

A HISTORY OF VETERINARY ANAESTHESIA

Historia de la Anestesia Veterinaria

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ABSTRACT:

The History of Veterinary Anaesthesia is reviewed from the time of the discovery of the anaesthetic properties of ether in birds in the 16th century to its first recorded use in humans and then in domestic animals in 1846. This was followed by the use of chloroform in man and animals. Chloral hydrate was used some years later at about the time that epidural anaesthesia was being used for the first time. An Anaesthetic Act followed in 1919 in the U.K. The 1930's saw the advent and development of the barbiturates. In the 1940's regional anaesthesia of the flank of the cattle was reported. The concept of balanced anaesthesia in small animals was developed in the 1950's. The discovery of halothane in 1956 was the real stimulus to the development of inhalational anaesthesia for large animals and it led to the development of equipment for that purpose. More recent developments have included the alpha 2-adrenoreceptor agonist and propofol. After the introduction of isoflurane there were further inhalational agents; desflurane and sevoflurane. The development of muscle relaxants from the time of Waterton's tripto South America to the present are also discussed.

Keywords: Anaesthesia. History. Veterinary.

RESUMEN:

Este trabajo revisa la Historia de la Anestesia Veterinaria desde el descubrimiento en el siglo XVI de las propiedades anestésicas del éter en aves, hasta la primera descripción de su uso clínico en humanos, y luego en animales domésticos, en 1846. Estos avances se siguieron del empleo de Cloroformo en seres humanos y animales. El Hidrato de Cloral se empleó más tarde, en la época en la que la anestesia epidural se utilizó por primera vez. La Ley sobre Anestesia reguló todos estos avances en el Reino Unido en 1919. La década de los 30 contempló el advenimiento y desarrollo de los barbitúricos. En los 40 la técnica de anestesia regional del flanco abdominal se describe en la vaca. El concepto de anestesia balanceada se desarrolló en pequeños animales en los años 50. El descubrimiento del halotano en 1956 fue el estímulo real para el desarrollo de la

anestesia inhalatoria en grandes animales, lo que condujo a la introducción de equipamiento específico con este propósito. Avances más recientes, incluyen la introducción de los agonistas alfa 2-adrenérgicos y del propofol. Tras la introducción del isoflurano, han seguido otros agentes inhalatorios como el desflurano y el sevoflurano. Se revisa también el desarrollo de los bloqueantes neuromusculares, desde la época de los viajes de Waterton por América del Sur hasta la actualidad.

Running Title: Historia Anestesia Veterinaria.

Keywords: Anestesia. Historia. Veterinaria.

The origins of anaesthesia, in both man and animals, are shrouded in the mists of time. However, it would appear that most of the early work was directed to the alleviation of pain in the human subject. Early records from the 15th Century B.C., in the Babylon papyrus of Eber, show that he used *Atropa mandragora*, henbane (Belladonna alkaloids) and poppy boiled in water as an analgesic mixture. The plant extracts were usually administered in the form of narcotic swabs. These swabs were soaked in the juice, dried and preserved. They were then rehydrated and placed in the nostril or mouths of the patients before operation. Wine and other forms of alcohol with the addition of hemp, opiates and lettuce were also used to produce narcosis and analgesia in man. Hippocrates (460-377 B.C) described the use of hemp to reduce pain.

In the Middle Ages the techniques of analgesia were developed mainly in Bologna and Salerno in the 10th and 12th centuries. A variety of prescriptions were described, which included similar constituents; poppy, belladonna, cicuta (hemlock) and hyoscinamine. The first authentic report of the use of ether to produce analgesia was in 1540 by Paracelsus. He administered it to chickens and allowed them to recover. It is interesting to note that around the same time, in 1543, Vesalius was passing a tube into the trachea of a pig, using a bellows to inflate the lung, and to keep the animal alive. He was studying the thoracic anatomy of the pig and his description was long and accurate.

It would appear that the first report of anaesthesia in the horse was that of Ruini in 1550. He administered belladonna alkaloids

mixed with distilled endive or barley water with the feed as a result of which they slept for a day. Alternatively the mixture was administered with an ounce of hemlock in the drinking water. He recommended that the animals should be revived afterwards with hellebore mixed with vinegar or castor oil pushed up the nostril. In the 17th and 18th centuries the techniques appeared to fall into disrepute and one veterinarian wrote *«it is impossible to operate on a horse for cataract: for a horse is an unreasonable creature and will not remain still»*.

The production of narcosis by the intravenous administration of drugs was known for a considerable period of time before the techniques were employed at a clinical level. Boyle in 1665 injected opium into the hind limb of a dog *«whereof the success was the opium being soon circulated to the brain; did within a short time stupefy though not kill the dog»*. The syringe was probably of the pattern designed by Sir Christopher Wren from a bladder and a quill. He injected opium into man and animals. The first injection in man unintentionally produced unconsciousness in about 1657. In 1742 Glover reported experiments, in which the intravenous injection of chloroform and bromoform produced, among other things, stupefaction. The introduction of intravenous injections into veterinary medicine is credited to Viborg in the early 1800's. He carried out experiments on various plant extracts and alkaloids in Copenhagen but he was only able to produce effective anaesthesia in dogs with a tincture of opium.

In 1774 Humphrey Davy, who was only 17 years old, described his experiments in cats. In

1800 he discussed the use of nitrous oxide as a remedy for operative pain in his pamphlet which was later incorporated into his famous book entitled «Researches chemical and philosophical chiefly concerning nitrous oxide and its respiration». He wrote «*into a mixture of one oxygen, and three nitrous oxide, a small guinea pig was introduced. He immediately began to struggle, and in two minutes reposed on his side, breathing very deeply. He made afterwards no violent muscular motion; but lived quietly for fourteen minutes: at the end of which time his legs were much convulsed. He was taken out and recovered.*».

During the early part of the 19th century a young Shropshire medical doctor, who was working on his own and virtually unknown to anyone, carried out experiments on small laboratory animals involving the use of carbon dioxide. This was Henry Hill Hickman who reported his finding in 1842. He tried to persuade surgeons in both England and France that his work was important but failed. He administered carbon dioxide to mice, puppies and an adult dog. Hickman, however, realised that anaesthesia may have been produced by asphyxia and turned to nitrous oxide. He died a somewhat disillusioned man at the early age of twenty nine and his work was not rediscovered until many years later.

Ether had long been known for the feeling of exhilaration which was produced by inhalation of its vapour. This led to the use of «*ether frolics*». It was on such an occasion that Crawford Long noticed that injuries could occur without the feeling of pain. As a result he realised that ether could be used for the relief of operative pain. Brodie had demonstrated the anaesthetic properties of ether some 20 years before it was administered to humans but it was not reported until 1851. He anaesthetised a guinea pig with ether in a bell jar until it stopped breathing in 8 minutes but the heart continued beating. Artificial respiration was administered by way of a tracheotomy and the animal recovered in a few minutes.

Morton is generally considered to be the pioneer of ether anaesthesia in man. Morton was a dentist and was employed as an assistant to Jackson. Morton experimented with various gases which he wished to reach the brain by inhalation techniques to prove that the «*seat of pain*» was in the brain and not as was generally supposed at the peripheral site of injury. He used «*analgesic drops*» given to him by Jackson in which he found ether to be the active principle. After successful experiments with laboratory animals and dogs during which he even constructed an anaesthetic mask, Morton carried out ether experiments on himself. He then proceeded to use it for dental extraction in his own practice. He gave the first public demonstration in the «*Ether Dome*» in Massachusetts General Hospital in Boston on 16th October 1846, with the surgeon Warren. Warren's famous and well known quote summarised the whole proceedings «*This is no humbug*». This information on ether anaesthesia was sent to England in a letter from Professor Bigelow to his friend Dr. Francis Booth in London. The letter travelled by ship to Liverpool and then by land to London. A demonstration was given by Dr. Booth in London on 21st December 1846 and this was claimed to be the first administration of ether anaesthesia in the United Kingdom. However, this was disputed in view of the fact that the ship's surgeon on that voyage was a young Scottish doctor from Dumfries. He took the information with him to Dumfries where an ether anaesthetic was administered at the Royal Infirmary there and the dates are still in dispute.

Within a year ether had been administered to most species of domestic animals and *The Veterinarian* published an article describing the use of ether in six dogs and two cats. The method of administration is of considerable interest «*I placed the sulphuric ether in a Florence flask, to the neck of which a large bladder was secured. The head of the animal was then introduced into the bladder and a spirit lamp applied to the*

flask». Few workers would have the courage to repeat such a procedure today. The results of this experiment were not calculated to inspire any very sanguine hopes. «*We cannot tell whether the cries emitted are evidence of pain or not; but they are suggestive of agony to the listener, and, without testimony to the contrary, must be regarded as indicative of suffering*». *The process, therefore is not calculated to attain the object for which in veterinary practice it would most generally be employed, namely, to relieve the owner from the impression that his animal was subjected to torture.* Consideration for the patient appears to have developed somewhat later in the history of anaesthesia. Further trials were reported on dogs, horses, asses and sheep, with more promising results. It was soon appreciated that asphyxia might also result from the methods employed for the administration of ether. Olden published a description of a mask designed to overcome this problem. An interesting comment is made in the editorial of *The Veterinarian* on May 1st 1847. A professor was criticised for saying to a meeting of the Royal Agricultural Society that nothing beyond «*a common soap-dish filled with aether and held to the animal's nose*» was required and that the odour was «*so delightful that the vapour is readily inhaled. When sufficiently affected the animal lies down and submits resistlessly to whatever is requisite to be done*». The editorial made the comment, «*The artist in his studio could hardly from his imagination have painted a picture more pleasing to the mind than this; and we shrewdly suspect our agreeable professor was seated in that pleasant backroom of his which looks out into the garden when he drew up for the Royal Agricultural Society his enchanting description of the effects of aether*».

In 1847 an article was published in *The Times* newspaper by Lucas a Liverpool veterinary surgeon. He successfully administered an ether anaesthetic to a Newfoundland dog for the removal of its spleen. Lucas was the first

President of the Veterinary Defence Society and a Vice-President of the Royal College of Veterinary Surgeons.

It was perhaps somewhat unfortunate that ether had only been used for a relatively short time of a few months before the advent of chloroform. This agent, used in Edinburgh by James Simpson, a gynaecologist, had many advantages over ether and as a result ether was neglected for many years. The use of chloroform was suggested to Simpson by Waldie who was a Liverpool pharmaceutical chemist. There were a number of advantages suggested for chloroform based on its greater «*potency*». The first reported veterinary use of chloroform was the reference by W. J. Goodwin, veterinary surgeon to Queen Victoria, to «*a fine sleek-looking bay carriage horse full of health and vigour lame from navicular arthritis*». There is a vivid and detailed description in *The Veterinarian* in 1848 in an editorial by Percival. Chloroform was given by means of a Sponge in a «*common leathern mask*». «*The groom impressed the muzzle upwards and so forced the sponge against the nostrils which caused the liquid to drop out from below. As a result the horse became wild and unmanageable, falling over backwards. The groom managed to pull the cavesson bridle and muzzle off the head. The horse recovered*». This account was followed by another where chloroform was «*poured on a piece of flannel cloth, below which was a sponge, the whole being placed in a tin case and, which was tied over the horse's nose and surrounded by a flannel bag. In three and a half minutes the animal fell over, and in five minutes it was perfectly insensible*». In this case the trial was more orderly and convincing. As a result of the struggling involved in the administration of chloroform, the editorial comment of *The Veterinarian* of September 1st 1848 was «*Abandoning the use of this potent chemical as an anaesthetic, at least for all practical purposes, let us turn our attention to it as an internal remedy*». In the same year Field

reported on his experiences. He stated «*However satisfied I may feel over the power of chloroform over the horse as an anaesthetic agent I cannot think of it in any way in lieu of hobbles in the fall of the animal it is too uncertain to admit of restraint or limitation and consequently violent injury may result in the struggle preparatory to its fall as well as in the fall itself*».

The popularity of chloroform, particularly in the human subject, was due mainly to the work of John Snow who administered it to Queen Victoria for the birth of her son Edward the Seventh. This led to the phrase «*narcose a la reine*». In man chloroform was responsible for many deaths; mainly due to cardiac failure. Ether was considered to be safer as respiratory failure occurred before cardiac failure but the controversy continued for many decades. In *The Veterinarian* of 1848 a description, by Professor Thiernesse of Belgium, was published of the observation that the arterial blood of dogs anaesthetised with chloroform or ether inhalation was darker in colour. If chloroform was given intravenously, then the arterial blood «*exhibited a florid red hue*». There was a belief for many years that anaesthesia was produced by asphyxia. It may well have been true but it was caused by the technique of administration and not by the specific agent. The difficulties associated with the administration led to the search for easier methods. By 1866 local anaesthesia by ether spray had been described.

Spencer Wells published an account of the use of chloral hydrate in 1869. It appears that administration was by subcutaneous injection in small doses and it was claimed that no local irritation occurred. He also stated that it was possible to produce narcosis in rabbits and other animals. Ore in France, after making preparatory tests in dogs in 1872, produced anaesthesia in man by the intravenous injection of chloral hydrate. There were several fatalities and by 1877 the method was discarded in man. Humbert is credited with the trial of this drug in the horse. Nocard in 1866 stated «*for years he had used*

no other general anaesthetic agent but chloral hydrate, in a solution of 1 to 3 of water, as an intravenous injection». This had been used in horse, ox and dog. In the horse and ox administration was by puncturing the jugular vein, and in the dog the external femoral vein was laid bare and punctured with a trocar, or hollow needle. In 500 to 600 injections he had had no anaesthetic death. It was Degive in Belgium, in the early part of the 20th century, who popularised the intravenous use of chloral hydrate. He wrote «*chloral hydrate injected into the jugular vein at a dose of 10 gr/100kg bodyweight in a 20 per cent solution produced in 1 to 2 minutes complete general anaesthesia without producing excitement in the animal. The method is most valuable when practiced with full aseptic precautions but it has been followed by several accidents which have put its value in doubt*».

Cocaine was introduced as a local anaesthetic in 1890 when Penhale reported on anaesthesia of the mucous membranes with this agent. A 4 per cent solution applied to the cornea «*had been found useful in removing foreign substances from the eye, especially in cattle*». In one operation on a dog he injected the solution near the corner of the eye, dropped some on the cornea and waited 3-4 minutes before removing the membrana nictitans. Penhale was one of the first people to suggest that less chloroform was required to anaesthetise the pregnant animal. It was probably Hobday who popularised the use of cocaine in veterinary anaesthesia but it had undesirable side effects after absorption. The introduction of procaine in 1905 enabled advances to be made in regional and local anaesthesia.

The status of veterinary anaesthesia at the turn of the 20th century was well described by Hobday, who wrote «*In my student days I had been taught that the administration of chloroform to the dog, the cat and other small animals was exceedingly dangerous. Deaths were of such frequent occurrence that the anaesthetic was*

used in the severest of cases, and then with extraordinary trepidation. Even in those days it was recognised that it was safer to chloroform a horse than a dog or cat, one indisputable reason being that the larger animal was perforce hobbled and secured in such a position that its lungs could expand and the chest was not pressed on by human hands». This resulted in Hobday developing a table for the restraint of small animals while they were being chloroformed. He also popularised the use of apparatus to give a steady flow of chloroform in a controlled manner. Hobday published a series of over 900 cases in which «only five deaths occurred altogether, and in all except one, the post mortem examination satisfactorily explained the cause of death. In this instance, owing to a misunderstanding, a post mortem examination was not made». In 1915 Hobday published the first text book completely devoted to veterinary anaesthesia. Most of the book was devoted to inhalational anaesthesia and regional and spinal anaesthesia were mentioned. One important point of interest was the use of premedication prior to chloroform anaesthesia by Iliesco in Bucharest. Scopolamine was used either by intravenous or subcutaneous injection and was sometimes combined with morphine. It was suggested that premedication reduced the excitement at induction, reduced the dose of chloroform and a more rapid recovery was seen. Merrillat, in his textbook on veterinary surgery in 1915 indicated that the use of anaesthesia was not universal at that time. «In veterinary surgery anaesthesia has no history. It is used in a kind of desultory fashion that reflects no great credit on this generation of veterinarians... Many veterinarians of rather wide experience have never in their whole lifetime administered a general anaesthetic in performing their operations... Anaesthesia in veterinary surgery today is a means of restraint and not an expedient to relieve pain. So long as an operation can be performed by forcible restraint without imminent danger to the technique, the operator or the animal, the

thought of anaesthesia does not enter into the proposition».

The comments of Hobday and Merrillat provided background for the introduction of the Animals Anaesthetic Act of 1919 in the United Kingdom. The Act made general anaesthesia compulsory for many types of operation. The general impression from the veterinary literature at that time was that the Act became law due to the pressure of public opinion rather than representations by the veterinary profession. In his memoirs Hobday wrote «Who can estimate the suffering relieved by these new methods backed by law? Thousands of operations had been carried out with no anaesthetic — a memory as disturbing as it is heartening to know that one had some share in bringing about so great an alleviation».

Although the 1919 Act ensured, as far as possible the universal use of general anaesthesia, it also delayed the introduction of new techniques particularly of regional anaesthesia, into veterinary anaesthetic practice. The 1919 Act was superseded by the Protection of Animals [Anaesthetic] Act 1954 which was modified in 1964, which allowed the veterinary surgeon to choose the type of anaesthesia employed as long as there was «adequate anaesthesia».

The use of tribromethanol was described in the cat in the late 1920's and it was administered by the rectal route and later intravenously. However, it was soon superseded by barbiturates in the 1930's. The first barbiturate to be used intravenously was butallylonal. Hexobarbital was used in dogs and cats by Ebert. Kreutzer in the United States was the first person to report the use of pentobarbitone in veterinary anaesthesia in 1931. It was administered by the intraperitoneal route. Some two years later in 1933, Wright reported the use of intraperitoneal pentobarbitone in a series of 100 dogs and cats. The great disadvantage of the technique was the tremendous variation in response. Barbiturates had earlier been administered intravenously in the human subject and reports soon followed in

small animals. It was shown that the onset of narcosis was more rapid by this route and it was therefore possible to inject the agent over a 3-4 minute period whilst assessing the degree of narcosis until the required depth was reached. As long as the drug was administered at a slow rate this method proved to be far in advance of the previously used anaesthetic techniques. Probably the greatest advantage was the quiet induction of anaesthesia. Later it was reported that for short periods of anaesthesia thiopentone was a very satisfactory agent. For a long period of time both pentobarbitone and thiopentone were widely used for small animal anaesthesia and it was not really until the wider use of halothane in the 1960's that their position was challenged. Indeed the use of thiopentone changed to that of an induction agent in which it is widely used at the present time.

The development of epidural anaesthesia owes a great deal to Brook. Spinal anaesthesia was first used by Corning in 1885, who injected cocaine solution into the region of the posterior thoracic interarcual spaces and produced anaesthesia of the hind limbs, penis, urethra and inguinal region. Brook (1935) suggested that it was Cuille and Sendrall in 1901 who were the first to use the technique in the horse, ox and dog by means of lumbo-sacral puncture. «True epidural anaesthesia» differs from spinal anaesthesia in that injection of local anaesthetic is outside the spinal membranes. This eliminates several of the disadvantages found in spinal injections. The first reported use of epidural anaesthesia in the horse was in Berlin in 1925 and Benesch in Austria developed the technique in cattle where it has proved to be a very popular and useful technique. Farquharson in America in 1940 developed the technique of paravertebral anaesthesia which was to prove extremely useful in ruminants. The spinal nerves are blocked as they leave the intervertebral foramina and this desensitises the skin and muscles of the flank region. Exposure of the bull's penis presented considerable difficulties from the anaesthetic

perspective. Epidural anaesthesia was effective but was not without its disadvantages. The development of pudendal nerve block by Larson in 1953 allowed the veterinary surgeon to produce effective penile relaxation and anaesthesia in the standing animal. Regional anaesthesia of the digits of ruminants of the limbs was a considerable advance. However, it depended on the accurate knowledge of and application of anatomy and it was not always practicable in the diseased limb. The development of intravenous regional anaesthesia by Bier in humans in the early 20th century was a considerable advance. It was abandoned and neglected in medical anaesthesia for many decades until it was reintroduced in the early 1960's. The technique was developed in cattle by Jones and Prentice in 1974.

The 1940's and 50's saw the development of two further inhalational agents: cyclopropane and trichlorethylene both of which had considerable disadvantages. They relied mainly on the development of endotracheal intubation for their administration in animals and in the case of cyclopropane on the use of a closed circuit which had been developed in the early 1940's by Waters. In 1954 a seminal paper was published by Hall and Weaver (1954) entitled «Some notes on balanced anaesthesia for the dog and cat». They developed the concept of balanced anaesthesia with premedication, induction of anaesthesia with an intravenous barbiturate and maintenance with an inhalational agent and oxygen. The greatest impetus in the development of inhalational anaesthesia in animals was the discovery of halothane by Suckling (1957) and Raventos (1956). The advent of a potent non-flammable agent stimulated the development of inhalational anaesthetic equipment for use in large animals by Fisher and Jennings in Glasgow followed by a number of other workers in Europe and North America. In the 1950's the phenothiazine tranquillising drugs, of which chlorpromazine was the first, were developed and found a place

in veterinary anaesthesia for premedication in all of the major species. In the late 1960's the first alpha-2-adrenoreceptor agonist, xylazine, was developed for use in ruminants. Its use was later extended to a number of other species including the horse, cat and dog. This was followed in the 1980's by three further compounds in the group, detomidine and romifidine for use in horses and medetomidine and the its reversal agent the alpha-2-adrenoreceptor antagonist atipamezole for use in dogs and cats. In the early 1970's, ketamine was introduced as a dissociative anaesthetic agent as a successor to phencyclidine. Whilst it is currently used in a wide variety of species in veterinary anaesthesia the development of its use was relatively slow and its use limited mainly to cats.

In the early 1980's the non-barbiturate intravenous agent propofol was introduced for use mainly as an induction agent. Its use is now widespread in human anaesthesia but its use in veterinary anaesthesia is mainly confined to small animals. The early 80's also saw the discovery of a new inhalational agent isoflurane. After initial trials, which were extremely promising, its use was suspended due to fears over its toxicity. However, subsequently these fears were found to be ill founded and the drug was reintroduced and is now in widespread use in veterinary anaesthesia. More recently two new inhalational agents, desflurane and sevoflurane have been introduced both of which have a low solubility and consequently a rapid mode of action.

Muscle relaxants have been known for a number of centuries but it is only since the middle of the 20th century they have been used in anaesthesia. It was Sir Walter Raleigh who first brought back the information from South America in the 16th century. Brodie was the first person to report experiments on animals in 1812. Waterton in 1847 described the administration of curare to a donkey and how he kept it alive

by the use of a bellows to inflate its lungs and following recovery it survived for 25 years. Claude Bernard was the first person to investigate the pharmacology of curare and the problems of consciousness under the effects of relaxants. His concerns led to the appointment of a royal commission on vivisection in the United Kingdom and the Cruelty to Animals Act of 1876 to regulate the practice of animal experimentation. In the early 1940's Griffiths and Johnson in Montreal first used the drug in human anaesthesia. This was followed some four years later by a report from Gray and Halton of its use in 1000 human patients. In the mid 1950's Hall and his co-workers described the use of suxamethonium in canine anaesthesia. In the early 1980's two new relaxants atracurium and vecuronium were developed for use in humans. Atracurium was a particularly interesting compound due to its novel metabolism by Hoffmann degradation. Their use in veterinary anaesthesia was investigated and they are now in widespread use horses dogs and cats. More recently two new drugs have been introduced. These are rocuronium, another amino-steroid and cis-atracurium which is one of the specific isomers of atracurium. The use of both agents has been reported in dogs.

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