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HISTORY OF MEDICINE

# A Brief History of Anaesthesia

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## Abstract

According to the definition of the International Association for the Study of Pain (IASP), pain is defined as: "Unpleasant subjective feeling and emotional experience associated with current or potential tissue damage of a particular localisation", which, as such, poses a challenge for epidemiological research to determine its frequency and prevalence.

We have all heard the motto that surgery has experienced its unprecedented development on the wings of anaesthesia. This is most certainly the case, since it is precisely the pain that prevents any invasive procedure on the human body, hence the very elimination of pain has opened up the way for the application and development of surgery. For this reason, the skill and now the science of anaesthesia are epochal civilizational achievements, which is why it is worth remembering the attempts and successes of its application. The very beginning of mankind cannot be imagined without the humans facing some sort of pain. As long ago as about 460 to 370 BC, the renowned Greek physician Hippocrates (in Greek: *Ἱπποκράτης*), who is nowadays considered the founder of modern medicine, stated: "To reduce pain is a divine deed" or, in Latin: *Sedare dolorem, opus divinum est*!

The article presents Morton's discovery of inhalation anesthesia, now as far back as in 1846, its development, introduction of other modes of anaesthesia, local, infiltration and regional, use of neuromuscular blockers and auxiliary procedures, such as endotracheal intubation and fiberoptic bronchoscopy, without which modern anaesthesia is inconceivable today.

**Key words:** Pain; Inhalation anaesthesia; Local anaesthesia; Infiltration anaesthesia; Regional anaesthesia.

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## Introduction

Over the centuries, people have resorted to various methods and means to get rid of the uncomfortable feeling of pain. Back in about 3000 BC in Mesopotamia, patients were anaesthetised by pressing the carotid arteries to make them unconscious and thus feel no pain. The Egyptians were the first to apply snow to cause analgesia by cooling, ie, by body hypothermia. The eastern Chinese tradition had developed acupuncture as a special form of analgesia. In the ancient times, surgical operations were rarely performed, while the use of cruel physical measures, such as suffocation, knocking-down and such, was noted for pain relief, all with the aim of causing a deep sleep in which one would cease to go through this unpleasant experience.

The use of the first means of analgesia was mentioned in the ancient Greek and Roman texts of Hippocrates, Theophrastus, Aulus Cornelius Celsius, Pedanius, Dioscorides and Pliny the Elder, whereas the period of great scientific advances began in the late eighteenth and early nineteenth centuries. A rapid development of natural sciences led to the rapid development of medicine. Anaesthesia, the development of microbiology, the


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discovery of X-rays, the discovery of blood groups and development of safe methods of blood transfusion and the discovery of penicillin and other antibiotics thereafter were the five major scientific advances that have enabled the development of modern surgery. Surgery was to experience its full take off on the wings of anaesthesia.

No real anaesthesia existed until the 19th century and the first research in this field began owing to the development of chemistry and physiology. In his book *The Century of the Surgeon*, Jürgen Thorwald wrote: "The century of modern surgery began in 1846 in the operating room of Massachusetts General Hospital in Boston. October 16 of that year marked the birth of the art of producing insensibility to pain by the inhalation of chemical gases. I believe that it is impossible for anyone in our times to grasp the vast significance of the revolution that began that day. Even to me it sometimes seems as if the cruel and frightful surgery, which I witnessed so often in my youth, never existed at all. Only a short time before that October 16 I had again watched another surgeon performing surgery of a cancerous tongue. I watched an operated woman fallen dead in shock when the broken iron began to squeak on the wound of the stump of her tongue. It was as if her last cry was still echoing the room, when the woman had already fallen dumb forever. And then, only a short while afterwards, a young man lay quietly under Warren's knife, uttering not a sound, unstirring, in a state of merciful insensibility, feeling none of the inconceivable pain that countless human beings had endured before him. Our whole world was transformed by an operation that lasted only a few minutes. A light burst forth from the darkness of those days, so bright that its first flash blinded us."[1]

The epoch-making discovery of ethereal anaesthesia was preceded by nearly fifty years of mental play and a series of attempts to relieve pain that had escalated in the consciousness of the humanity on that day. Subsequently, this new adjunct surgical device began to be successfully tested worldwide. The skill and science of anaesthesia have progressed steadily, contributing to the further development of surgery. The most important thing for anaesthesia is that it has become a separate specialisation. This has created a category of physicians who are both physiologists and high-level pharmacologists.

## A brief historical overview

The end of the 18th and beginning of the 19th century brought numerous researches in the field of gases and their discoveries. Thus, Joseph Black discovered carbon dioxide, Henry Cavendish hydrogen, Antoine-Laurent de Lavoisier nitrogen and oxygen. Joseph Priestley discovered nitrous oxide ($N_2O$) and its analgesic effects were quickly recognised. It was the first gas used to reduce pain. Initial experiments on animals with nitrous oxide to induce sleep were performed by Henry Hickman in 1824, a young English surgeon who was working in France at the time. He did not receive a license to work on humans from the French medical authorities and, discouraged, he returned to England, where he soon died. In the 19th century, the so-called laughing parties were popular among the upper classes in Britain, to which people came and inhaled large quantities of nitrous oxide gas, which was better known as "paradise gas" or "laughing gas". In the year of 1800, the British chemists Humphrey Davy and Thomas Beddoes described the analgesic properties of nitrous oxide, but the era of its use in surgery had not begun at the time. It was in 1818 when Michael Faraday discovered that ether had similar properties to nitrous oxide, whereas, in 1824 Hickman discovered that carbon dioxide could also be used in anaesthesia; however, the era of surgical anaesthesia had not begun at the time either.[2]

It was another physician, Crawford Williamson Long, from Danielsville, Georgia, USA, who, while working with nitrous oxide and ether, observed their similar properties and it was him who noted that ether had stronger anaesthetic effect. Long was the first to successfully apply ether anaesthesia, on 30 March 1842, during surgery, giving his friend James M. Venable an excision, cutting out one of two tumours from his neck. For unknown reasons, he made this discovery public only in 1849, three years after William Morton celebrated the demonstration of ethereal anaesthesia in Massachusetts.[3]

Horace Wells, an American dentist, was the first who extracted a diseased tooth to a patient under anaesthesia using nitrous oxide in 1844. Wells came to this idea by watching a public performance of Gardner Colton, a travelling chemist, who made money entertaining people by inhaling nitrous oxide. Wells noted that people did not feel pain when they were injured stumbling around

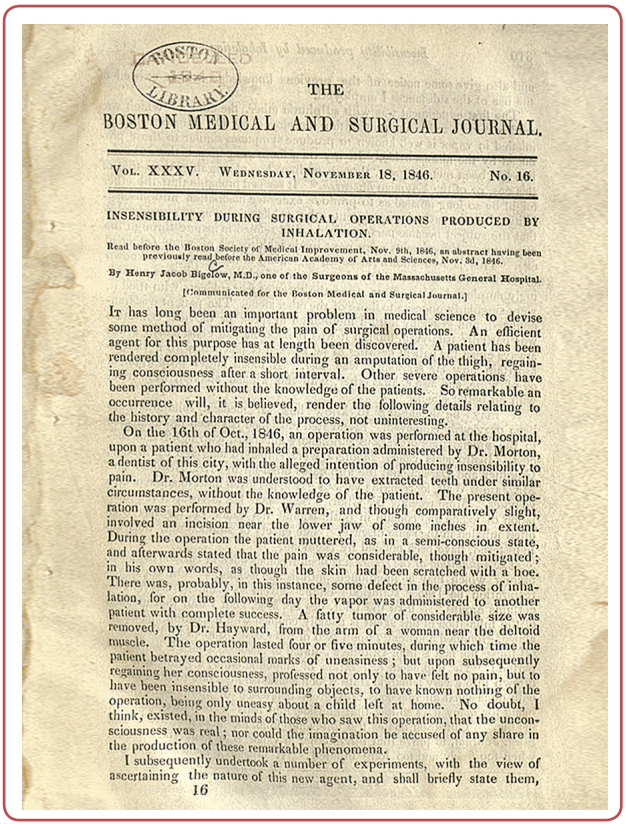
*Figure 1: Dr William Thomas Green Morton (1819-1868), pioneer of inhalation anaesthesia*

stunned with nitrous oxide. Unfortunately, he was unsuccessful in trying to publicise his method at the Massachusetts hospital and quickly lost the support of medical circles due to multiple professional errors, which caused Wells' disappointment and severe psychological depression, leaving his student, associate and colleague, William Morton (Figure 1), take over the primacy in anaesthesia.[4]

On 16 October 1846, William Thomas Green Morton (1819-1868), an American dentist, after unsuccessful attempt to administer nitrous oxide by his colleague Horace Wells, whom he successfully collaborated with, performed his famous demonstration of anaesthesia in surgery of the submandibular gland and tongue. He used ether as a stronger anaesthetic, as advised by his former mentor, Professor Jackson. The operation, performed by the Boston surgeon John Collins Warren, was to remove a large tumour from a man's face. Morton, at the same clinic where Wells failed, experienced the full success and recognition of his colleagues, after which the use of anaesthesia in surgery spread throughout the world. Therefore, 16 October 1846 is considered a date of discovery of anaesthesia (Figure 2). Morton's discovery was published next month and the news spread throughout the world (Figure 3).

*Figure 2: "First Operation Under Ether" by Robert C. Hinckley, painting, oil on canvas*

In 1847, James Young Simpson (1811-1870), a British obstetrician, proposed the use of chloroform, another significant drug in anaesthesia, discovered in 1831. The efficacy of chloroform has been proven by Simpson by using it in pregnant women to relieve childbirth pain. Thus, at the beginning of its development, in addition to nitrous oxide, anaesthesia received two more anaesthetic agents, ether and chloroform.[5]



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INSENSIBILITY DURING SURGICAL OPERATIONS PRODUCED BY INHALATION.

Read before the Boston Society of Medical Improvement, Nov. 9th, 1846, an abstract having been previously read before the American Academy of Arts and Sciences, Nov. 3d, 1846.

By Henry Jacob Bigelow, M.D., one of the Surgeons of the Massachusetts General Hospital.

[Communicated for the Boston Medical and Surgical Journal.]

IT has long been an important problem in medical science to devise some method of mitigating the pain of surgical operations. An efficient agent for this purpose has at length been discovered. A patient has been rendered completely insensible during an amputation of the thigh, regaining consciousness after a short interval. Other severe operations have been performed without the knowledge of the patients. So remarkable an occurrence will, it is believed, render the following details relating to the history and character of the process, not uninteresting.

On the 16th of Oct., 1846, an operation was performed at the hospital, upon a patient who had inhaled a preparation administered by Dr. Morton, a dentist of this city, with the alleged intention of producing insensibility to pain. Dr. Morton was understood to have extracted teeth under similar circumstances, without the knowledge of the patient. The present operation was performed by Dr. Warren, and though comparatively slight, involved an incision near the lower jaw of some inches in extent. During the operation the patient muttered, as in a semi-conscious state, and afterwards stated that the pain was considerable, though mitigated; in his own words, as though the skin had been scratched with a hoe. There was, probably, in this instance, some defect in the process of inhalation, for on the following day the vapor was administered to another patient with complete success. A fatty tumor of considerable size was removed, by Dr. Hayward, from the arm of a woman near the deltoid muscle. The operation lasted four or five minutes, during which time the patient betrayed occasional marks of uneasiness; but upon subsequently regaining her consciousness, professed not only to have felt no pain, but to have been insensible to surrounding objects, to have known nothing of the operation, being only uneasy about a child left at home. No doubt, I think, existed, in the minds of those who saw this operation, that the unconsciousness was real; nor could the imagination be accused of any share in the production of these remarkable phenomena.

I subsequently undertook a number of experiments, with the view of ascertaining the nature of this new agent, and shall briefly state them,

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*Figure 3: Boston Medical and Surgical Journal, 18 November 1846, describing the 16 October 1846 successful operation under ethereal inhalation anaesthesia*

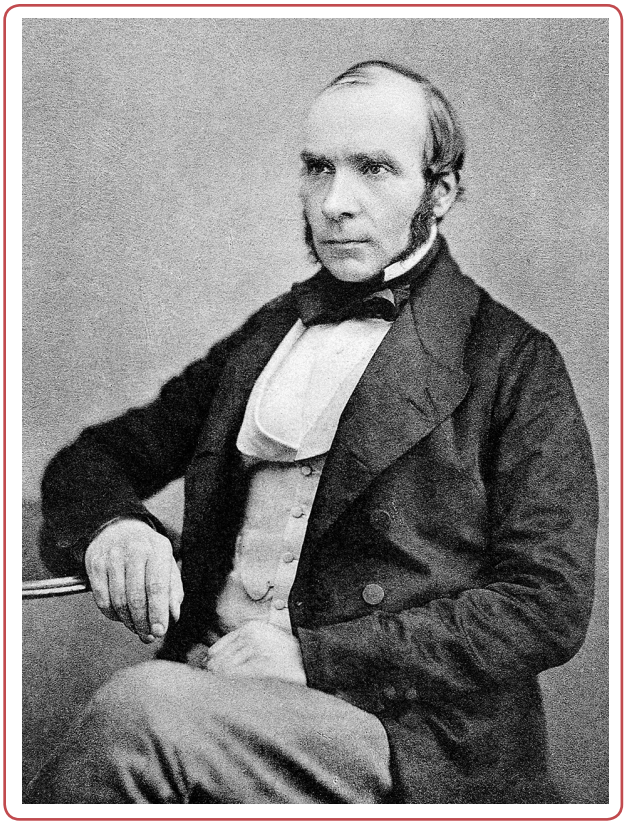

*Figure 4: Dr John Snow (1813-1858), first qualified anaesthesiologist and father of modern epidemiology*

In 1847, a Russian surgeon Nikolay Ivanovich Pirogov, performed the first successful operation under ether anaesthesia on the battlefield, which significantly reduced the mortality of the wounded on battlefields during the war as well as in the postoperative period.[6]

The first qualified anaesthesiologist was John Snow (1813-1858). This was a doctor who decided early on to deal exclusively with anaesthesia. Dr Snow was also involved in the practice of teaching, particularly of passing the knowledge to younger doctors. In 1841, he developed the first fan, called a pulmotor, for children in asphyxia. He also developed a type of inhaler through which the amount of ether given to a patient could be dosed. He discovered the importance of lack of oxygen as well as of problems occurring in the body due to the insufficient removal of carbon dioxide. Snow was the first to describe the stages of anaesthesia. He used chloroform in his work and became famous when he used the anaesthetic in 1853 during the childbirth of Queen Victoria with her eighth child, Prince Leopold. Snow gained fame beyond anaesthesia by alerting the public that cholera, with its London outbreak in 1854, was transmitted by water. As a result, the epidemic was stopped by the issuance of a regulation that all water had to be boiled before human use.[2,7] Dr John Snow thus remained remember not only as the first anaesthesiologist, but also as father of modern epidemiology (Figure 4). The first intravenous anaesthesia was used in 1872, which was performed with chloral hydrate by Pierre-Cyprien Ore (1828-1891). Due to delayed and slow recovery and high mortality of patients, this type of anaesthesia has long been unacceptable.[8]

The first anaesthesia using a cannula inserted through tracheostomy was performed by Friedrich Trendelenburg (1844-1924) in 1869 for successful performing of operations in the oral cavity,[9] while in 1878 the Scottish surgeon William McEwen (1848 - 1924) performed the first endotracheal intubation through the mouth as an alternative to tracheotomy, allowing the patient to breathe in oedema of the glottis, during general anaesthesia with chloroform. This anaesthesia technique is still in use today.[10]

The first local anaesthesia was performed in 1884 by Carl Koller (1857–1944), an Austrian ophthalmologist, anaesthetising the cornea of the eye by applying a solution of cocaine onto its surface, which was of great importance for further refinement of ophthalmic surgery. Due to reflex, involuntary eye movements that occur in response to a slightest touch, eye surgery without prior anaesthesia was difficult and limited. After numerous studies, Carl Koller discovered that a few drops of cocaine solution would solve this problem. Cocaine also causes mydriasis, an enlargement of the pupil of the eye, which is another trait for which it has also been used in ophthalmology.[11] It is interesting that Sigmund Freud, another prominent scientist of the time, mentioned in his autobiography his cooperation with Koller and commended him for his work.[12]

Already in the year of 1885, William Stewart Halsted (1852 - 1922), an American surgeon, performed the first blockade of the nerve with cocaine, only to become a victim of his own research. He became addicted to cocaine and morphine later in life, which was why he had to be sent to a sanatorium for treatment. Namely, during his stay in Europe, Halsted, along with his fellow students and doctors, experimented with cocaine. They injected cocaine into each other's nerves, which caused safe and effective local anaesthesia, but during the course of the study they became addicted to it.[13] A little later, in 1892, Carl Ludwig Schleich (1859–1922) in Germany demonstrated

his method of local analgesia by infiltration of cocaine into the tissue.[14] The field of use of cocaine as then only known local anaesthetic was in 1898 extended to anaesthetise nerve roots of the spinal cord when August Bier (1861–1949), a German surgeon, performed the first successful spinal anaesthesia by puncturing the dura mater.[15]

The development of local anaesthesia required discovery of anaesthetics that would work locally. In 1904 in France, Ernest Fourneau commercialised a new local anaesthetic amylocaine (Stovaine). Using the complex structure of cocaine, he invented the original molecule, with similar activities, but poorer toxic properties. This paved the way to developing of other local anaesthetics.[16]

Alfred Einhorn (1856 – 1917), a German chemist, patented novocaine the same year, which marked the beginning of the modern era of local anaesthesia. Until then, cocaine was used as a local anaesthetic, which due to side effects, including toxicity and addiction, forced scientists to search for new topical anaesthetics. Novocaine has been found to be relatively safe and effective, although its anaesthetic effects are slightly weaker than cocaine and some patients were allergic to it. However, no anaesthetic proved to be more effective than novocaine, so it quickly became the most commonly used topical anaesthetic. Although its use has been largely replaced by lidocaine today, novocaine is still in use, most commonly in dentistry.[17]

Using a mixture of ether and oil administered rectally to relieve birth pains, James Tayloe Gwathmey (1862-1944) introduced rectal anaesthesia to medical practice in 1913. This method of anaesthesia avoided inhalation of anaesthetics and their negative effect on the mother and foetus.[18, 19]

The introduction of neuromuscular blockers and the ability to control muscle tone is considered a turning point in the development of anaesthesia and, consequently, surgical work. In 1942, Harold Randall Griffith (1894-1985), a Canadian anaesthesiologist, introduced curare into anaesthesia (Figure 5). The introduction of curare, as a means of muscle relaxation, significantly reduced the amount of anaesthetic required, increased the volume of surgery, improved working conditions for the surgeon and reduced morbidity and mortality. The contribution of this Griffith's discovery to the further development of medicine and anaesthesia is best illustrated by medical historians, who often divide the development of anaesthesia into the periods before and after Griffith.[20, 21]

*Figure 5: Harold Randall Griffith (1894-1985), pioneer of use of curare and other neuromuscular relaxants during anaesthesia*

Another novelty introduced into anaesthesia practice, which modern anaesthesia is unthinkable without, was the use of a fibreoptic bronchoscope. Specifically, in 1967, Peter Murphy, an English anaesthesiologist, introduced it for tracheal intubation. By the mid-1980s, a flexible fibreoptic bronchoscope has become an indispensable instrument in pulmonology and anaesthesiology worldwide.[22]

## History of the central nerve blocks

With the development of general anaesthesia, experience and knowledge about its harmful effects on human body were accumulating, taking into account the generality of its action. This was the reason for seeking to anaesthetise only the part of the body that would undergo surgery. For this purpose, the techniques of local and regional anaesthesia have found their place of application. The two most accepted regional anaesthesia techniques are spinal and epidural anaesthesia, which block nerve conduction at the level of nerve roots upon their exit from the spinal cord, in all its modalities: autonomic, sensory and motor. The development of regional anaesthesia required the accumulation of knowledge in the fields anatomy and physiology of the nervous system and pharmacology of local anaesthetic agents.

*Figure 6: August Bier (1861-1949), pioneer of spinal anaesthesia*

It was Hippocrates (470-400 BC) who discovered cerebrospinal liquor, while treating hydrocephalus with ventricular puncture and called it "brain water". The Hippocratic school described in detail the brain with two halves, brain sheaths, crossed brain syndromes, inflammation and brain tumours, etc. The first serious experiments on the nervous system were made by Aurelius Galen or Claudius Galen (129 - 200 AD), better known as Galen from Pergamum (in Greek: Γαληνός, Galēnos). Galen was a prominent Roman physician and philosopher of Greek descent and probably the greatest medical scholar of the Roman era. He was the first to carry out more serious tests of the nervous system, such as experiments on the ligation of nerves, to substantiate the theory, which still stands today, that the brain controls all muscle movements through the central and peripheral nervous systems.[23] In 1692, Valsalva was the first who claimed the existence of water fluid around the spinal cord of the dog, while in 1764 Domenico Cotugno was the first to explain this fluid.[24] In 1825, François Magendie, a French physiologist, was the first to describe the circulation of the cerebrospinal fluid and provide an explanation for it. He also called it cerebrospinal liquor.[25, 26]

Puncture of the spinal canal was also a challenge for nineteenth-century physicians. In 1855, James Leonard Corning, a neurologist from New York, accidentally punctured dura mater when investigating the effect of cocaine on the spinal nerves of dogs. Corning is considered the father of epidural anaesthesia. However, the origin of the first lumbar dural puncture was attributed to Heinrich Quincke of Cologne, Germany, in 1890.[27, 28]

A German surgeon August Carl Gustav Bier (1861-1949) was the first to use cocaine intrathecally in six patients for lower extremity surgery in 1898. He is considered the father of modern intrathecal anaesthesia (Figure 6). He hypothesised that cocaine administered around the spinal nerve roots may induce adequate surgical anaesthesia. In 1898, he performed experiments on his assistant August Hildebrandt after giving him spinal anaesthesia by hammering an iron hammer at his legs, twisting his testicles, all to test their pain after injecting cocaine intrathecally. However, it turned out that all these stimuli were painless for Hildebrandt. Hildebrandt subsequently suffered from headaches, nausea and bruises on his legs. Thus, Bier's lumbar puncture also provided the first description of a nine-day post-dural puncture headache.

Bier attributed it to the loss of cerebrospinal fluid and stated the importance of using thin needles for puncture for its prevention.[15]

There is a controversy in the medical world as to whether the first spinal block was performed by Dr August Bier or the American neurologist James Leonard Corning (1855-1923), of Acorn Hall, Morristown, NJ. Corning is officially considered the father of epidural anaesthesia because he was the first to perform neuro-axial blockade by injecting 111 mg of cocaine into the dog's epidural space and of ten healthy male volunteers. He published this experiment in 1885 in the *New York Medical Journal*.[29] On 16 August 1898 in Kiel, Germany, Dr August Bier performed the first surgery under spinal anaesthesia. The experiments of Dr Bier were published in 1899.[15] There was a controversy as to whether Dr Bier or Corning performed the first spinal anaesthesia. Undoubtedly, the experiment of Dr Corning chronologically preceded Dr Bier's experiments. It is unclear whether Corning's injection was a subarachnoid or epidural blockage. The dose of cocaine used by Corning was several times higher than that used by Bier. Dr Corning did not describe seeing the flow of cerebrospinal fluid in his report in the *New York Medical Journal*, while Bier made it clear. This suggests that the injections of Dr Corning were in the epidural space, not in the subarachnoid space. Indeed, Dr Bier deserved credit for introducing spinal anaesthesia into the clinical

practice of medicine for the first surgery done under spinal anaesthesia. Still, Dr Corning created the first experiment with neuraxial anesthesia.[30]

A year later, in 1899, the first spinal anaesthesia in the United States was performed by Rudolph Matas (1860-1957), a vascular surgeon from New Orleans, using cocaine and probably the first to inject morphine in the subarachnoid space. He was also the first who described a fatal outcome after lumbar puncture.[31] The first spinal anaesthesia for therapeutic purposes for the treatment of painful conditions in syphilis was performed by US medical doctors from San Francisco, Dudley Tait and Guido Cagliri, who injected mercury iodide into cerebrospinal fluid. Their studies include work on animal models, corpses and living patients, all in an effort to determine the benefit of lumbar puncture for the treatment of syphilis.[32]

The continuous intrathecal technique with a flexible needle was first used by William T Lemmon (1896-1974) at the Mayo Clinic in 1940.[33] The first sitting block was described by Adriani and Roman-Vega in the USA[34] in 1946, whereas the first intrathecal injection of morphine to a patient with malignancy was reported by Wang at the Mayo Clinic in 1979.[35]

In Europe, the first caudal approach to the epidural space was performed by Jean-Anthanase Sicard and Fernand Cathelin in Paris in 1901. Radiologist Jean-Anthanase Sicard described the injection of a dilute solution of cocaine through the sacral hiatus to a patient who suffered severe pain in the sacral and lumbar region. Working independently, Cathelin published a similar report three weeks later. He assumed that sacral injection of cocaine could also be used in surgery.[36, 37]

The lumbar approach to the epidural space would be applied only twenty years after the caudal approach, being first performed by the Spanish surgeon from Madrid, Fidel Pagés Miravé (1886-1923). Twenty years later, in 1921, he reported on his work on lumbar epidural anaesthesia. The text was as the birth of the modern epidural anaesthesia (EA). In *Anaesthesia Metamerica* he talks about 43 cases of epidural anaesthesia performed for operations inguinal hernias, adhesions and lower extremities.[38] Pagés died quickly after his work was published and his idea of lumbar epidural anaesthesia remained dormant until the year of 1933 when it was reconfirmed and popularised by an Italian surgeon from Turin named Achille Mario Dogliotti (1897-1966). Doglioti wrote a book entitled *Anasthesia, Narcosis, Local, Regional, Spinal* and it was the first foreign book of anaesthesia translated into English. Dogliotti devoted one chapter to epidural anaesthesia. He advocated the use of EA in a wide range of different procedures. He was the first to describe the technique of loss of resistance. Although a surgeon by profession, he had a strong influence on the development of anaesthesia.[39] Therefore, Pagés in Spain and Dogliotti in Italy applied, independently of each other, lumbar EA.

In 1932, Vincent Ruiz and Alberto Gutierrez from-Buenos Aires, Argentina began their practice of EA in the USA and published their work in 1939. They discussed the history of EA, Doglotti's first caudal anaesthesia, their drip stroke technique and their experiences with EA. During 1933, 81.5 % of all their cases were done in EA, 12.5 % in local, 4 % in general, 0.25 % in spinal and 1.75 % without anaesthesia. They used 2 % procaine in a volume of 25 to 50 mL and their failure rate was 1 % .[40]

Dr Angelo Luigi Soresi, an Italian surgeon, combined the spinal and epidural techniques into one combined technique "episubdural anaesthesia" in 1937, in an effort to achieve good analgesia with minimal motor blockage.[41] However, this technique was not initially accepted, to be reintroduced forty years later Ioan Curelaru, who is thus considered a pioneer of regional anaesthesia in obstetrics.[42]

Thus, 120 years after the establishment of regional anaesthesia techniques, these both anaesthetic techniques for surgery have become popular, because of their cost and relative ease of delivery and advantages in terms of patient safety. They have also found their place in the treatment of acute and chronic pain conditions.

Anaesthesiology, as a young medical discipline, has grown rapidly thanks to the rocketing development of science and technology and is now classified as a broad, if not the broadest, field of medical activity. Its field of work has long gone beyond just caring for sleeping patients and because of their knowledge of pharmacology, physiology, pathophysiology, surgery, acute and chronic pain therapy, anaesthesiologists today stand at the helm of operating theatres, intensive care, emergency departments, outpatient pain therapy

clinics. Due to their broad medical knowledge and mastery of many skills, they are expected to be trained in a wide range of subspecialties, cardiology, pulmonology, sleep electrophysiology, pain therapy, intensive care, pharmacology, all for the purpose of contributing to the development of medical science. In addition to understanding the medical community, this activity requires their personal engagement as well.

## Acknowledgements

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## Conflict of interest

None.

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