History

The history of regional anesthesia and pain management is filled with fabulous stories and great characters. Ancient Egyptians used a variety of analgesics including hyoscyamine, scopolamine, opium poppy, beer, juniper, and yeast to treat a variety of ailments including “pains within the body.” Ancient Indian culture used herbal medicine and yoga to overcome pain and create internal balance, and the ancient Chinese used acupuncture to properly channel negative energies and treat pain. The ancient Greeks gave the world Hippocrates (460–370 BC) who believed in the healing power of nature and focused on a rational approach to diagnosis and treatment rather than one based on superstition (Raj 2010).

Early giants in the field of medicine and philosophy were concerned with characterizing and understanding pain. Early teachings from Aristotle (384–322 BC) described pain as an emotion that was situated in the heart and it was not until Galen of Pergamon (AD 130–201) that people recognized that the brain was the organ responsible for pain sensation. Avicenna (AD 980–1037) described how pain sensation could be altered in various disease states, and Newton (1642–1727) and Hartley (1705–1757) described the potential role of nerves in transmitting noxious stimuli from the periphery to the brain (Perl 2007). Despite these advances in knowledge, the Middle Ages remained an unpleasant period of time in which to require a surgical procedure when even invasive surgeries were performed without anesthesia.

Early attempts at medicinal pain control typically originated from plant material and included opium (Papaver somniferum), alcohols, mandrake (Atropa mandragora), belladonna (Atropa belladonna), and marijuana (Cannabis). Friedrich Wilhelm Sertürner (1783–1841) isolated morphine from the opium plant in 1803. Aspirin (acetylsalicylic acid) was released in 1899 by the Bayer Company and quickly became the common man’s “go to” therapy for mild to moderate pain relief (Raj 2010).

The natives of Peru are attributed with being the first to “use” a local anesthetic—the cocoa leaf, known for both its analgesic and hallucinatory properties. During surgical procedures, they obtained local anesthesia by chewing the leaves of the plant and allowing the resulting saliva to run into the fresh incisions. Chewing the leaves of the cocoa plant was also reported to “assuage the hungry,
invigorate the weary and brighten the depressed.”

The cocoa plant was also important in the Peruvian natives’ religious and political lives (Keys 1942; Fink 1985). The Spaniards who conquered the native Incan people initially described chewing cocoa leaves as the “work of the devil,” but when they recognized the profit that could be made, they legalized it and taxed the revenue from plant sales. Bernabe Cobo described the first analgesic use of cocaine in 1653 when he discussed the native Incan practice of using the cocoa leaves to cure a toothache. In 1859, Paolo Mantegazza described Peruvian natives using cocoa leaves for the treatment of “a furred tongue in the morning, flatulence and whitening the teeth.” While on a trip to South America, Scherzer noticed that the leaves numbed the tongue when they were chewed, and he went on to become the first person to make a report in the literature about its anesthetic qualities (Keys 1942; Deschner et al. 2007).

A necessary prerequisite to performing regional anesthesia was the development of the hypodermic needle and syringe. In 1836, Lafargue reported injection of morphine paste subcutaneously using a needle trocar. In 1839, Taylor and Washington began the practice of using hypodermic medication for relief of pain when they punctured the skin using lancets followed by injection of morphine solutions using syringes. In 1845, Francis Rynd described the potential benefits that could be obtained from perineural injections of opioids. In 1853, Alexander Wood invented the hollow needle and in that same year Charles Gabriel Pravaz attached an improvised hollow needle to a specially constructed syringe, completing the combination of equipment that we still use today (Raj 2010; Deschner et al. 2007).

In 1855, Friedrich Gaedcke was the first to isolate the active alkaloid from the cocoa plant, naming it “erythroxyl.” In 1860, Albert Nieman (1834–1861) isolated this ingredient in crystalline form (naming it “cocaine”) and reported anesthesia of the tongue when it was tasted (Cousins and Bridenbaugh 1988; Deschner et al. 2007). In 1872, Theodor Aschenbrandt, an Austrian army officer, secretly put cocaine into the water of his soldiers and found that it improved endurance (Fink 1985). In 1880, Vasili Konstantinovich Von Anrep (1854–1925) thoroughly studied the pharmacology of cocaine. He developed a solution of cocaine and found that it could both abolish the sensation of taste and create anesthesia when applied to the tongue. Von Anrep also injected cocaine subcutaneously under the skin of his own arm and discovered that he created an area of anesthesia that lasted about 35 minutes. At the same time, others were experimenting with use of cocaine solutions for blocking corneal reflexes in animals and for treating painful diseases of the larynx and pharynx (Keys 1942; Deschner et al. 2007).

With the groundwork completed, all that was now needed was for someone to apply what had been learned about cocaine and apply it to the surgical arena. The development and use of cocaine as a local anesthetic agent is primarily attributed to Karl Koller. While Koller was practicing as a house surgeon at the Vienna General Hospital, his friend Sigmund Freud happened upon the beneficial reports of cocaine and studied its use for curing patients with morphine addiction (Fink 1985). Koller wanted to be accepted into an ophthalmology training program and was well aware of the search for a topical anesthetic to allow surgery to be performed on the eye. Prior to the introduction of cocaine anesthesia into clinical practice, eye surgery was nearly impossible to perform, given that general anesthesia typically induced coughing and vomiting, consequences to be avoided during eye surgery. He had read the reports of cocaine causing anesthesia of the tongue and had even tried it on his own tongue before arriving at the realization that cocaine could be topically applied to the eye. He first applied topical cocaine to the eye of a frog and when the frog did not move in response to touching of its cornea, regional anesthesia was truly born. He reported these findings to the Ophthalmological Congress in Heidelberg in September 1884, and the world’s first surgery performed under regional anesthesia was completed as Koller anesthetized a patient’s eye with cocaine for glaucoma surgery. Dr. Koller’s assistant later wrote of the discovery:

“We could make a dent in the cornea without the slightest awareness of the touch, let alone any unpleasant sensational reaction.”

With that demonstration, the discovery of local anesthesia was complete and cocainization of the eye for production of local anesthesia was generally
adopted. “I rejoice that I was the first to congratulate Dr. Koller as a benefactor of Mankind,” wrote an assistant of Koller’s (Fink 1985; Leonard 1998; Deschner et al. 2007). Freud referred to his former colleague Koller as “Coca Koller” and Koller described Freud as his “muse” (Fink 1985; Deschner et al. 2007).

In 1884, William Halsted (1852–1922) was the first to describe cocaine application to accessible peripheral nerves to perform dental blocks, thus obtaining “conduction” anesthesia in peripheral regions. The mandibular nerve was the first nerve he blocked. Halsted and Hall also performed a variety of other peripheral nerve blocks on themselves and medical student “volunteers” (Cousins and Bridenbaugh 1988). The next challenge in the evolution of regional anesthesia was to locate and inject a peripheral nerve percutaneously and blindly.

G.L. Corning, a neurologist, was the first to report an intravenous injection of local anesthetic with proximal venous occlusion for distal anesthesia. Corning is also credited with inducing the first spinal anesthesia in a dog, when he injected cocaine into the space between two adjoining spinous processes in a dog in 1885 and uncovered the possibilities of spinal anesthesia. He reported that the injection of a cocaine solution into the space between the spinous processes of two inferior dorsal vertebrae resulted in anesthesia of the dog’s hind legs without affecting the anterior extremities. He subsequently performed a similar procedure in a man, resulting in anesthesia to the subject’s legs and genitalia (Cousins and Bridenbaugh 1988). He later pondered:

“Whether the method will ever find an application as a substitute for etherization in genito-urinary or other branches of surgery, further experiments alone can show.”

Corning is also credited with the first regional anesthetic peripheral nerve block after injecting a solution of cocaine around the median cutaneous antibrachii nerve in 1887 (Fink 1985; Ball and Westhorpe 2003; Deschner et al. 2007).

Carl-Ludwig Schleich (1859–1922) first described a technique for infiltration anesthesia to the German Congress of Surgeons in 1892. Previously in 1869, Pierre Edouard Potain used subcutaneous injections of water to provide skin anesthesia and Schleich described how both water and saline had weak anesthetic properties. Subcutaneous injections of water were associated with significant pain so Schleich took the next step and added cocaine to his injectate solution. Using his low-concentration cocaine solution for subcutaneous infiltration, Schleich was able to perform a variety of peripheral surgical procedures. Two years later, his methods had been widely adopted and were being used in the United States (Cousins and Bridenbaugh 1988; Deschner et al. 2007).

In 1897, Braun demonstrated that the toxicity of cocaine was in proportion to its rate of absorption, and recommended the addition of epinephrine to the solution of cocaine in order to decrease its rate of absorption and increase the duration of anesthesia—something anesthetists still commonly perform today (Braun 1914).

August Bier performed the first spinal anesthetics in 1898 when he injected the spinal canals of animals, himself, and an assistant (August Hildebrandt) with a solution of cocaine. Bier described the procedure of spinal anesthesia on six patients and one colleague in a manuscript written in 1899. First, Bier performed spinal anesthesia with intrathecal cocaine on his colleague Hildebrandt. Bier then subjected Hildebrandt to a series of painful insults including making a small skin incision on his thigh, applying a burning cigar to his legs, and applying strong blows to his shin with an iron hammer, without any apparent perception of pain on the part of Hildebrandt. Bier then went on to describe the problems associated with experimenting on himself and Hildebrandt when he detailed how Hildebrandt later developed pain in the distribution of his legs where “sensibility had been tested by crushing and heavy blows.” Bier also described what we would now recognize as postdural puncture pain but attributed it to:

“...Treating our bodies too lightheartedly. Instead of laying down and resting following the lumbar puncture and injection of cocaine, we went about our avocations, drank and smoked more than was good for us, and performed our normal work the next day.”

(Wulf 1998)

Between the time that Bier first performed spinal anesthesia and 1910, the techniques must have
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become widely adopted, because in 1909–1910, Tyrell Gray described performing spinal anesthesia in children and explained that his patients were comfortable enough to “eat cake throughout the duration of the surgical procedure” (Brown 2012).

In 1908, August Bier described the first use of intravenous regional anesthesia, the “Bier block” that still bears his name (van Zundert et al. 2008). In 1911, Georg Hirschel described the axillary brachial plexus block and D. Kulenkampff described the supraclavicular brachial plexus block (Cousins and Bridenbaugh 1988). Louis Gaston Labat (1877–1934) further popularized the use of regional anesthesia in the United States by authoring the text Regional Anesthesia: Its Technic and Clinical Application in 1920. Despite Labat himself commenting that the text was likely as popular as it was secondary to “the clear, concise descriptions carefully illustrated by half-nude women,” his text served as the definitive text on regional anesthesia for 30 years and clearly helped to expand and advance the practice of regional anesthesia (Cousins and Bridenbaugh 1988; Cote et al. 2003).

One of the dangers associated with cocaine regional anesthesia is that the drug has euphoric, hallucinogenic, and, ultimately, addictive properties. Sadly, many of the early names in regional anesthesia that experimented on themselves developed addictions to cocaine. Due to these properties, and with the advances in chemistry and manufacturing, alternative local anesthetic molecules were subsequently developed. Amylocaine was developed as an early alternative to cocaine but it was abandoned when it was found to be an irritant. Procaine was developed in 1904 and was introduced into clinical practice in 1905. Procaine very quickly replaced cocaine in practice but its use was limited by its short duration and the potential for it to produce allergic reactions. Dibucaine (1925) and tetracaine (1928) were synthesized to create local anesthetics of longer duration, but they continued to have unacceptably high allergenic potential. Lidocaine was developed in the mid-1940s, a revolutionary new amide local anesthetic with decreased potential for allergic reactions. Mepivacaine (1957), bupivacaine (1957), prilocaine (1969), and etidocaine (1972) were all subsequently released into clinical practice. Mepivacaine and bupivacaine are still commonly used. Recently, ropivacaine has been developed as another long-acting local anesthetic agent, and, compared to other agents, has less motor blockade and decreased potential for cardiac toxicity (Brown et al. 2010).

The use of regional anesthetic techniques in animals started near the turn of the twentieth century (Lumb and Jones 1973). Cuille and Sendrail induced subarachnoid anesthesia in horses, cattle, and dogs in France in 1901. Cathelin reported the use of epidural anesthesia in dogs in 1901, but it took until the 1920s for this technique to be adapted by Retzgen, Benesch, and Brook for use in large animals. Later, in the 1940s, Farquharson and Formston developed paravertebral techniques for cattle. By the 1960s, local anesthetic techniques were commonplace in veterinary practice and chapters that described their pharmacology and use were included in many veterinary textbooks. Many of the drawings and images that we still use today are based on figures from Wright’s Veterinary Anesthesia and Analgesia (first published in 1941, Hall 1966) and Lumb and Jones’ Veterinary Anesthesia (first published in 1973). Today, the science is catching up to the art, and local and regional anesthetic techniques continue to have an ever more important role in acute and chronic patient management of veterinary species.

Peripheral nerve blocks

Although the practice of neuraxial (spinal, epidural) anesthesia has changed minimally over the years, peripheral nerve blockade has undergone multiple shifts in both philosophy and technique. Originally, correct needle positioning was simply approximated by anesthesiologists who would use their knowledge of anatomy to estimate the locations of target nerves. Later, techniques involved asking the patient to report “paresthesias”—the nerve tingling in the distribution of the target nerve to be blocked after the needle had been inserted close to the target nerve. Anesthesiologists at that time were governed by the words of Moore “No paresthesia, no anesthesia,” and they relied heavily on patient feedback to finalize needle position prior to drug administration. Traditional techniques also relied upon the anesthesiologist sensing palpable and subjective “pops” or “clicks” as their needles traveled through various fascial planes, and detecting arterial pulsations transmitted along the length of their
needles as they came in close proximity to major arteries (Dillane and Tsui 2012).

Nerve stimulation

In 1780, Luigi Galvani applied static electricity-charged metal electrodes to frog sciatic nerves and showed that electrical stimulation of peripheral nerves would result in muscle contractions. In 1850, H. von Helmolz investigated isolated nerve-muscle specimens. Based on those studies, he formed the concept that when an electrical stimulus is applied to a nerve, a threshold must first be reached before an action potential can result in creation of a muscle contraction. Georg Perthes first reported the clinical use of electrical nerve stimulation for nerve blocks in 1912 in Germany. In 1962, Greenblatt and Denson reported their use of a portable nerve stimulator for nerve localization, and in 1966, battery powered portable nerve stimulators first appeared in clinical practice (Dillane and Tsui 2012). In 1984, specially designed needles became available for electrostimulation of nerves. These needles had electrically insulated shafts but naked metal tips that served as electrodes during nerve stimulation (Ford et al. 1984). This technological development resulted in worldwide growth and interest in medical nerve blocks. By being able to “find” target nerves through visualization of motor responses prior to injection of local anesthetic solutions, nerve stimulation was reported to increase the chances of successful nerve blockade while at the same time reducing the volume of local anesthetic that was required. There was a belief that at certain stimulating currents, target nerves could be identified before the needle tip contacted the nerve itself, thus minimizing the risk of patient injury during needle placement and/or injection of the local anesthetic. Nerve stimulation for nerve localization was found to be associated with a decreased incidence of nerve trauma and Gentili and Wargnier coined the phrase “no paresthesia, no dysesthesia” (Dillane and Tsui 2012).

Ultrasound visualization

Ultrasound guidance has become popular as a nerve localization tool in people, and its use during regional anesthesia has recently been called the “new gold standard.” The advantage of ultrasound guidance is that variation in individual patient anatomy no longer negatively affects block success rates. As target nerves can be “seen,” they can more effectively be located with a needle tip prior to injection of the local anesthetic solution. Compared with the use of nerve stimulation alone, ultrasound guidance has been shown to result in a higher rate of successful peripheral nerve blockade, decreased block set-up times and longer block durations. When Orebaugh et al. (2007, 2009) studied the use of ultrasound guidance versus nerve stimulation for peripheral nerve blockade performed by anesthesia residents, they found that ultrasound guidance resulted in decreased procedure times, needle insertions, and inadvertent vascular punctures (Orebaugh et al. 2007, 2009).

A study by Robards et al. (2009) demonstrated that nerve stimulation might not confer the added safety benefits with which it was initially credited. In their study using combined ultrasound guidance and nerve stimulation to perform sciatic nerve blocks in the popliteal fossa, they found that in 4/24 patients a current of 1.5 mA (a typical current used during regional anesthesia) failed to produce a visible motor response even though needles were placed intraneurally (Robards et al. 2009). Ultrasound guidance has the added benefit of being able to visualize vascular or other anatomical structures that should be avoided during needle placement (i.e. pleura, peritoneum, etc.), but its use is limited by equipment availability and operator skill. In theory, the decreased volume of local anesthetic that is required to block a nerve when ultrasound guidance is used should confer added safety to the patient. However, despite all of these reported advantages, in people there is no definitive evidence to support a safety benefit of using ultrasound guidance versus nerve stimulation, and the debate continues over the role of nerve stimulation and ultrasound guidance in the performance of regional anesthesia (Chin and Chan 2008; Griffin and Nicholls 2010).

Rationale for loco-regional anesthesia and analgesia

Why all of this excitement and interest in the field of regional anesthesia? For many practitioners,
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Regional anesthesia offers the potential to put the anatomical knowledge that they have acquired throughout the years into practice. The use of regional anesthesia is intellectually challenging and incredibly rewarding. The benefits for your patients are often quite obvious as you take a patient in excruciating pain and make them comfortable when they are in the vulnerable postoperative period.

The anesthesia literature is filled with studies further demonstrating the benefits of regional anesthesia. The list of indications for regional anesthesia continues to expand as the number of regional techniques expands or is improved upon to allow more peripheral techniques to be performed. Pain itself has been demonstrated to have a number of adverse effects throughout the body. It impacts the respiratory system by promoting atelectasis, ventilation-to-perfusion mismatching, arterial hypoxemia, hypercapnia, and pneumonia. In the cardiovascular system, pain has been shown to produce hypertension, tachycardia, myocardial ischemia, and cardiac dysrhythmias. Pain impacts the endocrine system by promoting hyperglycemia, sodium/water retention, and protein catabolism. It can cause urinary retention, decreased clotting ability, impaired coagulation, and decreased immune function (Stoelting and Miller 2007).

Decreases in morbidity and mortality, improved postoperative pain control and decreases in perioperative complications have been listed as potential benefits of regional anesthesia in people. A meta-analysis that compared intraoperative neuraxial to general anesthesia (141 randomized controlled trials, 9559 patients) demonstrated that neuraxial anesthesia was associated with a decrease in mortality from 2.8% to 1.9% (Rodgers et al. 2000). A study evaluating the Medicare claims database found that when an epidural was used for postoperative analgesia, mortality was reduced at 7 days (0.5% vs. 0.8%) and 30 days (2.1% vs. 2.8%) postoperatively (Wu et al. 2004). Another database analysis of 259,037 patients found that epidural anesthesia was associated with a decrease in mortality from 2.0% to 1.7% (Wijeysundera et al. 2008). Despite the exciting findings of the above-mentioned studies, other investigations have failed to find mortality benefits and it is likely that mortality benefits truly exist only for the sickest patients undergoing high-risk procedures (Peyton et al. 2003). Thoracic epidural anesthesia has been demonstrated to have more clear benefits with regard to perioperative cardiovascular (myocardial infarction and dysrhythmias) and pulmonary (postoperative pulmonary complications, pulmonary infections, and respiratory failure) events. Thoracic epidural and regional anesthesia has been associated with faster recovery of bowel function, improved postoperative rehabilitation, improved pain control, decreased opioid requirements, and fewer opioid-related side effects (Hanna et al. 2009). An exciting frontier of investigation in the world of regional anesthesia focuses on the ability of nerve blockade to attenuate the amount of perioperative immunosuppression typically encountered in the perioperative period. This may have important implications with regard to the incidence of recurrence or metastatic cancer following cancer resection surgery (Exadaktylos et al. 2006).

As with all areas of veterinary medicine, local and regional anesthetic techniques have evolved rapidly over the last 20 years. Veterinarians and their staff are very interested in techniques that contribute to pain management and patient care, and as a result, the use of local anesthesia is being “rediscovered” after playing a secondary role in pain management due to the widespread development and use of opioids and NSAIDs over the last few years. If what physicians have learned about the benefits of local and regional anesthetic techniques has any application to animals (which they would be expected to), then we can look forward to an exciting few years to come!

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