1 Introduction: Use, Definitions, History, Concepts, Classification, and Considerations for Anesthesia and Analgesia

William J. Tranquilli[1] and Kurt A. Grimm[2]
[1]College of Veterinary Medicine, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA
[2]Veterinary Specialist Services, PC, Conifer, Colorado, USA

Chapter contents

Introduction

Veterinary anesthesia continues to evolve as a science and specialty within the veterinary profession. The major drivers of change are advances in medical technology and pharmaceutical development for domesticated animals or those adapted from human anesthesiology; research in physiology, pharmacology, and clinical trials for human and veterinary patients that provide better evidence-based guidance for patient care; and socioeconomic and demographic changes in countries where animals serve evolving roles. Veterinary anesthesiologists will continue to be advocates for patient safety, humane care through education about pain management and quality of life, and educators of the profession and society at large about the current best practices in anesthesia, analgesia, and pain management.

Use of anesthesia, sedation, and analgesia

Proper use of anesthetics, sedatives, and analgesics can alleviate pain, create amnesia, and produce muscle relaxation essential for safe and humane patient care [1]. Important uses include facilitation of immobilization for various diagnostic, surgical, and therapeutic procedures; safe transportation of wild and exotic animals; and euthanasia and the humane slaughter of food animals. Anesthesia, sedation, and analgesic drug administration are not without significant patient risk and are not recommended for trivial reasons. The continued development of better techniques and drugs along with the concerted and continuing effort to educate veterinary care providers has minimized the overall risk of anesthesia and pain alleviation in an ever-increasing and more sophisticated patient care environment. Any discussion with the animal-owning public, such as that occurring with owners when obtaining informed consent, requires use of proper terminology to convey the issues central to the safe delivery of veterinary anesthesia and pain therapy.

Definitions

The term *anesthesia*, derived from the Greek term *anaisthaesia*, meaning 'insensibility,' is used to describe the loss of sensation to the entire or any part of the body. Anesthesia is induced by drugs that depress the activity of nervous tissue locally, regionally, or within the central nervous system (CNS). From a pharmacological viewpoint, there has been a significant redefining of the term general anesthesia [2]. Both central nervous stimulants and depressants can be useful general anesthetics [3].

Management of pain in patients involves the use of drugs which are often called *analgesics*. The term is derived from *an*, which is the negative or without, and *alges(is)*, meaning pain [4]. Clinical management of pain often results in varying degrees of effectiveness that represent states of *hypoalgesia*, or decreased sensation of pain. It is important to understand that the administration of an analgesic drug does not necessarily create the state of analgesia.

Several terms are commonly used in describing the effects of anesthetic and pain-inhibiting drugs:

1. *Analgesia* is the absence of pain in response to stimulation which would normally be painful. The term is generally reserved for describing a state in a conscious patient [5].
2. *Nociception* is the neural process of encoding noxious stimuli [5]. Nociception is the physiologic process that underlies the conscious perception of pain. Nociception does not require consciousness and can continue unabated during

Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones.
Edited by Kurt A. Grimm, Leigh A. Lamont, William J. Tranquilli, Stephen A. Greene and Sheilah A. Robertson.

general anesthesia if techniques that interrupt or inhibit the transduction, transmission, and modulation of nociceptive stimuli are not included.

3. *Pain* is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [5].
4. *Tranquilization* results in behavioral change wherein anxiety is relieved and the patient becomes relaxed but remains aware of its surroundings. Tranquilizers are drugs that result in tranquilization when administered; however, many prefer to use the term anxiolytic or anti-anxiety drug when describing drugs that result in both reduced anxiety and relaxation.
5. *Sedation* is a state characterized by central depression accompanied by drowsiness and some degree of centrally induced relaxation. The patient is generally unaware of its surroundings but can become aroused and is responsive to noxious stimulation. Sedatives are not recommended by themselves to immobilize a patient during times which painful stimuli are likely to occur.
6. *Narcosis* is a drug-induced state of deep sleep from which the patient cannot be easily aroused. Narcosis may or may not be accompanied by antinociception, depending on the techniques and drugs used.
7. *Hypnosis* is a condition of artificially induced sleep, or a trance resembling sleep, resulting from moderate depression of the CNS from which the patient is readily aroused.
8. *Local analgesia* (*anesthesia*) is a loss of pain sensation in a circumscribed body area.
9. *Regional analgesia* (*anesthesia*) is insensibility to pain in a larger, though limited, body area usually defined by the pattern of innervation of the effected nerve(s) (e.g., paralumbar nerve blockade and anesthesia).
10. *General anesthesia* is drug-induced unconsciousness that is characterized by controlled but reversible depression of the CNS and perception. In this state, the patient is not arousable by noxious stimulation. Sensory, motor, and autonomic reflex functions are attenuated to varying degrees, depending upon the specific drug(s) and technique(s) used.
11. *Surgical general anesthesia* is the state/plane of anesthesia that provides unconsciousness, amnesia, muscular relaxation, and hypoalgesia sufficient for painless surgery.
12. *Balanced anesthesi*a is achieved by the simultaneous use of multiple drugs and techniques. Drugs are targeted to attenuate specifically individual components of the anesthetic state, that is, amnesia, antinociception, muscle relaxation, and alteration of autonomic reflexes.
13. *Dissociative anesthesia* is induced by drugs (e.g., ketamine) that dissociate the thalamocortic and limbic systems. This form of anesthesia is characterized by a cataleptoid state in which eyes remain open and swallowing reflexes remain intact. Skeletal muscle hypertonus persists unless a strong sedative or peripheral or central muscle relaxant is co-administered.

Brief history of animal anesthesia

In 1800, Sir Humphrey Davy suggested that nitrous oxide might have anesthetic properties. Twenty four years later, H. H. Hickman demonstrated that pain associated with surgery in dogs could be alleviated by inhalation of a mixture of nitrous oxide and carbon dioxide. He reasoned that the latter increased the rate and depth of breathing, thus enhancing the effects of nitrous oxide. More recent studies have shown that unconsciousness can be induced in 30–40 s in piglets breathing carbon dioxide (50%) in oxygen (50%) [6].

It was not until 1842 that diethyl ether was used for human anesthesia. Two years later, a dentist, Horace Wells, rediscovered the anesthetic properties of nitrous oxide. Although this finding was neglected for several years, nitrous oxide was introduced to human anesthesia in 1862. C. T. Jackson, a Boston physician, was the first to employ diethyl ether extensively in animals [7].

Chloroform was discovered by Liebig in 1831, but it was not until 1847 that it was first used to induce anesthesia in animals by Flourens and in people by J. Y. Simpson of Edinburgh, Scotland. With the introduction of chloroform, reports began to appear in the veterinary literature of its use in animals. Dadd routinely used general anesthesia in animals and was one of the first in the United States to advocate humane treatment of animals and the application of scientific principles (i.e., anesthesia) in veterinary surgery [8].

In 1875, Ore published the first monograph on intravenous anesthesia using chloral hydrate; 3 years later, Humbert described its use in horses. Pirogoff was the first to attempt rectal anesthesia with chloral hydrate in 1847. Intraperitoneal injection was first used in 1892 in France. Thus, various routes of administration of general anesthetics to animals had been identified and minimally investigated by the end of the 19th century.

After the initial isolation of cocaine by Albert Niemann of Germany in 1860, Anrep, in 1878, suggested the possibility of using cocaine as a local anesthetic. In 1884, Kohler used cocaine for local anesthesia of the eye, and Halsted described cocaine regional anesthesia a year later. Its use was popularized by Sir Frederick Hobday, an English veterinarian. Thereafter, G. L. Corning was credited for using cocaine for spinal anesthesia in dogs in 1885. From his description, however, it would appear that he induced epidural anesthesia. In 1898, August Bier of Germany induced true spinal anesthesia in animals and then in himself and an assistant [9].

While local infiltration was popularized by Reclus (1890) and Schleich (1892), conduction regional anesthesia had been earlier introduced by Halsted and Hall in New York in 1884. These techniques increased in popularity with the discovery of local anesthetics less toxic than cocaine. These developments enabled Cuille and Sendrail (1901) in France to induce subarachnoid anesthesia in horses, cattle, and dogs. Cathelin (1901) reported epidural anesthesia in dogs, but it remained for Retzgen, Benesch, and Brook to utilize this technique in larger species during the 1920s. Although paralumbar anesthesia was employed in humans by Sellheim in 1909, it was not until the 1940s that Farquharson and Formston applied this technique in cattle. Despite these promising advancements in local analgesic techniques in the latter half of the 19th century, likely owing to the many unfavorable results, general anesthesia and humane surgery were not readily adopted by the veterinary profession until well into the 20th century. It is sad to say, but a 'heavy hand,' without analgesia/anesthesia or even sedation, was the stock in trade of many 'large animal' practicing veterinarians well into the latter half of the 20th century.

In smaller domestic animals, diethyl ether and chloroform were commonly administered in the early part of the 20th century. However, general anesthesia became more widely accepted after

the discovery of barbiturates in the late 1920s and, in particular, with the development of pentobarbital in 1930. Barbiturate anesthesia received an additional boost with the introduction of the thiobarbiturates and particularly thiopental in 1934. Because of rough, prolonged recovery, the acceptance of barbiturate general anesthesia in larger species of animals was delayed until phenothiazine derivatives were also introduced by Charpentier in France in 1950.

General anesthesia of large farm animals was further advanced by the discovery of fluorinated hydrocarbons and the development of 'large animal' inhalant anesthetic equipment for safe administration. The discovery of newer classes of drugs together with their safe co-administration (e.g., tranquilizers, opioids, α_2-adrenergic receptor agonists, dissociatives, muscle relaxants, and inhalant anesthetics) has further advanced the safety and utility of veterinary anesthesia for both large and small animal species [10].

The modern era of veterinary anesthesia was initiated during the last three decades of the 20th century facilitated by the establishment of anesthesia specialty colleges within North America and Europe. Stated organizational missions were the improvement of patient safety and the development of new techniques and knowledge paralleling the advances made in human anesthesia. New drugs and techniques are continually being evaluated for clinical usefulness in a variety of species and individual patient pathologies. In addition, an appreciation of patient monitoring for improved safety has led to the adaptation of technologies such as pulse oximetry, capnography, and blood pressure measurement. The veterinary anesthesiologist's value as a member of the patient care team has led to an ever-increasing presence in private veterinary practice. A more sophisticated approach to anesthesia care has become evident with an increasing patient age demographic. This demand will continue to expand the anesthesiologist's importance to our profession beyond the traditional roles of university instructors and pharmaceutical researchers. Demand has also been bolstered by the veterinary profession's quest to improve patient quality of life through better pain management. Many anesthesiologists have been leaders in this area through continued research and the creation of evidence-based species-specific pain-assessment scales and therapeutic guidelines.

History of North American organizations

During the late 1960s and early 1970s, a small group of physician anesthesiologists made it possible for a number of future diplomates of the American College of Veterinary Anesthesiologists (ACVA), now the American College of Veterinary Anesthesia and Analgesia (ACVAA), to participate in their training programs and to learn about the development of new anesthetic drugs and techniques. Among these physicians were Robert Dripps, University of Pennsylvania; Arthur Keats, Baylor University; Mort Shulman and Max Sadolv, University of Illinois; and Edmond I. Eger, University of California Medical College. During this same period, E. W. Jones (Oklahoma State University) and William Lumb (Colorado State University) were making significant contributions to the field of veterinary anesthesiology. Jerry Gillespie had made significant contributions through his work on the respiratory function of anesthetized horses and William Muir was reporting on the cardiopulmonary effects of various anesthetic drugs in various species.

Even though there were many dedicated faculty within North American veterinary colleges and research laboratories, it was not until 1970 that a major effort was made at organizing veterinarians interested in anesthesiology as a stand-alone specialty. Initially, the American Society of Veterinary Anesthesia (ASVA) was established. Membership of the ASVA was open to all individuals working in the veterinary profession who had an interest in veterinary anesthesiology. In 1970, the first organizational meeting was held in conjunction with the American Veterinary Medical Association (AVMA) to coordinate the efforts/interest of all those wishing to develop the specialty of veterinary anesthesiology. Their primary goal was to improve anesthetic techniques and to disseminate knowledge whenever and wherever possible. Charles Short was elected the first President of the new society. The ASVA was designed expressly to promote dissemination of information irrespective of individual training or background. Of major emphasis was the selection of individuals to speak at the ASVA and other scientific and educational meetings. As the ASVA developed, publication of original research and review articles seemed in order. Bruce Heath accepted editorial responsibilities for manuscripts submitted for the ASVA journal. In 1971, John Thurmon chaired the Ad Hoc Committee to establish the American College of Veterinary Anesthesiologists (ACVA). The AVMA had established guidelines for the selection of founding-charter diplomat of specialty organizations. The Ad Hoc Committee requirements for charter diplomat status in a specialty included 10 years of active service in the specialty, significant publication, intensive training, and either being a recognized head of an anesthesiology program or spending a major portion of one's professional time in anesthesia or a closely related subject area. Seven members of the ASVA were found to meet these qualifications becoming the founding diplomats of the ACVA.

Between 1970 and 1975, the constitution and bylaws were drafted and formalized. In 1975, the AVMA Council on Education recommended preliminary approval of the ACVA and it was confirmed by the AVMA House of Delegates in that same year. Thus, the ACVA was officially established in North America. Of importance throughout this process were the insight and efforts of William Lumb and E. Wynn Jones. They greatly assisted in the establishment of the ACVA because of their sincere interest in the sound principles of veterinary anesthesiology. During this same period, several didactic texts had been published further establishing anesthesia as a stand-alone discipline and specialty within veterinary medicine. The first edition of this text, *Lumb and Jones' Veterinary Anesthesia*, was published in 1973, *Clinical Veterinary Anesthesia*, edited by Charles Short, was published in 1974, and the *Textbook of Veterinary Anesthesia*, edited by Larry Soma, was published in 1971.

During the late 1970s, many of the founding diplomats established residency training programs in their respective veterinary colleges. From 1975 to 1980, the ACVA developed continuing education programs, programs in self-improvement, and programs for testing and certification of new diplomats. Along with residency training programs, anesthesiology faculty positions were being created in a number of universities across North America. In 1980, an effort headed by then president Eugene Steffey sought and achieved the full accreditation of the ACVA by the AVMA.

During the past four decades, a number of additional organizations have promoted and contributed greatly to the advancement of veterinary anesthesia. They include the Association of

Veterinary Anaesthetists of Great Britain and Ireland (AVA) and the Veterinary Anesthesia and Surgery Association in Japan. These associations along with the ACVA were instrumental in organizing the first International Congress of Veterinary Anesthesiology with its stated objective of globally advancing the field of veterinary anesthesiology. The first International Congress was held in Cambridge, England, in 1982, and has been held continually triannually ever since at various locations around the world on nearly every continent.

Concurrently, during the latter decades of the 20th century, organized veterinary anesthesiology was being advanced in Western Europe. Veterinary anesthesiologists in the United Kingdom had established the Association of Veterinary Anaesthetists and awarded the Diploma of Veterinary Anaesthesia to those with advanced specialty training. Later, interest in board specialization became increasingly evident in the United Kingdom and many European countries, resulting in the establishment of the European College of Veterinary Anesthesiologists (ECVA). In order to better recognize the central role anesthesiologists have in providing and advancing pain management, both the ECVA and ACVA subsequently sought and were granted approval to incorporate the word 'analgesia' into their names. Thus, the colleges were renamed the European College of Veterinary Anesthesia and Analgesia (ECVAA) and the American College of Veterinary Anesthesia and Analgesia (ACVAA). Currently, a number of veterinary anesthesiologists are boarded by both the ACVAA and ECVAA with both organizations recognizing the legitimacy of either credential, allowing residency training programs supervised by ACVAA diplomats to qualify candidates to sit the ECVAA Board Exam and vice versa. For further information concerning the early history of veterinary anesthesia, the reader is referred to additional sources [11–14].

The establishment of the ACVAA and the ECVAA has helped to advance veterinary anesthesia and pain management on a global scale through their efforts to promote research, create knowledge and enhance its dissemination via annual scientific meetings and publications. The ACVAA and ECVAA have as their official scientific publication the *Journal of Veterinary Anaesthesia and Analgesia*, which also serves as the official publication of the International Veterinary Academy of Pain Management (IVAPM).

During the early 2000s, in an effort to improve out-reach to practitioners interested in humane care and to increase pain management awareness and continuing education programs for practicing veterinarians, the IVAPM was initially conceived of at the annual Veterinary Midwest Anesthesia and Analgesia Conference (VMAAC) Scientific Meeting. The organization's stated mission was to advance the multidisciplinary approach to pain management within the wider veterinary community and was supported by an ongoing academic–pharmaceutical industry partnership, the Companion Animal Pain Management Consortium, led by ACVAA diplomats Charles Short (president of the original ASVA), William Tranquilli, and James Gaynor. Appropriately, the first President-Elect of the IVAPM was the then current President of the ACVA, Peter Hellyer. Interestingly, at the time of this writing (early 2014), the current IVAPM President-Elect, Bonnie Wright, continues to represent the legacy of ACVAA leadership in the field of veterinary analgesia and pain management.

Indeed, alleviating animal pain and suffering is an increasingly important and defining issue for 21st century veterinary medicine. Today, academic and private practice anesthesiologists, practitioners, veterinary technicians, research and industry veterinarians, and animal scientists alike are increasingly working together through organizations such as the ACVAA, ECVAA, IVAPM, AVA, AVTA, and others, toward the common goals of creating new knowledge, coordinating educational programs, and advancing veterinary anesthesia, analgesia, and pain management.

Anesthesiologist defined

A boarded *anesthesiologist* is a person with a doctoral degree who has been certified by either the ACVAA or ECVAA and legally qualified to administer anesthetics and related techniques [15]. The term *anesthetist* has more variable meaning because in some European countries an anesthetist is equivalent to an anesthesiologist, but in North America and many other countries anesthetist refers to a person who administers anesthetics who is not board certified or possibly not a physician or veterinarian. Perhaps the most appropriate way to define a *veterinary anesthesiologist* is by recognizing that the veterinarian has been extensively trained and supervised by either ACVAA or ECVAA diplomats and credentialed by a veterinary certifying anesthesia and analgesia specialty examination (i.e., either the ACVAA or ECVAA Certifying Board Exam) whose expertise consists of anesthetic and analgesic delivery and risk management across a wide array of species and medical circumstances.

Early conceptual stages of anesthesia

Throughout the early years of anesthetic administration (diethyl ether) to human and veterinary patients alike, the assessment of anesthetic depth was a learned skill, appreciated most fully by individuals with much experience and the courage to learn from trial and error. John Snow was the first physician to attempt to classify the depth of anesthesia based on observation of the patient [16]. Teaching new anesthetists how much anesthetic to administer required close oversight by an experienced person. This system became strained during periods of high demand for anesthetists such as was encountered during the First World War.

Dr Arthur Guedel was a physician from Indianapolis, Indiana, who served in the First World War. One of his tasks was to train orderlies and nurses to administer diethyl ether to wounded solders. Guedel thus developed guidelines through the use of a wall chart that could be used by anesthetists to gauge the depth of anesthesia (Table 1.1) [17].

While Guedel's original observations were made in human patients anesthetized with diethyl ether, they were subsequently adapted for use with other inhalant anesthetics such as halothane. Four progressive stages of anesthesia beginning at its initial administration and ending at near death were characterized. Within stage 3 there are three or four sub-classifications listed (Box 1.1). These planes of anesthesia represent the progressive central nervous system depression that can be observed while a patient is within a surgical depth of anesthesia.

Modern anesthetic techniques seldom utilize only inhalant anesthesia, which has led to less reliance on Guedel's classification. Incorporation of other drugs into balanced anesthetic techniques (e.g., antimuscarinics and dissociative anesthetics)

Table 1.1 Characteristics of the stages of general anesthesia.

Stage of Anesthesia								
		I	II	III				IV
				Plane				
				1	2	3	4	
System Affected	Characteristic Observed			Light	Medium		Deep	
Cardiovascular	Pulse[a]	Tachycardia		Progressive bradycardia				Weak or imperceptible
	Blood pressure[a]	Hypertension		Normal	Increasing hypotension			Shock level
	Capillary refill	1 s or less			Progressive delay			3 s or longer
	Dysrhythmia probability	+++	+++	++	+		++	++++
Respiratory	Respiratory rate[a]	Irregular or increased		Progressive decrease			Slow irregular	Ceased; may gasp terminally
	Respiratory depth[a]	Irregular or increased		Progressive decrease			Irregular	Ceased
	Mucous membrane, skin color	Normal					Cyanosis	Pale to white
	Respiratory action	May be breatholding		Thoracoabdominal, abdominal			Diaphragmatic	Ceased
	Cough reflex	++++	+++	+	Lost			
	Laryngeal reflex	++++	May vocalize	Lost				
	Intubation possible	No	Yes					
Gastrointestinal	Salivation	++++	+++	+	Diminished absent, except in ruminants			Absent
	Oropharyngeal reflex	++++	+++	+	Lost			
	Vomition probability	+++	+++	+	Very slight			
	Reflux (regurgitation) potential	None		Increases with relaxation				++++
	Tympany (rumen, cecum)	None		Potential increases with duration of anesthesia				
Ocular	Pupils	Dilated		Normal or constricted, progressive dilation				Acutely dilated
	Corneal reflex	Normal	+++	Diminishes, lost (horses may persist)				Absent
	Lacrimation	Normal	+++	+	Diminishes, absent			Absent
	Photomotor reflex	Normal	+++	+	Diminishes, absent			Absent
	Palpebral reflex	Normal	+++	+	Diminishes, absent			Absent
	Eyeball position	Normal	Variable	Ventromedial in dogs and cats or central				
	Nystagmus	++++	Especially horses and cows				+	None
Musculoskeletal	Jaw tone	++++	++++	Decreased, minimal			Lost	
	Limb muscle tone	++++	++++	Decreased, minimal			Lost	
	Abdominal muscle tone	++++	++++	++	Decreased, minimal			Lost
	Sphincters (anus, bladder)	May void		Progressive relaxation			Control lost	
Nervous	Sensorium	+++	+	Lost				
	Pedal reflex	++++	++++	Decreased	Absent			
	Reaction to surgical manipulation	++++	++++	+	None			

[a]Surgical stimulation causes increased heart rate, blood pressure and respiratory rate via autonomic responses that persist in plane 2. Vagal reflexes due to visceral traction persist in plane 3.
+ to ++++ = degree present.

greatly influence the reflexive and autonomic responses of the patient. In light of this, a greater reliance on monitoring patient physiologic parameters such as blood pressure, respiration, and neuromuscular tone has become common. Use of electroencephalographic monitoring of CNS activity (e.g., bispectral index monitoring) is currently of great interest and increasing in clinical application to insure adequate anesthetic depth for surgical procedures. Interestingly, a comparison of bispectral index monitoring with Guedel's classic signs for anesthetic depth in humans anesthetized with diethyl ether has a relatively good correlation (Fig. 1.1) [18]. Nevertheless, and despite the incorporation of many new monitoring modalities in daily practice, the anesthetist should continue to have some understanding of the correlation of changing physical signs with anesthetic depth progression. Thus, Guedel's early observational classification will likely continue to have relevancy.

Box 1.1 Stages of anesthesia observed during inhalant anesthesia.

Stage I. The stage of voluntary movement is defined as lasting from initial administration to loss of consciousness. Some analgesia may be present in the deeper phases of this stage. Excited, apprehensive animals may struggle violently and voluntarily hold their breath for short periods. Epinephrine release causes a strong, rapid heartbeat and pupillary dilation. Salivation is frequent in some species, as are urination and defecation. With the approach of stage II, animals become progressively ataxic, lose their ability to stand, and assume lateral recumbency.

Stage II. The stage of delirium or involuntary movement. As the CNS becomes depressed, patients lose all voluntary control. By definition, this stage lasts from loss of consciousness to the onset of a regular pattern of breathing. As a result of anesthetic depression of the CNS, reflexes become more primitive and exaggerated. Patients react to external stimuli by violent reflex struggling, breath holding, tachypnea, and hyperventilation. Continued catecholamine release causes a fast, strong heartbeat, cardiac arrhythmias may occur, and the pupils may be widely dilated. Eyelash and palpebral reflexes are prominent. Nystagmus commonly occurs in horses. During this stage, animals may whine, cry, bellow, or neigh, depending on the species concerned. In some species, especially ruminants and cats, salivation may be excessive; in dogs, cats, and goats, vomiting may be evoked. The larynx of cats and pigs is very sensitive at this stage, and stimulation may cause laryngeal spasms.

Stage III. The stage of surgical anesthesia is characterized by unconsciousness with progressive depression of the reflexes. Muscular relaxation develops, and ventilation becomes slow and regular. Vomiting and swallowing reflexes are lost.

In humans, this stage has been further divided into planes 1–4 for finer differentiation. Others have suggested the simpler classification of light, medium, and deep. Light anesthesia persists until eyeball movement ceases. Medium anesthesia is characterized by progressive intercostal paralysis, and deep anesthesia by diaphragmatic respiration. A medium depth of unconsciousness or anesthesia has traditionally been considered a light plane of surgical anesthesia (stage III, plane 2) characterized by stable respiration and pulse rate, abolished laryngeal reflexes, a sluggish palpebral reflex, a strong corneal reflex, and adequate muscle relaxation and analgesia for most surgical procedures. Deep surgical anesthesia (stage III, plane 3) is characterized by decreased intercostal muscle function and tidal volume, increased respiration rate, profound muscle relaxation, diaphragmatic breathing, a weak corneal reflex, and a centered and dilated pupil.

Stage IV. Extreme CNS depression. Respirations cease and the heart continues to beat for only a short time. Blood pressure is at the shock level, capillary refill of visible mucous membranes is markedly delayed, and the pupils are widely dilated. Death quickly intervenes unless immediate resuscitative steps are taken. If the anesthetic is withdrawn and artificial respiration is initiated before myocardial collapse, these effects may be overcome and patients will go through the various stages in reverse.

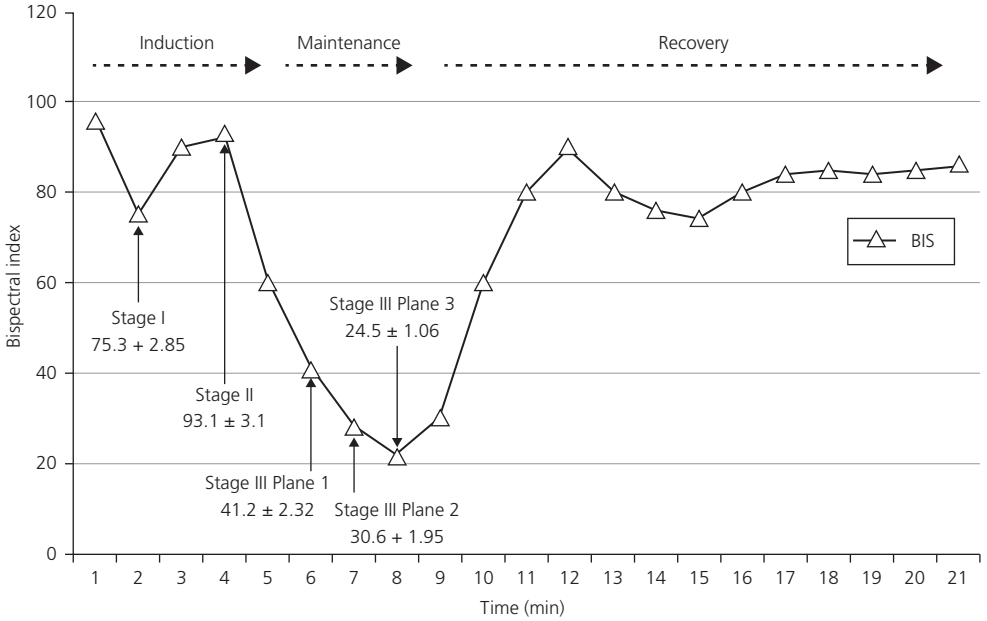

Figure 1.1 Bispectral index (BIS) values under various stages of ether anesthesia (mean ± SD). Source: [18]. Reproduced with permission of Lippincott Williams & Wilkins.

Classification of anesthesia

The diverse uses for anesthesia (as it relates to immobilization, muscle relaxation, and antinociception) and the requirements peculiar to species, age, and disease state necessitate the use of a variety of drugs, drug combinations, and methods. Anesthesic technique is often classified according to the type of drug and/or method/route of drug administration:

1 *Inhalation*: Anesthetic gases or vapors are inhaled in combination with oxygen.
2 *Injectable*: Anesthetic solutions are injected intravenously, intramuscularly, and subcutaneously. Other injectable routes include intrathoracic and intraperitoneal. These last two routes are not generally recommended.
3 *Total intravenous anesthesia (TIVA), partial intravenous anesthesia (PIVA) and targeted controlled infusion (TCI)*: Anesthetic techniques that utilize intravenous infusion of one or more drugs to produce a suitable anesthetic state. Some automated infusion systems are available that allow input of patient parameters and

pharmacokinetic information for specific drugs and allow the anesthesiologist to target a predetermined plasma drug concentration (TCI).

4 *Oral or rectal*: These routes are ordinarily used for liquid anesthetics, analgesics, or suppositories. There is often a greater degree of inter-species and inter-individual variability in the dose–response relationship of orally administered drugs due to differences in absorption and first-pass hepatic metabolism.
5 *Local and conduction*: Anesthetic drug is applied topically, injected locally into or around the surgical site (field block), or injected around a large nerve trunk supplying a specific region (conduction or regional nerve block). In the last instance, the injection may be perineural (nerve block) or into the epidural or subarachnoid space.
6 *Electronarcosis, electroanesthesia, or electrosleep*: Electrical currents are passed through the cerebrum to induce deep narcosis. Even though there have been successful studies, this form of anesthesia has never gained popularity and is rarely used in veterinary practice. Electronarcosis should not be confused with the inhumane practice of electroimmobilization.
7 *Transcutaneous electrical nerve stimulation (TENS, TNS, or TES)*: Local analgesia is induced by low-intensity, high-frequency electric stimulation of the skin through surface electrodes. TENS has many similarities to electroacupuncture.
8 *Hypnosis*: A non-drug-induced trance-like state sometimes employed in rabbits and birds.
9 *Twilight anesthesia*: A state of heavy sedation where the patient is still conscious, but cooperative, and has limited or no recall (amnesia). This technique is popular for outpatient anesthesia in human medicine for diagnostic procedures and for minor surgical procedures when combined with local anesthetics and additional analgesic drugs. *Twilight anesthesia* is a term in common use by laypeople to connote heavy sedation and does not refer to a specific anesthetic procedure or technique.
10 *Acupuncture*: A system of therapy using long, fine needles to induce analgesia. Additional modalities of acupuncture point stimulation have been utilized, including mechanical and electrical stimulation.
11 *Hypothermia*: Body temperature is decreased, either locally or generally, to supplement insensitivity and decrease anesthetic drug requirement, and reduce metabolic needs. It is primarily used in neonates or in patients undergoing cardiovascular surgery.

Environmental considerations

Concerns about potential adverse effects associated with the use of anesthetic drugs fall into three general categories. The first is patient-experienced adverse drug reactions, which can be classified into seven types: dose-related (Augmented or type A), non-dose-related (Bizarre or type B), dose-related and time-related (Chronic or type C), time-related (Delayed or type D), withdrawal (End of use or type E), failure of therapy (Failure or type F), and genetic reactions (type G) [19]. Specific patient-experienced adverse drug reactions are reviewed in other areas of this text.

A second type of adverse effect is experienced by health and veterinary care providers exposed to anesthetic drugs and gases during the performance of their daily tasks. Acute exposure through accidental needle penetration or through accidental spillage of drugs will always be a risk. Many employers have standard operating procedures in place, instructing employees how to limit their exposure and how to proceed if exposure occurs. Chronic workplace exposure to low levels of inhalant anesthetic agents has been a concern since their use began and, although studied repeatedly, questions still exist about the relative risk of toxicity such as infertility, miscarriage, cancer, and other chronic health problems. Part of the difficulty in determining safe levels of exposure is related to the apparently low incidence of adverse effects and the potentially long lag period between exposure and expression of toxicity. Usually the question is approached through large epidemiological studies of healthcare providers that are administering anesthetics. This introduces many confounders such as provider age, agents in use, coexisting health problems, and measurement of actual provider exposure, which may make interpretation and generalization of results problematic. Occupational exposure to inhalant anesthetics is addressed in Chapter 16, Inhalant Anesthetics.

The third type of anesthetic adverse effect is environmental. Historically, drug development and clinical use of anesthetic agents did not consider the resources consumed to produce drugs, or their ultimate fate once eliminated by the patient. Of the inhalant anesthetics in clinical use, desflurane is responsible for the largest greenhouse gas emission (both carbon dioxide and halogenated compounds) during its lifecycle. It is approximately 15 times that of isoflurane and 20 times that of sevoflurane on a per MAC-hour basis. The concurrent use of nitrous oxide to facilitate delivery of inhalant anesthetics further increases emissions. The impact of the contemporary inhalant anesthetics on ozone depletion has also been studied [20]. Although these agents do have some potential for ozone depletion, their relative contribution is low and the impact on global warming through this mechanism is minor. For all of the inhalation anesthetics, their eventual release as waste anesthetic gases into the atmosphere is the largest contributor to their greenhouse gas footprint and global warming potential.

Propofol's impact on greenhouse gas emission is much smaller, by nearly four orders of magnitude, than that of desflurane or nitrous oxide. The greenhouse gas emission associated with propofol and many other injectable anesthetic drugs is primarily related to their production and consumption of fossil fuels needed to manufacture and deliver the drugs [21,22].

References

1 Short CE. The management of animal pain: where have we been, where are we now, and where are we going? *Vet J* 2003; **165**: 101–103.
2 Heavner JE. Veterinary anesthesia update. *J Am Vet Med Assoc* 1983; **182**: 30.
3 Winters WD, Ferrer AT, Guzman-Flores C. The cataleptic state induced by ketamine: a review of the neuropharmacology of anesthesia. *Neuropharmacology* 1972; **11**: 303–315.
4 Askitopoulou H, Ramoutsaki IA, Konsolaki E. Analgesia and anesthesia: etymology and literary history of related Greek words. *Anesth Analg* 2000; **91**(2): 486–491.
5 International Association for the Study of Pain. *IASP Taxonomy*. http://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698 (accessed 15 September 2014).
6 Thurmon JC, Benson GJ. Anesthesia in ruminants and swine. In: Howard JL, ed. *Current Veterinary Therapy*, vol. **3**. Philadelphia: WB Saunders, 1993; 58–76.
7 Jackson CT. Etherization of Animals. *Report of the Commissioner of Patients for the Year of 1853*. Washington, DC: Beverly Tucker, Senate Printer, 1853, **59**.
8 Dadd GH. *The Modern Horse Doctor*. Boston: JP Jewett, 1854.
9 Keys TE. The development of anesthesia. *Anesthesiology* 1942; **3**: 11–23.
10 Stevenson DE. The evolution of veterinary anesthesia. *Br Vet J* 1963; **119**: 477.
11 Clark AJ. Aspects of the history of anesthetics. *Br Med J* 1938; **ii**: 1029.
12 Smithcors JE. The early use of anesthesia in veterinary practice. *Br Vet J* 1957; **113**: 284.
13 Lee JA. *A Synopsis of Anesthesia*, 4th edn. Baltimore: Williams & Wilkins, 1959.
14 Miller RD. *Anesthesia*, 2nd edn. New York: Churchill Livingstone, 1986.
15 Medical Dictionary. *Medical Dictionary, Medical Terminology*. http://www.medi-lexicon.com/medicaldictionary.php (accessed 1 December 2012).

16 Snow J. *On the Inhalation of the Vapor of Ether in Surgical Operations*. London: Churchill, 1847.
17 California Pacific Medical Center. http://www.cpmc.org/professionals/hslibrary/collections/guedel/ (accessed 15 September 2014).
18 Bhargava AK, Setlur R, Sreevastava D. Correlation of bispectral index and Guedel's stages of ether anesthesia. *Anesth Analg* 2004; **98**(1): 132–134.
19 Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. *Lancet* 2000; **356**(9237): 1255–1259.
20 Langbein T, Sonntag H, Trapp D, *et al*. Volatile anaesthetics and the atmosphere: atmospheric lifetimes and atmospheric effects of halothane, enflurane, isoflurane, desflurane and sevoflurane. *Br J Anaesth* 1999; **82**(1): 66–73.
21 Sherman J, Le C, Lamers V, Eckelman M. Life cycle greenhouse gas emissions of anesthetic drugs. *Anesth Analg* 2012; **114**(5): 1086–1090.
22 Ryan SM, Nielsen CJ. Global warming potential of inhaled anesthetics: application to clinical use. *Anesth Analg* 2010; **111**(1): 92–98.