

Edmond I Eger II
Lawrence J. Saidman
Rod N. Westhorpe
Editors

The Wondrous Story of Anesthesia

 Springer

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To those responsible for the discovery and evolution of anesthesia.

Preface

This story describes events in three succeeding eras: first, events during the time preceding and immediately after the demonstration of anesthesia; then those in the subsequent 90 years of slow evolution of the specialty, ending in the 1950s; and finally those from the 1950s to the present, a period of explosive growth. Our lives span the last of these, the era in which modern anesthesia evolved from empiricism—“doing what worked”—to a practice relying on science and evidenced-based medicine. We sought to tell this story before too many grand participants died or were unable to tell their story. Many died in the past decade: Safar (2003); Marx (2004); Greene (2005)—including since we began this project in 2007—Haglund, Ibsen and Keats (2007); Gray (2008); Parsloe (2009); Smith and Terrell (2010); Gordh, Morris and Pierce (2011). We would have lost too many opportunities had we failed to act.

We enlisted 100 authors to construct 53 chapters (The Individual Stories) describing specific aspects of the evolution of anesthesia: people, countries, drugs, science, organizations, education, and more, each a thread in the tapestry of a larger story, each chapter written by anesthesiologists and others who lived this history. These 53 chapters make up the second part of our book. The first part wove stories from these chapters into chronologies described in 14 additional chapters (The Woven Stories) which provide a coherent picture of the development of anesthesia, a framework that facilitates an understanding of how events and people described in the second part of the book jointly shaped the development of the specialty.

Our contributors represent the Americas, Europe, the Middle and Far East, and Australia and New Zealand. They were chosen because of demonstrated expertise and/or actual participation in the development of a specific subject or of the specialty in a specific geographic area. Several chapter titles may seem idiosyncratic for a history book and were chosen because the subjects seemed to represent existing trends that were likely to influence the future.

A book of this breadth could not have been produced without the help supplied by our 100 contributors. Each endured multiple suggestions, changes, requests for no fewer than four revisions and a gentle nagging for more and more and more that in retrospect probably bordered on abuse. A few did not tolerate our intrusiveness and withdrew before completing their assignments. Fortunately, replacements were found and despite a shortened timeline for completion they met our deadlines. To all of these dear friends we offer our gratitude—we are in your debt!

The book is a story, not a recitation of pharmacology or physiology. It is not intended to educate the student in techniques or mechanisms. It describes the issues that shaped anesthesia, the incidents and humor, the anecdotes that put a human face to this wonderful specialty. We hope it shows the interactions between diverse forces that made this great specialty grow, and provides a sense of where those forces may take us in the future.

We three editors (Fig. 1) and many of our contributors hail from English speaking countries. While our respective forms of English are nearly identical they do differ slightly in spellings, e.g., an(a)esthesia, vapo(u)r, (o)esophagus, antagoni(s)ze, and many more. Rather than dictating the use of American English throughout, we elected to use the spelling common to the country of the chapter's author(s).

Redundancy in the descriptions of subjects, persons, and events is a frequent complaint lodged against multi-authored books, especially those like ours wherein the stories span centuries. Rather than purging the text of such repetitions, we allowed them to remain where and



Fig. 1 The three editors, from left to right: Edmond (Ted) Eger, Lawrence J. Saidman, and Rod N. Westhorpe

whenever they obviously belonged. The largest example, the discussion of Danish anesthesiologist Bjørn Ibsen's impact upon intensive care medicine, intensive care units, and associated issues appears in five chapters, each with its own focus.

Finally, a tribute to **The Power of Three** (Fig. 1). As might have been expected, in the 6 years over which we wrote and re-wrote this book, we disagreed regarding the how, who, when, where, why, and whether of many things. We settled each of these disputes (mostly) without rancor by taking a vote. For anyone anticipating a similar future exercise, we advise avoiding an even number of participants.

It has been a wonderful journey that has allowed us to re-live lives we loved.

San Francisco, CA, USA
Stanford, CA, USA
Melbourne, VIC, Australia

Edmond I Eger II
Lawrence J. Saidman
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Part I

The Woven Story of Anesthesia: Eras, Exemplars, and Looking Forward

Summary

Surgeons in ancient times undertook diverse operations, usually at great speed to diminish the duration of suffering. Skulls from 5,000 BCE show trephination, the removal of a piece of bone from the head. Egyptians in 3,600 BCE performed circumcisions and tracheotomies. In 1700 BCE, Babylonians excised tumors. Egyptians cauterized breast tumors and excised peripheral aneurysms. The Roman surgeon, Galen, in the second Century CE, treated cataracts to restore sight, and he cut out the uvula to cure chronic coughing. Surgeons in Europe might be physicians, monks or barbers who in the thirteenth and fourteenth centuries wrote books on surgery. They gained recognition by their study of the anatomy of cadavers. Thus, in 1543 Vesalius published “*On the Fabric of the Human Body*”, demolishing centuries of errors, and opening the door to the performance of accurate surgery.

The horrors of pain, shock, and infection hindered surgeons. Operations brought infection, an added threat to life. Surgeons had surprising remedies, some desperately wrong (e.g., venesection), and some perhaps surprisingly wise (e.g., irrigating wounds with alcohol).

Before the advent of anesthesia, humans used diverse means to diminish pain, including pressure or ice to numb extremities. They administered herbal potions including mandragora, hemp-marijuana, opium, and alcohol. The Incas may have known of the topical effect of coca/cocaine, but they had no way to inject it other than spit coca-laced saliva into the wound. That might have some effect, but the amount of active cocaine was small and the effect probably too little to produce anesthesia.

Some potions contained hallucinogens, particularly scopolamine. Some prescriptions with wonderful names had unknown components: In 500 BCE, Hua Tuo gave “mafeisan” or “cannabis boil powder”. In the Middle Ages, patients might suck liquid or breathe vapors from soporific sponges. And since the 1700s, we knew that we could produce immobility with a curare tipped dart, but we now know that would not eliminate pain.

Practitioners applied positive thinking and forms of suggestion, including modern magical rings, necklaces, and charms for the parturient. Greeks applied oils and warm compresses during labor, anticipating the warm compresses, massage and herbal teas used today. Were they placebos (which can have positive effects)? Mesmer’s late eighteenth century creation of animal magnetism may have also relied on suggestion, perhaps a form of hypnosis that inconsistently assuaged surgical pain.

World Events Before 1798

The Jews credited 3761 BCE as the date of creation, but scientists suggest it was billions of years earlier. By 4000–3000 BCE, civilizations had arisen in China, Korea, Japan, Mesopotamia, and Egypt, aided by the development of ag-

riculture, domestication of animals, invention of the wheel (including the potter’s wheel), and writing. The Bronze Age appeared in 3000–2000 BCE, and the Egyptians constructed the pyramids. Parallel great kingdoms ruled Egypt and China, and an egalitarian civilization arose in the Indus Valley. In 2000–1000 BCE, Central Asian Indo-European invaders on horse-powered chariots overran Egypt and Babylonia. The Iron Age appeared in 1000–0 BCE, and Judaism, Zoroastrianism, Hinduism, Jainism and Buddhism developed. Greece conquered Persia, and the Romans conquered Greece and established the Roman Republic. In the first century CE, Rome dominated Europe, North Africa and the Near East, and the Han Dynasty ruled China. In the second century, Cai Lun invented paper, and Roman civilization peaked. The Prophet Muhammad began the Muslim conquests in 622 CE. In this century, India gave smallpox to Europe, and the world’s population shrank to 200 million. In the eighth century, Arabian expansion continued,

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and Charlemagne came to power. Vikings repeatedly invaded Britain in the ninth century. The eleventh century saw the worst of Europe's Dark Ages (500–1500 CE), but great advances in science took place in China. Gutenberg invented mechanical movable type printing about 1439. The Spanish Inquisition began in 1492 the same year that Columbus landed in America. Copernicus proposed the sun as center of the universe in the 1540s. In the seventeenth century, Newton invented the calculus and his Laws of Motion. The eighteenth century saw French, American, and industrial revolutions, including invention of the steam engine.

Ancient Approaches to Pain Relief

We cringe, thinking of Galen, a prominent physician and surgeon in ancient Rome, ¹ performing uvulectomy, cataract extractions, caesarean sections, and amputations in unanesthetized patients. We cringe, thinking of children forcibly restrained to allow surgery to proceed. Despite the absence of any clear path to pain-free surgery, surgeons in ancient times undertook diverse operations, usually at great speed to diminish the duration of suffering. How did these ancient surgeons deal with the issue of pain?

Ancient civilizations may have used pressure or ice to numb extremities. Magical herbs, including marijuana, might have been given. Perhaps the first known use of anesthesia came from China, where in 500 BCE, Hua Tuo combined herbs and wine into a concoction known as “mafeisan” or “cannabis boil powder”.

In 40–90 CE, the Greek, Pedanius Dioscorides, used opium or mandragora to minimize pain during surgery. However, such therapies might be lethal or ineffective, or both. Opium could cause patients to stop breathing. Belladonna drugs in mandragora might lead to a fatal increase in temperature. Other surgeons experimented with opioids, alcohol, or a blow to the head—imperfect techniques that did not offer the control and reversibility required for anesthesia. Alcohol, for example, needed to be consumed in precisely the right quantity to cause unconsciousness, but not death. Persuading the underdosed inebriate to drink more might be impossible, and in the meantime, their irrational behavior and propensity to vomit made such a remedy ineffective.

Some remedies may have anticipated modern approaches. South American Indians may have chewed coca leaves and spat into the surgical field, thereby applying the first local anesthetic. However, the lack of cocaine alkaloids available in raw coca leaves may have limited its effectiveness [1].

Surgery Without Anesthesia: A Painful Proposition

The Earliest Surgeries

A history of anesthesia is not complete without a discussion of the history of surgery. Anesthesia is a recent invention relative to surgery. Brutality attended the earliest surgeries. One early procedure appeared in all parts of the world except the Far East. Called “trephination,” it involved making a hole through the patient's skull to expose the brain. Archeologists have unearthed skulls dating to 10,000 BCE, that show evidence of the practice. Some such skulls had healed, indicating that the holes resulted from a deliberate surgical act. The purpose of trephination remains a matter of speculation. Did it have religious implications? Did it release evil spirits?

Even in ancient times, humans performed complex surgical procedures. By 3,600 BCE, Egyptians performed tracheotomies, cutting a hole in a patient's windpipe to ease airflow. In 1,700–1,600 BCE, Egyptian surgeons operated on tumors and aneurysms. They used cautery to remove breast cancers and treat other ailments, literally burning away the offending body part.

So common were surgical procedures, that the 1,700 BCE Code of Hammurabi (Babylon) dictated the cost of surgeries, including incisions of tumors, giving discounts for operations on slaves. The Code dealt harshly with surgical failure: “if a physician make a large incision with the operating knife, and kill him, or open a tumor with the operating knife, and cut out the eye, his hands shall be cut off.” We may assume that malpractice was rare.

Egyptian and Greek surgical practices may have anticipated modern therapies. *The Edwin Smith Papyrus*, an Ancient Egyptian medical text and the oldest known surgical treatise on trauma, described the healing of injuries in 3,000 BCE, and suggested the application of meat to wounds to decrease bleeding, possibly using tissue clotting factors to achieve hemostasis. The ancient Greeks treated wounds with wine, perhaps acting to sterilize the incisions.

Records indicate the types of care given to wounds during this period, and the diversity of surgical procedures, but few records indicated attempts to dull the pain of surgery. How did ancient humans endure having a quarter-sized hole bored into their skull, the extraction of tumors, and the destruction of maladies by burning? The agony is difficult to imagine.

As the new millennium approached, surgeries became more complex, and the center of progress shifted from Greece to Rome. The Romans contributed to the knowledge essential for conducting surgery. The ancient Roman physician, Celsus (25 BCE–CE 50), accurately described the body's response to trauma or infection, using terms characteristic of inflammation—redness, swelling, heat and pain. The great Roman surgeon, Galen (CE 129–199), performed

¹ In the second century CE, Galen treated cataracts to restore sight and cut out the uvula to cure the chronic cough.

cataract extractions, perhaps by displacing the opaque lens into the vitreous humor with a needle. A surgeon to gladiators, he made major contributions to the knowledge of anatomy through his observations of normal and abnormal structure. He dissected pigs and apes because human dissection was forbidden. However, by relying on dissection of animals, some of his extrapolations to human anatomy initiated errors that continued for centuries, errors sustained because of Galen's fame.

Ancient Jews in the Middle East also conducted surgeries. The Talmud described the suturing of wounds, the reduction of dislocations, the amputation of limbs, and the performance of Caesarian sections. The Jews had quaint remedies including the application of onions to wounds, a therapy for preventing infection that has modern support [2].

Dealing with the Pain of Surgery in the Ninth Through Twelfth Centuries

Church edicts during the Middle Ages, particularly the Dark Ages, diminished the use of surgery, and in 1163, the church forbade monks from shedding blood—and thus from performing surgery. Enter the barbers, men taught surgery by the monks before the Church's prohibition. These barber-craftsmen continued performing surgeries. They repaired hernias, removed bladder stones and cataracts, among other procedures, thereby preserving a modicum of surgical craft.

Pain always accompanied surgery; what to do about the pain? In the Middle Ages, patients might suck liquid or breathe vapors from sponges which offered mandrake, henbane or other hallucinogens such as hyoscyne and scopolamine [3]. It sounds wonderful, a sponge to cause sleep, to shield its beneficiaries from the cruelty of the knife.

“The most popular method of inducing narcosis was the so-called soporific sponge, *spongia somnifera*. Historians have found descriptions of it in manuscripts dating to the ninth century. Nicholas of Salerno described its ingredients in the twelfth century as opium, hyoscyamine, mulberry juice, lettuce seed, hemlock, mandrake and ivy. A fresh sea-sponge was to be soaked in the mixture and allowed to dry ‘in the sun during the dog-days until all the liquid is consumed.’ When required for use, the concoction was re-constituted by dipping the sponge in water. Because the medieval manuscripts recommended applying the sponge to the subject's nostrils, it has been thought that this was meant to be a form of inhalation anesthesia, but there is good evidence that the potion was usually administered as a drink [4].”

Medieval physicians even thought of an antidote: “Reversal of the narcotizing effect was to be attained with the juice of fennel-root or with vinegar [4].” But the soporific sponge probably could not produce anesthesia. Patients given scopolamine may not remember the agony of surgery, but they would move in response to the inflicted pain, and they might move vigorously [5].

Thirteenth–Fourteenth Centuries: Ether is Synthesized and Surgery Grows

In 1275, Spaniard Raymond Lully (Fig. 1.1) created a compound that, centuries later, would become the world's most important anesthetic. He combined sulfuric acid with wine to produce ethyl ether, which he called sweet oil of vitriol. But Lully did nothing further with his discovery, and patients everywhere would have to wait nearly 600 years for ether to be used to produce anesthesia.

Italian and French surgery resumed, growing as the Middle Ages ended. Published in Salerno, the earliest book on operations, the Bamberg Surgery, elevated the prestige of Italian surgery. Italian and French barber-surgeon guilds competed with each other and with so-called “masters of surgery”, for royal recognition and support. Italian master surgeon, Lanfranc of Milan, irrigated wounds with wine (as had Greek physicians 1,500 years earlier) before closure of the wounds. In 1,290, Lanfranc left for France, thereby transferring considerable surgical authority from Italy to France. His 1296 book, *Practice and Art of All of Surgery*, further inspired French surgery.

French master surgeon Guy de Chauliac's 1368 book, *Inventory of the Complete Works of Surgery*, supplemented Lanfranc's work. Both Lanfranc's and de Chauliac's books appeared in Latin, and thus were inaccessible to most barber-surgeons until translated into French and other European languages. This contributed to the stiff competition between the master surgeons (who were likely to speak Latin) and the barber-surgeon guilds. The books guided surgery in France, and to some extent in England, for two centuries. They advised treatment of tumors, sores, and fractures, and prescribed antidotes and drugs. England however, remained a backwater controlled primarily by barber-surgeons, who competed with the less numerous military surgeons.

Fifteenth and Sixteenth Centuries

The 1425 translation of Guy de Chauliac's book from Latin into French and English, aided the barber-surgeons (known as the “surgeons of the short gowns”) in their mounting competition with Latin-educated university surgeons (the “long gown” academic surgeons). Barber-surgeons grew more numerous than their long-gown counterparts, in part because the barber surgeon was more accessible. Although the barber-surgeons lacked social status or academic rank, the public found them to be more approachable, and eventually recognized that they also possessed superior skills that decreased complications and mortality.

Two self-educated Frenchmen, Pierre Franco and Ambroise Paré, advanced surgery in France and the reputation of such surgery in the world. They learned to perform surgery



Fig. 1.1 In 1275, Raymond Lully (pictured with words coming from his mouth) synthesized diethyl ether (“ether”) by mixing wine and sulfuric acid, calling it sweet oil of vitriol, but he made nothing of it

from itinerant lithotomists and herniotomists (Franco), and barber-surgeons (Paré). Franco is thought to have fought charlatans, and Paré helped bridge the divide between the barber-surgeons and academic surgeons.

The Renaissance generated a new era of discovery in surgery. The Renaissance diminished the power of the Church and thereby limited its power to prevent human dissection. As a consequence, surgeons gained important new insights into anatomy that materially advanced surgery. In 1543, 29 year-old Andreas Vesalius published his classic book *On the Fabric of the Human Body*, demolishing centuries of errors based on Galen’s dissections of animals, or ignorant imaginings [6, 7].

A half-century later, in 1597, Gaspare Tagliacozzi published *The Surgery of Defects by Implantations*, a treatise on the management of mutilating injuries—plastic surgery in 1597. Tagliacozzi precisely instructed surgeons on the reconstruction of noses and ears. The uncomplaining immobilized

patient waited for two or three weeks for the skin graft from the arm to gain circulation from the nose [6, 7]. Plastic surgery without a drop of anesthesia.

It was not for lack of an anesthetic. It was not for lack of an observation that the anesthetic might block pain. As Lully had done three centuries earlier, in 1540, 25 year-old Valerius Cordus (Fig. 1.2a) once again produced ether (sweet oil of vitriol) by adding sulfuric acid to wine [8, 9]. About the same time, Theophrastus Bombastus von Hohenheim (Fig. 1.2b), better known as Paracelsus [10] noted that ether “has associated with it such a sweetness that it is taken even by chickens, and they fall asleep from it for a while but awaken later without harm.” Paracelsus continued, “On this sulphur no other judgment should be passed than that in diseases which need to be treated with anodynes (pain killers) it quiets all suffering without any harm, and relieves all pain, and quenches all fevers, and prevents complications in all illnesses [8].”

Why did no one notice? A potent painkiller, ether would eventually be widely used as an anesthetic, but Paracelsus died in 1541 without demonstrating this possibility. Had anyone tumbled to the possibilities inherent in Paracelsus’ observation that ether put chickens to a reversible sleep, one which relieves all pain, anesthesia might have been discovered three centuries sooner.

Perhaps Italian scholar, polymath and playwright, John Baptista Porta, had discovered the anesthetic potential of ether. In his 1597 work on “*Natural Magic*,” Porta noted:

At last shall be related a wonderful method by which any sleeping person may inhale a soporific medicine. From what we have said, any one will easily know that he is liable to suffer severely after sleep caused by medicine, and to have his suspicions aroused [11].”

“But the quintessence is extracted from a number of the above named medicines by somniferous (sleep-inducing) menstrual. This is put into leaden vessels perfectly closed, lest the least aura should escape, for the medicine would vanish away. When it is used, the cover being removed, it is applied to the nostrils of the sleeping person, he draws in the most subtle (sic) power of the vapour by smellings, and so blocks up the fortress of the senses that he is plunged into the most profound, sleep, and cannot be roused without the greatest effort. After the sleep, no heaviness of the head remains nor any suspicion of trick or fraud. These things are plain to the skilful physician, but unintelligible to the wicked [11].”

Although he does not describe what chemicals he uses, Porta (who sometimes was called a “professor of secrets”) could have been describing ether. Much later, John Snow (author of *On Chloroform and other Anaesthetics: Their Action and Administration*) reflects on Porta’s 1597 book and makes his own astute observations concerning Porta’s description. Snow states,

“The author [Porta] does not make known what the ‘somniferous menstrual’ were, with which the ‘quinta essentia’ were

Fig. 1.2a Using the approach used by Lully nearly three centuries earlier, Valerius Cordus (I.2) synthesized ether in 1540.

1.2b However, this time someone—Paracelsus (I.3)—made observations on pharmacological qualities of the new compound: “...it quiets all suffering without any harm, and relieves all pain...”



extracted. As sulphuric ether had been described more than fifty years before he published his work, it is not improbable that this was the evanescent substance which required the vessel be carefully closed up, and that the profound sleep was simply caused by this, as the narcotic principles dissolved in it would remain in the bottle in the form of extracts...Porta does not say that operations were performed under the influence of the inhalation, or in fact, that it was applied to any useful purpose whatever [11].”

Why didn’t Porta apply his observations to relieve the pain of surgery? Why didn’t Paracelsus do the same? As Winston Churchill observed: “Men stumble over the truth from time to time, but most pick themselves up and hurry off as if nothing happened.”

And what of possibilities other than ether might there been to diminish pain? Shakespeare reminds us of remedies such as the Mandrake root:

“Not poppy, nor mandragora,
Nor all the drowsy syrups of the world,
Shall ever medicine thee to that sweet sleep
Which thou ow’dst yesterday.”
Shakespeare: Othello III.iii

Just like the soporific sponge, the Mandrake root contains deliriant hallucinogenic tropane alkaloids, such as hyoscyamine and scopolamine [12]. Those who take sufficient hyoscyamine (an alkaloid precursor of scopolamine) may lapse into a coma, one that adds a risk of lethal increases in temperature because scopolamine can prevent sweating [13]. Enormous doses of scopolamine or its sister, atropine, have been used in the treatment of depression, so they are relatively safe as long as the ambient temperature does not require

sweating to keep cool [14, 15]. As already noted, although such doses may eliminate the remembrance of surgery, they do not produce anesthesia. They do not produce a patient who is immobile in the face of noxious stimulation [5].

The Seventeenth Century

By the turn of the seventeenth century, surgical procedures became more complex (and thus more painful), and the practice of medicine more professional. The scientific revolution was in full swing, and experimentation began to replace speculation. William Harvey’s 1628 book, *An Anatomical Exercise on the Motion of the Heart and Blood in Living Beings*, described his momentous discoveries concerning the anatomy and physiology of the circulation of blood, how blood moved from heart to artery to vein and back again [7]. And Hieronymous Fabricius ab Aquopendente, a teacher to Harvey, not only demonstrated venous valves but also used a technique for tracheotomies—puncturing the windpipe to allow passage of air—that is similar to the approach used today. Adding to Harvey’s contribution, in 1661, Marcello Malpighi described the capillaries and their function.

In the 1500s–1600s, Colleges of Physicians arose in England, Scotland and Ireland, acquiring the Royal prefix by the 1600s. This brought prestige to physicians (internists), but little to the surgeons. Surgeons continued to struggle for recognition in their field. French barber-surgeons eventually received the legal right to treat all wounds. As is the case today, the “private practice” barber-surgeons received higher fees

than their academic competition, the master surgeons. Even so, to make ends meet, in addition to doing surgery, barber-surgeons performed bloodletting and mundane wound care. They became more technically proficient than the academicians but did not contribute to advances in knowledge.

The seventeenth century saw the first demonstration of the possibility of intravenous anesthesia. In 1656, Christopher Wren (the architect for St. Paul's cathedral and a founder of the Royal Society) infused wine and ale from a syringe made of dog's bladder, through a goose quill needle into the vein of a dog [16, 17]. Wren wrote "I have injected wine and ale in a living dog into the mass of blood by a veine (sic), in good quantities, till I have made him extremely drunk, but soon after he pisseth it out." The dog survived the experiment. The dog, incidentally, was provided by Robert Boyle, author of Boyle's law. Wren later gave opium intravenously via a quill to dogs, causing unconsciousness in some animals but killing others [17]. Wren's experiment was the first known injection to produce anesthesia.

The Eighteenth Century: The Verge of Discovery

The eighteenth century brought the professionalization of medicine to Europe and eventually, to the US. By the 1700s, academic surgeons gradually became recognized as professionals equal to physicians, largely because they demonstrated the importance and interdependence of pathological (diseased) anatomy and pathophysiology (diseased function). French surgical training increasingly included teaching an accepted body of knowledge in courses and schools. Two events moved French surgery closer to a profession. One was the 1731 establishment of the Royal Academy or College of Surgery. Second was a 1743 Royal Declaration, forbidding master surgeons to work as barbers. Laws promulgated after the initiation of the French Revolution in 1789, added to the rise of surgery in France. The Faculty of Medicine and the College of Surgery were abolished in 1792, replaced in 1794 by the School of Health that imposed identical educational requirements for those practicing medicine and surgery [6, 7].

In the last half of the eighteenth century, surgery in Great Britain also progressed rapidly. In 1745, the British Parliament separated surgeons from the barber guilds by enacting a bill that formed a Corporation of Surgeons. Led by Percival Pott and John Hunter, [6, 7] Britain displaced France as the most important European center for surgical education and training. Pott and Hunter's knowledge of anatomy advanced surgery as a scientific discipline. Hunter made important observations, describing, for example, the pathophysiology of surgical diseases, and supplying observations on malignant tumors and the growth of collateral circulation after arterial occlusion. This information was particularly important to

treatment of aneurysms.² Pott connected the occupation of chimneysweeps with their development of scrotal cancer.

Medicine and surgery were stagnant in North America from 1600 to 1750, and self-educated "physicians" served most medical needs. As 1800 approached, Americans increasingly admired physicians, prompting progressive numbers of Americans to obtain training from the more advanced European system of medical education.

Eighteenth century internal medicine sped forward in diagnosis and treatment. The parallel development of eighteenth century pathological anatomy and experimental physiology strengthened the connection of internal medicine and surgery. Surgeons increasingly correlated disease with anatomical (pathological) changes. This reflected the view long held by physicians, that disease processes had physiologic consequences. Regardless of these developments, without anesthesia and antisepsis, surgery advanced slowly.

Several important discoveries were made during this period. One was by Englishman Joseph Priestly, who had committed himself to the ministry, but believed that understanding nature would further the aims of religion. Priestly's experiments resulted in the discovery of new gases or "airs", among them oxygen and nitrous oxide. He produced nitrous oxide by heating iron filings with nitric acid in 1772, publishing his studies three years later. However, like Paracelsus' oversight about the possibilities of ether two and a half centuries earlier, Priestly missed the significance of his discovery and little was then made of the new air.

Perhaps the most important discovery of the time originated from a 1735 expedition, led by French explorer Charles de la Condamine into South America's Amazon River region, where he observed the natives using blowpipes to propel poisonous arrows with lethal effects while hunting [18]. In 1769, while in South America, English physician Edwin Bancroft wrote of his observations of the natives concentrating the poisonous mix of bark and roots, noting that they avoided exposing wounds in their skin to the confection [19]. Bancroft brought samples of the poison, known as curare, back to England.

In 1811, English surgeon Benjamin Brodie, reported that although the poison caused breathing to cease in a donkey, the heart continued to beat, [20] and beating could be sustained if ventilation was supported [21]. In an 1814 demonstration, Brodie and Sewell, a veterinary surgeon, dramatically demonstrated the innocuousness of curare if ventilation

² Ironically, Hunter had angina pectoris, presciently noting that "my life is in the hands of any rascal who chooses to annoy and tease me." A fatal heart attack at age 65 followed an argument at St. Georges Hospital on 14 October 1793. Pott described the anatomy of congenital inguinal hernias in his "Treatise on Ruptures." He advocated emergent operations for incarcerated hernias. Most famous was his 1775 *Chirurgical Observations*, a 5-page essay correctly connecting scrotal cancer in chimney sweeps to their exposure to tars.

was supported. Sykes, a well-known surgeon described the experiment as follows [22]:

A she-ass received the wourali poison in the shoulder, and died apparently in 10 min. An incision was made in its windpipe, and through it the lungs were regularly inflated for two hours with a pair of bellows. Suspended animation returned. The ass held up her head and looked around; but the inflating being discontinued, she sunk once more in apparent death. The artificial breathing was immediately recommenced, and continued without intermission for two hours more. This saved the ass from final dissolution; she rose up, and walked about; she seemed neither in agitation nor in pain. The wound, through which the poison entered, was healed without difficulty...and by Midsummer (the ass) became fat and frisky...The kind hearted reader will rejoice on learning that Earl Percy, pitying her misfortunes, sent her down from London to Walton Hall, near Wakefield. There she goes by the name Wouralia. Wouralia shall be sheltered from the wintry storm; and when the summer comes she shall feed in the finest pasture. No burden shall be place on her and she shall end her days in peace."

To survive the paralytic effects of curare, Wouralia the donkey had a tracheotomy and ventilation with a bellows. Wouralia did just as Sykes described, and lived another 25 years in peace. The local paper supplied an obituary.

Prior to Brodie and Sewell's experiments, interest had already developed in approaches to secure the airway. As a result, their efforts built on the practice of earlier surgeons like Hooke, Kite, Herholdt and Rafn. In 1667, Robert Hooke performed an extraordinary and cruel sequel to Vesalius' 1550s experiment. Hooke showed that blowing air down the windpipe and out through multiple punctures in the lungs of an awake dog sustained life, even though the lungs were still. In 1788, Kite ventilated a drowning victim's lungs through a tube he placed blindly through the oropharynx and into the windpipe. Nearly a decade later, Herholdt and Rafn described blind digitally assisted tracheal intubation, to resuscitate drowning victims.

Some aspects of modern surgery and management of the airway arose early. Concentrating cohorts of war casualties or victims of epidemics in one place enhances their monitoring and care—in ancient or modern times—anticipating the development of hospitals. The Bible implies the use of mouth-to-mouth respiration (2 Kings, iv, 34), and midwives used it to revive the new-born. Slowly, science and medicine would bring together the airway and ventilatory necessities, the concentrating of patients to supply the intensive care that became part of modern anesthesia.

And What About Positive Thinking?

Other than Priestly's discovery of nitrous oxide, little else anticipated the approaching demonstration of anesthesia in 1846 besides the mind control that physicians and others long had practiced. Practitioners have seemingly forever

applied positive thinking and various forms of suggestion, including modern magical rings, necklaces and charms for the parturient. Greeks applied oils and warm compresses during labor, anticipating the warm compresses, massage and herbal teas used today. Were these placebos (which can have positive effects)? In the latter part of the eighteenth century, Franz Mesmer created "theories of animal magnetism," perhaps a form of hypnosis. Mesmerism provided an inconsistently effective management of the pain of surgery. The scientific establishment noted the absence of any rationale for Mesmerism's effectiveness.

Reprise

By the nineteenth century, the surgeon had become a full member of the medical community, contributing to the knowledge of human anatomy and pathology, and to an elaboration of surgical procedures. The operations performed included amputations, cataract removal, cesarean sections, cosmetic surgery, removal of bladder stones, ligation of major arteries, excision of superficial tumors, excision of anal fistulas, and repair of hernias. The range staggers the imagination, more so, given the absence of anesthesia. Surgeons focused on acute processes, conditions requiring immediate care: simple fractures, dislocations, and abscesses. Infection compromised treatment and was a constant threat to life. But most of all, pain limited the number of surgeries that might be performed, and thus limited progress in surgery.

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Summary

The gases and vapors later known as anesthetics had been synthesized or isolated before (ether, nitrous oxide and carbon dioxide) or would be synthesized in (chloroform) the period from 1798 through 1846. They served various purposes. In 1798–1800, Humphry Davy used nitrous oxide for recreation and research, noting its capacity to diminish or even abolish pain. He suggested its use for surgery, but no one noticed. In 1823, Hickman used carbon dioxide to cause what he called “suspended animation”, a state that permitted apparently painless surgery in animals. But no one noticed. In the 1840s, Clarke, Long, and Smilie each administered ether in amounts sufficient to permit surgery to be undertaken without pain. But they thought too little of what they had done, or didn’t know what they had done, to request public credit for their accomplishment. And no one noticed.

As indicated in the preceding chapter, despite the absence of anesthesia, despite the agony of surgery, despite the great risk of infection and death from infection, surgery intruded into any immediately accessible structure thought to need attention. The exemptions might be abdominal, thoracic, and intracranial operations, but surgeons might go even there. The agony of remembrance of surgery was expressed vividly, revealing what we know today as post-traumatic stress disorder (PTSD).

World Events in the Half Century Before Ether Day

In 1799 Napoleon staged a coup d’état, becoming First Consul of France, five years later crowning himself Emperor. With the 1803 Louisiana Purchase, the US more than doubled its size, buying The West. The steam engine appeared in 1804. Nelson defeated Napoleon’s fleet at Trafalgar in 1805, and winter defeated Napoleon’s army in Russia in 1812. After his defeat he was exiled to Elba (1814), but he escaped the next year, and began the Hundred Days leading to his final defeat at Waterloo. In 1820, a Russian expedition discovered Antarctica. Three years later, James Monroe declared his eponymous Doctrine (any effort by European nations to interfere with governance in North or South America or colonize land would be viewed by the US as an act of aggression). The first electric motor appeared in 1829 and in 1836, Samuel Colt

manufactured his six shooter. Several inventors made “telegraphs”, the one by Samuel Morse in the late 1830s being the most successful. Rowland Hill introduced the postage stamp in 1840. The first publicly funded telegraph line in 1844 sent Morris’ message: ‘What hath God Wrought?’ Two Opium Wars waged from 1839 to 1860 forced China to make many concessions to France, the UK, the US, and Russia, greatly weakening China’s power.

A Chronology of Major Themes up to Ether Day

1798–1800: Humphry Davy Misses the Gold Ring

In Bristol, England, Thomas Beddoes established the Pneumatic Institution to treat pulmonary tuberculosis with “new airs”, various gases including nitrous oxide. Traveling in 1798, he met the precocious 20-year-old Humphry Davy (1778–1829) and recruited him to superintend his laboratory. Davy (Fig. 2.1) vigorously pursued his charge, particularly in studies of nitrous oxide, studies involving self-experimentation to the point of addiction. Well, we might say, of course, but Keys points out that this took a bit of courage: “...an American chemist and physician, Samuel Latham Mitchill, administered nitrous oxide to animals with such dire results that he came to the conclusion that this gas was very poisonous [1].” We know now, that lack of oxygen rather than the nitrous oxide itself caused death, but who knew that then? “He (Mitchill) also believed that nitrous oxide

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Fig. 2.1 Humphry Davy, the precocious superintendent of the Pneumatic Institution in Bristol, described the capacity of nitrous oxide to prevent pain, suggesting its use in surgical procedures, but no one took up his suggestion

might possibly be the contagium for the spread of epidemics [1].” In addition, 5 years before Davy’s discoveries, Mitchill described the “anesthesia” produced by inhalation of nitrous oxide [2]. Thus, a mixture of courage, bravado, foolishness and addictive behavior probably underlay Davy’s inhalation of nitrous oxide. Keys wrote that “instead of dying, he (Davy) experienced many pleasurable sensations; he felt an agreeable sense of giddiness, a relaxation of the muscles, noticed his hearing to be more acute, and in general felt so cheerful that he was compelled to laugh.” By 1800, Davy had written a 580 page book describing his adventures [3], displaying more than a passing fondness for its properties: “... a desire to breathe (nitrous oxide) is always awakened in me by the sight of a person breathing, or even by that of an air-bag or an air-holder.” His is an early example of the potential of anesthetics to produce addiction.

On page 465 of Davy’s book, he described his self-treatment for the pain associated with eruption of a wisdom tooth:

“In cutting one of the unlucky teeth called *dentes sapientiae*, I experienced an extensive inflammation of the gum, accompanied with great pain, which equally destroyed the power of

repose and consistent action. On the day when the inflammation was most troublesome, I breathed three large doses of nitrous oxide. The pain always diminished after the first four or five respirations; the thrilling came on as usual, and uneasiness was for a few minutes swallowed up in pleasure. As the former state of mind returned, the state of organ returned with it; and I once imagined that the pain was more severe after the experiment than before.”

Part of this fits with what we now believe about the effects of nitrous oxide. It may decrease the perception of pain (i.e., cause analgesia), in part, by activating the receptors turned on by opioids such as morphine [4]. Tolerance (a decreased effectiveness) develops with nitrous oxide, especially with repeated administration, possibly explaining enhanced pain on recovery [5].

On page 556 of his book, we find Davy’s famous quotation suggesting the possibility of surgical anesthesia: “As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place [3].” His suggestion went unnoticed. This meteor of a man went on to discover several elements including sodium, and construct the miners’ safety lamp, but his inaction regarding nitrous oxide cost him anesthesia’s gold ring, the greatest discovery in all of medicine. He was immortalized by Edmund Clerihew Bentley’s poem (a *clerihew* is a poetic 4-line verse that takes the form AA, AA, BB, BB). The first-ever clerihew was perhaps written during a particularly boring chemistry lecture:

Sir Humphry Davy
Was not fond of gravity
He lived in the odium
Of having discovered sodium.

1800–1810

As the nineteenth century began, the US had but 4 medical schools. Benjamin Rush (1745–1813), professor at the foremost school, the University of Pennsylvania, had attempted to minimize labor pain by applying leeches to remove blood. Since the pain of childbirth caused stimulation, he reasoned that bloodletting would offer relief by producing an opposing depression. In defense of higher learning in the US, note that Rush obtained his medical education at the University of Edinburgh and St Thomas’ Hospital in London. Others shared his belief in the curative power of the removal of blood by venesection (Stanley, p 54) [6]: “In 1809, The Times reported on an American, Captain James Niblett, who over two months had been bled of 600 ounces of blood, more than fifty instances in addition to leeches.”

In 1803, Serturmer isolated morphine from opium.

Fig. 2.2 The agony of surgery without anesthesia and the violence of the response to surgery are readily imagined



1810–1820

Numerous reports describe the agony of surgery and the lingering after effects, what we might now call post traumatic stress disorder (PTSD). Columnist David Brooks wrote [7]: “In 1811, the popular novelist Fanny Burney learned that she had breast cancer and underwent a mastectomy without anesthesia:

“‘I felt the instrument—describing a curve—cutting against the grain, if I may so say, while the flesh resisted in a manner so forcible as to oppose & tire the hand of the operator who was forced to change from the right to the left...I began a scream that lasted intermittingly during the whole time of the incision—& I almost marvel that it rings not in my ears still.’ The surgeon removed most of the breast but then had to go in a few more times to complete the work: ‘I then felt the Knife racking against the breast bone—scraping it! This performed while I yet remained in utterly speechless torture.’”

Brooks noted that Burney wrote about more than the immediate experience. She described the recurring impact on her emotions. “Not for days, not for weeks, but for months I could not speak of this terrible business without nearly again going through it!... I dare not revise, nor read, the recollection is still so painful.” PTSD, indeed!

A patient of Scottish surgeon James Simpson provided another vivid description of the agony of remembrances of surgery [8]:

“Suffering so great as I underwent cannot be expressed in words...but the blank whirlwind of emotion, the horror of great darkness, and the sense of desertion by God and man, which swept through my mind, and overwhelmed my heart, I can never forget...Those are not pleasant remembrances. For a long time they haunted me, and even now they are easily resuscitated; and though they cannot bring back the suffering attending the events which gave them a place in my memory, they can occasion a suffering of their own, and be the cause of a disquiet which favors neither mental nor bodily health.”

It might have been nearly impossible for four strong men to restrain a terrified woman or man subjected to the knife (Fig. 2.2). And the struggles of the consenting patient could be sufficient to cause the operating table to disintegrate [9].

Yet surgery continued despite the woe it induced, despite the agony, despite the haunting memories. For some, pain was something to be borne, a misery that nonetheless did not preclude surgery or surgical advancement.

In 1818, Michael Faraday noted parallels between the effects of ether and nitrous oxide [10, 11]:

“When the vapour of ether mixed with common air is inhaled, it produces effects very similar to those occasioned by nitrous oxide...In trying the effects of the ethereal vapour on persons who are peculiarly affected by nitrous oxide, the similarity of sensation produced was very unexpectedly found to have taken place. One person who always feels a depression of spirits on inhaling the gas, had sensation of a similar kind produced by inhaling the vapour.”

Faraday raised a caution regarding ether [10]: “By the imprudent inspiration of ether, a gentleman was thrown into a very lethargic state, which continued with occasional periods of intermission for more than 30 hours, and a great depression of spirits; for many days the pulse was so much lowered that considerable fears were entertained for his life.”

Surgeons used counter-irritants “to inflict pain in the hope of healing [6].” They would apply blistering agents. They would remove blood with lances and leeches. In 1819, Sir Walter Scott, plagued with stomach cramps was subjected to

“profuse bleeding and liberal blistering” causing him to scream “without interval through the night, terrifying his family and servants...Looking back on the ordeal Scott reflected wryly that his doctors had told him that ‘mere pain cannot kill’...The suffering inseparable from treatment before or besides surgery, however, explains how the acute pain of surgery was perhaps merely an intensification of a regime in which prolonged pain was seen as an inevitable part of healing [6].” (p 56)

1820–1830

In the first half of the nineteenth century, surgeons devised operations of increasingly greater complexity, invasiveness and duration. Stanley [6] reported (pp 64–5) that in 1822,

“Working in a cottage in poor light Liston excised a tumour beneath McNair’s shoulder blade...I began by making an incision of a foot long...I felt my finger and knife dip into the body of the tumour...I immediately thrust my sponge into the cavity, so as to command the haemorrhagy. The patient, who had borne the operation well...now dropped his head off the pillow, pale, cold, and almost lifeless. I then...saw that nothing but a bold stroke of the knife could save the boy from immediate death. Pulling out the sponge, therefore, with one rapid incision I completely separated the upper edge of the tumour...After removing the tumour, I found it necessary to saw off the ragged and spongy part of the scapula, so as to leave only a fourth part of that bone....’ Liston’s patient survived the operation but died four months later....”

The Lancet was first published in 1823. Five years later, the *Boston Medical and Surgical Journal* (later the *New England Journal of Medicine*) began publication. Such journals plus newspapers described medical discoveries, including ether’s anesthetic properties just two decades later.

In 1823 and 1824, a young English surgeon, Henry Hickman (1800–1830), gave animals carbon dioxide to breathe, causing a “suspended animation” that allowed apparently painless amputation. Hickman reported his observations to the Royal Society and to Charles X in France, but neither responded. Well, he tried and then died of tuberculosis. Credit him with advancing the idea that surgery might be undertaken painlessly by the inhalation of an agent whose elimination could rapidly reverse the pain-relieving effect. This idea may have been crucial to the discovery of anesthesia. Otherwise the widespread belief of the inevitability of pain would prevent a search for a remedy.

In 1829, Babbington viewed the glottis, the opening to the larynx, using indirect laryngoscopy, i.e., viewing the larynx using mirrors. Increasingly we shall see attempts to control the freedom of the passage of air to the lungs. Viewing the larynx was important to such attempts.

1830–1840

The great surgeon, James Syme, operated on 95 patients in Minto House in 1830 [6]: 10 major amputations of the legs; 9 minor amputations of fingers or toes; 7 novel excisions of elbows or knees (i.e., removal of a diseased portion of the knee or elbow, thus avoiding amputation); 4 breast resections for cancer; excision of an upper jaw; removal of 11 tumors; 4 lithotomies (for bladder stone); ligation of 2 aneurysms; and repair of a strangulated hernia. He performed several minor operations: 6 for hemorrhoids; 4 for anal fistulas; 3 nasal

polyps; and 1 for cataract. All this in 1 year when Syme was aged 30.

In 1831, von Liebig, Soubeiran and Guthrie independently discovered chloroform.

1840: The State of Medicine and Surgery

By 1840, the US had 30 medical schools. The curriculum typically occupied two four-month blocks, and covered seven courses. Ability to pay entrance fees determined admission to most schools. Physicians supplemented their training with apprenticeships, the “house pupil” experience, or they traveled to Europe for advanced training. No medical students were women.

Latin American surgeons undertook operations in homes, hospitals, or local inns. In Europe, surgery and delivery might be accomplished in hospitals. Despite the absence of anesthesia, there seemed little that surgeons would not do. Nordic surgeons performed major operations; they removed the mandible, performed gastrectomies, and repaired inguinal hernias and cleft lips. In Chap. 3, Stanley [6] noted the many major procedures done in Great Britain that were improved upon in the first half of the nineteenth century, including trephination, amputation, herniotomy and lithotomy, each with multiple surgical approaches. The rectum offered 23 operable conditions.

“By the 1840s over twenty arteries could be ligated (for aneurism consequent to the considerable incidence of syphilis), most frequently the aorta, the popliteal (in the thigh), the inguinal (in the groin), the subclavian (near the collarbone), and the carotid (in the neck)...In 1832 in the distant colony of New South Wales, Australia, William Bland, one of Sydney’s most prominent surgeons attempted to ligate a subclavian aneurism of William Mullen, a convict. Mullen, whose wife had paid Bland twenty pounds, died after eighteen days. Bland attempted a second operation in 1837, keeping the patient on the table for five-and-a-half hours.” (Stanley pp 76–7)

Fergusson performed more than 200 cleft palate repairs in unanesthetized children – with a mortality rate of only 1% [12]. Most procedures were accomplished with dispatch. In London, Liston famously said before he began surgery: “Time me, gentlemen, time me!” Infection and mortality were ever present.

What could be done to diminish the agony of surgery? Latin American clergy and shamans used opium, herbal extracts, and alcohol to decrease surgical pain. Patients required restraint. In Australia and New Zealand, neither the aborigines nor the Maori used “anesthesia”, although aborigines chewed “pituri” or “pedgery”, herbs producing intoxication or hallucination. Pituri could cause respiratory arrest and death in animals.

Stanley (p 203) [6] argued that courage supported the surgeon as well as the patient. The surgeon dreaded the pain

he (no female surgeons) inflicted. He knew the immediate, sometimes bloody, disasters that awaited his actions. Loss of blood might kill the patient sooner, and infection later. “The desire to finish an operation quickly (whether from concern for the patient or for reputation) imposed a peculiar strain on operators. Some expressed this tension by shouting at the patient, colleagues or dressers. The tension showed in the haste with which, as Samuel Cooper said, surgeons sawed through bone with ‘short, very rapid, and almost convulsive strokes’.” Operations were done speedily to diminish the anguish of the patient. Amputations of the upper or lower extremities might be accomplished in 15 to 30 seconds with closure to follow (Stanley, pp 226–7) [6]. Although the operation might be accomplished with dispatch, cleaning up and closure could impose an hour of great misery: “As dressers wiped a sponge over the raw surface ‘perhaps studded by the truncated ends of large nerves,’ patients would twitch and gasp. At each ‘catch of the forceps and noosing of the ligature’ the patient might shriek” (Stanley, p 229) [6].

“The surgeon might lament what he had to do, ending surgery with tears in his eyes or retiring to vomit in solitude. Surgeons were known to faint mid-operation and their assistants had to supervene. Appetite lessened and sleep came hard.” (Stanley, p 205) [6] A tension existed between the necessity of surgical pain and the desire to heal. The focus of the surgeon might be intense: “After performing an amputation by transfixion in the Adelaide Hospital, (George Mayo) remarked ‘How quiet the patient has been!’ A colleague, startled at his absorption, retorted ‘Why, man, he was screaming all the time’” [6].

But there was a certain resignation. As the French surgeon Alfred Velpeau said in 1839, “The abolishment of pain in surgery is a chimera. It is absurd to go on seeking it...knife and pain are two words in surgery that must forever be associated in the consciousness of the patient.” Again, note this impediment to the discovery of anesthesia, the remedy that Velpeau said could not exist.

One also sees the foolishness of physicians in this time. In the early 1840s, surgeons treated stuttering by operation: “Yearsley...excised the patients’ uvula and tonsils...(giving) the patients ‘instantaneous’ relief.’ Patients previously ‘scarcely able to articulate half a dozen words’ became able to speak ‘with a wonderful degree of fluency’.” (Stanley, p 248) [6]—shades of Galen.

1840–1846: The Non-discovery of Ether Anesthesia

In the 1840s, several physicians/dentists discovered the anesthetic effects of ether before Ether Day, but either didn’t publicize their findings at the time, or didn’t appreciate what they had found. They knew of the inebriating effects of ether and employed it in one or a few patients. These early timid



Fig. 2.3 In 1842, Crawford Long used ether to deliberately provide anesthesia. He did not report this, despite his repeated successful application of ether for anesthesia. Like many others, he missed the gold ring. (Courtesy of the University of Pennsylvania Art Collection, Philadelphia, PA)

successes illustrate the caution and apprehension of those who didn’t realize that they had succeeded. Perhaps success required audacity, a daredevil ego, and greed. In 1842, William Clarke, who “was in the habit of entertaining his companions with inhalations of ether,” anesthetized a Miss Hobbie with ether poured on a towel [13]. Dr. Elijah Pope then extracted a tooth from Miss Hobbie “without pain” [13]. “This would appear to be the first use of ether anesthesia on record; it antedated the work of Crawford Long (1815–1878) by at least two months. Apparently Clarke considered his contribution of no importance, for it is not mentioned in an account of his life in Stone, RF: *Biography of Eminent American Physicians and Surgeons*, Indianapolis, Carlton and Hollenbeck, 1894, p. 89” [13]. Clarke’s failure to publicize his discovery cost him his place in history.

Like Clarke, Long (Fig. 2.3) had engaged in ether frolics; he knew the inebriation it produced and that ether might be safe to breathe, at least to levels that produced inebriation.

“The first patient to whom I administered ether in a surgical operation, was Mr. James M. Venable, who...consulted me on several occasions in regard to the propriety of removing two small tumours situated on the back part of his neck, but would