DRUG	DOSE AND ROUTE	COMMENT
Opioid Analgesics		•respiratory depression •pruritus •nausea/vomiting •sedation •reversal agents
morphine	0.1-0.2 mg/kg IV	•histamine release
fentanyl	1-2 mcg/kg IV 5-15 mcg/kg OTFC	•titrate incrementally •Oralet™ lozenges
sufentanil	1-3 mcg/kg IN	
Benzodiazepines		•anxiolysis, amnesia •lack analgesia •respiratory depression •± muscle relaxation •reversal (flumazenil)
midazolam	0.05-0.1mg/kg IV 0.5-0.7 mg/kg PO 0.2-0.4 mg/kg IN	•immediate onset; titrate •onset 20-30 minutes •onset 5-15 minutes
diazepam	0.1-0.2 mg/kg IV	•venous irritation
lorazepam	0.02-0.05 mg/kg IV	•longer half-life
Barbiturates		•full gamut sedation •lack analgesia •respiratory depression •hypotension
thiopental methohexital pentobarbital	1-6 mg/kg IV 20-30 mg/kg PR 2-6 mg/kg IV/IM/PO	•rapid induction anesthesia •contraindicated TLE •onset 10-15 minutes IM
DRUG	DOSE AND ROUTE	COMMENT
Other pure sedatives		
chloral hydrate	50-75 mg/kg PO/PR	•max dose 100 mg/kg •↓respiratory depression •lack analgesia •slow onset (45-60 min) •liver toxicity w/overdose
propofol	1-3 mg/kg IV bolus 100-200 mcg/kg/min	•rapid general anesthetic •lack analgesia •respiratory depression •hypotension •pain on injection •+anti-emetic effects •rapid awakening •infection concern
sedative-analgesic		
ketamine	 1-2 mg/kg IV 4-10 mg/kg IM 6-10 mg/kg PO/PR 3-6 mg/kg IN	•dissociative anesthesia •somatic analgesia •sympathomimetic •supports ventilation •emergence delirium •increase ICP •secretions •myoclonic movements •onset w/in minute •duration 5-15 minutes •peak onset 5 minutes •duration 30-120 min

dix 1 of the COD guidelines) should minimize patient risk for central nervous system and/or cardiorespiratory depression after completion of the procedure, and discharge from observation by trained personnel.

SEDATION AND ANALGESIA: PHARMACOLOGIC CONSIDERATIONS

In the effort to achieve satisfactory sedation and analgesia, a variety of agents have been utilized, alone and in combination, in a variety of routes. Safety and predictability remain an issue, especially for agents that are purported to provide "conscious" sedation. Due in part to interpatient variability, it is difficult to achieve conscious sedation without the potential for unanticipated deep sedation. This can occur by a direct overdose, drug-drug interactions or increased sensitivity. In short procedures, this might occur after the procedure is completed, either through delayed drug absorption, or the sudden lack of stimulation. Biban reported two cases of significant airway obstruction (requiring bag ventilation) in toddlers with obstructive sleep apnea (due to enlarged adenoids) that had received 80 mg/kg of chloral hydrate.[6] As noted previously, surveillance and monitoring must occur until suitable discharge criteria are met, as per institutional operating room guidelines. Cote reported 9 sedation "disasters" occurring after discharge, including three children found dead in car seats upon arrival home.[7]

Specific agents utilized in sedation and analgesia fall into several categories. These include pure analgesics, pure sedatives, and sedative-analgesics. For information regarding specific agents, please refer to Appendix 3.

A PRACTICAL APPROACH TO SEDATION

I. General considerations

Anesthesiologists emphasize a rational, consistent approach to sedation. Our institutional guidelines at Rhode Island Hospital closely mirror those of the AAP, and emphasize patient preparation, monitoring, and documentation of events. Informed consent is not a

The importance of the anesthesia community in the preparation of patient sedation protocols is predominantly the emphasis on a systematic approach to patient evaluation and preparation, monitoring and record keeping, drug and fluid management, recovery and discharge — elements that are not intuitive to non-anesthesiologists.

separate document, but confirmation of patient or parental assent is included on a standardized procedural sedation form. Having reviewed general consideration and specific pharmacologic agents, one must now develop a rational plan for each individual sedating event, beginning with the following questions:

i. is the procedure painful or non-painful?
ii. what is the duration of the procedure?
iii. is a motionless patient mandatory?
iv. what are unique patient considerations (including NPO status)?
v. is the procedure urgent or elective?
vi. who should provide the sedation?

The question of who should provide sedation to patients outside the operating room is controversial at the present time. Obviously, situations must be individualized, taking into account the age and physical status of the patient, complexity of the planned procedure, skill of non-anesthesia practitioners who would be called upon to provide the sedation, and availability of anesthesiologists. Clearly, someone skilled in basic life support and familiar with the routine monitors (especially pulse oximetry) must be designated as solely responsible for monitoring and sedation; this practitioner must not be re-

sponsible for the procedure itself.

II. The Painful Procedure

Painful procedures might be elective (as a bone marrow aspiration for a child with leukemia), or urgent (as setting a fracture or suturing lacerations in the emergency department). The ideal approach in these situations is the integrated approach, including psychological assessment, developmental evaluation, and simple behavioral intervention, including distraction through music, tactile stimuli, or even hypnosis. These techniques may reduce the need for pharmacologic sedation/analgesia, certainly an advantage in the emergency department, where virtually all patients must be assumed to have inadequate gastric emptying. In this setting, true "conscious sedation" is always the goal, usually with the reassuring presence of a parent as a useful adjunct; the parent must be counseled about not only the relative risks and benefits of any proposed sedation/analgesia, but also about its limitations in any given setting.

Although drug combinations may be more effective than single agents in certain situations, the risk of drug interaction and potentiation of respiratory depression[8] emphasizes the need to appropriately reduce the dose of each component as well as the need to continually monitor respiratory function. It is my personal bias that solitary agents provide an added margin of safety; whenever intravenous agents are titrated to effect, especially in combination, "deep sedation" may occur.

Sandler designed a randomized, double blind, crossover study comparing IV midazolam (0.2 mg/kg) or fentanyl (4 mcg/kg) for painful pediatric oncology procedures.[9] A majority of children (range 3-21 years) preferred midazolam, despite its lack of analgesic property. Apparently, if a single agent is to be utilized, the anxiolysis and amnesia provided by a benzodiazepine (in conjunction with local anesthesia) might be advantageous compared to a short acting opioid. If an opioid is to be utilized, fentanyl would appear to be a logical and easily administered choice, although emesis, pruritus and respiratory depression may occur. Similarly, oral ketamine

(10 mg/kg) has been shown to alleviate distress associated with pediatric oncology procedures.[10] I would consider all of the above to be reasonable in the emergency department.

When deep sedation is required for painful procedures, reasonable options include parenteral ketamine (usually with a benzodiazepine) or titrated bolus dosing of a benzodiazepine and opioid in combination. It must be stressed that these drug combinations greatly increase the possibility of respiratory depression; both during and after the procedure.

Deep sedation in the emergency department is problematic due to the "full stomach" status of patients in this setting. Thus, the first consideration might be towards the potential combination of conscious sedation with local anesthesia and mild restraint, if needed. If deep sedation is deemed necessary, the need to proceed must be weighed against the benefit of delaying the procedure to ensure maximal gastric emptying. Even a four-hour delay in urgent surgical procedures has been shown to reduce gastric volume by one-half.[11] It would be reasonable during this time period to institute pharmacologic measures that reduce gastric volume and acidity, such as metoclopramide (0.2 mg/kg) and cimetidine (7.5 mg/kg). Endotracheal intubation must be considered in such patients in the event loss of consciousness occurs. Most guidelines ensure that practitioners in this situation be "attending physicians trained in critical care and airway management."

III. ANESTHESIA IN THE RADIOLOGY SUITE

The major requirement in the radiology suite is that the patient remains motionless. Pain is generally not an issue, and opioids are not indicated. Although in-

fants and toddlers may be successfully sedated with chloral hydrate (and gentle restraint) for even long MRI studies, frightened children between 2-8 years of age will usually require deep sedation. Reasonable alternatives include oral or IM pentobarbital, rectal methohexital, and propofol. At Rhode Island Hospital, anesthesiologists provide most deep sedation for radiologic procedures; obviously, this is an institutional decision.

Important considerations in the radiology suite include duration (some radiation therapy interventions take literally minutes, while MRI studies can take two hours), use of oral contrast, environmental concerns (especially in the MRI suite), and proximity to recovery units and emergency medical support.

CONCLUDING REMARKS

The importance of the anesthesia community in the preparation of patient sedation protocols is predominantly the emphasis on a systematic approach to patient evaluation and preparation, monitoring and record keeping, drug and fluid management, recovery and discharge — elements that are not intuitive to non-anesthesiologists. Although guidelines are not meant to represent absolute standards of care, but rather recommendations that allow practitioners to make rational decisions about health care, AAP and ASA guidelines have clearly led to the purchase of crucial equipment and aided in formulating institutional policy designed to provide safe, efficient sedation outside the operating room. The authors expect this issue to be an on-going challenge for many years as more and more procedural specialties perform their work in multiple and decentralized sites. Quality control and improvement will require frequent review of institutional practices for compliance with updates to existing guidelines.
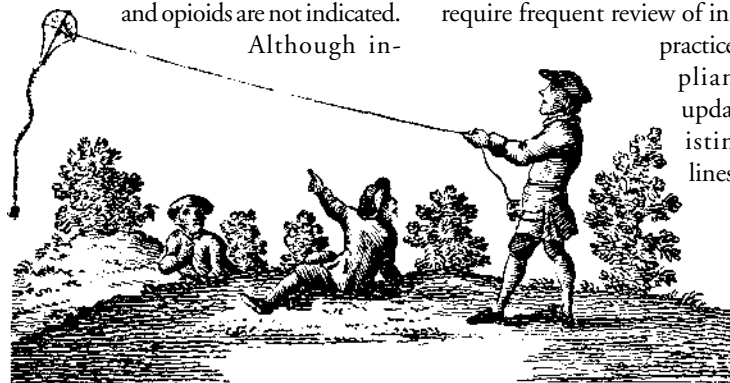
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Sedation in Critically Ill Patients: A Review

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Critically ill patients are forced to endure a variety of noxious stimuli throughout their intensive care stay. Included among these are fresh surgical wounds, wound cleansing and dressing changes, invasive procedures, and indwelling catheters and tubes. Nursing care measures and components of physical therapy can contribute to the patient's discomfort, at least temporarily. Furthermore, the intensive care environment represents a significant departure from normal, with limited freedom of movement, profound restriction of activity and, in many cases, loss of day-night sensory input.

The above constellation of circumstances can be associated with behavioral and biochemical consequences. Behavioral consequences include agitation[1] and delirium.[2] A significant number of patients may manifest a substance withdrawal syndrome.[3] All of these may interfere with medical and nursing management of the patient and may lead to patient injury and/or unplanned removal of endotracheal tubes, invasive monitors and indwelling catheters. Biochemical consequences, especially of painful conditions, include stress hormone responses which may not only elevate systemic blood pressure and heart rate but also contribute to a hypercoagulable state.[4]

The aim of adequate sedative therapy is to minimize the above consequences of critical illness. The topic of sedation in critically ill patients has been reviewed extensively[5] and the **Society of Critical Care Medicine (SCCM)** (with the **American College of Critical Care Medicine (ACCM)**) has published practice parameters for intravenous analgesia and sedation in the intensive care unit.[6] An ideal sedation strategy meets the goals of pain relief and anxiolysis and allows the patient to tolerate the various aspects of the ICU experience while leaving the sensorium relatively intact and permitting meaningful neurological evaluation. This balance of therapeutic aims is often difficult to realize in the face of the rapid changes in drug handling that may accompany critical illness.[7] Changes in drug handling influence dosage requirements and create the potential for overdose and prolonged mechanical ventilation, especially when drugs are administered by continuous infusion.[8] The goal of this review is to summarize pharmacological and clinical data that underlie various sedation strategies in the intensive care unit in adult patients.

> *The "ICU" syndrome occurs in 15-20% of general hospital admissions and in almost 40% of postoperative patients.*

SEDATION STRATEGIES

Sedation strategies encompass diagnosis, choosing a pharmacological regimen and monitoring. Diagnosis requires distinction between anxiety and delirium. The pharmacological regimen should be appropriate for the clinical disorder. Monitoring involves not only determination of effectiveness of the drug regimen but also repeated assessment of the underlying behavioral disturbance with a view to reduction or discontinuation of the pharmacological intervention.

DIAGNOSIS

Delirium is distinguished from simple anxiety and pain by the acute onset of generalized cognitive impairment[2] which may include a fluctuating level of consciousness, poor orientation and perceptual disturbances, such as hallucinations.[9] Included under the diagnostic umbrella of delirium is the "ICU" syndrome, also known as "ICU" psychosis, postoperative delirium and, in heart surgery patients, postcardiotomy delirium.[9] The "ICU" syndrome occurs in 15-20% of general hospital admissions[2] and in almost 40% of postoperative patients requiring ICU care. Older age and premorbid impaired cognitive status are independent predictors of the "ICU" syndrome while the relationship among sleep deprivation, the intensive care environment and delirium has not been conclusively established.[9] The diagnosis of delirium or "ICU" syndrome should prompt an exhaustive search for organic causes which include metabolic disturbances, electrolyte disorders, systemic infections, substance withdrawal syndromes and a variety of drugs.

PHARMACOLOGICAL REGIMENS

There is a large choice of sedatives available to the clinician to alleviate simple anxiety and pain, as well as to treat delirium. The ACCM and the SCCM have jointly published practice parameters for intravenous analgesia and sedation for adult patients in the intensive care unit in order to help clinicians make rational choices of sedatives and analgesics.[6] The authors recommended that morphine be the preferred intravenous analgesic in the intensive care unit and listed fentanyl and hydromorphone as acceptable alternatives. The use of meperidine was discouraged. Either midazolam or propofol were the preferred agents for short-term (<24 hours) sedation while lorazepam was recommended for long-term (>24 hours) sedation for anxiety. Haloperidol was strongly recommended for the treatment of delirium.

All of the suggested medications, except haloperidol, blunt ventilatory response to carbon dioxide to some extent. Because analgesic and sedatives are respiratory depressants, caution must be exercised when using these agents in the intensive care setting. The patient must be conscious enough to protect his or her airway from pulmonary aspiration and must be evaluated frequently, both clinically and with arterial blood gas measurements, for the need for mechanical ventilatory support. If the patient re-

quires mechanical ventilation or is comatose, the airway should be secured with an endotracheal tube.

ANALGESIA

Morphine is a naturally occurring alkaloid of the phenanthrene class of opium derivatives. It is lipophobic and only a small fraction crosses the blood brain barrier, with slower onset but longer duration than more lipophilic agents. It has excellent analgesic properties but also causes drowsiness, respiratory depression, decreased gastrointestinal motility, nausea and hypotension, partly through histamine release. It cumulates in most parenchymal tissues but does not persist in them beyond 24 hours after the last dose in short term use. Morphine is metabolized in the liver to morphine glucuronide, which has very little activity, and subsequently excreted by the kidney. The half-life of morphine is between 2.5-4 hours in young healthy patients but is likely longer in older and in critically ill patients. The low activity of morphine glucuronide may be important in prolongation of opiate effect on patients with renal failure. The loading dose of morphine is 0.05 milligrams per kilogram (mg/kg) of body weight and most patients require 4-6 milligrams per hour of maintenance.[6] Patients with hepatic metabolic and renal excretory abnormalities may need a lower maintenance dose, while substance abusers may have higher requirements.

Fentanyl is a synthetic opioid that is much more potent than morphine and highly lipophilic, which allows rapid passage across the blood brain barrier and accounts for its rapid onset of action. It has many of the same therapeutic and adverse effects as morphine. However, fentanyl does not release histamine and therefore causes less systemic hypotension. It may cause significant muscle rigidity if injected rapidly. At low dose, fentanyl has a short duration because of redistribution of drug into adipose tissue. At high dose or with continuous infusion, duration of action is much longer because the adipose depot continually releases accumulated drug to the blood after cessation of administration. This phenomenon results in a long half-life of 3-8 hours. Fentanyl is transformed in the liver to several metabolites with

minimal opioid activity and then excreted by the kidney. Loading dose is 1-2 micrograms per kilogram (μ/kg) and maintenance is between 1-2 μ/kg per hour (μ/kg/hr).[10] This dose may also require modification in liver or kidney disorders and in substance abusers.

There is little information about the use of hydromorphone in continuous infusion. In most circumstances it is administered as a bolus. Typical requirements range from 0.5-2 milligrams per hour (mg/hr).[6] Meperidine is discouraged because its major metabolite, normeperidine, may accumulate and cause central nervous system excitation.

SEDATION

Midazolam is an imidazobenzodiazepine that is water soluble in acidic media but highly lipophilic at physiologic pH, allowing the formulation to be non-irritating to veins and accounting for the very rapid onset of action with intravenous administration. Its properties include anxiolysis, hypnosis, antegrade amnesia, muscle relaxation, anticonvulsant effects, mild respiratory depression and a modest drop in systolic blood pressure due to a decrease in systemic vascular resistance. The drug is oxidized by the liver to compounds that have some pharmacological activity. Half-life is 1-4 hours in healthy young individuals and up to twice as long in the elderly and morbidly obese.[11] Half-life may be as long as 12-24 hours in the critically ill.[5] Loading dose is 0.03 mg/kg and maintenance dosage starts at 0.03 mg/kg/hr. Because of the lipophilic nature of midazolam, it can accumulate in adipose tissue and long term administration can result in prolongation of the drug's sedative effects.[6]

Propofol is a phenol with low aqueous solubility requiring a commercial formulation as an oil-in-water emulsion of glycerol, egg phosphatide and soybean oil which is irritating to veins. Propofol's high lipid solubility accounts for its rapid onset of action. It is a potent sedative/anesthetic agent that can cause central nervous system excitability at low dosage and systemic hypotension at higher doses. In long term use, patients develop tolerance to propofol. In addition, propofol infusion over greater than seven days can present a caloric load and raise

serum triglyceride levels. Furthermore, the emulsion supports bacterial growth and might theoretically contribute to infection, although this is rare if proper sterile handling technique is used. The remarkable feature of propofol is its short duration of action after discontinuation of even long term infusions. The rapid fall in plasma concentration occurs partly because of drug redistribution but mainly because of rapid hepatic and extrahepatic (possibly pulmonary) metabolism. Sedative dosages start at under 50 μ/kg/min.[12]

Lorazepam is an intermediate acting benzodiazepine, which is longer acting than midazolam in the short term, but causes less hypotension. After long term infusion, cessation of action is of similar duration to that of midazolam. Its lower cost makes it more desirable for long term intravenous sedation. Starting dose is 0.02 mg/kg/hr but onset of action is slow and a faster agent such as midazolam may be required for initial sedation.[6]

Diazepam accumulates in the adipose tissues and has too long a duration of action to be of practical use in the intensive care setting.[5]

Haloperidol is a butyrophenone which is efficacious in the treatment of delirium in the intensive care patient. It can be used intravenously in dosage increments of 2 mg., has an onset of action of about 30 minutes and a duration of action of 4-8 hours. Significant side effects include movement disorders, prolonged QT interval, and Torsade de Pointes and limit the widespread use of haloperidol.[13]

MONITORING

Frequent physical examination is warranted to assess level of sedation. Ideally the patient should be calm or somnolent but easily arousable. Small incremental adjustments should be made if "fine tuning" is required. Several sedation scoring systems exist, but neither have they been validated, nor are they in widespread use.[14] The use of bispectral analysis of a continuous electroencephalogram has been advocated and may hold promise in the future.[15]

SUMMARY

The most commonly used sedatives in the intensive care setting are

midazolam, propofol and lorazepam. The ACCM/SCCM recommendations provide reasonable options for selection of therapeutic agents. Choices may differ, however, in specific cases. For example, where frequent neurological evaluation is necessary, propofol may be the sedative of choice in long term sedation. Abrupt withdrawal of any sedative may precipitate withdrawal symptoms and infusion dosages should be reduced gradually. Finally, any sedation strategy should be devised in cooperation with the ICU nursing staff to be certain that both medical and nursing requirements converge with the patientís needs.

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Opioid Therapy for Chronic Painful Conditions

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Over the past 2 decades, a dramatic change has occurred in the way healthcare providers, patients, and society in general view pain and pain treatment. Throughout history, pain was viewed as the natural and unavoidable accompaniment of disease, injury, and death. Acceptance of pain often took upon a sense of religious purification and penance. Opiate analgesics have been available since the beginning of recorded history, but have long been regarded with disdain by many societies over their potential for addictive use. Even today, the opioids continue to be regarded as medically risky, their use the subject of intense suspicion and scrutiny by legal and medical regulators. Legal barriers limiting opioid prescribing, fear of addiction, and the potential for causing harm have created a sense of personal jeopardy among physicians prescribing opioids, even in the treatment of acute pain. As the hospice care approach began to evolve during the past 20-30 years, aggressive opioid treatment of intractable cancer pain was introduced and championed. This led to greater medical and social acceptance of long-term opioid analgesia. The success of this aggressive pain management approach for cancer pain, coupled with the recognition that aggressive postoperative pain management can produce improvements in perioperative morbidity and mortality, has stimulated interest in adapting rational opioid prescribing to the chronic noncancer pain patient.[1]

EVIDENCE OF OPIOID EFFICACY FOR CHRONIC NONCANCER PAIN.

Portenoy and Foley were among the first to extrapolate their experiences with chronic cancer pain to the general chronic pain population.[1] In 1986, they reported on a series of thirty-eight chronic non-cancer pain patients who were treated with a variety of oral opioids for 1 to 14 years. Thirty-one patients were treated for 2 years or longer. The purported benefits of opioid therapy included a reduced emphasis on seeking invasive alternatives to control their pain, improved function, and safety.

Zenz and associates reported on a series of 100 chronic noncancer pain patients treated with a variety of opioids.[2] Fifty-one patients rated their pain relief as good, with greater than 50% improvement. Twenty-eight patients reported partial relief, and 21 patients did not experience any improvement in their pain. The patients experiencing good relief demonstrated the greatest improvement in function, as estimated by the Karnofsky scale. Problematic side effects were not identified. These reports strongly suggest that opioid therapy may be regarded

as helpful by a subset of chronic pain patients.

Another group of chronic, non-cancer pain patients has neuropathic pain. Neuropathic pain is generally regarded as responding poorly to opioid analgesics. Interestingly, the chronic pain patients with neuropathic pain identified in the Zenz series appeared to respond as well as the nonneuropathic pain patients.[2] Portenoy and associates have indicated that neuropathic pain conditions may respond to opioid therapy, but may require higher doses to produce their analgesic effect.[3] Pappagallo and Campbell reported that long-term opioid analgesics were helpful in the management of neuropathic pain of postherpetic neuralgia.[4] Watson and Babul reported similar findings in another group of patients with postherpetic neuralgia in a double-blind crossover trial treated with controlled-release oxycodone or placebo.[5] Their patients reported improvements in constant pain, allodynia, and paroxysmal pain. These reports challenge the widespread dogma that opioids are ineffective for neuropathic pain.

In a randomized prospective trial, Jamison and colleagues looked at the treatment of 36 low back pain patients treated with and without opioids.[6] The opioid groups demonstrated greater improvement and satisfaction with their treatment. Interestingly, there was little change in pain score between groups; however, the anxiety and mood parameters were significantly improved in the opioid groups.

From the above discussion, several conclusions may be drawn. First, it would appear that not all chronic pain patients benefit from opioid therapy. However, in a significant subpopulation chronic opioids may play a useful role in providing pain relief, improving mood, and restoring some degree of function.
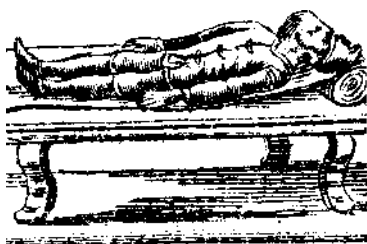
Addiction-prone individuals may develop addiction behavior upon exposure to an opioid, but an otherwise normal person exposed to opioids is unlikely to become addicted.

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THE NEGATIVE ASPECTS OF OPIOID THERAPY

Is there a downside to the use of chronic opioids? As an analgesic class, the opioids have many advantages over other analgesic alternatives. Although widely prescribed and utilized, the **nonsteroidal anti-inflammatory drugs (NSAIDS)** suffer from significant toxicity. The number of annual deaths each year attributed to complications produced by the NSAIDS is equivalent to the number of patients dying annually from AIDS (>16,000).[7] Opioids are relatively safe with respect to organ system toxicity, with little impact on hepatic, renal, and cardiac function. However, opioid analgesics are not devoid of side effects. The most feared, but rarely encountered side effect, is respiratory depression. This is an individual and dose-related effect, but rarely impacts on chronic treatment. The more common problems, nausea, vomiting, constipation, fatigue, and dry mouth can limit opioid use in many patients. Constipation and dry mouth are universally present, increasing with dose escalation. Constipation should be anticipated and treated proactively with a combination of laxatives and stool softeners. The dry mouth produced by the opioids is poorly recognized and rarely addressed by most physicians. Dental caries and tooth loss often develop in this population, particularly if other pain adjuvants, such as the tricyclic antidepressants are employed.[8] Encouraging sugar-free candy and good oral hygiene can help reduce this problem.

The most significant concern limiting the widespread acceptance of opioid analgesics for the treatment of chronic pain is the risk of addiction. Physiologic adaptation to long-term opioid use, such as physical dependence and tolerance, are a fact of life, but should not be confused with addiction. Addictive behavior is more of an individual response, triggered by opioid exposure, but not caused by opioid exposure. Addiction-prone individuals may develop addiction behavior upon exposure to an opioid, but an otherwise normal person exposed to opioids is unlikely to become addicted. Extrapolating from the experience with cancer pain treatment and from the reports discussed above, patients with chronic pain can be treated for years with relatively stable doses. True addictive behavior is characterized by preoccupation with obtaining the drug, utilizing escalating doses to produce euphoria, and compulsive use of the drug despite personal harm. This does not describe the behavioral pattern witnessed in the pain population. Occasionally, a situation may develop in which a patient experiencing inadequate pain relief will behave in an aggressive manner to obtain additional medication. This type of behavior has been labeled as pseudoaddiction, as it represents a response to inadequate pain relief and does not represent addiction.[9]

MEDICOLEGAL ISSUES

It would be naïve to presume that substance abuse is not a consideration in evaluating opioid use in chronic pain. While many patients experience successful pain control using an opioid analgesic on a chronic basis, between 2-20% of the general population are at risk for addiction. Jamison and colleagues recently reported, in a survey of patients undergoing methadone maintenance therapy for opioid addiction, that 61% of this group reported suffering from chronic pain.[10] Of these patients with pain, 44% believed that their use of opioid medication to treat their pain contributed to their addiction problem. Obviously, the methadone

maintenance population represents a skewed population, but illustrates the potential for problems.

PATIENT SELECTION

Since not all patients with chronic painful conditions will respond well to opioid therapy, the decision to pursue treatment with chronic opioids must be made jointly with the patient, taking care to carefully explain the controversies, risk of physical dependence, the risk of withdrawal, side effects, and opioid addiction. The patient must exhibit a clear comprehension of the undertaking, know to watch for and respond to side effects, and must realize that complete pain relief is unlikely to be achieved. Based on the published data in the medical literature, most patients experience very modest reductions in pain, but often exhibit improvement in function, mood, anxiety, and sense of well-being. Goal setting should target limiting dose escalation, identifying patient responsibility for adhering to the treatment plan, and linking medication use to improvement in function. Opioid contracts are a useful means of documenting that the patient was provided with an informed consent, acknowledged their responsibility to adhere to the guidelines for obtaining refills, accept the need for unannounced drug screening, and the need to adhere to the contracted dose.

Once the decision has been made to begin opioid therapy, patients will generally fall into one of four patterns of use. The Type I patient often has a clear pathologic basis for his/her pain, has good social supports, exhibits improved physical function, and exhibits a very stable opioid usage pattern. The Type II patient has a pathologic basis for their pain, has good social support, but may not show improved function and/or displays a tendency to escalate their medication. The Type III patient does not have a clear explanation for his/her pain, and displays a tendency to escalate or experiences inadequate relief. The Type IV patient may have a history of substance use that was unrecognized, escalates their opioid without permission, constantly seeks early refills, or reports lost medication.

Obviously, the Type I pattern is the least contentious and represents the successful use of opioid therapy for chronic pain. The Type II and III pattern bear close monitoring and guidance. Ultimately, they may be maintained on long-term analgesic therapy, but will require frequent redirection. The Type IV behavioral pattern represents a failure pattern, and these patients should be withdrawn from opioid treatment, or rigidly supervised, including drug monitoring. Ultimately, Type IV patients may require referral to an opioid rehabilitation program.

OPIOID SELECTION

There is no single opioid analgesic that provides optimal results for every pain patient. The only inappropriate opioid selection is meperidine. Oral meperidine is poorly absorbed, has a short duration of effect, and can lead to the accumulation of the neurotoxic metabolite; normeperidine.[11] Generally, the longer-acting opioids or sustained-release formulations have been advocated. Long-acting opioids, such as methadone and levorphanol, offer the advantage of prolonged blood levels, good bioavailability, and minimal cost (Table 1). However, a lack of familiarity with these agents by most

physicians, the stigma of drug addiction associated with methadone, and the possibility for gradual accumulation have limited their acceptance. Any physician with a controlled substance license may prescribe methadone, provided the prescription contains the words "for pain".

The sustained/controlled-release preparations of oxycodone, morphine, and the soon-to-be-available controlled-release hydromorphone, have become widely prescribed for cancer, and increasingly for chronic noncancer pain. The ability to deliver these preparations as infrequently as once or twice daily provides sustained pain relief, improves compliance, and helps to reduce the focus on the relationship between the patient's pain and pill taking. However, many patients want to take medication more frequently. This may reflect the limited pain relief produced by the opioid, often referred to as "taking the edge off", and the patients need to interact with their pain. Several recent studies have suggested that sustained release opioids do not necessarily produce better analgesia than the conventional immediate-release opioid tablets, and appear to be associated with a much higher dose requirement.[6,12] The rate of rise in the blood opioid level produced by the immedi-

Table 1. Common Long-Acting Opioid Preparations

Agent	Equivalent Oral Dose (mg)	Dose Interval (hours)	Expense Ratio
Methadone	5	6-8	1
Morphine Extended Release	15	8-24	10-16
Oxycodone Extended Release	10	8-12	17

ate-release opioid analgesics may contribute to more effective transfer of the opioid into the central nervous system, producing a greater analgesic effect. Patients receiving sustained release preparations or around-the-clock dosing appear to require 2-3 times more opioid, when compared with conventional opioids, but with little improvement in their pain scores.[6,12,13] Thus, patients obtaining good relief with modest doses of an immediate release opioid are probably better served by leaving them on this medication regimen. The sustained release products are significantly more expensive than the generic immediate release tablets or methadone. Finally, the abuse potential of the sustained release products appears to be much more significant than originally assumed. Crushing and swallowing, chewing, or inhaling the crushed tablets can lead to immediate release of the active drug.

Transdermal fentanyl is a useful alternative to the oral route of administration.[14] The advantages of the transdermal delivery system may include less constipation, sustained drug levels, less focus on pill taking, and less abuse potential. The disadvantages include poor skin adherence in some patients, difficulty in making dose adjustment, expense, and variability in absorption of the drug depending on skin characteristics and body habitus.

MEDICOLEGAL CONSIDERATIONS

Unlike the majority of medications prescribed by physicians, the opioids are subject to very close monitoring by law enforcement agencies. Although governmental laws, rules, and regulations are not intended to impact on therapeutic decisions relating to patient care, they have become a significant barrier limiting pain medication prescribing. The key to avoiding legal or professional entanglement is to adhere to the prescribing guidelines established by Federal and State regulatory agencies (see the Model Guidelines for the Use of Controlled Substances for the Treatment of Pain, published by the Federation of State Medical Boards of the United States, Inc, 1998). This requires the physi-

cian to provide regular follow-up visits, creation of a treatment plan, close monitoring of the patient for signs of abuse or diversion, referral to appropriate specialists, and careful documentation. The Rhode Island State Medical Board has established guidelines for opioid prescribing that acknowledge the physician has a responsibility to treat pain, and has adopted the recommendations of the Federation of State Medical Boards. Furthermore, the Rhode Island Legislature has passed an Intractable Pain Law, so that physicians will not be subject to legal action for providing opioid treatment for patients with intractable pain unresponsive to standard medical treatment. The importance of careful documentation, however, cannot be overemphasized.

CONCLUSION

Long-term opioid therapy may be appropriate for the management of chronic pain states unresponsive to more definitive medical treatment, and has been endorsed by the American Pain Society and the American Academy of Pain Medicine. Pain relief may be modest with long-term opioid therapy, but can be associated with improvements in mood and sense of well being. Based on the current medical literature, long-term opioid therapy appears to be beneficial for a select population. Clinicians are reminded that careful monitoring and documentation are the hallmarks of good medical practice when prescribing opioids for chronic pain.

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Nonsteroidal Anti-inflammatory Drugs for Perioperative Pain Control

Frederick W. Burgess, MD, PhD, and Richard A. Browning, MD

The **nonsteroidal anti-inflammatory drugs (NSAIDs)** are an important mainstay of analgesic therapy in medicine. Since the synthesis of acetylsalicylic acid in 1899, the NSAIDs have evolved into the most widely prescribed class of oral analgesic medications. NSAIDs provide analgesia and anti-inflammatory therapy, which can be very beneficial for promoting healing and providing comfort for the post-operative patient. This treatment modality is often overlooked in the management of the acute trauma or post-operative patient. NSAID avoidance is attributable to concerns over bleeding complications. These concerns are largely overstated as demonstrated in the post-marketing surveillance data collected for ketorolac.[1] Their data revealed a minimal risk of perioperative bleeding at the surgical site following perioperative ketorolac administration. Despite this, many physicians and surgeons continue to advise their preoperative patients to discontinue the use of NSAIDs prior to surgery. The authors and others feel, for a majority of patients, there is a clear rationale for prescribing an NSAID on the day of surgery.[2]

The NSAID class produces its analgesic action through the inhibition of cyclooxygenase synthetase, at the site of injury in the periphery and possibly through actions within the central nervous system. Tissue trauma liberates phospholipids from damaged cellular membranes, which are in turn converted by phospholipase into arachidonic acid. Cyclooxygenase converts the arachidonic acid into prostaglandin precursors responsible for the development of regional pain, edema, and vasodilatation. Within the central nervous system, prostaglandins appear to have a role in the transmission of pain signals, independent of their peripheral inflammatory actions. Animal and clinical data have demonstrated a potent central analgesic effect of NSAIDs when delivered intraspinally.[3,4] The importance of this central mechanism to the analgesic effects of most NSAIDs is uncertain, but

may provide a useful target for future analgesic development.

There are a large number of different NSAIDs currently on the market. Fortunately, it is not necessary to become familiar with every agent. NSAID selection may be made on the basis of duration of action desired, and on the side effect tolerance profile. The most potent anti-inflammatory effect is provided by indomethacin; however, adverse reactions and side effects have led to a decline in the use of this compound. For short-term therapy, ibuprofen remains one of the least expensive and best-tolerated NSAIDs. The one disadvantage of ibuprofen is its short duration of action, which creates a need for multiple daily doses (Table1). Even with pain relievers, compliance can be a problem, often resulting in poor pain control and dissatisfaction with the treatment. Longer-acting agents, such as naproxen or piroxicam offer greater convenience of dosing, but appear to carry a greater risk of gastrointestinal bleeding and ulceration.[5] This increased risk of gastric perforation and bleeding may relate to the sustained inhibition of the cycloxgenase enzyme provided by the prolonged half-lives of these drugs. Ketorolac deserves

mention, as it is the only NSAID available for parenteral delivery in the United States, making it convenient for intraoperative and postoperative administration. Unfortunately, ketorolac has received a black box warning by the **Food and Drug Administration (FDA)** to limit parenteral administration to not more than 5 days. This resulted from post-marketing data that revealed an increase in gastrointestinal bleeding when ketorolac was administered parenterally for greater than 5 days.[1] Associated risk factors included age greater than 70 years and concomitant medical illness.[1]

SELECTIVE INHIBITION OF CYCLOOXYGENASE

The newest group of **NSAID** drugs is the selective cyclooxygenase inhibitors. Cyclooxygenase exists as two isoenzymes.[6] **Cyclooxygenase-1 (COX-1)** is a constitutive enzyme, which is continuously expressed in many tissues, including the gastric mucosa, platelets, and the kidney. A second isoenzyme, **cyclooxygenase-2 (COX-2)**, is an inducible enzyme usually associated with inflammation and healing.[6] It is now possible to selectively target the COX-2 enzyme for inhibition, which can greatly reduce unwanted effects on platelet function and the mucosal integrity of the GI

Table 1

Nonsteroidal Anti-inflammatory Agents

Agent	Dose Range mg	Dosing Interval hours	Maximum Dose mg	Half-life Hours	Platelet Inhibition
Nonselective COX Inhibitors					
Ibuprofen	200-800	4-8	2,400	2-2.5	Yes
Naproxen Sodium	275-550	6-8	1375	12-15	Yes
Indomethacin	25-50	8-12	100	2	Yes
Ketorolac	15-60 i.m. 10 p.o.	6	120	6	Yes
Diclofenac	50	8	150	1-2	Yes
Piroxicam	20-40	24	40	50	Yes
Etodolac	200-500	6-12	1000	7	Yes
Nabumetone	500-2000	12-24	2000	24	Yes
COX-2 Selective					
Celecoxib	100-200	12	400	11	No
Rofecoxib	25-50	12-24	50	17	No

tract.[7] Preliminary data from studies on two new COX-2 selective compounds, celecoxib and rofecoxib, reveal a much lower risk of gastric erosion and ulceration relative to nonselective COX inhibitors such as ibuprofen and naproxen.[8,9,10] Furthermore, celecoxib and rofecoxib do not appear to impact on platelet function. They are devoid of the antiplatelet effects, which are associated with COX-1 inhibition.[7] The COX-2 selective inhibitors may be particularly advantageous during the perioperative period, as they do not need to be discontinued and may be administered on the day of surgery to provide perioperative analgesia. Paracoxib, the prodrug form of Valdecoxib, a parenteral COX-2 inhibitor is currently under study and may supplant the use of ketorolac during the perioperative period.

Although the COX-2 inhibitors represent a major step forward in safety, several important points must be emphasized. It is important to recognize that the COX-2 inhibitors are safer than the nonselective COX inhibitors, but do not provide better analgesia or anti-inflammatory effect. Thus, in circumstances where a less expensive nonselective agent for a short-term course of therapy could suffice, the nonselective COX inhibitors remain the best choice for the sake of economy. Also, the selective COX-2 inhibitors are not entirely devoid of the potential for gastrointestinal ulceration.[8,9,10] Among patients with known peptic ulcerations, the COX-2 inhibitors should be avoided. COX-2 is a component of the healing response and can be identified in healing ulcers. Administration of a COX-2 inhibitor in this setting will interfere with the healing process and can contribute to further injury and perforation. The COX-2 inhibitors cannot be used with impunity, particularly in the long-term setting. Finally, the COX-2 inhibitors do have the potential to impair renal function.[11] This will be most pronounced in the elderly and/or volume depleted patient. Peripheral edema and renal failure may accompany their use and should be carefully monitored in the high-risk patient.

OPIOID REDUCTION WITH NSAID USAGE

For the perioperative patient, combining an NSAID with an opioid can

… for a majority of patients, there is a clear rationale for prescribing an NSAID on the day of surgery.

result in a 30-40% reduction in opioid requirement.[12] Rarely will an NSAID provide adequate analgesia as a solitary analgesic, but as a component of a combined analgesic regimen, it can improve the quality of pain relief and reduce opioid related side effects.[12-15] The opioid sparing effect is most evident in the orthopedic and dental surgery populations. The advantage of combining an NSAID with an opioid may become evident in a faster return of bowel function, less constipation, less nausea, and improved analgesia.[12] Parenteral ketorolac has been shown to be a useful adjuvant to epidural opioid analgesia.[13,14]

With the availability of the COX-2 inhibitors, more widespread use of NSAIDs during the perioperative period should result in improved analgesia. Reuben and Connelly have recently demonstrated the value of rofecoxib when administered as a single 50 mg preoperative oral dose to patients undergoing spinal fusion surgery.[15] They found no increase in perioperative blood loss, relative to placebo, and showed a substantial reduction in morphine consumption during the first 24 hours. The prolonged half-life of rofecoxib allowed for a sustained opioid sparing effect, which was not seen with celecoxib. When compared to the cost of multiple doses of ketorolac that would be needed during the postoperative period, rofecoxib offers a cost savings. Furthermore, the lack of platelet interference allows the COX-2 inhibitors to be administered very early in the treatment of the surgical patient, provided renal perfusion and volume status are carefully considered and managed.

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Obstetric Anesthesia and Analgesia: Options for Pain Relief During Childbirth

Sung-Hee R. Lee, MD, and Yusef Barcohana, MD

Analgesic options for labor and delivery have improved dramatically over the last several decades. Today, many women are able to participate fully in the birth process, remaining alert and aware, while still enjoying significant pain relief with minimal effects on the fetus. Recent reports have noted the increased use and acceptance of epidural analgesia during labor among American women giving birth today.[1] More widespread utilization of labor epidural analgesia has been accompanied by greater safety of obstetric anesthetic techniques, improving the overall care of obstetric patients.

TECHNIQUES

Parenteral Analgesics

In patients for whom regional anesthetic techniques (epidural, spinal) are contraindicated or in centers where full-time anesthetic services are not available, intravenous or intramuscular injections of opioids, such as Demerol® (meperidine) or Stadol® (butorphanol) are commonly used. These agents are effective in earlier stages of labor, though less so as labor progresses. Due to the episodic nature of labor pain, systemically used medications often lead to inadequate analgesia during the peak of a contraction, followed by somnolence during the intervals between contractions. Furthermore, parenterally administered drugs may cross the placenta to the fetus, increasing the possibility of respiratory depression in the neonate.

Neuraxial Techniques

The two most commonly used neuraxial techniques for labor and delivery are epidural and spinal analgesia. Epidural analgesia involves placing a catheter to provide continuous analgesia into the epidural space, a potential space surrounding the dura that covers the spinal cord. Spinal analge-sia is accomplished by a single injection of medication into the subarachnoid space, inside the dura, where spinal nerves and cerebral spinal fluid are located.

Contraindications to neuraxial analgesia include:

1. Coagulopathy, which increases the risk of epidural hematoma formation

2. Skin or soft tissue infection or lesion at the site of regional anesthesia placement, due to the risk of seeding infection to the spinal column

3. Uncorrected severe hypovolemia, such as in ongoing severe hemorrhage

4. Increased intracranial pressure due to an intracranial mass, in which dural puncture may lead to brainstem herniation

Epidural Analgesia

Epidural analgesia is an effective and versatile means of achieving pain relief during labor. Placement of a temporarily indwelling catheter allows great flexibility for the varying needs of different stages of labor and delivery. The catheter is placed in a lower lumbar interspace, aiming for the nerves that transmit contraction pain, T10 through L2, during the first stage of labor, and the sacral nerves that supply the perineum during the second stage of labor. Typically, analgesia is initiated and maintained with low-concentration solutions of local anesthetics combined with opioids. Commonly used local anesthetics include bupivacaine and the newer ropivacaine, which both provide long-acting, excellent sensory analgesia with lesser degrees of motor block. Opioids, such as fentanyl or sufentanil, work synergistically with low concentration local anesthetics to provide analgesia equal to a higher concentration local anesthetic alone. In this way, optimal analgesia is achieved with less motor block.[2] If operative delivery, such as forceps-assisted or cesarean delivery, becomes necessary, the epidural medication can be switched to higher concentration local anesthetics to induce a denser degree of anesthesia.

Spinal Analgesia:

Due to the unpredictable time course of labor, spinal analgesia alone, which is of limited and unrenewable duration, is rarely used. The development of the **combined spinal epidural** (CSE) technique, however, gains the advantages of both spinal and epidural analgesia. Spinal analgesia provides highly effective analgesia with a faster onset, while the epidural catheter can administer continuous analgesia until delivery of the baby. Spinal opioids, such as fentanyl or sufentanil, sometimes together with a small dose of local anesthetic, leads to intense and rapid analgesia with virtually no motor block, thus making it possible for the patient to continue ambulating during labor. (Hence the name "walking epidural", as it is called in the lay press.) Analgesia duration is approximately 90 minutes.[3] Yeh and colleagues report even longer duration of spinal analgesia by combining a low dose of morphine with fentanyl and bupivacaine.[4] Use of the CSE is also highly effective when used very close to delivery, since the faster onset can give the woman immediate analgesia and the lack of motor block will not impede her pushing efforts during the second stage of labor.[3]

ADVANTAGES OF REGIONAL ANALGESIA

The parturient receiving regional analgesia is alert, and often more cooperative and actively involved in the birth process than either a patient writhing in pain or one who is medi-

cated into somnolence. No longer does childbirth need to be a time of excruciating pain and terror to be endured.

While spinal and epidural analgesia afford excellent analgesia to the mother, the effects on the fetus are minimal. Especially when compared to parenteral opioid analgesia, several studies have shown better pH values in the babies of mothers receiving epidural analgesia.[10] The relief of pain for the mother also reduces the level of circulating catecholamines and decreases maternal hyperventilation, two effects that can be detrimental for the fetus.

A further advantage of epidural analgesia is that it allows the anesthetist, in the event of an emergency, to quickly and easily administer deeper levels of anesthesia, should an operative delivery, whether forceps-assisted or cesarean delivery, become necessary. This is especially important, since it avoids the need for general anesthesia. General anesthesia is more risky in the pregnant woman because of the following reasons:

1. Anatomic changes due to weight gain and increased body water content cause swelling in the airway, making endotracheal intubation more difficult than in the nonpregnant population,[5] increasing the chance of maternal hypoxia.

2. Increased oxygen consumption due to needs of both the mother and the fetus decreases the time window available for securing the airway, significantly decreasing the time before hypoxia develops.

3. The relaxed lower esophageal sphincter tone and decreased gastric emptying during labor increase the risk of pulmonary aspiration of gastric contents during induction of general anesthesia, increasing the risk of aspiration pneumonitis.

The improvement in safety in obstetric anesthesia has been attributed to the greater usage and safety of regional anesthesia.[6] In many obstetric anesthesia practices, it is common to place epidural catheters in patients deemed high risk for cesarean delivery (nonreassuring fetal evaluations, fetal macrosomia, attempted vaginal birth after cesarean, etc.), especially in those who may be difficult to tracheally intubate.

Especially in high-risk patients, regional analgesia allows the avoidance of general anesthesia, thus making anesthesia safer overall.

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DISADVANTAGES OF REGIONAL ANALGESIA

Adverse effects may occur immediately with initial placement and dosing of regional anesthesia or later in the parturient's course. Fortunately, most of these can be easily recognized and treated. Immediate effects that may occur with epidural analgesia include:

1. Hypotension. Decreases of systolic blood pressure to less than 100 mm Hg may occur after either conventional epidural or combined spinal epidural placement, reported at less than 10% in one series for both and requiring treatment in about half these cases.[7] This is easily treated with additional intravenous hydration, ensuring that the weight of the uterus is kept off the patient's inferior vena cava, and administration of the beta-adrenergic vasopressor ephedrine.

Systemic symptoms from inadvertant intravascular injection of local anesthetics. The epidural space is filled with a plexus of veins. If the epidural catheter enters a vein, which may occur about 10% of the time,[8] local anesthetics may be injected directly into the bloodstream.

2. Systemic reactions to local anesthetics range from benign (perioral numbness, tinnitus) to life-threatening (convulsions, cardiovascular collapse), depending on the total dose of drug given and the rate of administration. The decreased incidence of fatal local anesthetic toxic reactions has been attributed to the practice of giving epidural medication in smaller increments so that any systemic reactions may be detected before symptoms of toxicity develop.[6] Furthermore, the development of new, softer tipped epidural catheters has significantly decreased the incidence of intravenous cannulation by epidural catheters.[9]

3. Respiratory depression. This may occur in two ways. If the epidural catheter is inadvertently placed in the spinal space, administered local anesthetic agents may cause profound motor block that impairs the muscles of respiration. Secondly, opioids given in a combined spinal epidural may rarely cause central respiratory depression.[3] The key to handling both reactions is close monitoring of neuraxial analgesia, especially immediately after administering spinal or epidural medications, for both reactions, if detected immediately, can be either reversed or minimized. Often only supplemental oxygen is required and rarely is temporary ventilatory support necessary.

4. Motor block. Local anesthetic agents given epidurally will eventually block all nerve fibers, both sensory and motor, especially when given in higher concentrations. Some patients develop significant degrees of motor block, especially over time, that may eventually impede their pushing efforts. Today, however, this effect has been decreased with the increased use of the combined-spinal-epidural technique and epidurals dosed with low concentration anesthetic solutions combined with opioid.

5. Effects on the fetus. Overall, the effects on the fetus are thought to be benign. Transient fetal bradycardia may occur, however, after placement of neuraxial analgesia. Epidural analgesia may lead to hypotension, and this may affect utero-placental blood flow if not treated promptly. Fetal bradycardia has also been seen after combined spinal epidural analgesia, unassociated with hypotension, possibly due to a brief increase in uterine activity.[3]

4. Itching is a common side effect after both combined spinal-epidural and epidural analgesia, reported at over 40% after spinal sufentanil by Norris and colleagues,[7] and in 20%-30% of patients receiving either epidural fen-

tanyl or sufentanil with bupivacaine.[11,12] Usually this is a benign symptom and well tolerated by most patients. In the rare patient who experiences severe pruritis, it can be reversed by removing the opioid from subsequent epidural medications or by the administration of a small dose of an opioid antagonist.

Some effects of epidural analgesia may not appear until several days after an epidural analgesic has been completed. Again, the important issue is prompt recognition and treatment.

1. **Postdural puncture headache (PDPH).** This is the most common significant complication (approximately 1-2% incidence) of regional anesthesia and may occur after either known or occult puncture of the dura with an epidural or spinal needle. The typical presentation is a postural headache, which is more pronounced with upright posture but relieved when the patient is supine. The headache may be accompanied by other symptoms, such as photophobia, neck stiffness, or nausea and vomiting. Persistent leaking of cerebral spinal fluid is thought to cause downward traction on the meninges when the patient is upright, thus causing pain. Conservative treatment may be effective in mild cases, including maintaining hydration, ingestion of caffeinated beverages, and oral analgesics. In severe or persistent cases, the definitive treatment is the epidural blood patch. The patient's blood is drawn in a sterile fashion and injected in the epidural space in close proximity to the original dural puncture site, thus "patching" the dural hole and allowing it to heal. Relief from the headache is immediate. The success rate is high, 90-95%, so that failure to relieve the symptoms will prompt a search for other causes of postpartum headache. While PDPH is generally a benign condition, which usually will resolve spontaneously with time, untreated PDPH can cause difficulties for a mother with a new baby, and rarely, can lead to more severe neurologic symptoms.

2. Neurologic sequelae. The most dreaded complication of neuraxial analgesia, spinal mass causing neurologic sequelae, is fortunately extremely rare, occurring infrequently even in series of thousands of anesthetics.[13] Regional analgesia may be associated with two such complications: epidural abscess and epidural hematoma. It is important to note that both may also occur spontaneously without a previous regional anesthetic.[13] While most cases of postpartum neurologic symptoms are mild or unrelated to anesthesia,[14] if a patient should develop neurologic signs after delivery, it is important to evaluate each patient thoroughly and promptly to exclude more serious complications.

Options for analgesia during labor and delivery now allow many women to enjoy relief from pain during childbirth, with a minimum of bothersome side effects. More importantly, the risks of neuraxial analgesia have been decreased by safer anesthetic techniques and close monitoring of patients undergoing regional analgesia. Especially in high-risk patients, regional analgesia allows the avoidance of general anesthesia, thus making anesthesia safer overall.

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Utility of Transesophageal Echocardiography in Non-Cardiac Surgery

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Intraoperative **transesophageal echocardiography (TEE)** was introduced into clinical practice in the early 1980s. Since then its application has been established in the cardiac surgery population, with several outcome analyses supporting its efficacy, particularly when surgery involves heart valves or congenital heart defects. In non-cardiac surgery, baseline cardiac function and tolerance to stress has been correlated with perioperative cardiac morbidity and mortality.[1] While preoperative echocardiography is often utilized to evaluate heart function and tolerance to stress, its use during noncardiac surgery has not been systematically evaluated. Suiani et al[2] reported on 123 high-risk noncardiac surgical patients in which intraoperative TEE was utilized. TEE had a major impact on clinical management in nineteen patients (15%); nine resulted in potentially life saving therapies. In fifty-seven patients, due to discordance with other monitors, TEE was subsequently used to monitor intraoperative cardiovascular function. Brandt et al[3] reviewed the impact of emergency intraoperative TEE in 66 patients. Indications included preoperative hemodynamic instability, major chest trauma or hypoxemia. Previously unsuspected findings were reported in 53 patients (80%), resulting in a change of operative plan in 15 patients (23%). Although no prospective randomized study of patient outcomes has been performed, a number of clinical scenarios of non-cardiac surgery in which TEE has been useful and may have a beneficial effect on outcome are described. The purpose of this article is to highlight the available literature and our experience regarding the application of TEE during non-cardiac surgery.

HEMODYNAMIC ASSESSMENT

Hemodynamic assessment includes evaluation of cardiac volume (preload), contractility, afterload, valvular func-tion, intracardiac defects or masses, and pericardial pathology. Echocardiography is not only capable of assessing all these aspects of cardiac function, but is superior to clinical judgment, with or without invasive monitoring.[3]

Intraoperative TEE assessment predominantly utilizes two dimensional echocardiography supplemented by Doppler assessment of blood flow. Common indications for TEE are evaluation of ventricular systolic function and volume. A transgastric short axis view of the left ventricle is the standard plane for quantitative and qualitative analysis of ventricular contractility. When assessing ventricular volume, the most reliable measurement is at end-diastole. Reich et al[4] studied whether experienced echocardiographers were able to differentiate normovolemia from hypovolemia in real time. They reported high predictive values (> 80%), confirming visual qualitative differentiation between hypovolemia and normovolemia. For experienced echocardiographers intraoperative decision making is based largely on qualitative visual evaluation, supplemented with quantitative measures when necessary.

Echocardiographic evaluation has become the standard for assessing valvular function. The combination of 2-D and Doppler echocardiography can determine the presence, severity, and cause of valvular pathology. While severe stenotic and regurgitant lesions are apparent with qualitative 2-D and color flow Doppler imaging, we often quantitate stenotic lesions. Accurate knowledge of the severity of regurgitant or stenotic lesions alters anesthetic management in non-cardiac surgery.

ISCHEMIA MONITORING

The association between coronary artery disease, perioperative myocardial ischemia, and cardiac morbidity and mortality is established and has resulted in an interest in the detection, preven-tion, and treatment of perioperative myocardial ischemia.[5] While the specificity and negative predictive value of ischemia monitoring modalities is high (> 80- 90%), the sensitivity and positive predictive value of these technologies are poor. A growing body of literature has examined the role of TEE in detecting ischemia during both cardiac and non-cardiac surgery.

The response of myocardium to ischemia manifests initially with abnormal relaxation followed sequentially by diminished wall thickening or inward motion during systole, electrocardiographic changes, and clinical symptoms and/or hemodynamic aberrations. Clinicians have postulated that **pulmonary artery catheter (PAC)** monitoring for acute increases in "wedge" pressure, or TEE imaging for **segmental wall motion abnormalities (SWMA)** or decreased thickening, are more sensitive monitors of intraoperative ischemia than electrocardiography. Of the echocardiographic techniques available, assessment of inward segmental motion and/or wall thickening during systole are most commonly employed. Echocardiography is also useful to evaluate for complications of myocardial ischemia such as infarction, heart failure (including differentiation between right and left heart failure), valvular regurgitation, septal defects, thrombi, pericardial effusions, and free wall rupture.

There is ample evidence from controlled laboratory settings, both animal and human, supporting myocardial ischemia as an etiology of SWMA and decreased wall thickening. Results from perioperative TEE studies have been disappointing, however, in correlating detected SWMA and adverse cardiac outcomes. There are multiple reasons for this including acute changes in preload, after-load, heart rate and contractility which occur in response to surgical stimulation and may cause transient SWMA which are not ischemia related.[6]

We conclude that TEE ischemia monitoring is not routinely indicated during noncardiac surgery, but its use may be justified in select high risk patients where significant abnormalities (i.e. left bundle branch block) of the electrocardiogram exist.

TRAUMA SURGERY

Major trauma often results in hemodynamic instability from cardiac and pulmonary injury. In these patients prompt and accurate diagnoses of cardiac injuries is critical to survival. Of 204 trauma patients sustaining cardiac injury, 128 survived to be treated at the hospital, and 90 required emergency surgical therapy.[7] Echocardiographic evaluation provides quick and accurate assessment of cardiac or vascular injuries as the cause of hemodynamic instability, and allows appropriate triage of patients. Plummer et al[8] evaluated 49 trauma patients with penetrating chest injuries, with (28 patients) and without echocardiography (21 patients). Cardiac evaluation and diagnosis was achieved within 15 minutes in the echo group compared to 42 minutes in the non-echo group. Survival was 100% in the former and 57% in the latter. They concluded that echocardiography provided immediately available accurate bedside diagnoses that resulted in reduced mortality in this population.

The choice of diagnostic testing depends on a number of variables including the mechanism of injury, stability of the patient, availability of resources, and institutional preferences. Although a stable patient with a normal ECG and chest radiograph is unlikely to have a significant cardiac injury, experience supports obtaining additional diagnostic tests if suspicion of cardiac injury is high. A normal echocardiogram in these patients essentially excludes a significant cardiac pathology.

Cardiac injuries after blunt and penetrating chest trauma detectable by echocardiography include cardiac contusion, intramyocardial hematoma, pericardial effusions and/or tamponade (hemopericardium), cardiac rupture, cardiac thrombi, coronary artery injury, septal defects, valve rupture or laceration,

hemothorax, and aortic injury. In patients with blunt and penetrating trauma, the right ventricle and atrium are commonly injured, due to the anterior location. Death after chest trauma is often a result of cardiac rupture which may remain undiagnosed until irreversibly advanced. Prompt diagnosis may be lifesaving and has been accomplished using two dimensional echocardiography. Several reports demonstrate a significant incidence of residual intracardiac injuries in penetrating chest trauma and recommend follow-up evaluation with the more sensitive imaging TEE modality. We suggest there be a low threshold to evaluate all major chest trauma with TEE.[7]

With greater experience, we expect that TEE will become the first line test to assess for all suspected traumatic cardiac or aortic injuries.

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While echocardiography is the diagnostic test of choice for suspected cardiac injuries, the optimal diagnostic test for suspected aortic injuries is less defined, and guided by institutional preferences. Magnetic resonance imaging is considered the most accurate test to assess aortic disruption. Despite the high sensitivity and specificity of TEE evaluation for aortic dissection or transection, aortography remains the preferred study in most institutions in unstable patients. Most studies demonstrate a low but increased false negative rate with TEE in comparison to aortography. A recent study showed TEE to be equivalent to aortography in the diagnosis of aortic dissection, and more accurate in the diagnosis of minor aortic injuries (intramural hematoma).[9] Which test is acquired first is dependent on the institutional availability of personnel to perform each, the expertise of the echocardiographer, and the stability of the patient. Additionally, TEE not only evaluates the aorta, but provides a simultaneous cardiac exam. Of-

ten this exam can be obtained significantly faster than other studies, and therefore, reduce the time to obtain a diagnosis. With greater experience, we expect that TEE will become the first line test to assess for all suspected traumatic cardiac or aortic injuries.

VASCULAR SURGERY

Vascular surgical patients are at high risk for perioperative cardiac morbidity, with 60-90% having angiographically significant coronary artery disease. Cardiac complications constitute the overwhelming majority of perioperative morbidity and mortality in these patients. Studies evaluating TEE utility in vascular surgery have been limited by small size, poor controls, and do not permit definitive outcome or cost-benefit analyses.

The relationship between cardiac ischemia and adverse cardiac outcomes in surgical patients is established. Although TEE may be a sensitive monitor of intraoperative myocardial ischemia and its complications, its routine use, even in this high risk patient population has not proven warranted. A high incidence of SWMA is detected by TEE during vascular surgery, especially major aortic surgery. SWMA occurring during aortic surgery is commonly reported during clamping and unclamping of the aorta, and is more frequent as the aortic clamp is applied closer to the heart. Yet SWMA detected by TEE does not correlate with perioperative morbidity in this population. There is also a discordant relationship between SWMA and ischemic ECG changes in this population. Presently only postoperative ischemic ECG changes are associated with adverse cardiac outcome.

As a hemodynamic monitor during aortic surgery, TEE has, however, been shown to be a superior modality compared to PAC monitoring or clinical impression. Clinical management of 9 of 17 patients undergoing thoracoabdominal aneurysm repair was significantly altered by TEE findings not apparent by simultaneous PAC monitoring.[10] The discrepancies between LV preload, predicted based on pulmonary artery catheter pressures, or measured

by TEE, were significant, both at the time of aortic cross-clamping and unclamping. TEE provides more accurate analysis of ventricular volume than does PAC pressure monitoring in the dynamic setting of acute afterload changes with aortic surgery. TEE is more likely to be a useful monitor and diagnostic modality for treating hemodynamic instability during major vascular surgeries than alternate technologies. A new approach to repairing aortic aneurysms involves endovascular stenting. TEE has been shown to confirm appropriate deployment and function of these stents.

NON-CARDIAC THORACIC SURGERY:

Intraoperative TEE has been utilized in patients undergoing pneumonectomy. TEE identified unsuspected tumor embolus in the pulmonary veins necessitating surgical removal in one report and significant RV systolic dysfunction with reduced LV volume loading after pneumonectomy in the other.[11,12] While monitoring biventricular function, TEE may be helpful to guide fluid management and intraoperative use of vasopressors, both of which are controversial topics, in this surgical population.

Mediastinal tumors are associated with cardiac or pericardial involvement. Echocardiography provides dynamic intraoperative assessment of hemodynamic instability occurring with surgical manipulation of these tumors. Subsequently, TEE can image for residual pathology after resection but prior to completion of the surgery. Information regarding the presence and extent of pericardial disease, with or without tamponade physiology, and cardiac involvement will have a significant impact on the management of surgery and anesthesia for this population. TEE has also been useful to assess resectability of mediastinal masses, and differentiate malignant from benign processes.

ORTHOPEDIC SURGERY

Intraoperative TEE has been utilized in patients undergoing knee and hip replacement, or major spinal reconstruction for kyphoscoliosis in the prone position. Intraoperative systemic complications associated with hip replacement include systemic vasodilatation, bronchospasm, hypoxemia and cardiac arrest. The etiology of these events can be related to the patient's underlying medical condition, but are often due to unique aspects of this surgery. The breakdown products of the methylmethacralate ("cement"), used to secure the prosthesis, are known to cause vasodilatation and significant hypotension. The high intramedullary pressures sustained during reaming, and cementing of the prosthesis, results in varying sizes and amounts of intracardiac emboli, detected within minutes by TEE.[13] These emboli, of either bone marrow, fat or thrombus in origin, are capable of producing mild to catastrophic hemodynamic instability, the severity correlating with their size and volume. These emboli result in significant blood pressure decreases, increased pulmonary artery pressures, reduced oxygen saturations, increased shunt fractions, and diminished end tidal carbon dioxide concentrations. With TEE monitoring, studies have demonstrated the omission of methylmethacralate and/or venting of the femoral shaft (to reduce pressure) results in decreased emboli and improved hemodynamic stability.[14]

Emboli have also been diagnosed by TEE in patients undergoing total knee replacement with use of a thigh tourniquet. Within minutes after tourniquet deflation, emboli are imaged passing through the right side of the heart into the pulmonary vasculature. The hemodynamic consequences of emboli in these patients appears less clinically significant in comparison to elderly patients undergoing hip surgery, but have resulted in hypotension.

Surgical repair of kyphoscoliosis has potential for significant cardiovascular instability. This is due to a combination of major blood loss, mediastinal compression in the prone position, and pre-existing cardiopulmonary disease. Patients with severe kyphoscoliosis have decreased lung volumes, pulmonary hypertension, and right heart dysfunction. The use of intraoperative TEE in this patient population has been reported by Soliman et al.[15] TEE analysis demonstrated a reduction in left ventricular volumes in the prone position with minimal changes in measures of ventricular contractility. Right heart function was unchanged. The hemodynamics reported suggest restricted cardiac filling in the prone position. In addition, our own ongoing TEE experience indicates a high incidence of pre-existing cardiac abnormalities in patients with muscular disorders and kyphoscoliosis.

NEUROSURGERY

Patients undergoing craniotomy for either tumor resection or aneurysm clipping are at risk for cardiovascular instability. Procedural factors include patient positioning (sitting versus supine), blood loss, the use of diuretics to lower intracranial pressure and edema, and the risk of **venous air embolism (VAE)**. The use of ultrasound devices to detect VAE remains widespread. VAE occurs between 25-50%, and as high as 76% of craniotomies performed in the sitting position. Ultrasound is the most sensitive monitor for VAE. This includes either precordial or transesophageal echocardiographic probes.

Another neurosurgical procedure in which TEE has been useful is the resection of giant intracranial aneurysms during deep hypothermic circulatory arrest utilizing cardiopulmonary bypass. TEE guides the placement of venous cannula from extra-thoracic insertion sites to ensure proper venous drainage. TEE monitors cardiac function during surgery, especially during the rewarming phase, and guides fluid and pharmacological therapy used to achieve hemodynamic stability when separating from cardiopulmonary bypass.

CONCLUSIONS

Perioperative echocardiography in noncardiac surgery is useful for diagnosing cardiovascular pathology and assessing hemodynamics in unstable patients. An echocardiographic evaluation can be performed quickly at the bedside allowing prompt diagnosis and treatment of the offending pathophysiology. Compared to transthoracic echocardiography, transesophageal

echocardiography provides more accurate and complete imaging and is a more practical tool during the majority of surgical procedures. While, the benefits of routine monitoring of cardiovascular function and ischemia are not established, there are several surgical procedures in which TEE may prove to be worthwhile. These include major aortic surgery with proximal cross clamping, major spine surgery in the prone position, surgery involving mediastinal tumors or tumors with vena caval involvement, and noncardiac surgery requiring cardiopulmonary bypass. Transesophageal echocardiography should also be considered a first line procedure to assess acute severe hemodynamic instability in any surgical patient, or patients with major trauma, especially when the thorax is involved. Compared to alternate intraoperative modalities, TEE compares equally to or improves accuracy in cardiac assessment.

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TEE for Intra-op Monitoring and Management of Vena Caval Tumor

Arthur A. Bert, MD, and Andrew Maslow, MD

Transesophageal echocardiography (TEE) has been utilized for detecting or monitoring for intraoperative embolism during cardiac and non-cardiac surgery. A number of neoplasms are associated with vena caval extension and potential intracardiac embolism including renal cell carcinoma, hepatic cell carcinoma, pheochromocytoma, transitional cell carcinoma, adrenal cortical carcinoma, lymphoma, and endometrial sarcoma. Renal cell carcinoma has a particular propensity for venous invasion with 4-10% of patients having vena caval involvement at the time of presentation, including a 1% incidence of extension to the right atrium.[1] While these tumors can present as recurrent pulmonary emboli, most often the tumor thrombus is nonobstructive within the vena cava or the tumor has invaded the vena caval wall. In the absence of metastatic disease, aggressive surgical resection of renal cell carcinoma and its tumor thrombus improves survival. Hatcher et al[1] demonstrated that while survival of patients was not dependent on the level of thrombus progression up the vena cava, including extension to the right atrium, failure to resect tumor thrombus invading vena caval wall resulted in a shorter life expectancy. Over the past few years we have managed a number of these patients at the Rhode Island Hospital, utilizing intraoperative TEE. TEE offers an effective real time diagnostic and monitoring modality in these patients with the potential to affect perioperative management and patient outcome.

The surgical approach to renal cell carcinoma depends on accurate assessment of the extent of any vena caval tumor. Optimal surgical therapy includes a radical nephrectomy with extraction of the tumor thrombus from the inferior vena cava and right atrium, including resection of any vena caval wall invasion. While MRI remains the preferred preoperative diagnostic study for demonstrating both the presence and extent of caval involvement, a number of studies and our own experience confirm the utility and accuracy of intraoperative TEE assessment of caval tumor extension.[2,3] Cases where intraoperative TEE imaging has documented more cephalad tumor extension than identified by preoperative testing have been reported.[3,4]

> *The advent of multiplane TEE probes has facilitated visualization of the heart and major vessels.*

The advent of multiplane TEE probes has facilitated visualization of the heart and major vessels. Specifically, the longitudinal views (50-90°) of the inferior vena cava (IVC) provide continuous imaging of an intracaval tumor during removal without intrusion into the sterile field or interruption of the surgery. A number of surgical techniques can be utilized to remove intracaval tumor. If the tumor thrombus does not extend above the hepatic veins, a tourniquet is applied subhepatically to the IVC and the tumor excised. Extension of the tumor above the hepatic veins increases the difficulty and risks of resection. A number of techniques have been successfully applied including liver mobilization and temporary occlusion of the hepatic veins and subdiaphragmatic IVC to balloon catheter tumor thrombectomy . When unable to safely manipulate and resect vena caval tumor thrombus with these techniques or when the tumor extends to the right atrium, we have utilized **cardiopulmonary bypass (CPB)** with circulatory arrest.

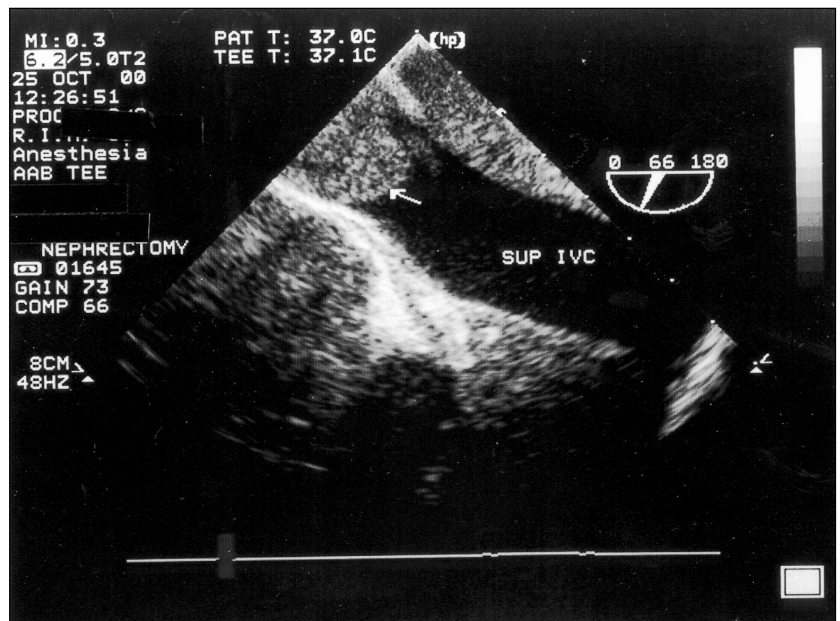While no randomized trials of TEE efficacy in improving outcomes are ever likely to be conducted with

Figure 1. —Transgastric longitudinal imaging plane view of tumor thrombus in superior portion of IVC. Arrow shows irregular head of tumor, with fragment (above arrow) which was mobile and vigorously oscillating.

such an uncommon patient population, a number of reports have cited instances where individual outcomes have been affected. Sigman et al[4] utilized TEE in thirteen patients with vena caval tumor thrombus undergoing surgical resection. TEE identified unrecognized, life-threatening intraoperative complications in two of these patients. One patient suffered a large tumor embolus as the specimen was manipulated during venacavotomy. TEE visualized the embolus in the right atrium and resulted in immediate atriotomy and tumor removal without postoperative patient morbidity. In a second patient undergoing tumor resection with CPB, TEE visualized a large amount of air trapped in the right atrium after closure of the atriotomy. The air was aspirated prior to closure of the chest and the patient recovered without sequelae.

Tumor embolism is a recognized and potentially fatal complication of caval tumors.[5,6] Although massive pulmonary tumor embolism occurs relatively rarely in the non-operative setting, this risk is significant during surgical treatment of these patients because of IVC manipulation. TEE offers real-time dynamic visualization of tumor mass during surgical manipulations. Moreover TEE can assess the mobility of the tumor head, demonstrating either its friability or adherence to the caval wall. Figure 1 demonstrates the transgastric longitudinal imaging plane we maintain during IVC manipulation. In this case a mobile fragment of the renal cell carcinoma, which oscillated with venous flow, indicated a high risk for tumor embolism and resulted in an IVC tourniquet prior to any tumor manipulation. Right atrial tumor masses have been reported to prolapse into the right ventricle resulting in acute tricuspid valve obstruction, severe hypotension or

cardiac arrest during surgical manipulation.[7,8] In this setting, Doppler color flow imaging can demonstrate blood flow around the tumor mass or diagnose complete obstruction and facilitate surgical manipulations to reverse it. TEE has proven useful for tumor thrombus monitoring during surgical excision, can diagnose tumor embolism, and facilitate prompt surgical interventions, as noted in these case reports.

When right atrial tumor mass is present, central venous and pulmonary artery catheterization is relatively contraindicated to avoid potential tumor embolization. Intraoperative hypotension is commonly encountered during these radical surgeries and has multiple potential etiologies. Reduction in venous return or right heart failure may be the result of massive bleeding, caval compression, tumor embolism or tricuspid obstruction. On-line visual assessment of cardiac preload is highly accurate in diagnosing hypovolemia and facilitating volume loading to regain hemodynamic stability. Two-dimensional imaging of the right sided cardiac chambers during caval manipulation can ascertain whether resection can be performed safely or whether CPB is necessary. TEE has proven useful for precise placement of venous cannulae for CPB to avoid tumor dislodgment. Finally, TEE monitoring confirms, in real time, completeness of the surgical resection of tumor mass prior to the conclusion of surgery. This is a critical advantage since prognosis is greatly improved if all tumor and any involved vena cava wall is resected. The authors conclude that TEE is a necessary intraoperative diagnostic and monitoring technology for these patients.

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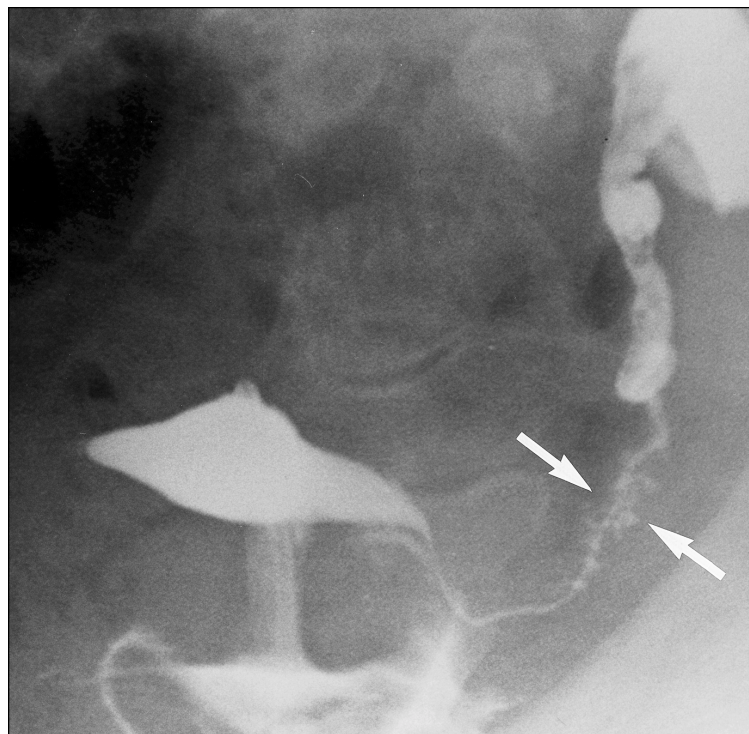fax: (401) 444-5083
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IMAGES IN MEDICINE

Edited by John Pezzullo, MD

Salpingitis Isthmica Nodosa

A 29 year-old female presented for **hysterosalpingogram (HSG)** in the evaluation of primary infertility. The contrast study demonstrates non-filling of the right fallopian tube. The left fallopian tube is markedly irregular with multiple outpouchings of contrast in the isthmic portion (arrows). Contrast did not spill from the left tube indicating tubal obstruction.

Salpingitis Isthmica Nodosa (SIN) is a disease entity of unclear etiology, and poorly understood pathophysiology. Proposed causes include infectious, inflammatory, congenital, and hormonal etiologies. It is a bilateral process in 50% of cases. Patients almost invariably have objective findings of prior pelvic infection, and the natural history of the disease is eventual complete obstruction of the fallopian lumen. There is an increased risk of ectopic pregnancy.

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Primary and Secondary Prevention of Coronary Artery Disease

As part of Rhode Island Quality Partners' continuing effort to provide Rhode Island physicians with current clinical evidence helpful to their practice, this column addresses the prevention of **coronary artery disease (CAD)**, since CAD continues to be the leading cause of mortality in the United States for both men and women. Several recent articles underscore the importance of addressing risk factors that can reduce the risk of acute cardiac events.

CIGARETTE SMOKING

Cigarette smoking remains a common practice in adults of all ages, and contributes to excess morbidity and mortality not only in cardiac disease, but also pulmonary, skin and oral cancers. Smoking cessation is one of the critical elements to longer and healthier lives for your patients, yet medical records in Rhode Island continue to lack documentation of smoking cessation counseling for hospitalized patients.

Measures to help people stop smoking have improved dramatically in recent years. Jorenby and colleagues' double-blind, placebo-controlled trial compared sustained-release bupropion alone, nicotine patch alone, bupropion plus a nicotine patch or placebo in approximately 900 smokers (excluding those who were clinically depressed). The authors reported a continuous abstinence rate after 1 year of 23% with the combination therapy compared to 18% with bupropion alone, 10% with the nicotine patch alone and 6% for placebo. Former smokers gained less weight when both active measures were used in combination. Behavioral measures should not be neglected: ask the patient to agree to quit date, actively offer effective pharmacological measures, and celebrate successes.

> Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *NEJM* 1999:340:685-91.

EXERCISE & OBESITY

Many Americans are sedentary and overweight. Vigorous exercise has been promoted to enhance cardiovascular health, but many patients are reluctant to engage in an exercise program. New research suggests that mild to moderate exercise may be as beneficial as vigorous exercise in preventing coronary events.

When nearly 72,500 participants in the Nurses' Health Study (40 to 65 years of age and free of cardiovascular disease at baseline) were followed for 8 years, a strong inverse association was evident between physical activity and risk for coronary events (nonfatal infarction or death from coronary artery disease). In multivariate analysis, the relative risk among women who walked at least 3 hours per week at a pace of 3 miles per hour or greater was 0.64 (95% CI, 0.47 to 0.88) compared with those who walked infrequently. The effect was comparable to the 30% to 40% risk reduction associated with regular vigorous exercise (running, cycling, swimming, aerobic dancing, and the like). Those who walked somewhat more slowly, at an average pace of 2 to 3 miles per hour, had a relative risk of 0.75 (CI, 0.59 to 0.96). Women who began exercising in middle age had fewer coronary events than their peers who remained sedentary. To optimize their cardiovascular health, women (especially those with coronary risk factors) should be advised to engage in a vigorous half-hour workout at least three times per week or walk regularly at an average or brisk pace. Walking will also lessen the risk for osteoporosis.

> Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. *NEJM* 1999:341:650-8.

CHOLESTEROL & TRYGLYCERIDES

Elevated cholesterol and triglycerides predispose patients with known coronary artery disease (and presumably those without known disease) to future cardiac events. Several articles point out that aggressive medical management using different agents to lower serum lipid levels results in dramatic reductions in future coronary events. Reducing lip levels does decrease the risk of cardiac events.

This double-blind trial from the LIPID Study Group included 9014 patients who had had a myocardial infarction or had been hospitalized for unstable angina and whose baseline plasma cholesterol level ranged from 155 to 271 mg/dL. Patients were randomly assigned to receive 40 mg of pravastatin once daily or a matching placebo. Cholesterol levels decreased by an average of 39 mg/dL in patients given pravastatin, a reduction 18% greater than that in placebo recipients. Levels of **low-density lipoprotein (LDL)** cholestmrol and triglyceride also decreased, and **high-density lipoprotein (HDL)** cholesterol levels increased 5% more than in the placebo group. After an average follow-up of 6.1 years, patients given pravastatin had a relative risk re-
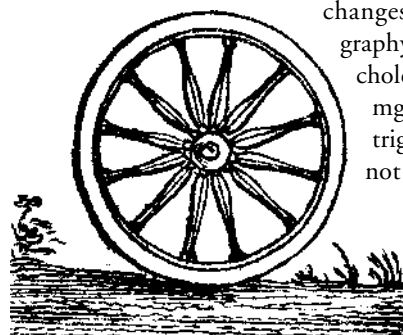
duction for fatal coronary heart disease of 24% (CI, 12% to ;5%)3 the absolute rate decreased from 8.3% to 6.4%. Overall mortality declined by 22%, and all cardiovascular events (myocardial infarction, stroke, bypass surgery, and angioplasty) were significantly reduced in the pravastatin group (P=0.001). Pravastatin caused no clinically important side effects. This trial enrolled patients ranging in age from 31 to 75 years, and benefit was apparent even in the oldest patients. Improvement was also seen in women, although the risk reduction was less striking than in men.

The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. *NEJM* 1998;339:1349-57.

This report by Rubins et al describes a double-blind, placebo-controlled trial of slow-release gemfibrozil, 1200mg/d (later 600mg of regular gemfibrozil twice daily). Participants were 2531 male veterans younger than 75 years of age with documented coronary heart disease. Patients assigned to receive gemfibrozil had 6% higher HDL cholesterol levels and 31% lower triglyceride levels at a median follow-up of 5.1 years, but LDL cholesterol levels did not change significantly. The absolute risk for a primary event (nonfatal infarction or death from coronary heart disease) decreased from 21.7% in the placebo group to 17.3% in the gemfibrozil group, an absolute risk reduction of 4.4% (number needed to treat for benefit [NNTB], 23 patients to prevent one event) and a relative risk reduction of 22% (CI, 7% to 35%). The overall risk for a primary event or stroke decreased by 24% (P=0.0001). Transient ischemic attacks decreased by 59% with active treatment and the need for carotid endarterectomy declined by 65%. Medication was generally well tolerated, although dyspepsia was somewhat more frequent with gemfibrozil.

Rubins HB, Robins SI, Collins D, et al. Cholesterol Intervention Trial Study Group. *NEJM* 1999;341:410-8.

This randomized trial was intended to compare the outcome of percutaneous coronary angioplasty (sometimes followed by lipid-lowering treatment) with the outcome of therapy with atorvastatin, 80 mg/d. The 341 patients had stable coronary artery disease, had relatively normal left ventricular function, and were asymptomatic or had mild to moderate angina. For inclusion, they were required to complete 4 minutes of a Bruce protocol treadmill test or bicycle exercise at 20W/min without marked ischemic changes on electrocardiography. The serum LDL cholesterol level was 115 mg/dL or higher, and triglyceride levels could not exceed 500 mg/dL. At least one coronary artery was narrowed by 50% or more, and treat-

ment assignments were stratified according to whether the patient had single-or double-vessel disease. Atorvastatin therapy reduced the average serum LDL cholesterol level by 46%, to 77 mg/dL. During the 18-month follow-up, ischemic events (cardiac arrest or death, nonfatal infarction, stroke, bypass surgery or angioplasty, or worsening angina leading to hospital admission) occurred in 13% of patients assigned to atorvastatin and 21% of those assigned to angioplasty. Patients in the angioplasty group had an 18% reduction in LDL cholesterol level, to 119 mg/dL. Ischemic events were 36 % less frequent in the atorvastatin group than in the angioplasty group after 18 months, but this finding was not statistically significant after adjustment for interim analyses. The difference between groups was in part a result of fewer angioplasties, bypass operations, and hospitalizations for symptomatic worsening in patients receiving atorvastation therapy. The time to a first ischemic event was, however, significantly longer in the atorvastatin group. At the end of the study, anginal symptoms were improved in 41% of the atorvastatin group and in 54% of the angioplasty group. Patient-rated quality of life improved in both groups but was slightly higher in the angioplasty group.

Pitt B, Walters D. Brown WY, et al. Aggressive lipid-lowering therapy compared with angioplasty in stable coronary artery disease. *NEJM* 1999; 341:70-6.

This column was adapted from Eagle, K. Update in Cardiology. *Ann Intern Med* 2000;133:439-46. The American College of Physicians-American Society of Internal Medicine is not responsible for the accuracy of the translation.
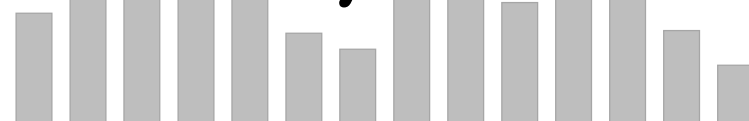
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Health by Numbers

Complications of Anesthesia

Edward F. Donnelly, RN, MPH, and Jay S. Buechner, PhD

Many surgical procedures and many invasive diagnostic and therapeutic procedures by non-surgeons are carried out under anesthesia or sedation. Anesthetic agents are administered by a variety of routes including topically, by inhalation, and intravenously, and all involve some risk to the patient in addition to that associated with the procedure itself.[1] Cardiovascular, renal, and neurologic adverse effects have all been associated with the administration of anesthesia.

Many of the procedures requiring the administration of anesthesia are performed in the hospital inpatient setting. Hospitals have reported patient-level discharge data for inpatients to the Department of Health since 1989, and these data include diagnostic codes for complications of anesthesia. This paper presents a descriptive analysis of the complications of anesthesia reported by hospitals over a ten-year period ending in 2000.

Table 1. Complications of anesthesia among hospital inpatients, by type of complication, Rhode Island, fiscal years 1991-2000.

ICD-9-CM Diagnosis Code	Complication	Number of Discharges
668	Complications of anesthesia during labor and delivery	139
763.5	Fetus or newborn affected by maternal anesthesia	42
968, excluding 968.5	Poisoning by central nervous system depressants and anesthetics, excluding surface and infiltration anesthetics (e.g., cocaine)	137
995.4	Shock due to anesthesia	9
995.86	Malignant hyperpyrexia due to anesthesia, etc.	2
995.89	Hypothermia due to anesthesia, etc.	27
E938	Drugs causing adverse effect during therapeutic use: Central nervous system depressants and anesthetics	397
E876.3	Misplacement of endotracheal tube during anesthetic procedure	0

Methods

All acute-care hospitals in Rhode Island submit a specified set of line-item data from every hospital inpatient stay in accordance with licensure regulations. Up to eleven diagnoses made during the hospital admission are included as codes from the **International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).**[2] Any discharge with one or more of eight ICD-9-CM codes or code groups identified as complications of anesthesia (Table 1) was considered a case for this analysis. (One type of complication, "poisoning by central nervous system depressants," include effects that may result either from the incorrect administration of anesthetics in the hospital or from illicit use of drugs prior ro admission. In order to exclude events of the latter type, codes for poisonings from anesthetics known to be abused by illicit users (e.g., cocaine) were excluded from the definition.) The analysis included all such discharges during the ten-year period from October 1, 1990, through September 30, 2000, corresponding to hospital fiscal years 1991-2000.

Hospital discharge data do not contain an indicator for the administration of anesthesia during procedures performed during the inpatient stay. An estimate of the proportion of patients undergoing anesthesia was therefore constructed using charges reported by the hospitals for anesthesia services. Because of variations in hospital reporting and billing practices for anesthesia charges, the estimate was
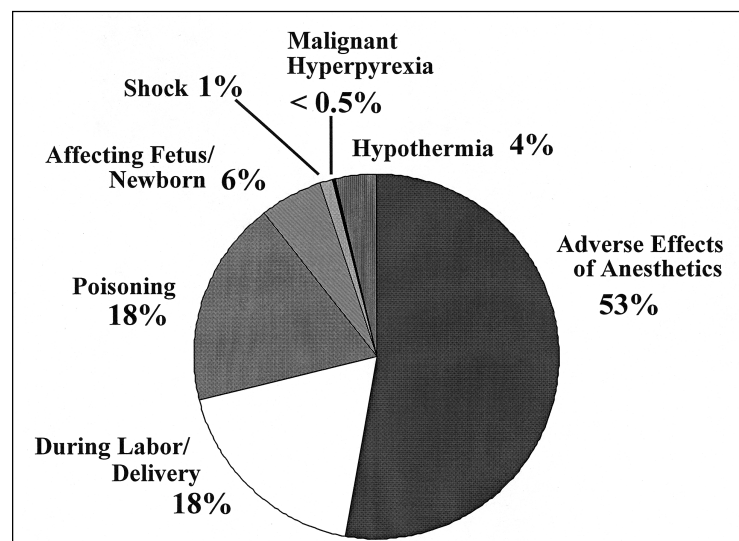

Figure 1. Complications of anesthesia among hospital inpatients, by type of complication, Rhode Island, fiscal years 1991-2000.
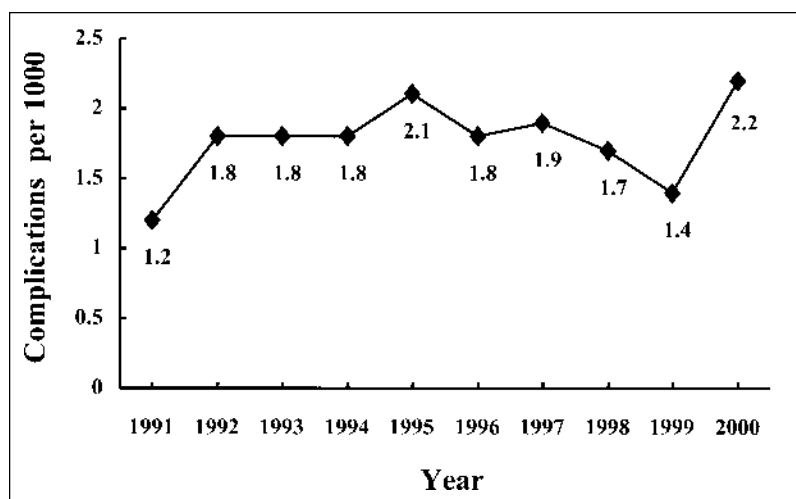
Figure 2. Complications of anesthesia per 1000 anesthetized hospital inpatients, by year, Rhode Island, fiscal years 1991-2000.

Figure 3. Complications of anesthesia among hospital inpatients, by age group and sex, Rhode Island, fiscal years 1991-2000.

based on data from six hospitals for fiscal years 1997-2000, comprising over 300,000 discharges. Among this subset, 31.12% of discharges had anesthesia charges reported. This proportion was applied to all discharge data included in the analysis to estimate the number of patients at risk for a complication of anesthesia. The number of events each year was divided by the estimated population at risk to arrive at annual rates of complications per 1000 persons anesthetized.

Results

Over the ten-year period, there were 730 hospital discharges of patients with one or more complications of anesthesia reported, among a total number of discharges equaling 1,319,685, of which an estimated 410,686 involved anesthesia. There were 23 discharges with more than one of the eight diagnosis codes representing these complications. The most commonly reported complications were adverse effects of central nervous system depressants and anesthetics (reported in 54.4% of the 730 discharges), complications of anesthesia during labor and delivery (19.0%), and poisonings by central nervous system depressants and anesthetics (18.8%). (Table 1; Figure 1)

The overall rate of complications of anesthesia for the

ten-year period was 1.8 per 1000 persons anesthetized (estimated). Annual rates ranged from a low of 1.2 per 1000 in FY1991 to a high of 2.2 complications per 1000 in FY2000. (Figure 2) There was no significant trend in the rate over time.

There were strong variations in the occurrence of anesthesia complications by age group and sex. (Figure 3) A small peak during infancy to age four was followed by low numbers during middle childhood, but the highest numbers were found in young adulthood rather than in old age. This was especially true among women, who comprised 64.8% of all hospitalizations with complications of anesthesia; the peak in early adulthood represented primarily women undergoing an obstetric procedure. For males, there was no discernable pattern of procedures to account for their relatively smaller peak in early adulthood; the most common types of procedure reported for males with complications of anesthesia were in the group ìmiscellaneous diagnostic proceduresî (28.7% of discharges).

Inpatient mortality was lower among patients who had a complication of anesthesia than was generally found among hospitalized patients during the ten-year period. Eleven of the 730 patients with complications (1.5%) were discharged dead, whereas 2.6% of all hospitalizations ended in death. The hospital discharge data do not contain information that links the cause of an inpatient death to a specific diagnosis, such as an anesthesia complication.

Conclusions

Based on information reported in hospital discharge data, complications of anesthesia are rare occurrences among inpatients in Rhode Island hospitals. Fewer than one-quarter of one percent of patients receiving anesthesia experience such complications. It should be noted that anesthesia complications are only reported in the source hospital discharge data if the complication is mentioned in the medical record and is coded during data abstraction. There is no independent verification of the completeness or accuracy of reporting for these complications.

Women ages 15-44 years and men ages 35-44 were more likely than hospitalized persons of other ages to have a reported complication of anesthesia. The number of women of child-bearing age experiencing complications is elevated primarily due to their increased risk during labor and delivery. For males, no specific surgical procedure or group of surgical procedures was associated with complications of anesthesia. Finally, there is no apparent increased risk of mortality among patients with these complications; inpatient mortality is actually lower among these patients than among all inpatients, perhaps reflecting the better underlying health of surgical patients.

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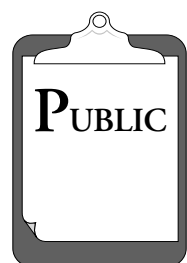
PUBLIC HEALTH BRIEFING

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by John P. Fulton, PhD

Asthma and Flu Vaccination

John P. Fulton, PhD

Respiratory infections including influenza are recognized as important asthma triggers. For this reason, influenza vaccine is recommended for asthmatics by the **Centers for Disease Control and Prevention** (CDC):

"Vaccination is recommended for the following groups of persons who are at increased risk for complications from influenza: … adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma."[1]

and by the National Heart, Lung, and Blood Institute:

"Annual influenza vaccinations are recommended for patients with persistent asthma. It is well established that viral respiratory infections can exacerbate asthma, particularly in children with asthma under the age of 10. . . The role of infections causing exacerbations of asthma also appears to be important in adults."[2]

The efficacy of influenza vaccine is recognized internationally. The CDC, for example, characterizes influenza vaccination as "the primary method for preventing influenza and its severe complications."[1] Vaccination prevents the onset of illness "in approximately 70%-90% of healthy persons aged <65 years," and may induce herd immunity in closed settings if vaccination rates are high.[1] Vaccination has also been shown to prevent asthma exacerbations in young children (ages 1-6).[3]

There are few drawbacks to the use of influenza vaccine, other than occasional allergic reactions to residual egg protein and the development of mild, transient symptoms (fever, malaise, myalgia) in some persons, especially young children.[1] Despite occasional anecdotal reports that the use of influenza vaccine in itself may exacerbate asthma symptoms, recent studies have demonstrated the contrary.[4,5,6,7] Additionally, "minor illnesses with or without fever do not contraindicate the use of influenza vaccine, particularly among children with mild upper respiratory tract infection or allergic rhinitis," and "children at high risk for influenza-related complications can receive influenza vaccine at the same time they receive other routine vaccinations."[1] A recent study also concluded that "influenza vaccination can be given safely and effectively to asthmatic children regardless of asthma symptoms or concurrent prednisone therapy when necessary."[8]

Unfortunately, the influenza vaccination rate for persons at increased risk for complications in the United States is low. The CDC recently reported a vaccination rate of only 31% (in 1998) "for adults aged 18-64 years with high risk conditions," and even lower rates (9%-25%) for asthmatic children.[1] As a result, in its most recent advisory on Prevention and Control of Influenza, the CDC asserts:

"Increasing vaccination coverage among persons who have high-risk conditions and are aged <65 years, including children at high risk, is the highest priority for expanding influenza vaccine use."

Physicians are urged to take every practical opportunity to vaccinate asthmatics for influenza.

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Judicial Diagnosis

The Medical Malpractice Implications of End-of-Life Care and Tretment

E. Paul Grimm, JD, and Patrick C. Barry, JD

"End-of-life" care is a growing area of medical treatment. The use of "**Do Not Resuscitate (DNR)**" orders, hospice care, and heavy narcotics for pain management in terminal patients is increasing across the country. A corresponding increase in potential civil (and even criminal) liability can be identified as well. This article will review some cases dealing with the possibility of liability arising from treatment by a physician or hospital in various end-of-life situations.

Excluding suicide, all courts recognize a patient's right to die. If the right to die is indeed a legally cognizable right, it logically follows that the loss of that right is compensable. The doctrine which embraces the compensation anticipated by the loss of the right to die has been labeled "wrongful prolongation of life." When a medical professional negligently or intentionally disregards the express wishes of a patient, the harm inflicted may give rise to monetary damages. The test for this type of liability is whether the unwanted prolongation of life would not have occurred but for the conduct of the medical professional.

This is by no means the only area of potential malpractice liability with regards to end-of-life care, however, as the following cases indicate. The wishes of the family, as well as the patient's need for pain management and other palliative care must be considered. One case even suggests potential criminal liability of medical professionals for mishandling the care of a patient in an end-of-life context.

There are very few cases on this subject. Fifty different state court systems, as well as the numerous federal circuits, are slowly developing this area of law. Courts, however, do not make statutory law, which is often clearer and well-defined. Rather, courts make specific decisions, based upon the facts of a particular case. Although the language of a decision may seem to have a very wide breadth, it may be applied differently to a case with different facts. Consequently, as different cases develop, unique facts will be used by the various court systems to carve out exceptions, and also to clarify or expand, the holdings discussed here. Thus, there are no clear rules yet in this area of medical malpractice.

1. ANDERSON V. ST. FRANCIS-ST. GEORGE HOSPITAL[1]

This is a leading case regarding liability for failing to follow a "Do Not Resuscitate" order. Generally speaking, a hospital will not be liable for general damages resulting from a negligent failure to honor a DNR request, but may be liable for other special damages. These would include medical expenses, but not general damages for the pain and suffering of a wrongfully prolonged life.

In *Anderson*, an elderly man was admitted to the hospital with chest pains and told his doctor not to resuscitate him if his heart failed. The doctor entered a DNR order on the charts but kept the man on a heart monitor. When the patient became tachycardiac, a nurse responded with a defibrillator and revived him. The patient suffered a stroke two days later, and lived for nearly two years partially paralyzed, although he was able to visit and communicate with his family.

The Ohio Supreme Court rejected the claim for a "wrongful prolongation of life." The analysis was as follows: The court recognized a "duty to accede to a patient's express refusal of medical treatment." Such duty arises out of a patient's constitutionally valid right to die and to refuse treatment. The court also recognized that a patient could prove causation in such cases by showing that but for the doctor's treatment, the patient would have died. The court refused to recognize, however, any legally cognizable harm or damages resulting from the patient's continued life, and would not allow the request for general damages. (Other cases, which also recognize that general damages are not recoverable, recognize that special damages could be recovered, such as extraordinary medical costs, etc.)

The *Anderson* court held that continued human life cannot be a compensable harm, partly because it is impossible to measure "being vs. nonbeing." The court also noted that such cases "demonstrate the outer bounds of liability." The facts of this case, however, are not very compelling, and another court could conceivably reach a different conclusion on different facts. For instance, what if the patient technically was revived, but only into a vegetative state? Here, the patient was revived without complication and later suffered a stroke; there was no proof that the resuscitation efforts caused the stroke.

2. STRACHAN V. J.F.K. MEMORIAL HOSPITAL[2]

This case also involves a DNR order, directed by the family rather than the individual patient. *Strachan* shows the importance of having in place policies and procedures to handle requests to turn off life support and release the body of a family member. In this case, a young man shot himself in a suicide attempt and was rushed to the hospital, where he was pronounced brain dead and placed on respirators. The family asked that the respirators be turned off and the young man's body be turned over for burial. The hospital, which had asked the family to donate the man's organs, waited three days before complying with the family's request, in order to discuss organ donation and consult the hospital's legal counsel.

The family sued, claiming that: 1) The hospital had a duty to have procedures, policies, forms, and the like, in place and ready to use, in order to effectuate the family's wishes, and 2) The hospital must turn over the body upon request.

The court held that the hospital had no separate duty to have procedures and policies in place to handle a request to remove life support. The court did recognize, however, the separate duty to act reasonably in the face of the request and the additional request to turn over the man's body. Furthermore, the court held that the failure to have procedures and policies in place could be evidence of a failure to act reasonably in the circumstances presented. The court also allowed an emotional distress claim by the parents, who watched their brain dead child "lying in bed, with tubes in his body, his eyes

taped shut, and foam in his mouth," for three days.

This case suggests that hospitals should have in place affirmative policies and procedures, discussed with legal counsel beforehand, designed to reasonably and appropriately respond to such requests.

3. FENLEY V. HOSPICE IN THE PINES [3]

This "hospice care" case shows the potential liability that may arise when palliative care is provided without determining whether it is appropriate. The plaintiff, wife of the deceased, sued the hospice care center where her husband died and the individual doctor who served as its medical director. The trial court granted summary judgment in favor of the doctor and hospice, but the appellate court reversed and sent the case back for trial.

The husband had been misdiagnosed with an inoperable brain tumor and given six months to live. He was admitted to the hospice and treated with narcotics, which caused a ruptured colon, infection, and ultimately death. The wife then learned that the husband did not have a brain tumor, but only a subarachnoid cyst that did not require any treatment, accompanied by sinus pain. Thus, he never should have been admitted to hospice nor administered the heavy narcotics.

The appellate court found that the medical director, as the doctor who admitted the husband to hospice and served on the hospice care team, "had a duty to independently determine the appropriateness of hospice-type care." The medical director breached this duty by merely "signing off" on the husband's admission to hospice. The medical director testified that his action in admitting the patient was "just a formality" because another doctor had certified that his condition was terminal.

This case demonstrates the need for careful consideration of whether hospice or palliative care is proper, and suggests that formal, stringent procedures should be in place.

4. KELLY V. ST. PETER'S HOSPICE [4]

This hospice care case is more interesting for its factual circumstances than its holding. The plaintiff, husband of the deceased, sued the hospice center where his wife died. The case was dismissed on summary judgment because the plaintiff did not submit an affidavit or any other evidence demonstrating any negligence. The underlying facts, however, show why end-of-life care may expose physicians to unexpected liability.

The wife, suffering from cancer, checked herself into the hospice center with the help of her daughter. She signed consent forms indicating that the hospice center would not treat her disease, but only alleviate her symptoms. The wife and husband were not living together at the time. When the wife died at the hospice center, the husband brought suit, claiming that he had no knowledge of his wife's presence at the center. The husband contended that the hospice failed to aggressively and curatively treat her disease, despite the existence of the consent forms and the traditional notions of hospice care.

The suit may have been allowed to proceed if the plaintiff had submitted sufficient evidence regarding the standard of care. In any event, the case demonstrates the conflicts that may exist between family members, even husbands and wives, about the desire or appropriateness of certain types of end-of-life care, such as DNR orders, pain medications and hospice care.

5. KANSAS V. NARAMORE [5]

This criminal case demonstrates the potentially broad scope of liability beyond a civil malpractice suit. This case also suggests that recognizable standards of care are emerging, which require active pain management in end-of-life situations, even where such medication increases the risk of death. A Kansas doctor was convicted of murder and attempted murder for his treatment of two terminally ill patients. The state supreme court reversed the conviction, finding that the medical evidence could not support a finding of guilt "beyond a reasonable doubt" because the evidence showed disagreement about — and even support for — aggressive pain management.

The alleged attempted murder is relevant to our discussion. The doctor treated a terminally ill patient with Versed, Fentanyl and Morphine to alleviate her pain. Upon the start of administration, the patient's condition noticeably deteriorated, while the doctor asked the family to join hands and began reciting "Into The Woods" by Robert Frost. A family member directed the doctor to stop the drugs, and then transferred the patient to another hospital. The patient died a few days later, and the doctor was charged with attempted murder for allegedly overdosing the patient.

The court ultimately held that the evidence could not sustain a criminal conviction, which had to be proved "beyond a reasonable doubt." The court cited numerous medical sources and suggested an emerging standard of care that requires the alleviation of pain, even when a risk of death is thereby increased, when a terminal patient is suffering. "Thus, a health care provider is ethically permitted, and perhaps even required, to implement pain medication and palliative care, with the consent of the patient or the patient's family, notwithstanding the potential for hastening death." The court noted a pronouncement by the AMA Council on Ethics and an article in the *New England Journal of Medicine*. A breach of this duty would seem to give rise to a claim for pain and suffering for the patient, and possibly a "bystander" claim for the family, for the negligent infliction of emotional distress caused by watching a family member suffer in pain.

The emerging scope of potential liability for end-of-life care is still developing and is not clear. These cases suggest, however, that physicians should consider having in place effective procedures and controls to handle DNR orders and the wishes of family members. Likewise, decisions by physicians regarding the appropriateness of hospice care and aggressive pain management need to be carefully considered. All of these issues create the potential for civil liability for malpractice, and even suggest possible criminal liability in extreme cases.

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– A Physician's Lexicon –

A Nail-Biting Experience

The word, onychophagia, does not commonly arise in everyday conversations. Nor indeed does it crop up when physicians list their diagnostic thoughts in a patient's chart. But while onychopagia does not constitute a life-threatening disease, it is, nonetheless, a commonly observed human failing. The word describes the act of nail-biting.

The *onycho-* root stems from the Greek word, *onyx*, meaning a fingernail or claw. The ancient Greeks also applied the word *onyx* to a crystalline quartz, akin to agate, which bore some resemblance to a fingernail. Onyx, as a semiprecious stone, is also cited in the Bible. Numerous medical derivatives of the root, *onycho-* , include onychopathy [diseases of the nails], onychoptosis [falling off of the nails], onychorrhexis [pathologic brittleness of the nails] and paronychia [inflammation of the skin fold surrounding the nail.]

The other part of the word, *-phagia*, is derived from the Greek, *phagos*, meaning to eat or feed upon. In 1884, the Russian immunologist Eli Metchnikoff coined the word, phagocyte, to define those mobile cells capable of devouring bacteria or other alien substances. [The *-cyte* root is from the Greek, meaning a hollow vessel; but in current scientific terminology it now refers to cell as in words such as cytology, cytoplasm and cytotoxin.]

The *phagos* root also crops up in words such as geophagia [the abnormal act of eating soil and gravel], xylophagy [the eating of wood, usually applied to certain genera of insects], phagology [an obsolete term for dietetics] and anthropophagy [the technically complex but polite word for cannibalism.]

Then there is the word, esophagus. The prefix *eso-* means within as in the adjective esoteric [something understood by a select few, something held within a small circle]; and when combined with the root, *phagos*, it serves to describe the anatomical structure connecting the oral cavity and the stomach for purposes of conveying food.

Some of the ancient Greek coffins reserved expressly for royalty were carved from blocks of limestone. And since the interred flesh of the corpse, in time, seemed to be consumed by the massive stone container, such an ornately embellished coffin was called a sarcophagus [*sarc-* , a Greek root meaning flesh as in the words sarcoma and sarcoplasm. A sarcophagus was thus a flesh-eating casket.]

The *sarc-* root also appears in such nonmedical words as sarcasm, a taunting remark literally to tear the flesh. Sardonic, a words that sounds somewhat similar to sarcastic, describes a bitter, scornful smile or laughter. Eating a particular toxic herb resident to the island of Sardinia was said to produce involuntary facial contractures simulating a bitter smile. The pathological grimace of tetanus intoxication is sometimes called *risus sardonicus*.

Except in archeological descriptions, people rarely use the word sarcophagus. Most people prefer the word, coffin, which is also of Greek origin. A *cophinus* was a wicker box or basket. And not until the 16th Century was the word coffin applied specifically to a corpse-containing box designed for burial in its grave [where, incidentally, onychophagia is no longer encountered.]

– Stanley M. Aronson, MD, MPH

Vital Statistics

Rhode Island Monthly Vital Statistics Report

Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	October 2000	12 Months Ending with October 2000		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	258	3,126	316.2	3,962.0
Malignant Neoplasms	202	2,431	245.9	6,580.0
Cerebrovascular Diseases	39	512	51.8	815.0
Injuries (Accident/Suicide/Homicide)	31	332	33.6	5,868.5
COPD	36	493	49.9	350.0

Vital Events	Reporting Period		
	April 2001	12 Months Ending with April 2001	
	Number	Number	Rates
Live Births	1277	13,251	13.4*
Deaths	846	10,125	10.2*
Infant Deaths	(3)	(103)	7.8#
Neonatal deaths	(3)	(87)	6.6#
Marriages	735	8,620	8.7*
Divorces	245	3,362	3.4*
Induced Terminations	400	5,407	408.0#
Spontaneous Fetal Deaths	56	1,001	75.5#
Under 20 weeks gestation	(53)	(936)	70.6#
20+ weeks gestation	(3)	(65)	4.9#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 988,480

(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

* Rates per 1,000 estimated population   # Rates per 1,000 live births

NINETY YEARS AGO
[OCTOBER, 1911]

Aimé Paul Heineck, MD, Surgeon to the Grace, Reliance and Cook County Hospitals, Chicago, contributed "When and How to Operatively Treat Varicocele in the Male." From January 1906 to July 1, 1910, 155 patients (ages 11 to 57) with varicocele had been operated on at Cook County Hospital. "At least as many other patients were refused operative relief." Dr. Heineck argued against operations in cases of pseudo-varicocele: "The surgeon must not accede to the importunities, to the requests of hypochondriacs and of neurasthenics who insist upon being operated on for an imaginary varicocele. Many of these individuals are hardened, pessimistic and dangerous neuropaths."

V. Lee Fitzgerald, MD, in "Constipation: Its Causes and Treatment," listed as one of the principal causes, "the neglect of persons to go to the closet when they feel the desire to go." Women were particularly susceptible: "Women suffer …very much more frequently than men….They lead a rather sedentary life, take little outdoor exercise, and their manner of dressing: the corset prevents the normal development of the abdominal muscles…." Dr. Fitzgerald also cited as a cause, "too little water and insufficient fat or not enough cellulite in the food."

FIFTY YEARS AGO
[OCTOBER, 1951]

The Journal printed papers from a symposium on Management of the Infertile Couple, presented before the Providence Medical Association. William A. Reid, MD, presented "Cervical and Vaginal Factors;" Charles Potter, MD, "Tubal Factors;" Sumner I. Raphael, MD, "Special Procedures;" Nathan Chaset, MD, "Diagnosis of Male Infertility;" and Ernest Landsteiner, MD, "Treatment of Male Infertility."

In "Hormonal Therapy for Diseases of the Genito-Urinary Tract," Clyde L. Deming, MD, discussed cases of cryptorchidism, pseudohermaphrodites,

Frohlich's syndrome, climacterium in the male, and cancer of the prostate.

An editorial on Workmen's Compensation Amendments discussed the proposed statute to limit the maximum charge for treatment by diathermy and massage to $75.

In "Fifth in Nation," the Journal reported that the Medical Society's Physician Service, the nonprofit prepaid voluntary sugical-medical insurance program, which started January 1950, was now 5th in the nation in the percent of the eligible population enrolled.

TWENTY FIVE YEARS AGO
[OCTOBER, 1976]

The Rhode Island Medical Society adopted a formal resolution, endorsing "the concept of free standing ambulatory surgical units within the state…."

Alan S. Cohen, MD, Alan Rubinow, MD, Don L. Goldenberg, MD, all from Boston University School of Medicine, contributed "Amyloidosis: Disturbances in immunoregulatory mechanisms may be an important step in the pathogenesis of amyloid disease," the report from a lecture given at Rhode Island Hospital, sponsored by its House Officers' Assoication.

William H. Harris, MD, Chief, Hip and Implant Surgery Unit, Department of Orthopaedic Surgery, Massachusetts General Hospital, presented the Chapin Oration, "Detection and Prevention of Thromboembolic Disease." He called for "better evaluation of risk factors and improved diagnosis, prophylaxis, and threatment with fewer side effects…."

Daniel S. Liang, MD, in "Value of Enzyme Studies after Prostatic Surgery," noted that "Enzyme studies after TUR [transurethral resection]… are generally unreliable for the diagnosis of myocardial infarction."