Keira P. Mason *Editor*

Pediatric Sedation Outside of the Operating Room

A Multispecialty International Collaboration

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This book is primarily dedicated to my mother and father, whose sacrifice, love, and encouragement enabled me to pursue my goals and dreams. Leading by example, they showed me to persevere, remain positive, optimistic, and to always strive to achieve my personal best. I thank my husband, Ed, for continuing in my parents' footsteps of encouragement, love and support. Finally, thanks to God for the gift of Tyler and Colin, my sons whom I can only hope to guide, nurture, and provide for as my parents did for me.

Preface

I am honored to present this book as a representation of the passion and expertise of all the contributing authors who are committed to the field of pediatric sedation. *Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration* is intended to represent all specialties from around the world. The authors represent some of the many leaders throughout all the specialties, both in the United States and abroad, in the field of sedation. I am very appreciative of their efforts. Each chapter has been revised and edited a minimum of three times (some as many as eight) and I extend a sincere "thank you" to each author.

This book represents a unique contribution to the field. It is the first book which is directed to all specialties and which specifically acknowledges and reviews the contributions and viewpoints of international societies and specialists. Sedation has evolved to include all specialties. Each chapter is written by a specialist in that particular area and intended to be of value to all sedation providers. For example, even the emergency medicine physician will learn something in the *Sedation of Pediatric Patients for Dental Procedures* chapter, which he will be able to apply or consider in his practice.

Each clinically-oriented chapter concludes with case studies, which present challenging clinical scenarios. This is a unique finale as it is the author's presentation of real-life cases. The intent of these case studies is to guide the reader through the challenges, thought process, and management options for each situation. Certainly there are many possible solutions to each scenario; exploring them through the eyes of the experienced author offers a unique and valuable perspective.

This book may be read cover-to-cover or read a chapter at a time, out of succession. There is intentional, albeit minimal, repetition in the book. The repetition is intended not only to solidify important information for the reader but also to convey relevant information for those who may not be reading the book cover-to-cover. Even the "repetition" is presented in a different style by the individual authors, in most cases masking the repeated elements.

This book went to the publisher in September 2011. Every chapter was updated the first week of September, complete with any recently published papers. Drs. Roelofse, Leroy and Sury were even so generous to share their specialty guidelines, each of which are detailed in this book but had not even been published at the time this book went to press. Dr. Thomas shared his propofol outcome data and protocols in Chap. 12: *The Anesthesia Directed*

Sedation Service: Models, Protocols, and Challenges, again prior to being published elsewhere. Even the emergency medicine update of the Clinical Practice Guideline for Emergency Department Ketamine Dissociative Sedation as well as the American College of Emergency Medicine Physicians updated Procedural Sedation and Analgesia in the Emergency Department: Recommendations for Physician Credentialing, Privileging, and Practice was included. This policy will be published in October 2011.

This book represents collaboration between multiple specialists all over the world. Currently the field of sedation is being challenged by politics, differing viewpoints, and our inability to reach a consensus. Our ability to come together, outside of this book, will be essential to the future of our pediatric patients who receive sedation.

There will continue to be new clinical and research studies which contribute to our knowledge of sedation. There may, in the far future, be new sedatives which come to market. However, the approach to sedation and the information conveyed in these chapters is intended to distinguish this book as a timeless relic which marks an important era in the field of sedation.

Boston, MA
August 2011

Keira P. Mason, MD

Acknowledgments

I cannot offer this book without acknowledging my family. Thanks to my husband, Ed, and my two sons, Colin and Tyler, for bearing with the numerous "motherless" weekends and evenings as I worked on this project. I especially thank my son Tyler, who kept me company and read over my shoulders, trying to help me as I edited and revised chapters on many occasions. Likewise, I am grateful for the companionship of my younger son Colin, as he sat next to me during many late nights in order to offer encouragement, keep me awake and ask me "do you need help?"

I would like to express my respect, gratitude, and appreciation to Shelley Reinhardt, Senior Editor in Clinical Medicine and Portia Levasseur, Developmental Editor of Springer. Their encouragement, gentle prodding, attention to detail, kindness, expertise, and professionalism inspired me to meet all deadlines. Most importantly, they were committed to this project: Committed to supporting all efforts to produce Pediatric Sedation Outside of the Operating Room as a contribution to the field.

My final and most important acknowledgement is to Ms. Amanda Buckley, the clinical coordinator and administrator who committed herself for the past 3 years to this project. From the inception of this book to the final moment of galley proof approval, she devoted even the after-hours to ensuring that all

references and source information were accurate, the grammar and typos corrected, the copyrights were obtained, and that everything from the table of contents to the final chapter flowed appropriately. Her commitment and belief in this project inspired me to drive this book to completion. She has read this book cover-to-cover more than once. I will always be appreciative.

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Part I

Pediatric Sedation Outside the Operating Room

The History of Sedation

1

Robert S. Holzman

The history of induced altered states as a means of tolerating the intolerable is as old as man and for eons has been associated with a loss of self-control alternately welcomed, worshipped and vilified [1]. Ironically, as in ancient times, these three attitudes often coexist, and our professional duty is to care for and educate our patients and public, controlling the end-effects while minimizing the risks, therefore enhancing the safety [1–3].

Is the history of sedation different from the history of anesthesia? They were, and often continue to be, inseparable, particularly for children [4]. This chapter will focus on the various modalities and practices over time, emphasizing the differences but remaining in awe of the similarities through the ages.

Ancient History

The emperor Shennung (2737–2697 Before the Common Era, BCE) made the earliest systematic study of herbal medicine. The Shennung Herbal (c. 200 BCE) mentioned the medicinal uses of 365 drugs, including the opium poppy, *Papaver somniferum*, for pain relief [5].

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The Sumerians codified many of their practices on at least 800 of 30,000 clay tablets from the time of Ashurbanipal of Assyria (568–626 BCE) [6]. Beers were an especially well-developed intoxicating drug in Babylon; hemp (*Cannabis indica*) was a well-acknowledged agent, producing ecstasy and exaltation, and was also recognized as a minor pain-relieving agent. Jewish potions were prepared by the priesthood for pain relief and the imparting of sleep during surgical procedures, venesection and leeching; *Samme de shinda* was probably a hemp potion [7].

The Charaka and Susruta, Hindu medical documents thought to have been written about 1,000 BCE, describe the use of wine and fumes of hemp "to produce insensibility to pain." There were over 700 medicinal plants detailed in the Susruta, including the depressant effects of *Hyoscyamus* and *Cannabis indica* [6].

Classical History

Greek Medicine

Chaldo-Egyptian magic, lore and medicine was transferred to the coasts of Crete and Greece by migrating Semitic Phoenicians or Jews and the stage was then set for incorporating ancient Egyptian drug lore into Greek medicine. Two prominent medical groups developed on the mainland of Asia Minor: the group on Cnidos, which was the first, and then the group on Kos, of which Hippocrates

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(460–380 BCE) was one member. While they were accomplished surgeons, they generally eschewed drugs, believing that most sick people get well regardless of treatment. Although Hippocrates did not gather his herbal remedies, he did prescribe plant drugs, and a cult of root diggers (*rhizotomoi*) developed, as did a group of drug merchants (*pharmacopuloi*). In Greece, plants were used not only for healing but also as a means of inducing death, either through suicide or execution; perhaps the best example was the death of Socrates.

Later, Theophrastus (380–287 BCE), a pupil of Aristotle (384–322 BCE), classified plants and noted their medicinal properties. This was a departure from previous recordings, as Theophrastus analyzed remedies on the basis of their *individual* characteristics, rather than a codification of combinations as in Egyptian formularies. He provided the earliest reference in Greek literature to mandragora [8].

Roman Medicine

After the decline of the Greek empire following the death of Alexander the Great (323 BCE), Greek medicine was widely disseminated through the Roman Empire by Greek physicians, who often were slaves. Dioscorides described some 600 plants and non-plant materials including metals. His description of mandragora is famous – the root of which he indicates may be made into a preparation which can be administered by various routes and will cause some degree of sleepiness and relief of pain [9]. In the first century, Scribonius Largus compiled *Compositiones Medicorum* and gave the first description of opium in Western medicine, describing the way the juice exudes from the unripe seed capsule and how it is gathered for use after it is dried. It was suggested by the author that it be given in a water emulsion for the purpose of producing sleep and relieving pain [6]. Galen (129–199 CE), another Greek, in *De Simplicibus* (about 180 AD), described plant, animal, and mineral materials in a systematic and rational manner. His prescriptions suggested medicinal uses for opium and hyoscyamus, among others; his formulations became known as galenicals.

Islamic Medicine

In 640 CE, the Saracens conquered Alexandria, Egypt's seat of ancient Greek culture and by 711 CE they were patrons of learning, collecting medical knowledge along the way. Unlike the Christians, who believed that one must suffer as part of the cure, the Saracens tried to ease the discomfort of the sick. They flavored bitter drugs with orange peels and sweets, coated unpleasant pills with sugar, and studied the lore of Hippocrates and Galen. They translated Greek texts into Syriac and spread the knowledge of Hellenic culture throughout the East. Persian physicians became the major medical teachers after the rise of the Baghdad Caliphate around 749 CE, with some even penetrating as far east as India and China. By 887 there was a medical training center with a hospital in Kairouan in Northern Africa.

The most prominent of the Arab writers on medicine and pharmacy were Rhazes (865–925 CE) and Avicenna (930–1036 CE), whose main work was *A Canon on Medicine*. The significance of this thread of ancient medical philosophy was that during the eleventh and twelfth centuries, this preserved knowledge was transmitted back to Christian Europe during the Crusades. Avicenna recognized the special analgesic and soporific properties of opium, henbane, and mandrake [10] (Fig. 1.1).

Medieval Medicine

The first Christian early medieval reference to anesthesia was found in the fourth century in the writings of Hilary, the bishop of Poitiers [11]. In his treatise on the Trinity, Hilary distinguished between anesthesia due to disease and "intentional" anesthesia resulting from drugs. While St. Hilary does not describe the drugs that lulled the soul to sleep, at this time (and for the following few centuries) the emphasis remained on mandragora.

3BFrom 500 to 1400 CE the church was the dominant institution in all walks of life, and medicine, like other learned disciplines, survived in

Fig. 1.1 Avicenna (930–1036 CE) "If it is desirable to get a person unconscious quickly, without his being harmed, add sweet-smelling moss or aloes-wood to the wine. If it is desirable to procure a deeply unconscious state, so as to enable the pain to be borne, which is involved in painful application to a member, place darnel-water into the wine, or administer fumitory opium, hyoscyamus (half dram dose of each); nutmeg, crude aloes-wood (4 grains of each). Add this to the wine, and take as much as is necessary for the purpose. Or boil black hyoscyamus in water, with mandragora bark, until it becomes red, and then add this to the wine." [10]

Western Europe between the seventh or eighth and eleventh centuries mainly in a clerical environment. However, monks did not copy or read medical books merely as an academic exercise; Cassiodorus (c. 485–585), in his efforts to bring Greek learning to Latin readers and preserve sacred and secular texts, recommended books by Hippocrates, Galen, and Dioscorides while linking the purpose of medical reading with charity care and help. Therefore, while preserved, the herbal of Dioscorides was accorded blind acceptance as the authoritative source on medical plants for virtually the entire 1,000-year interregnum of the Dark Ages.

Conventional Greco-Roman drug tradition, organized and preserved by the Muslims, returned to Europe chiefly through Salerno, an important trade center on the southwest coast of Italy in the mid 900s. Since an increasing number of monks now spent more time pursuing their medical aims and less time fulfilling their religious duties, medical practice and reliance on medicine were taking on a more secular and specialized caste. Salerno's medical melting pot was a hub of knowledge derived from sources as diverse as the ancient Greco Roman tradition (still present in southern Italy), monastic medicine, and Jewish, Arabic and Oriental practices of the Middle East and Northern Africa [12]P.

One of the more impressive practices documented at Salerno was intentional surgical anesthesia, described in *Practical Chirugiae* in 1170 by the surgeon Roger Frugardi (Roger of Salerno), in which he mentions a sponge soaked in "narcotics" and held to the patient's nose. Hugh of Lucca (c. 1160–1252) prepared such a sleeping sponge according to a prescription later described by Theodoric of Cervia (c. 1205–1296). As an added precaution, Theodoric bound his patients prior to incision. The description of the soporific sponge of Theodoric survived through the Renaissance largely because of Guy de Chauliac's (1300–1367) *The Grand Surgery* and the clinical practices of Hans von Gersdorff (c. 1519) and Giambattista della Porta (1535–1615), who used essentially the same formula of opium, unripe mulberry, hyoscyamus, hemlock, mandragora, wood-ivy, forest mulberry, seeds of lettuce, and water hemlock (Fig. 1.2).

Ether

Ether was discovered in 1275 CE by the Spanish chemist Raymundus Lullius. This new discovery was given the name "sweet vitriol." In 1540 CE, the synthesis of ether was described by the German scientist Valerius Cordus (1514–1544 CE) who carefully specified the materials to be used, the apparatus, and the procedure to be followed in order to distil "strong biting wine" (alcohol) with "sour oil of vitriol" (sulfuric acid). This was

Fig. 1.2 The alcohol sponge [22]. "Take of opium, of the juice of the unripe mulberry, of hyoscyamus, of the juice of hemlock, of the juice of the leaves of mandragora, of the juice of the wood-ivy, of the juice of the forest mulberry, of the seeds of lettuce, of the seeds of the dock, which has large round apples, and of the water hemlock - each an ounce; mix all these in a brazen vessel, and then place in it a new sponge; let the whole boil, as long as the sun lasts on the dog-days, until the sponge consumes it all, and it is boiled away in it. As oft as there shall be need of it, place this sponge in hot water for an hour, and let it be applied to the nostrils of him who is to be operated on, until he has fallen asleep, and so let the surgery be performed. This being finished, in order to awaken him, apply another sponge, dipped in vinegar, frequently to the nose, or throw the juice of the root of fenugreek into the nostrils; shortly he awakes." [23]

a far leap from the conventional secrecy and esoteric rites of the alchemists. Thinking the product to be liquid sulfur, he noted its lack of color, its rapid evaporation, its tendency to cause salivation, and its safety. He recommended it for the relief of cough and pneumonia [13]. Paracelsus (1493–1541), a contemporary of Cordus, came surprisingly close to the recognition of ether as an anesthetic [14]. Later, in 1730, German scientist W.G. Frobenius changed the name of sweet vitriol to ether.

Varied Preparations of Varying Potencies

If the constituents of the plants were combined with fats or oils, they would penetrate through the skin or could be easily absorbed via the sweat ducts in the axillae or body orifices such as the vagina or rectum. This would allow the psychoactive tropane alkaloids, especially hyoscine, access to the blood and brain without passage through the gut, thus avoiding the risk of

Fig. 1.3 John Arderne (1307–1380) "An ointment with which if any man be anointed he shall suffer cutting in any part of his body without feeling or aching. Take the juice of henbane, mandragora, hemlock, lettuce, black and white poppy, and the seeds of all these aforesaid herbs, if they may be had, in equal quantities; of Theban poppies and of poppy meconium one or two drachms with sufficient lard. Braize them all together and thoroughly in a mortar and afterwards boil them well and let them cool. And if the ointment be not thick enough add a little white wax and then preserve it for use. And when you wish to use it anoint the forehead, the pulses, the temples, the armpits, the palms of the hands and the soles of the feet and immediately the patient will sleep so soundly that he will not feel any cutting." [24, 25]

Fig. 1.4 Andres de Laguna (1499–1560 CE) " … a pot full of a certain green ointment … with which they were annointing themselves … was composed of herbs … such as hemlock, nightshade, henbane, and mandrak … I had the wife of the public executioner annointed with it from head to foot … she … had completely lost power of sleep … no sooner did I annoint her than she opened her eyes, wide like a rabbit, and soon they looked like those of a cooked hare when she fell into such a profound sleep that I thought I should never be able to awake her … after a lapse of 36 h, I restored her to her senses and sanity." [26]

poisoning. A few prominent surgeons offered statements about the mode of application of such salves or "oyntments." John Arderne (1307–1380), known for his success curing fistula in anus, and Andres De Laguna (1499–1560), physician to Emperor Charles V and Philip II, provided unambiguous descriptions of soporifics (Figs. 1.3 and 1.4).

The Transitional Epoch-Secular and Non-Secular Ambivalence and the Mistrust of Drugs

The uncertainly of the potency and action of the narcotic drugs rendered their application dangerous and by the end of the sixteenth century such anesthetics had largely fallen into disuse. Indeed, even if physicians tried to use "narcotic" herbals in the middle of the seventeenth century, they were condemned, arrested, and fined or tried for practicing witchcraft [15]. Many of the early books were herbals, and Gerard (1545–1612) warned of the

alkaloids "… this kind of Nightshade causeth sleepe … it bringeth such as have eaten thereof into a ded sleepe wherein many have died" [16].

The Scientific or Modern Epoch

The divergence of herbalism (botany) and medicine began in the seventeenth century as part of the larger movement known alternatively as natural philosophy, scientific deism, and the scientific revolution. An attempt to develop quantitative methodology characterized science, and at the forefront of these attempts was the chemical analysis of the active ingredients in medicinal plants.

Following his clinical observation of poisoning in children who had mistaken water hemlock for parsnip root, Johann Jakob Wepfer (1620–1695) demonstrated dose-dependent toxic effects in dogs of the alkaloids eventually isolated as strychnine, nicotine, and conine [17, 18]. Thus, this early quantitative approach gave rise to the development of modern chemistry and pharmacology. This was first successfully applied to anesthetic pharmacology by Friedrich Wilhelm Adam Serturner (1783–1841) who, in 1805, described the isolation of meconic acid from the crude extract of opium and in 1806, extracted opium. He further experimented with this crystal on dogs, finding that it caused sleep and indifference to pain and called this new substance morphine, in honor of the Greek god of dreams, Morpheus. This science of pharmacology – the interaction of chemistry with living matter – thus began to replace the ancient and descriptive materia medica of herbalism, and set the stage for the advances of the second half of the nineteenth century, which included modern surgical anesthesia.

The Modern Story of Anesthesia

The modern story of anesthesia began with the reaction in Philadelphia to Humphrey Davy's (1778–1829) account of nitrous oxide and its biological effects. In 1808, William P.C. Barton (1786–1856) emphasized the brain disorientation caused by inhaling nitrous oxide, and cited Davy. Meanwhile, an anonymous note, often ascribed to Michael Faraday, indicated that the inhalation of ether would produce effects similar to those of nitrous oxide [19].

In 1839, William E. Clarke (1818–1878) in Rochester, NY began the fad of ether frolics among young people. He is said to have given ether for extraction of a tooth in 1842. In Jefferson, GA, Crawford W. Long (1815–1878) noted that one of the participants in an ether frolic fell heavily, but seemed to lack pain. On March 30th, 1842, Long gave ether by inhalation to a patient for removal of a neck tumor; there was no evidence of pain. Unfortunately, he failed to report his anesthetic success for several years. William T.G. Morton (1819–1868), a student at Harvard Medical School, learned of sulfuric ether, and practiced anesthetizing various small animals at his home. He tried to perfect an inhaling device, and a demonstration was arranged at the Massachusetts General Hospital on October 16PthP, 1846, a turning point in the history of medicine. Gardner Quincy Colton (1814–1898) first gave nitrous oxide for anesthetic purposes to Horace Wells in 1844 and revived its use in dentistry for dental extractions in 1863. Alfred Coleman (1828–1902) became the chief advocate for the use of nitrous oxide in dentistry.

There were additional "sleep-producing" agents available in the second half of the nineteenth century. For example, it was recognized by Robert Glover that potassium bromide would cause drowsiness in animals and by Charles Locock that it would effectively treat epileptic seizures in obstetrical patients being treated for dysmenorrheal. Behrend reported its use for the treatment of insomnia, nervous excitement, and irritability. This led to the therapeutic use of "bromides" (of lithium, sodium and potassium) as anticonvulsants. It was only a short time later that chloral hydrate was introduced by Liebreich as a soporific for medical purposes [20], as well as for more nefarious purposes (it was the chief ingredient in the "Micky Finn" cocktail, for which the bartender, Michael Finn, was tried in 1903 in Chicago). Additional soporifics were paraldehyde, ethanol, sulphonal, diethyl-malonyl-urea (Veronal, or barbital), and phenyl-ethyl-malonylurea (Luminal, or phenobarbital).

Following its introduction and promotion as a short-acting intravenous dissociative anesthetic in 1962, ketamine became a favorite for anesthetics administered outside of the operating room; it avoided the appearance of general anesthesia while providing motionlessness and analgesia (in anesthetic doses). Frequent practitioners of the technique quickly noted that tachyphylaxis developed after only a few administrations in most patients requiring serial sedations, for example, for radiation therapy. This prompted a variety of pharmacologic strategies that were ultimately replaced when propofol was introduced in 1989.

"Modern" Sedation and Analgesia Services

There is an inseparable continuum, particularly in pediatrics, between general anesthesia and sedation and analgesia. Not surprisingly, it was the early efforts of dental surgeons at the beginning of the twentieth century that spearheaded ambulatory anesthesia, as early general anesthesia was associated with dental procedures. Ralph Waters (1883–1979) opened the Downtown Anesthesia Clinic in Sioux City, Iowa in 1916, caring for dental and minor surgery patients! Intermittently, pediatric anesthesiologists filled the role of sedation experts in order for children to tolerate unpleasant diagnostic procedures (Fig. 1.5). Nevertheless, Waters' prescience was followed by a long gap, until the 1960's, when increasing interest in employing shorter-acting anesthetic strategies with more rapid return to "street-fitness" predated the explosion onto the medical diagnostic scene of computed tomography (1974), magnetic resonance imaging (1977), interventional radiology procedures, cardiac catheterization (diagnostic and interventional), and various other imaging modalities. In addition, further miniaturization and engineering improvements continued for both gastrointestinal and pulmonary endoscopy and the use of radiation therapy as an adjunct to surgical and medical treatment of cancer patients. All of these took place in nontraditional anesthetizing locations, popularly known as "outfield" anesthesia [21]. These services, which often require sedation and analgesia or general anesthesia, occupy such a large (and increasing) fraction of pediatric anesthesia practice that at Children's Hospital Boston we currently provide such services for more than 9,000 procedures per year (Table 1.1).

Table 1.1 Anesthesia encounters (sedation and general anesthesia) outside the operating room

Children's Hospital Boston	2010
Interventional radiology	2,000
Cath Lab	1,500
Diagnostic radiology (CT, MRI)	3,899
Gastrointestinal endoscopy	1,450
Oncology	540
Radiation therapy	368
Total	9,757

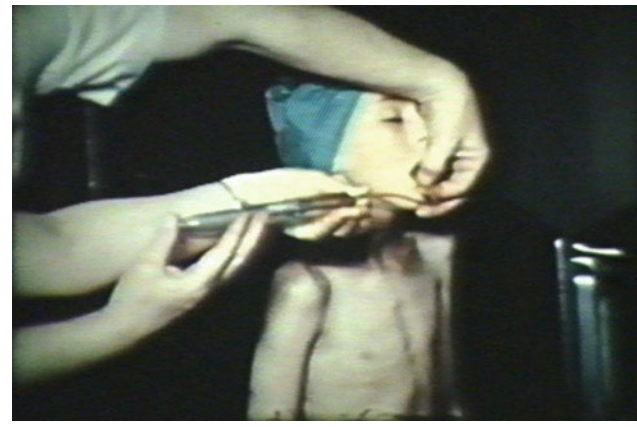

Fig. 1.5 A cachectic child undergoing intrapulmonary contrast injection via an intratracheal catheter for radiographic evaluation of tuberculosis. (From a pediatric anesthesia training film made by Dr. M. Digby-Leigh in 1947)

The Future of Sedation

As an increasing number of procedures are developed that are accessible by percutaneous, intravascular or natural orifice routes, they will be less painful in both the awake and asleep state. However, the need for motionless conditions for children as well as adults will remain, especially as these imaging techniques and procedures are likely to be longer and require increasingly sophisticated instrumentation. At the same time, progress will inevitably continue in understanding the neurophysiology of pain mechanisms as well as consciousness, and we are perhaps not that far removed from the "tricorder" settings in Star Trek to noninvasively control mediators of pain, attention, and neuromuscular competence, all in scalable fashions.

Anesthesia and sedation in the absence of surgery is not a new idea; indeed, it is an idea that has persisted through the eons and is likely to evolve exponentially as our diagnostic procedures and interventions become more sophisticated and our knowledge about neurophysiology grows.

References

1. Holzman R. Uncertainty by choice: anesthesia and the children of night. J Clin Anesth. 2002;14:46–51.
2. Committee on Drugs, American Academy of Pediatrics. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. Pediatrics. 1992;89:29–34.
3. Holzman R, Cullen D, Eichhorn J, Philip J. Guidelines for sedation by nonanesthesiologists during diagnostic and therapeutic procedures. J Clin Anesth. 1994; 6:265–76.
4. Kallar S, Dunwiddie W. Conscious sedation. In: Wetchler B, editor. Outpatient anesthesia. Philadelphia: Lippincott; 1988. p. 93–100.
5. Veith I. The Yellow Emperor's Classic of Internal Medicine. Berkeley, CA: University of California Press; 1972.
6. Leake C. An historical account of pharmacology to the 20th century. Springfield, IL: Charles C. Thomas; 1975.
7. Friedenwald H. The Jews and medicine. Johns Hopkins: Baltimore; 1944.
8. Holzman R. The legacy of Atropos, the fate who cut the thread of life. Anesthesiology. 1998;89:241–9.
9. Anazarbos, Dioscorides: the Greek Herbal of Dioscorides, Illustrated by a Byzantine A.D. 512, Englished by John Goodyer A.D. 1655. Oxford: Oxford University Press; 1933.
10. Avicenna. Qanun dar tibb (Canon of Medicine). Tihran, Surush, 1987.
11. Humphrey J, Oleson J, Sherwood A. Greek and Roman technology: a sourcebook: annotated translations of Greek and Latin texts and documents. Routledge: London; 1998.
12. Caton D. The secularization of pain. Anesthesiology. 1985;62:493–501.
13. Cordus V. Annotationes in Pedacii Dioscorides Anazarbei de materia medica. Strassburg; 1561.
14. Temkin O, Rosen G, Zilboorg G, Sigerist H. Defensiones, in four treatises of Theohrastus von Hohenheim called Paracelsus. Johns Hopkins: Boston; 1941.
15. Summers M. The history of witchcraft and demonology. New York: Alfred A. Knopf; 1926.
16. Gerard J. The herball, or generall historie of plantes. London: Adam Islip, Joice Norton, Richard Whitakers; 1633.
17. Eichenberger P. Autobiographic material on Johann Jakob Wepfer (1620–1695) in correspondence with Johann Conrad Brotbeck (1620–1677). Gesnerus. 1967;24:1–23.
18. Maehle A. Scientific and moral justification of toxicologic animal trials in the 17th century. Johann Jakob Wepfer and Johann Jakob Harder. Gesnerus. 1986;43:213–21.
19. Faraday M. Effects of inhaling the vapour of sulphuric ether. Miscellanea. Q J Sci. 1818;4:158–9.
20. Liebreich O. Das Chloralhydrat: Ein neue Hypnoticum und Anaestheticum. Arch Deutsch Ges Psychiat. 1869;16:237.
21. Mason K, Zgleszewski S, Holzman R. Anesthesia and sedation for procedures outside the operating room. In: Motoyama EK, Davis PJ, editors. Smith's anesthesia for infants and children. Philadelphia, PA: Mosby Elsevier; 2006. p. 839–55.
22. Schilling D. Diebold Schillings Spiezer Bilderchronik: kommentar zur Faksimile-Ausgabe der Handschrift Mss. hist. helv. I. 16 der Burgerbibliothek Bern/ herausgegeben von Hans Haeberli und Christoph von Steiger; mit Beiträgen von Vinzenz Bartlome. Faksimile: Luzern; 1990. p. 1513.
23. Borgognoni T. The surgery of Theodoric … Tr. from the Latin. New York: Appleton-Century; 1955.
24. Fraenkel W. Uber Narkosen und Weckmittel des John Arderne. Leipzig: Schmerz-Narkose-Anesthesie; 1937.
25. Piomelli D, Pollio A. A study in Renaissance psychotropic plant ointments. Pubbl aStazione Zool Napoli Sect Ii Hist Phil Life Sci. 1994;16:241–73.
26. Rothman T. De Laguna's commentaries on hallucinogenic drugs and witchcraft in Dioscorides' Materia Medica. Bull Hist Med. 1972;46:562–7.

Procedural Sedation: Let's Review the Basics – The Pediatrician's Perspective

2

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For the welfare of children

–Motto, American Academy of Pediatrics

Pediatricians, by their very nature, are patient advocates. As such, it is no wonder that pediatricians have taken a leadership role in trying to define standards around the management of pain, anxiety, and motion in children undergoing medical procedures. In 1985, the American Academy of Pediatrics published its first set of guidelines for the elective use of conscious sedation. These guidelines have continued to evolve over the last 20-plus years [1]. In this time, our understanding of pediatric pain experiences as an interplay of genetic, experiential and developmental factors has grown considerably [2, 3]. Simultaneously, the widespread availability of noninvasive monitoring, short-acting opioids and sedatives, and specific opioid and benzodiazepine antagonists has greatly increased our ability to provide procedural sedation in a wide array of practice settings [4].

The practice of procedural sedation, however, is not simply the administration of pharmacologic agents to remove all pain. In every clinical setting, pediatricians must weigh the balance of all the risks and benefits of their potential treatment. Virtually every agent in the procedural sedation armamentarium can have negative effects on a patient's cardiovascular and/or respiratory status and the physician providing sedation must be prepared to handle these potential adverse effects. Furthermore, there are a number of adverse reactions, such as nausea and vomiting, that may also result from the provision of procedural sedation. As much as pediatricians serve as the advocates for their patients to minimize pain and anxiety, they are also their patient's advocates with regard to their safety. For example, it is unlikely that procedural sedation would ever be routinely used for procedures such as venipuncture or vaccine administration [3].

In a pediatrician's practice, there are a number of indications for the provision of procedural sedation. This chapter aims to provide a framework for procedural sedation from a pediatrician's point of view, including understanding of the practice setting, the patients and the procedures themselves. This chapter is designed to apply to all sedation providers across specialties. Additionally, in trying to create an approach to procedural sedation, it is equally important to consider when the risks of the sedation outweigh the benefits which may be achieved by the procedure.

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Questions to Be Asked

Prior to the initiation of any procedural sedation, the following questions need to be considered:

1. What are the goals of the procedural sedation? Eliminating or reducing pain (analgesia)? Alleviating or reducing anxiety (anxiolysis)? Maintaining motionlessness for an imaging procedure?
2. Do I have the appropriate personnel to provide the therapy, both with regard to knowledge and experience? The proper equipment? The time to do the procedure and to monitor the patient during the recovery period?
3. Does the patient have an underlying medical condition that may complicate the provision of procedural sedation?
4. Am I prepared to handle an adverse reaction or unanticipated complication of the procedural sedation?

This chapter will attempt to provide a framework for these questions and will lay the foundation for future chapters.

Setting

First and foremost, the provision of sedation in a safe manner requires a setting that has immediately available personnel, equipment, monitoring, and protocols to manage emergency and rescue situations [5]. In particular, practitioners providing sedation must be prepared to handle the patient who has a compromise of the airway or depressed respiratory effort, both of which can result in airway obstruction, hypoventilation, hypoxemia, apnea and at worst, frank respiratory arrest. Fortunately, most severe outcomes are extremely rare. One large study found that even in centers with dedicated and specialized sedation services, one in every 200 sedations outside of the operating room required airway and ventilation intervention and one in every 400 procedures is associated with stridor, laryngospasm, wheezing or apnea [6]. While it is difficult to predict when and for whom adverse events will occur, advanced preparation may be the most critical factor in minimizing an adverse outcome [7, 8].

Personnel

Properly trained personnel are of the utmost importance in the provision of procedural sedation and there should be, at a minimum, two trained professionals present at each sedation.

The primary caregiver is the one who is responsible for providing the sedation itself. This person must be credentialed to provide sedation and should have current training in both basic (e.g., BLS) and advanced (e.g., PALS) life-support. Simple certification, however, is not enough. This primary practitioner needs to be able to recognize all potential complications of the sedation, especially the earliest signs of airway difficulties, and to manage them accordingly [9]. According to the Joint Commission, this level of competence requires not only training and education, but experience as well [10].

The secondary provider's primary responsibilities are to monitor the patient during the procedure and to inform the primary provider of any changes in the patient's cardiovascular or respiratory status. Most, if not all healthcare facilities, require that all providers be properly trained and educated as well as take part in a minimum number of sedations annually in order to ensure competence and maintain sedation privileges.

Equipment

The space where the procedural sedation takes place must have the proper equipment to minimize any adverse consequences. Table 2.1 lists the minimum equipment that must be available to provide sedation and rescue a sedated patient [5, 11].

Monitoring

A number of physiologic parameters should be monitored to ensure the safety of the patient. The