

Edward Jenner (1749-1823), the pioneer of vaccinology. On the bicentenary of his death

**Radosław Karaś¹, Konrad Barszczewski¹, Martyna Białasiewicz¹, Halina Kulik¹,
Tomasz Lepich²**

¹ Department of Propaedeutics of Nursing, Faculty of Health Sciences in Katowice, Medical University of Silesia in Katowice, Francuska Street 20/24, 40-027 Katowice, Poland

² Department of Anatomy, Medical University of Silesia in Katowice, Medyków street 18, 40-762 Katowice, Poland

Abstract

Edward Jenner (1749-1823), a doctor originating from England, is the man who initiated the vaccination process against smallpox. This disease had been decimating the world's population for hundreds of years, while at the same time, due to its high infectivity, making treatment of other diseases impossible. Throughout this time, mankind was losing the unequal battle against the virus with tragic results. Understanding the nature of the problem smallpox posed at the time made Edward Jenner's discovery revolutionary. The depth of knowledge concerning the disease, the numerous observations, and the experiments carried out made it possible to begin the process of universal vaccination. The English doctor's professional life was clearly subordinated to intensive work on combating the virus effectively. During the doctor's lifetime, praise for Edward Jenner's feat was expressed by such figures as Napoleon Bonaparte and Empress Catherine II. His discovery of variolysis against smallpox revolutionised medicine, enabled the subsequent eradication of this viral disease, and provided the impetus for further attempts to combat infectious ailments. (*Farm Współ* 2023; 16: 91-97) doi: 10.53139/FW.20231610

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Introduction

The pandemics affecting the world over the past decade or so have led to a significant popularisation of topics related to immunology and infectious diseases. Influenza, AIDS, and COVID-19 are just a few examples of diseases that, by causing the deaths of millions of people, have become major social problems worldwide. Widespread globalisation and access to information sources of unidentified origin mean that science-based content is increasingly becoming the subject of disputes and arguments, such as the validity of vaccination. At such moments, it is worth reflecting on the history of diseases that have severely affected humanity over the centuries, causing the deaths of millions of people. Particular attention should be paid to those who have had a revolutionary impact on the history of medicine by initiating new branches of medical science. Their innovative views required not only diligent work but

also courage and strength in disseminating them. A prime example is the English physician Edward Jenner, the discoverer of smallpox vaccination.

When on 14 May 1796, he vaccinated an eight-year-old boy James Phipps against cowpox, the method was initially met with much disbelief and even derision. Many doctors considered it dangerous, and in applying it, they deliberately made mistakes, the consequences of which were attributed to Jenner. There was also no shortage of collective actions aimed, under widely various appearances, at combating this method of eradicating a massively fatal disease.

The chorus of dissenting voices included even a statement by Pope Leo XII: "Anyone who submits to such vaccination is not a son of God.... Smallpox constitutes a divine judgment.... Vaccination is a challenge from heaven". It was even said that the vaccinated would grow cow horns. Some called the Jenner method "the

greatest villainy committed in the last semicentenary”, while others paid a fortune for a thread soaked in pus from cow’s udder [1].

Despite these difficulties, Jenner’s vaccine began to be used widely around the world, and in less than two centuries, the disease was defeated. In 1980, the World Health Organisation declared smallpox wholly eradicated. It is worth mentioning that not much before that, in 1963, Wrocław became a victim of smallpox. The source of the outbreak in this city was an intelligence worker who came to the country directly from Delhi (India). Despite previous vaccination, the virus was transmitted to Poland. The officer recovered, but he became a source of infection for more people; 99 people became ill, and seven died. Introducing a sanitary regime and vaccination campaigns helped minimise the further development of the epidemic [2].

A brief history of smallpox

Smallpox is a contagious disease to which modern people are no longer exposed. However, it has been ranked among the greatest human disasters decimating the world’s population throughout the centuries. The history of the disease dates back to the dawn of mankind. It probably originated in Africa, from where it was transferred to Asia, mainly India, by Egyptian traders. Although the first descriptions of this disease date only from the 4th (China) and seventh (India and the Mediterranean) centuries AD, traces of infections can be found on ancient Egyptian mummies and writings [3,4]. The existence of a cult of ‘sacred smallpox matter’ in China around 1500 BC indicates that the disease was well-known there [5].

One of the largest population centres in antiquity was the Nile Valley. It is estimated that around one million people inhabited the land in the 3rd century BC. Such a high concentration of people and the paramount economic and commercial importance of this region meant that Egypt was probably the place from which smallpox began its worldwide spread [3]. The first traces of skin lesions that may indicate getting over smallpox were discovered on Egyptian mummies dating from 1570-1085 BC. It includes the mummy of the pharaoh Ramses V, who died in 1157 BC [6].

During the abovementioned period, Greece was the main centre of social life and consequently a densely populated area in Europe. Around 400 BC, it had approximately 3 million inhabitants. The multiple migrations and social transformations characteristic

of the early Christian era resulted in the transfer of the main centre of the continent from Greece to Rome. Although the first unequivocal descriptions of smallpox in Europe date from the sixth century, it has been suggested that the disease decimated the continent’s inhabitants much earlier. Smallpox is believed to cause the so-called Athenian plague in the fifth century BC. The disease was said to have originated in Ethiopia and then spread via Egypt and Libya to the Mediterranean and the port of Piraeus, and from there further to Athens. The 6th century was the first time the Latin term ‘variola’ was used, from ‘vurius’ = mottled or ‘vurus’ = pimple. The author of the term was the bishop and chronicler Marius of Aventicum, who used it to describe epidemics in France and Italy [3].

What is surprising is that smallpox is not mentioned in the ancient guiding books. The subject is omitted from both the New and Old Testaments and from classical Greek and Roman literature. Therefore, all analyses are based on chroniclers’ descriptions, such as Tukidides (Greece, 5th century BC).

The Persian physician Rhazes (865 – 925 AD, chief physician of the Baghdad hospital, considered one of the greatest physicians of the Islamic world), who first described measles and smallpox in his classic monograph ‘A Treatise on Smallpox and Measles’, stated that it was Galen who first recorded it in the 2nd century. Although the disease was known in China and India around 1000 BC, it is widely believed that the first recorded epidemic occurred in 570 AD in Arabia. At this time, the Abyssinian army, under the command of the Christian leader Abrah Ashram, was about to launch an attack on Mecca, to destroy the Kaaba (the holy shrine of the Arabs). The soldiers carrying out the raid were tragically decimated. A report of the event can be found in the Koran (Islam’s holy book), according to which God would send flocks of birds showering the attacking army with stones that caused ulcers and pustules. Historians estimate that this was the first smallpox outbreak. Following this, smallpox was transmitted to North Africa and Europe by Arab invaders in the sixth, seventh, and eighth centuries. On an inordinately wider scale, the disease was spread to the Old Continent by the Crusaders returning from the wars to reclaim the Holy Land (1096 – 1291) [7].

Also of interest is the English term for this disease – smallpox (small pox). The term ‘variola’ was used in Europe until the 15th century. However, during this time, a new disease emerged in Europe that also mani-

fested as pustules, but of a larger size than smallpox. As it mainly affected adults, it was therefore referred to as 'greatpox'. It should be clarified that the mentioned disease was syphilis [3,4].

Smallpox was brought to the Americas by Spanish conquistadors in the late 15th and early 16th centuries. There, it decimated the indigenous population and contributed to the collapse of the Inca state in western South America and the Aztec empire [3,6].

In the 17th and 18th centuries, smallpox had a tragic course in Britain; the disease even affected Queen Mary II in 1694, being the cause of her premature death at the age of 32. The virus ravaged European cities, responsible for 400,000 deaths yearly, and those who recovered had severe complications such as blindness [7].

Over time, it was noticed that people who had previously recovered from smallpox became immune when they were exposed to the virus again. As a result, doctors were deliberately infecting patients in appropriate cases in the hope that such an initiated infection would prove less severe in its consequences. The immunization method consisted of administering pus from pustules, vesicles, or scabs which is a material taken from infected individuals. Approximate methods of acquiring immunity gained popularity in China, where patients were advised to snort powdered scabs of smallpox pustules through their nostrils. In the same country, 100 years before Jenner's discovery, tablets of cow fleas were administered to a healthy part of the population, which is now recognized as the first recorded example of oral vaccination. The variolation technique was spread by merchants traveling in caravans, who were at exceptional risk of getting infected and, at the same time, could quickly spread pathogenic microorganisms. The acquiring of immunity was also practised in the Ottoman Empire, with the variolation technique being introduced by Cherokee merchants in 1760. Innovative methods of combating smallpox began to reach Europe from Istanbul in the early 18th century. Despite the crisis associated with the rapid development of the disease, which was slowly devastating society, the conservative English medical community was quite sceptical of news from the East [8].

It is unthinkable to imagine what the present would look like if it were not for the groundbreaking achievement of English physician Edward Jenner. What is certain is that smallpox would take an even more significant toll, causing the deaths of an additional million

people. Characteristics of the 20th century, developments in science and technology, and achievements in molecular techniques have allowed scientists to trace the history of the spread of smallpox using historical evidence. Therefore, nowadays, we can undoubtedly claim that it was one of the most devastating diseases in the history of mankind. It is precisely why we can consider the initiation of the vaccination process by Edward Jenner as a watershed moment in the history of medicine and humanity.

Life and activities of Edward Jenner

Edward Jenner was born on 17 May 1749 in Berkeley. He was the third son of the clergyman Stephen Jenner. Edward's brothers: Stephen and Henry, followed in their father's footsteps. A particular role in Edward's life was played by Stephen, who looked after his younger brother when their parents died. Edward was five years old at the time. As a child, he suffered severely from smallpox. Perhaps this unpleasant event in his life was the reason for his later interest in fighting this disease [9-11].

Young Edward began his education at the age of eight at Wotton-under-Edge and then at a grammar school in Cirencester. From the beginning, he showed a strong interest in nature and natural history. He was interested in ornithology by studying the biology of cuckoos and bird migration. Jenner studied the behaviour of cuckoos, which involves appropriating a nest and throwing the chicks of other birds outside the appropriated nest. He even described the anatomical adaptations of the dorsum of cuckoos that facilitate this foul act. Although he was not wrong, his theses did not initially receive wide recognition and, moreover, were repeatedly ridiculed. In addition, Jenner conducted research on the state of hibernation among hedgehogs [9,12].

In his spare time, he also played the violin [13]. At the age of 12, he came under the wing of the surgeon Daniel Ludlow (1720-1784), who practised in Sodbury, near Bristol. There, for the next nine years, Edward Jenner gained knowledge and practice in surgery and pharmacy. Jenner and Ludlow may have been distantly related through descent from the Nelme family of Stinchcombe [9,10,14]. In 1770, at the age of 21, Jenner moved to London to continue his surgical training at St. George's Hospital. In the capital, his teacher and friend was Dr. John Hunter (1728-1793), whose house he lived in for the next two years [4,9-11]. At that

point a few words should be said about John Hunter and his achievements. Born in 1728, this farmer's son left school at the age of thirteen. Shortly afterward, he moved from Scotland to London, where he helped his older brother William to procure cadavers for his newly established anatomical school. He did this by working with grave robbers. Then he came under the wing of the highly regarded surgeon William Cheselden at the Royal Hospital Chelsea. Among other things, Hunter described the process of bone growth and healing. He improved many descriptions of anatomy, discovered with his brother the separation of maternal and fetal blood circulation, and performed mastectomy operations. He also collected many natural history specimens (about 14,000). He stored them in his house, which also contained a dissecting room and lecture theatre. In 1767, Hunter became a member of the Royal Society [15,16]. It shows that Edward Jenner learned the art of medicine from the best. The student's capacity for analytical thinking and precise preparation and drawing made his work very helpful to Hunter. With these skills, Jenner was employed by Sir Joseph Banks on the recommendation of his master. His job was to describe the natural specimens brought by Captain Cook from his first expedition of 1771. After this work, he was even reportedly offered the position of onboard naturalist on the captain's next planned voyage. However, Jenner was said to have declined the offer, which he supposedly explained by his attachment to his hometown and his loved ones [4,11]. Edward Jenner returned to Berkeley in 1773. Here he practised medicine and enjoyed great popularity in his hometown community [9,10].

A friend of Jenner's from his school years was Caleb Hillier Parry. They both shared a passion for fossils and natural history. Both also associated their future with medicine. Parry conducted successful research on angina pectoris and arterial pulse [10]. In 1808 Jenner met Dr John Baron, with whom he also became friends. After his death, it was Baron who was entrusted with his late friend's notes and the task of compiling a biography of the doctor. Baron worked meticulously over the following years, feeling the responsibility of the task given to him. The final result of his work was published in 1827 in the form of a two-volume book, which was widely acclaimed for its exceptional detail [11].

In 1778 Edward Jenner married Catherine Kingscote. They had three children: two sons and a daughter. The eldest son, Edward Robert, was born in 1801, and his godfather was John Hunter [4,10-12,17].

While staying at Sodbury, Jenner witnessed a conversation between a villager (who milked cows for a living) and D. Ludlow. During this discussion, the woman stated that she could not get smallpox because she had a history of cowpox [10,11,13,14]. Among other things, these words prompted the young medical student to consider and research the question of the immunity to smallpox that previous exposure to cowpox can provide. Cowpox is a viral disease that mainly affects domestic cats and cattle. However, it can also affect humans and manifests itself as pustules on the body. Nowadays, the disease is almost non-existent. However, it was different when Edward Jenner lived [18]. Jenner shared his thoughts with Hunter, to which Hunter replied – “*Jenner, don't think, try*”. Jenner, however, decided to do both. He was prepared for failure and ridicule. Having this in mind and following in the footsteps of Galileo or Copernicus, he tried to confirm the thesis he had put forward [4].

Jenner conducted his first experiment on his son Edward Robert in November 1789 and inoculated him with swine pox. Carrying out this experiment on his child shows how much Jenner believed in the veracity of his theory. After eight days, the boy developed the disease with the appearance of pustules, but after some time, the illness receded. Jenner then re-injected the swine pox material into his son's arm, but the son did not develop symptoms. He also repeated the attempt to infect him in 1791 and 1792. Each time the disease did not occur, which was a testament to the effectiveness of the vaccination [4,10,11].

At this point, it should be noted that Jenner was not the first originator of this type of vaccination. Mary Wortley Montagu, the wife of an ambassador at the Ottoman court, wrote a letter to her friend Sarah Chiswell of Adrianople in 1717, describing an experiment of vaccination against smallpox. She also confessed that she trusted the method and planned to have her son vaccinated, which she did in March of the same year. The procedure was performed by an old Greek woman assisted by Dr. Maitland – the embassy surgeon. Part of Mary Wortley Montagu's plan was also to persuade doctors in England to start vaccinating the population. It resulted in the publication of the first essay recommending smallpox vaccination in England in 1721. However, it gained relatively little popularity at the national level. In 1722, selected Newgate inmates sentenced to capital punishment were offered a reprieve if they submitted to vaccination. It was primarily to

assess the safety of this procedure. Six prisoners acceded to the offer. In each case, the process proved to be safe. Citizens of the UK were very sceptical about vaccination at the time. Robert Sutton, a specialist in surgery and pharmacy, was involved in the process of their promotion, and in eleven years, beginning in 1757, vaccinated about 2500 inhabitants of the country against smallpox [4,10].

In a book entitled 'An inquiry into the causes and effects of the variolae vaccinae, a disease discovered in some of the western countries of England, particularly Gloucestershire and known by the name of the cow-pox', published in 1800, Edward Jenner describes twenty-three cases of people he vaccinated. It is where the case of 14 May 1796 is described. Edward Jenner took fluid from the skin bladder of the hand of milkmaid Sarah Nelmes, who was suffering from cowpox. Then he inserted the collected contents through a scratch wound on the arm of 8-year-old James Phipps. The boy subsequently developed a mild illness from which he quickly recovered. On 1 July that year, Jenner inoculated James with smallpox. The disease did not develop, nor did it after a second administration in the spring of 1797. It was a key moment in vaccine research [4,9-11,13,19].

After the experiment, Jenner made a report, but it was rejected by the president of the Royal Society – the most significant scientific tribunal in England. The position of president at the time was held by the botanist of James Cook's first expedition, Sir Joseph Banks. At the insistence of friends, Jenner published the report independently the following year. He dedicated it to his friend Dr. Parry of Bath [4,10,11]. In London, Jenner's manifesto was supported by Mr Cline, of St Thomas' Hospital. He carried out further inoculations, writing of the discovery itself "it is one of the greatest improvements ever made in medicine". A year after Jenner published his pamphlet, a manifesto appeared on the validity and efficacy of smallpox vaccination. This manifesto was topped by the signatures of more than seventy London doctors [4,11,13].

Beginning in 1800, when Jenner was hosted by the Prince of Wales, the world recognised Jenner's achievement on a wide scale and smallpox vaccination took over the globe. Compliments came, among others, from Napoleon and the then Empress of Russia, Catherine II. The Empress ordered that the first child vaccinated in her country be named Vaccinoff; she would also provide the child with an education and a living wage.

Catherine II had a crucial influence on the dissemination of vaccinations in the then Russian Empire. In turn, Napoleon ordered that all his soldiers who had not yet suffered from smallpox should be vaccinated against the disease. Moreover, at Jenner's request, he released several English captives, which he argued with the words "*what that man asks is not to be refused*" [3,4,10,11]. However, not everyone believed in the validity and effectiveness of Jenner's proposed method. In London, Jenner's opponents were Dr. Woodville and Dr. Pearson. Opponents of vaccination created caricatures depicting Jenner as a breeder of children with cow horns [4,13]. Nevertheless, smallpox vaccination was made mandatory in England from 1853 onwards. It is worth noting that such an obligation already existed in at least five countries on the old continent [4].

Since 1798, Jenner had claimed that vaccination gave permanent immunity against smallpox. Three years later, he was forced to change his position, which he explicitly admitted in 1808. In 1804, he concluded that in some cases, revaccination, what we would call today a booster dose, was necessary. This conclusion was based on observations that indicated that herpes could reduce the effectiveness of vaccination. Such a change of opinion only demonstrates the maturity of the doctor and the conscientiousness of his observations. When Jenner was at his home in Berkeley, he carried out mass vaccinations, and the vaccination point was a hut in his garden. Its constructor was a friend of the host, Robert Ferryman [12].

Despite such widespread worldwide recognition, it was not until 1801 that parliament decided to award Jenner a grant of £10,000. However, this was not paid until three years later and was reduced by £1,000. Five years after that deliberation, a second grant of £20,000 was awarded to him almost unanimously [4,9,10]. It should be noted that, up to this point, Jenner had covered the cost of vaccination with his private money. In 1793, Jenner obtained a doctorate from St Andrews University in Scotland [4,9,17]. In the same year, Jenner's friend Dr. Hunter died [10]. Two years later, Jenner took a job at the health resort at Cheltenham, where he worked during the summers until 1815 [4,12,17]. In 1813, Oxford University awarded him the degree of doctor honoris causa.

Edward Jenner was the founder of two medical societies: The Gloucestershire Medical Society (1788) and the Convivio-Medical Society, whose membership also included Daniel Ludlow jr. (1757-1802). At

the conventions of these societies, he dissertated not only on smallpox but also on angina and its relation to coronary heart disease. This is another indication of Jenner's strong social commitment and the breadth of his interests [10,12,17].

Until the end, Jenner remained grateful to James Phipps and funded his house in Barkley. From 1968 the building housed Jenner's museum, which in 1982 was moved to the doctor's former home [12,14,20].

Although carrying out vaccination of the population, a smallpox epidemic broke out in England in 1816, lasting three years. Jenner blamed the failure to protect the population on incorrectly carried out vaccination operations. He pointed out the importance of checking whether the vaccination was effective and, if it was ineffective, called for the vaccination activity to be repeated [12].

Jenner's work became the seed for the subsequent research of Louis Pasteur. Also, Von Pirquet – author of the term “allergy” – dedicated the first sentence of his publication to Edward Jenner [12]. The reason for this was the anaphylaxis described by Jenner, which occurred after vaccination in 31-year-old Mary Barge [17].

In 1810, the physician's eldest son died, and five years later, on 13 September 1815, his wife Catherine passed away. The cause of death was presumably tuberculosis [4,11,13,17]. A year before, this was the last time Edward Jenner visited his country's capital. He published his final paper in 1822, entitled ‘On the Influence of Artificial Eruptions in Certain Diseases’ [4,11]. On 6 August 1820, Jenner suffered a mild stroke. However, three years later, he had a second attack, which turned out to be fatal. Edward Jenner died on 25 or 26 January 1823 at the age of 73 [9,11,13]. Le Fanu described Jenner as “*He spent 24 years growing up, 24 years as a country surgeon, and 24 years as the apostle of vaccination*” [12]. Edward Jenner was buried on 3 February 1823 with his family in Barkley Church. The doctor's funeral gathered crowds to bid farewell to a great doctor, scientist, and social activist [10,11,17]. In 1858, a monument depicting Jenner was erected in central London. Four years later, however, the monument was relocated to Kensington Gardens. Certainly, this scenery would have pleased Jenner personally even more [4].

Conclusion

What emerges from Edward Jenner's biography is a picture of a doctor and scientist who, through his discovery, saved millions of people from death. In retrospect, however, we tend to forget and underestimate the achievements of earlier eras and our predecessors.

Nowadays, it is hard to imagine the further evolution of infectious disease medicine without the courageous discovery of Edward Jenner. His work inspired subsequent researchers and initiated successive victories in the fight against infectious diseases. Given the very low level of development of virology from the 18th/19th century, the English doctor's discovery was spectacular because, thanks to him, we could celebrate the eradication of smallpox in 1980. Edward Jenner is an example of a doctor and a good man who, through his determination and passion for medicine, changed the course of events, making a revolutionary change. His achievement, the creation of a vaccine, has also shown that this is a complex and challenging process that requires very specialised knowledge of how the human body functions, perseverance, and courage. All the more reason that work on new generations of vaccines should be continued. Smallpox can potentially be a biological weapon, especially for terrorist and non-democratic states and governments. In light of ongoing conflicts and globalisation, this problem should be viewed with particular awareness and responsibility. Continuing Edward Jenner's mission, the scientific world should focus on upgrading the available vaccines.

Conflict of interest

None

Correspondence address

✉ Radosław Karaś

Department of Propaedeutics of Nursing, Faculty of Health Sciences in Katowice, Medical University of Silesia in Katowice, Poland

Francuska St. 20/24, 40-027 Katowice

☎ (+48 32) 252 80 06

✉ s82860@365.sum.edu.pl

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