

## ARTYKUŁ POGŁĄDOWY / REVIEW PAPER

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# Historia anestezji – praca poglądowa *History of anaesthesia – reviewpaper*

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## Streszczenie

Anestezja wywodzi się od dwóch greckich słów, które dosłownie oznaczają „bez zmysłu”. Można zatem stwierdzić, że anestezja polega na przerwaniu przewodzenia impulsów nerwowych w obie strony, zarówno impulsów nerwowych aferentnych z komórek receptorowych oraz eferentnych do komórek efektorowych. Anestezja też jest określana jako znieczulenie ogólne lub potocznie narkoza. Cechą charakterystyczną każdego znieczulenia ogólnego jest możliwość jego zakończenia i przywrócenia świadomości pacjenta z powrotem do stanu wyjściowego. Historia anestezji opisuje stopniową realizację ludzkiego marzenia, aby wszystko co nieznanne i bolesne przespać i obudzić się szczęśliwym i bez złych wspomnień. Początkowo korzystano ze środków naturalnych. Później do niwelowania bólu wykorzystywano znieczulenie gazowe. Natomiast współcześnie najpowszechniejsze jest znieczulenie dożylnie. *Anestezjologia i Ratownictwo 2023; 17: 49-55. doi:10.53139/AIR.20231707*

*Słowa kluczowe: anestezja, podtlenek azotu, eter, chloroform*

## Abstract

Anaesthesia is derived from two Greek words that literally mean “senseless”. It can therefore be concluded that anaesthesia consists in interrupting the conduction of nerve impulses in both directions, both afferent nerve impulses from receptor cells and efferent nerve impulses to effector cells. Anaesthesia is also referred to as general anaesthesia or colloquially narcosis. A characteristic feature of any general anaesthesia is the ability to end it and return the patient’s consciousness back to its initial state. The story of anaesthesia describes the gradual realization of a human dream to sleep through everything unknown and painful and wake up happy and without bad memories. Initially, natural resources were used. Later, gas anaesthesia was used to eliminate pain. In contrast, intravenous anaesthesia is the most common nowadays. *Anestezjologia i Ratownictwo 2023; 17: 49-55. doi:10.53139/AIR.20231707*

*Keywords: anaesthesia, nitrous oxide, ether, chloroform*

## Introduction

Undoubtedly, pain has caused great problems for both patients and doctors since ancient times. It is safe to say that it was an important hindrance that inhibited the development of surgery. Doctors, trying to relieve patients, used natural

remedies to relieve pain. Only in the 19th century there was a breakthrough, because nitric oxide, ether and chloroform were discovered. This was already a small progress, however, the use of these substances was associated with high risks. Effective intravenous anaesthesia was not used until the 20th century.

## Ancient and medieval anaesthesia

For a very long time, both in antiquity and in the Middle Ages, natural remedies were relied on. The Babylonians, in order to minimize toothache, used henbane [1]. It is a plant with hallucinogenic properties. It was 2200 BC. The Chinese, on the other hand, began using acupuncture in 1600 BC to stimulate circulation and relieve pain [1]. In addition to the substances mentioned, mandrake was also often used [2]. Its various forms, whether tincture, or in combination with flour or cooked in wine, were recommended for depression, wound healing, and pain relief in people who had burnt diseased tissues. Aconite was also used as an anesthetic. This plant is poisonous, but in small doses the aconitine contained in it has analgesic properties. Arthritis was once treated with it. In India in the 6th century B.C.E. cannabis vapors were used [3]. It can be said that these were the first beginnings of inhalation anaesthesia. It is also necessary to mention here the technique of anaesthesia of the Assyrians, who, before operations, especially cataracts, used pressure on the carotid artery to induce loss of consciousness [3].

In the Middle Ages, the so-called sleeping sponge was very popular. It was a material impregnated with a mixture of the previously mentioned substances: opium, mandrake, hemlock and henbane mixed in the right ratio with water [4]. Later, such a soaked sponge was dried in the sun, and just before the procedure, boiling water was poured over it and small pieces of it were inserted into the patient's nostrils. To wake the patient up, a sponge soaked in warm vinegar was inserted into his nostrils. The method of anaesthesia was very effective, but the problem was that not everyone was able to wake up after the procedure [4]. In Europe, high-percentage liquors were also very popular when it came to relieving surgical pain. The sleeping sponge also found its supporters here, especially in Italy, where it was used in a slightly modified composition until the eighteenth century [4]. For anaesthesia in sponges, the following were used in Europe: lettuce seeds, poppy pods, climbing ivy juice and unripe berries. Patients were awakened by inserting fennel roots into their nostrils. It is not known why this method of anaesthesia was finally abandoned. Theories say that these practices came to be associated more with magic than with medicine, and another says that alternative, more effective methods were simply discovered.

One of the researchers who undoubtedly made history when it comes to modern achievements in the field of anaesthesia was Valerius Cordus. He has a considerable achievement to his credit, which was the synthesis of ether. He did it in 1540 [1]. Valerius Cordus was a doctor of German origin, he discovered ether by dehydration of ethanol with sulfuric acid. Some sources confirm that Cordus learned this method thanks to Portuguese travelers who brought this knowledge from India [5]. Another doctor who undoubtedly contributed to the development of modern anaesthesia is William Harvey. He is an English biologist who in 1628 published a work in which he described the discovery of blood circulation in the human body [1]. This means that the injected substance will be distributed throughout the body. Based on Harvey's discovery, other researchers began working on intravenous therapies. For example, Christopher Wren and Robert Boyle began experimenting with opium and injecting it into dogs. They have proven that the substance administered in this way affects their entire body.

## The milestones a modern anaesthesia

### Laughing gas

The history of laughing gas dates back to 1772 [6]. It was then that Priestley isolated nitrous oxide, commonly known today as laughing gas due to its euphoric properties. Originally, however, it was given the term "dephlogisticated air" [7]. Later, more studies were carried out and various experiments were carried out with the use of nitrous oxide. One of the chemists, Humphry Davy, experimented with nitrous oxide on himself and concluded that it "appears to be capable of destroying physical pain, and probably can be successfully used in surgical operations where there is no high blood effusion." [8] However, nitrous oxide didn't work as well as Davy initially suspected. Its use was limited to recreational use as "laughing gas" in the early 19th century. However, in 1844 he was reinstated to medical practice [6]. American dental surgeon Horace Wells used it during tooth extraction. The failed procedure and its wide publicity saw nitrous oxide removed from the medical arena and replaced by noteworthy inhalation anesthetics. Laughing gas was appreciated only about 100 years after its first discovery [9]. It was especially effective in dentistry, later also its use extended to surgery and obstetrics. Since then, the administration of nitrous

oxide has undergone numerous advances, increased safety and reliability. Nowadays, the use of nitrous oxide as an auxiliary inducing agent of anaesthesia in dentistry and in the operating room has been well established [9].

### Ether

October 16, 1846 is a memorable date in the entire history of anaesthesiology [5]. It was on this day, and more specifically on Friday, that the world's first successful demonstration of ether in the form of vapor as a means of neutralizing surgical pain was made. It was presented by dentist William Thomas Green Morton at Massachusetts General Hospital in Boston, USA [5]. The history of ether begins with Valerius Cordus and the year 1540 [5]. Cordus named the substance he discovered "sweet vitriol oil" and recorded its healing properties. Both ether and nitrous oxide were used as entertainment intoxicants until the 19th century. It is not known why doctors have been fighting for so long to eliminate pain from doctor's offices. It is highly likely that the euphoria of ether and nitrous oxide obscured any potential for practical application. Morton, hoping to make a fortune, decided to patent ether [5]. He tried to introduce a patented mixture called Letheon, which was a mixture of ether and orange oil, but it was unsuccessful. The Europeans used to reward scientists with large sums of money in exchange for the fact that they bestowed the goods of science on humanity. The Americans, however, did not honor such a rule. Until the end of his days, Morton applied for \$100,000 in Congress, which was supposed to be compensation for his kindness [5]. Other scientists, Jackson and Wells, claimed that it was they who made the basic discovery and were opposed to Morton receiving any reward for his achievements [5]. In the end, however, all three scientists ended badly. Wells committed suicide [5]. Jackson never got the recognition he certainly deserved because he was the one behind the invention of ether. He also felt bitter because he was convinced that he also gave Morse the idea for the telegraph. Eventually he ended up in an insane asylum [5]. Morton, on the other hand, was rightly honored with numerous medals and fame for what he had done, but he never acquired the wealth he sought so much.

### Chloroform

The year 1831 is assumed to be the date of discovery of chloroform [10]. It was then that Guthrie,

Soubeiran and Liebig independently reported the discovery of a compound that was formed by the distillation of a mixture of concentrated ethyl alcohol and calcium chloride [11,12,13]. Three years later, another scientist, Dumas, determined the chemical formula for this compound -  $\text{CHCl}_3$  and named it chloroform [11, 12, 13]. Soubeiran and Liebig were aware that they had made a phenomenal discovery of a new compound, while Guthrie thought he had discovered a simpler and cheaper method of producing chlorine ether [14]. He read about chlorine ether and its properties from Silliman's Elements of Chemistry of 1831 [15]. After reading, he was fascinated by the commercial possibilities of using this product. Although the common date for the discovery of chloroform is 1831, it is likely that chloroform existed as early as 1830. Its discoverer was supposed to be a German pharmacist from Frankfurt (Oder) – Moldenhawer [16, 17]. It was he who, in the early fall of 1830, published a new process for removing impure fusel oil from ethyl alcohol prepared from potatoes. Delving into the various methods used to purify alcohol, Moldenhawer mentioned Zeise's procedure [18], which involved adding one-quarter lotha (2.5 g) of calcium chloride to one-quart (1 L) of ethyl alcohol, shaking it frequently and vigorously mixture for 20-24 h and distilling the alcohol (lot and quart are German measures of that period). Moldenhawer found fault with Zeise's method: he found fusel oil in the distillate and none in the residue. He also noticed that shaking the mixture vigorously released a strong smell of what he thought was chlorine ether. Therefore, it seems that chloroform may have been discovered by Moldenhawer. He, like Guthrie, mistakenly labeled the substance chlorine ether because of its similar smell.

### Ethyl chloride

Ethyl chloride was introduced into surgery in 1848 by Johan Heyfelder [19]. The anesthetic properties of this compound were described by Flourens in 1847 [19]. Heyfelder used it to anesthetize three patients, but soon realized that ethyl chloride had no future due to cost and volatility. In 1894, the substance was restored to favor by Carlson McCardie, a Swedish dentist [19]. It turned out that ethyl chloride works great in local anaesthesia. It was then that this substance became popular among dentists. Although in the first half of the 20th century this substance was used on a large scale, this agent never gained widespread approval of

anaesthesiologists. In the last decade, the vast majority of centers resigned from its use [19].

### Chloral hydrate

Chloral hydrate appeared in the 18th century [2]. The first person to use it was Matthias Liebreich in 1869. The beginning of general anaesthesia is considered to be the intravenous use of chloral hydrate by the surgeon Pierre Ore in 1874 [2]. With this substance, he put a 52-year-old man in the acute phase of tetanus to sleep. He was anesthetized with 9 g of chloral hydrate dissolved in 10 g of water [2]. The patient fell asleep almost immediately. During the procedure, Ore gave the patient anaesthesia three more times. In total, the patient slept for 11 hours [2]. It was a great success for Ore. He immediately decided to inform the French Academy of Sciences about his achievement, but the high mortality rate during dosing of this anaesthesia meant that it did not gain universal approval. We had to wait a little longer for intravenous anaesthesia, which is the standard today.

## Modern advances in anaesthesia

### Intravenous anaesthesia

At the latest, only in the 20th century, intravenous general anaesthesia was introduced. In 1932, hexobarbital was introduced in short operations [1]. Then, in 1934, thiopental was used [1]. Intravenous anesthetics have the advantage over inhalation anesthetics that they cause a rapid onset of anaesthesia after a single dose, and loss of consciousness occurs within 10-15 seconds from the start of the injection [1]. In addition, intravenous anaesthesia does not cause irritation of the respiratory tract or malignant hyperthermia.

Since the introduction of thiopental, propofol, ketamine, etomidate, dexmedetomidine and benzodiazepines have gained in importance among intravenous drugs [20,21]. Scientists are constantly trying to develop newer drug formulas and introduce new chemical compounds to improve effectiveness, safety and minimize side effects. One of the widely used intravenous drugs is midazolam. It has a sedative and anxiolytic effect [20]. The disadvantages of this drug include the lack of analgesic effect, as well as prolonged convalescence in patients with liver dysfunction [20]. Remidazolam is a new drug, a short-acting anesthetic. It was created on the basis of esters, and its metabolism is not dependent on liver and kidney enzymes [20,22].

It is currently in phase III clinical trials in the United States [20, 22]. Remidazolam combines the properties of two drugs commonly used in anaesthesia: midazolam and remifentanyl [20].

Etomidate was first introduced into general use in 1972 [20, 23]. Its popularity was mainly due to its mild effect on the cardiovascular and respiratory systems. Side effects may include pain at the injection site, myoclonus, as well as nausea and vomiting. In addition, it is very dangerous to administer etomidate by long intravenous infusion, as it is associated with increased mortality in critically ill patients. It is currently not used as an extended infusion and is limited to a single bolus. Although the administration of etomidate, even in limited doses, is very controversial [20,23].

Propofol is a drug that has been transforming ever since it was introduced into clinical practice [20,24,25,26]. It still enjoys widespread recognition among anaesthesiologists and is still considered an almost ideal anesthetic [20,24,25,26]. It owes its success primarily to the quick onset of action, short duration of action and minimal side effects [20,24,25,26]. It is called an almost ideal anesthetic because it has several significant disadvantages: its oily consistency increases the risk of bacterial contamination and hyperlipidemia [20,26]. There may be severe pain during injection and a potentially fatal risk of propofol infusion syndrome [20,25]. The truth is that the perfect anesthetic does not exist. However, work is currently underway to modify propofol to further minimize the side effects of this drug [20,26].

### Inhalational anesthetics

Despite the huge progress in research on the use of intravenous drugs, inhalation anesthetics continue to be an important element of general anaesthesia. Inhalational anesthetics include isoflurane, enflurane, sevoflurane, desflurane and halothane [27,28,29,30,31]. Isoflurane and enflurane are relatively rapidly absorbed and excreted. Like halothane, they have a depressant effect on breathing, with enflurane more strongly than isoflurane. In addition, they also have a sensitizing effect on catecholamines and reduce peripheral vascular resistance. Enflurane metabolites are nephrotoxic [32]. In addition, tonic-clonic muscle contractions have been reported during general anaesthesia with enflurane. Therefore, it should not be used in predisposed patients, e.g. epileptic patients [32].

Sevoflurane and desflurane, created by replacing chlorine atoms with fluorine, are, like laughing gas, easy to control [27,28]. This means that the patient can be woken up quickly after the procedure. In terms of their effects on the respiratory, cardiovascular and muscular systems, they resemble the properties of isoflurane [29]. Sevoflurane stands out from other modern ether derivatives in that it is the only one that is not metabolized to toxic trifluoroacetic acid [27]. Among the main advantages of desflurane is that it is neither nephrotoxic nor hepatotoxic. However, its disadvantage is strong irritation of the respiratory tract [28].

Halothane has a very weak analgesic and myorelaxant effect. It is the only halogenated hydrocarbon. It has a pleasant smell. The advantages of halothane include the fact that it does not create explosive mixtures with air or oxygen, has a strong anesthetic effect, does not irritate the mucous membranes, and reduces the tension of the bronchial muscles [30,31]. However, there are many disadvantages in favour of its increasingly rare use, such as the respiratory depressant effect, the possibility of cardiac arrhythmias, liver damage when using high concentrations, and the narrow range of anaesthesia [30,31]. It is also worth adding that halothane has a rather historical value, which explains why it was discussed last.

### Musclerelaxants

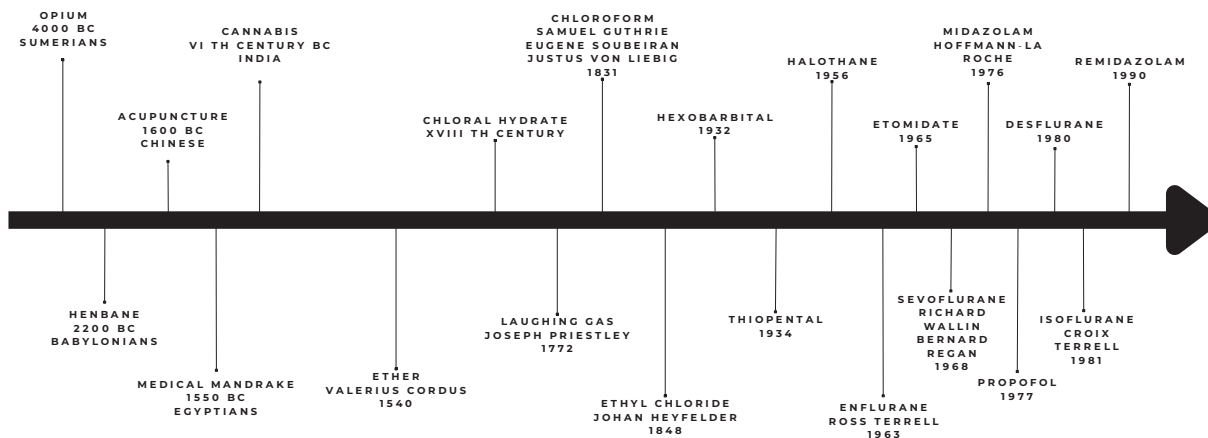
Muscle relaxants are part of anaesthesia, they do not have an anesthetic effect, but thanks to muscle relaxation, they facilitate ventilation of the patient and create better operating conditions for the surgeon.

## Discussion

The tasks of the first anaesthesiologists of the second half of the 19th century included primarily focusing on how to minimize the pain experienced by the patient during surgical procedures, as well as the issue of patient safety after using a given agent. The vast majority of operations at that time concerned the surface of the body [5]. The introduction of the principles of antisepsis and then asepsis made it possible to expand the scope of operations in the 1880s [5]. This was also associated with the introduction of changes in anesthetic techniques. The changes, however, became an impulse for further discoveries. For example, the use of local anesthetics in regional anaesthesia began, muscle relaxants, new safer inhalants and intravenous anesthetics were used [5]. The tremendous development and progress that has been made in the field of anaesthesiology, both in terms of monitoring and a better understanding of issues related to pain and awareness, mean that there are now hardly any fears about the use of anaesthesia. Anaesthesia, which is now much safer than before, can be used in any patient undergoing any surgical operation, regardless of health or age.

## Summary

The history of anaesthesiology dates back to antiquity. Anaesthesiology has been constantly developing since then, thanks to which today we have highly effective and safe drugs that minimize or almost completely eliminate the pain associated with surgical procedures. Many



Rycina 1. Historia anestezji

Figure 1. History of anaesthesia

names have gone down in history, whose discoveries shaped the contemporary image of the field of anaesthesiology. It is worth noting that most of the important discoveries were made by ordinary people who were not discouraged by failures and setbacks. Today, we owe a safe and painless operation to those who boldly took their first steps in the world of science, to pioneers who discovered new benefits for humanity, often at the expense of their own interests. One of them was certainly Morton, who was the discoverer of inhalation anaesthesia. Modern medicine will forever be grateful to Morton and the other unsung heroes who gave us anesthetics.

Konflikt interesów / Conflict of interest  
Brak/None

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