

HISTORICAL OVERVIEW OF THE DEVELOPMENT OF VACCINATION UNTIL THE END OF THE 19TH CENTURY

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Abstract. *Immunization is the process by which a person, due to a vaccine received, is immune or resistant to an infectious disease. The story of vaccination does not begin with the first medically framed vaccine by Edward Jenner, but with the understanding of the risks of infectious diseases in humans and in ancient times and attempts to provide immunity to that disease. Around 1100 AD, variolation techniques had been developed in Turkey, China, many African countries and some parts of Europe, which involved inoculating children and adults with dried scab material obtained from smallpox patients. This paper aims to systematically present the events that influenced the development of the process of passing laws or regulations on the obligation of mass immunization of people by the end of the 19th century. Thanks to the awareness of prominent people of that time, about the risks of spreading epidemics of serious infectious diseases, various techniques of variolation from many distant countries of the Old World were brought to Europe and America. This stimulated work on medical techniques to prevent the occurrence of deadly infectious diseases. Some of these prominent people are: Mrs. Mary Wortley Montagu, wife of the English ambassador to Turkey, English physician Charles Maitland, 17th century inventor Benjamin Franklin, Scottish physician Francis Home, Russian Empress Catherine the Great, English physician Thomas Dimsdale, as well as George Washington, then commander of the Continental Army in the US Civil War. After 1888 and the founding of the Pasteur Institute in Paris, the era of introducing public health laws began, which included a segment related to mandatory, recommended or absolutely voluntary immunization, thus beginning the modern era in human immunization.*

Keywords: infectious diseases, variolation, Jenner, vaccination, laws

Introduction

Immunization is the process through which a person becomes immune or resistant to an infectious disease as a result of vaccination. A vaccine stimulates the body's own immune system, providing protection against disease or future infection. Immunization is widely recognized as one of the most effective tools in preventing infectious diseases and has significantly reduced disability, mortality, and health inequalities across the globe (1). It is also one of the most cost-effective investments in public health, with well-defined strategies designed to reach even the most vulnerable and hard-to-access populations. Vaccination programs can be efficiently implemented in the field and do not require any changes in the lifestyle of vaccinated individuals (2).

Smallpox is considered one of the oldest known infectious diseases, responsible for hundreds of millions of deaths throughout history. The earliest written records of the

disease date back to 4th-century China. Some studies suggest that lesions resembling smallpox have been identified on Egyptian mummies, indicating that the disease may have existed for at least 3,000 years (3).

Although more than 300 years have passed since the discovery of the first smallpox vaccine in the late 18th century, the history of vaccination predates Edward Jenner's scientifically documented use of cowpox material to protect humans against smallpox. The story of immunization begins much earlier, with the understanding that individual health conditions could impact entire communities, and with early efforts to induce immunity by using material from infected individuals.

Historical sources indicate that as early as the 4th century BCE, Hippocrates described several diseases, including mumps, diphtheria, and epidemic jaundice (4). By the 12th century CE, variolation techniques had been developed, involving the inoculation of children and adults with dried material taken from smallpox scabs (5). The historian Joseph Needham, who researched the origins of vaccination in China, suggested that variolation may have been invented around the year 1000 CE by a Taoist or Buddhist monk—or possibly a nun. The practice, combining medicine, technique, and mystical traditions, was passed down orally and surrounded by cultural taboos, which likely prevented written documentation.

Other sources claim that vaccination practices existed in India thousands of years ago, citing references in ancient Sanskrit texts. These descriptions suggest a method involving the dipping of a sharp iron needle into a smallpox pustule and repeatedly puncturing the skin in a small circle, typically on the upper arm (6). Writing in 1731 about smallpox inoculation in Bengal, Oliver Coult reported that the procedure was first performed by Dununtary, a physician from Champanagar, around 1580 (6). It is also believed that Indian communities intentionally exposed children to a milder form of the disease by wrapping them in blankets contaminated with smallpox material. Similar variolation techniques were recorded in Turkey, Africa, and parts of Europe during this time (7).

The first Western physician to accurately describe smallpox was Ahrun (610–641), a Greek Christian Egyptian scholar from Alexandria. The most detailed early description of smallpox, including a clear differentiation from measles, was provided in the 10th century by Abu Bakr Muhammad ibn Zakariyya al-Razi (854–925), one of the most prominent physicians of his time. Soon after, documentation of variolation techniques emerged in various parts of the Ottoman Empire (8).

Many prominent historical figures recognized the dangers of epidemic outbreaks and their devastating mortality rates, especially among children. Their understanding of this threat facilitated the transfer of variolation techniques from non-European regions to Europe and, later, to the Americas. This exchange laid the foundation for scientific research aimed at preventing infectious diseases through systematic medical interventions (8). Key contributors to the advancement of vaccination include Lady Mary Wortley Montagu, English physician Charles Maitland, American inventor Benjamin Franklin, Scottish physician Francis Home, English physician William Heberden, Russian Empress Catherine the Great, English physician Thomas Dimsdale, George Washington, then-commander of the Continental Army during the

American Revolutionary War, and Edward Jenner, widely regarded as the father of modern vaccination. This paper aims to systematically trace the events and discoveries that paved the way for mass vaccination, documenting the development of immunization practices around the world up to the end of the 19th century. It is also necessary to note that we find new motivation for this reminder of the ancient roots of vaccination in the not-so-new anti-vaccination movement, which, unfortunately, also has repercussions in our country and region.

Study Design and Methods

This study employed a comprehensive literature review to examine the historical development of immunization practices up to the end of the 19th century. Sources included the PUBMED database, Google Scholar, publicly available documents from medical school websites, educational centers specializing in immunization, and the official website of the World Health Organization (WHO). A structured search strategy was used, relying on key terms such as infectious diseases, variolation, Jenner, vaccination, and legislation. All retrieved literature was critically reviewed, and the extracted data were organized and presented in chronological order to provide a clear and systematic overview of the evolution of vaccination systems worldwide.

Results and Discussion

Ian and Jennifer Glynn, in their book *The Life and Death of Smallpox*, note that by the late 16th century, Emperor K'ang Hsi—who had survived smallpox as a child—had been inoculated. The method involved grinding scabs from smallpox pustules and insufflating the powdered material into the nostril. In China, it is believed that the technique of variolation was introduced from India during the 11th century. Inoculation could also be performed by scratching the skin with material taken from smallpox sores (9). Chinese practitioners intentionally sought to transmit infection to susceptible individuals in order to render them immune. They observed that opening pustules on infected patients, drying the material on cotton, and then introducing it into the nostrils of healthy individuals could transmit the virus and, in some cases, confer immunity. These instructions were compiled in a medical text titled *Yizong Jinjian* (Golden Mirror of Medicine), published in 1749. Determining the precise origins of these practices is difficult, as some sources claim they date back as early as 200 BCE (10).



Figure 1. Technique of dry variolation in traditional Chinese medicine
(Source: “Development of Variolation and its Introduction to Joseon-era Korea”)

Emmanuel Timonis, who served as Vice-Rector of the University of Padua in 1691 and later earned his doctorate from Oxford, published two significant works on this subject: *Istoria variolarum qua per incisionem excitantur* (A History of Smallpox Induced by Incision), printed in Constantinople in 1715, and *Tractatus de nova variolas per transmutationem excitanti method* (A Treatise on the New Method of Inducing Smallpox by Transmutation), published in Leiden in 1721. Timonis' works were translated into several languages, including English, Italian, and French. He is known to have conducted experiments in Constantinople, Chios, and elsewhere. His case is notable because, despite being educated in Padua and Oxford, he placed considerable trust in traditional medicine, which caused skepticism among British physicians regarding his methods (8).

Lady Mary Wortley Montagu, whose husband was the British ambassador to Turkey, was left severely scarred by smallpox around 1715. After learning about variolation upon her arrival in Turkey, she wrote in 1717 to her friend Charles Maitland: “*Smallpox, so fatal and so general among us, is here entirely harmless by the invention of engrafting, as they call it. There is a set of old women who perform this operation every autumn. An old woman comes with a walnut shell full of the best sort of smallpox matter, and asks which vein you please to have opened. She immediately rips open that vein with a large needle, and puts into it as much venom as can lie upon the head of her needle. Every autumn thousands undergo this operation, and there is not one instance of any dying in it. You may believe I am well satisfied of the safety of the experiment, since I intend to try it on my dear little son. I am patriotic enough to try to bring this useful invention into fashion in England, and I should not fail to write to some of our doctors about it.*” In 1718, while in Constantinople, Lady Montagu had her son variolated by Dr. Charles Maitland, who later introduced the practice in England, where he first variolated his own two-year-old daughter (11).

Renowned 17th-century scientist and inventor Benjamin Franklin suffered a personal tragedy on November 21, 1736, when his four-year-old son died of smallpox because

Franklin had not chosen to inoculate him. Shortly after the boy's death, Franklin wrote: *"I long regretted bitterly, and still regret, that I had not given him the inoculation, which I mention for the sake of parents who omit that operation, under the supposition that they should never forgive themselves if a child died under it. My example shows that the regret may be the same either way, and that, therefore, the safer should be chosen"* (12).

The expansion of variolation and vaccination practices in the 18th century further demonstrated the growing scientific understanding of infectious diseases. In 1738, a smallpox epidemic struck Charleston, South Carolina. Among the 441 individuals who were variolated, nearly 4% died, whereas the mortality rate among those infected naturally was 18%. These results strongly encouraged proponents of variolation, despite reports that the same epidemic killed approximately half of the nearby Cherokee population (13).

In 1757, Scottish physician Francis Home conducted an experiment to demonstrate that measles was caused by an infectious agent. He attempted to replicate the variolation process for smallpox by introducing measles infection through inoculation. Home collected blood samples from infected patients and injected them into healthy individuals, successfully transmitting measles to ten out of twelve subjects. This experiment provided the first clear evidence of a "measles virus in human blood" (14).

In 1759, at the suggestion of his friend Benjamin Franklin, English physician William Heberden published a pamphlet entitled *Some Account of the Success of Inoculation for the Smallpox in England and America*, accompanied by simple instructions that allowed ordinary individuals to perform the procedure and guide patients through recovery. Franklin contributed a preface documenting the success of inoculation in Boston and arranged for the pamphlets to be distributed free of charge throughout the American colonies, thereby encouraging parents to inoculate their children (15).

A landmark moment in the acceptance of vaccination occurred in Russia under Empress Catherine the Great. On October 12, 1768, Catherine personally requested to be inoculated with smallpox material, demonstrating leadership in addressing the disease's high endemicity in Russia. That year, she enlisted English physician Thomas Dimsdale, who had refined inoculation methods, to carry out the procedure. Following Catherine's successful inoculation, which was widely publicized, Dimsdale inoculated over 140 members of the nobility. The Empress's public endorsement of the procedure sparked widespread acceptance of variolation throughout Russia and inspired investment in hospitals, training programs, and overall improvements in public health infrastructure. By 1805, vaccination against smallpox was formally declared mandatory by law, marking the beginning of official vaccination campaigns in Russia (16).

In the context of military medicine, George Washington, commander of the Continental Army during the American Revolutionary War, issued the first known medical order in United States military history in January 1777. Concerned about the devastating effects of smallpox outbreaks among his troops, Washington required that all soldiers who had not previously contracted the disease undergo inoculation.

Recruits passing through Virginia were inoculated in Alexandria, establishing one of the earliest large-scale military vaccination campaigns (17).

The most significant breakthrough in the history of immunization came with Edward Jenner's experiments in 1796. Jenner hypothesized that infection with cowpox—a mild bovine disease transmissible to humans through contact with infected cows—could protect individuals from smallpox (18). On May 14, 1796, Jenner inoculated eight-year-old James Phipps with material taken from cowpox pustules on the hand of a milkmaid named Sarah Nelmes. Phipps developed a localized reaction and experienced mild illness for several days but recovered completely. In July 1796, Jenner deliberately exposed Phipps to fresh smallpox material in a procedure similar to variolation. Remarkably, Phipps did not develop smallpox (19). Jenner's subsequent experiments confirmed that cowpox material could be transmitted from person to person, conferring immunity to smallpox. Although Jenner himself was not fully certain of the exact nature of the protective material, his findings laid the foundation for modern vaccination, ushering in a new era of preventive medicine and public health.

Recent genetic analyses of historical smallpox vaccine samples have revealed that many specimens were more closely related to the horsepox virus than to the cowpox virus. Today, it is understood that the cowpox virus belongs to the Orthopoxvirus genus, which also includes the horsepox virus, the monkeypox virus, and the variola virus—the causative agent of smallpox (20).

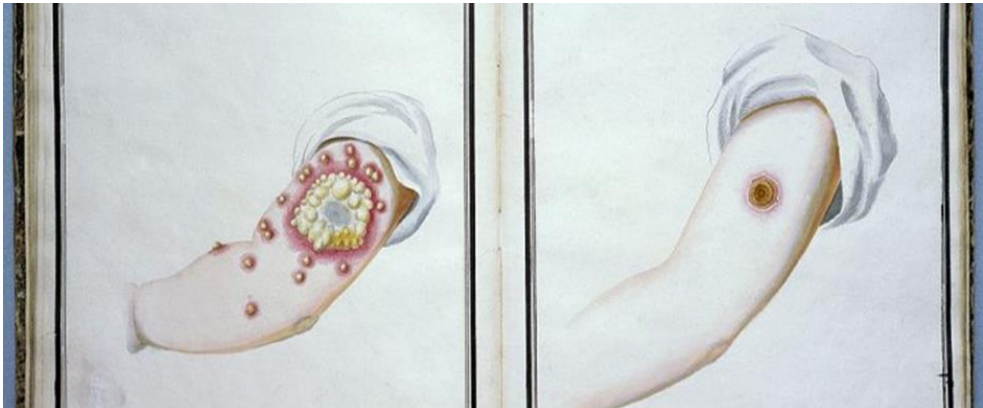


Figure 2. Difference between variolation against smallpox and cowpox vaccination, 16 days post-application; Color engravings by George Kirtland, 1802 (20).

At the beginning of 1799, Benjamin Waterhouse received a copy of Edward Jenner's seminal work, *An Inquiry into the Causes and Effects of the Variolae Vaccinae*, from his London colleague Dr. John C. Lettsom. Shortly thereafter, Waterhouse published a brief report on Jenner's discovery in the *Columbian Centinel*, a Boston newspaper, on March 16, 1799. Additional reports soon followed, and by 1800 several American physicians were actively introducing cowpox virus inoculation. On July 8, 1800, Waterhouse achieved a milestone by vaccinating his son Daniel. On August 2, after vaccinating six more members of his household, he requested Dr. William Aspinwall, who maintained a specialized hospital in Brookline, to

test their immunity by variolating one of them with smallpox material. The test was unequivocally successful (21).

Expansion of Vaccination as an Organized Public Health Measure

In Canada, vaccination was first introduced around 1798, when Reverend John Clinch, a medical missionary in Trinity, Newfoundland and a former colleague of Edward Jenner, requested and received vaccine supplies directly from Jenner (22). New Scotia moved quickly to contain the spread of smallpox, implementing restrictions on inoculation in 1799, and later became the first British North American colony to legislate vaccination through an act passed in 1850 (23).

In 1803, Spanish King Charles IV commissioned royal physician Francisco Xavier de Balmis to bring vaccination to Spanish colonies in the New World. Balmis embarked on the expedition aboard a ship accompanied by 22 orphaned children and a team of assistants. The plan involved sequentially vaccinating pairs of boys throughout the voyage to maintain a live vaccine supply. Upon arrival in Caracas, Balmis successfully launched South America's first mass vaccination campaign (24).

In the Italian kingdom at the time, the Royal Decree on Medical Policing of 1806 formalized public health administration, creating a centralized, multilayered system for disease control and vaccination promotion. By 1809, under the leadership of Luigi Sacco, Italy had established a well-coordinated vaccination infrastructure across all departments. Approximately 1.5 million Italians were vaccinated by the end of 1809. In 1821, Italy implemented a comprehensive regulatory framework mandating vaccination, licensing vaccinators, organizing mandatory vaccination sessions, and maintaining systematic parish-level vaccination records (25).

In the United States, Congress passed and President James Madison signed the Vaccine Act of 1813, establishing the National Vaccine Agency and appointing Dr. James Smith of Baltimore as its director. The Act mandated the U.S. Postal Service to deliver smallpox vaccine material weighing up to 0.5 kg free of charge, representing one of the earliest federal initiatives to ensure equitable vaccine distribution (26).

In Britain, vaccination legislation evolved rapidly. In 1840, William Farr criticized the National Vaccine Act in *The Lancet*, noting that despite free vaccination services, five London children still died daily from smallpox. The Act marked Britain's first provision of free medical services and banned private variolation, restricting the practice to qualified medical professionals. The 1853 Vaccination Act made smallpox vaccination mandatory for infants within the first three months of life, introducing penalties for noncompliance (27). The 1867 Act extended vaccination requirements to all individuals up to age 14 (28).

Similarly, in the United States, Milton, Massachusetts became the first city to offer free smallpox vaccination in 1809. That same year, Massachusetts enacted a state law mandating smallpox vaccination, though it was later repealed under the belief that smallpox had been eradicated. However, due to renewed outbreaks and high child mortality rates, Massachusetts reinstated mandatory smallpox vaccination for schoolchildren in 1855. By 1900, 13 additional U.S. states had adopted similar laws, making proof of vaccination a prerequisite for school enrollment (29).

France, which initially lacked legislation mandating vaccination, began to respond to concerns over the potential transmission of diseases such as syphilis through arm-to-arm vaccination. Inspired by Neapolitan practices, Parisian physicians began using calves as a source of vaccine material in 1864. This innovation spread widely across Europe and the United States, though Britain did not adopt calf lymph vaccination until 1881 and formally banned arm-to-arm transmission in 1898 (30).

Germany enacted its mandatory vaccination and revaccination law on April 8, 1874. Mortality rates declined dramatically thereafter: between 1875 and 1886, Prussia reported an average annual mortality of only 1.91 deaths per 100,000 inhabitants. By 1897, just five smallpox-related deaths were recorded in the entire German Empire, which had a population of 54 million at the time (31).

Finland began its first nationwide smallpox vaccination campaign in 1802 and introduced a system of vaccination districts in 1825. The first mandatory vaccination law, passed in 1883, required all parents to vaccinate children under one year of age, with monetary fines imposed for noncompliance beginning in 1885 (32).

On July 6, 1885, Louis Pasteur successfully demonstrated the efficacy of his rabies vaccine in humans. Joseph Meister, a nine-year-old boy from Alsace, had been bitten 14 times by a rabid dog. As Pasteur was not a licensed physician, he enlisted Dr. Grancher to administer a series of 13 injections over 10 days, using progressively fresher preparations of rabid rabbit spinal cord tissue that had been attenuated through drying. Meister never developed rabies, becoming the first human to receive the vaccine (33). In September 1885, Pasteur successfully treated a second patient, Jean-Baptiste Jupille, a 15-year-old shepherd bitten by a rabid dog. These cases marked the public debut of the rabies vaccine. In 1888, Pasteur established the Institut Pasteur in Paris, a center dedicated to rabies treatment and scientific research. The institute soon expanded its vaccination programs internationally and today operates 30 international branches and 146 research units focused on infectious diseases, public health, and education (34).

The advancement of vaccination laws was paralleled by the emergence of organized anti-vaccination movements. The introduction of Britain's 1840. Vaccination Act triggered opposition, which grew in both Europe and the Americas. The first national organization, the Anti-Compulsory Vaccination League, was founded in England in 1867. in response to the new mandate, marking the beginning of widespread resistance to state-mandated immunization policies (35).

Conclusion

In recent years, the eradication or near elimination of life-threatening infectious diseases such as smallpox and rabies has created a sense of security that these illnesses no longer pose a significant risk. However, the historical development of immunization clearly demonstrates that achieving lasting solutions to prevent large-scale epidemics required centuries of systematic observation, experimentation, and innovation in medicine and public health. This historical perspective emphasizes the necessity of continuous evaluation and long-term commitment to immunization strategies to ensure their sustainability and effectiveness.

The remarkable advances in immunology and vaccine technology in the 21st century must not overshadow the pioneering work of early advocates and scientists who laid the foundations of modern vaccination. Through the efforts of influential figures such as Lady Mary Wortley Montagu, Charles Maitland, Benjamin Franklin, Francis Home, and Thomas Dimsdale, vaccination became a cornerstone of preventive medicine, saving millions of lives. Their legacy remains a testament to the transformative power of scientific progress, legislation, and global collaboration in controlling and eliminating infectious disease.

Literature

- [1] Vanessa Rémy, York Zöllner & Ulrike Heckmann (2015) Vaccination: the cornerstone of an efficient healthcare system, *Journal of Market Access & Health Policy*, 3:1, 27041, DOI: 10.3402/jmahp.v3.27041 Available from: <https://www.tandfonline.com/doi/pdf/10.3402/jmahp.v3.27041>
- [2] World Health Organisation; Vaccines and immunization. Available from: <https://www.who.int/topics/immunization/en/>
- [3] Saleh A, Qamar S, Tekin A, Singh R, Kashyap R. Vaccine Development Throughout History. *Cureus*. 2021; PMID: 34462676; PMCID: PMC8386248. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8386248/#REF4>
- [4] Mammias IN, Spandidos DA. Paediatric Virology in the Hippocratic Corpus. *Exp Ther Med*. 2016 DOI: 10.3892/etm.2016.3420. Epub 2016 Jun 3. PMID: 27446241; PMCID: PMC4950906. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4950906/>
- [5] Hajj Hussein I, Chams N, Chams S, El Sayegh S, Badran R, Raad M, Gerges-Geagea A, Leone A, Jurjus A. Vaccines Through Centuries: Major Cornerstones of Global Health. *Front Public Health*. 2015 Nov 26;3:269. doi: 10.3389/fpubh.2015.00269. PMID: 26636066; PMCID: PMC4659912. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4659912/>
- [6] Boylston A. The origins of inoculation. *J R Soc Med*. 2012 Jul;105(7):309-13. doi: 10.1258/jrsm.2012.12k044. PMID: 22843649; PMCID: PMC3407399. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3407399/>
- [7] Vaccine History Timeline. Immunize.org. Available from: <https://www.immunize.org/vaccines/vaccine-timeline/>
- [8] Kyrkoudis T, Tsoucalas G, Thomaidis V, Bakirtzis I, Nalbandi E, Polychronidis A, et al. Vaccination of the Ethnic Greeks (Rums) Against Smallpox in the Ottoman Empire: Emmanuel Timonis and Jacobus Pylarinos as Precursors of Edward Jenner. *Erciyes Med J* 2021; 43(1): 100–6. Available from: https://jcpres.com/storage/upload/pdfs/EMJ_43_1_100_106.pdf
- [9] Jan and Jennifer Glaynn, *The Life and Death of Smallpox*. Cambridge University Press, 2004. Available from: <https://assets.cambridge.org/97805218/45427/sample/9780521845427ws.pdf>
- [10] K. Hwang. Development of variolation and its introduction to Joseon-era Korea *J Trauma In* (2024) Available from: <https://www.jtraumainj.org/upload/pdf/jti-2022-0044.pdf>
- [11] Riedel S. Edward Jenner and the history of smallpox and vaccination. *Proc (Bayl Univ Med Cent)*. 2005 Jan;18(1):21-5. doi: 10.1080/08998280.2005.11928028. PMID: 16200144; PMCID: PMC1200696. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC1200696/>
- [12] Best M, Katamba A, Neuhauser D. Making the right decision: Benjamin Franklin's son dies of smallpox in 1736. *Qual Saf Health Care*. 2007 Dec;16(6):478-80. doi:

- 10.1136/qshc.2007.023465. PMID: 18055894; PMCID: PMC2653186. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC2653186/>
- [13] McCandless P. Epidemics. University of South Carolina, Institute for Southern Studies, 2016. Available from: <https://www.scencyclopedia.org/sce/entries/epidemics/>
- [14] World Health Organization; Fenner, Frank, Henderson, Donald A, Arita, Isao, Jezek, Zdenek, Ladnyi, Danilovich et al. (1988). Smallpox and its eradication. Available from: <https://iris.who.int/handle/10665/39485>
- [15] “Preface to Dr. Heberden’s Pamphlet on Inoculation, 16 February 1759,” Founders Online, National Archives, <https://founders.archives.gov/documents/Franklin/01-08-02-0073>. [Original source: The Papers of Benjamin Franklin, vol. 8, April 1, 1758, through December 31, 1759, ed. Leonard W. Labaree. New Haven and London: Yale University Press, 1965, pp. 281–286.] Available from: <https://founders.archives.gov/documents/Franklin/01-08-02-0073>
- [16] Chorba T, Esparza J. A Head of State Leading by Example. *Emerg Infect Dis*. 2022(10):2141–3. doi: 10.3201/eid2810.AC2810. PMCID: PMC9514359. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9514359/>
- [17] Smallpox, Inoculation,” Boston National Historic Park; Ann M. Becker, “Smallpox in Washington’s Army: Strategic Implications of the Disease during the American Revolutionary War,” *Journal of Military History* 68, No. 2 (2004): 415-419; John Adams to Abigail Adams, June 26, 1776, in Founders Online, National Archives, Available from: <https://founders.archives.gov/documents/Adams/04-02-02-0013>
- [18] Riedel S. Edward Jenner and the history of smallpox and vaccination. *Proc (Bayl Univ Med Cent)*. 2005 (1):21-5. doi: 10.1080/08998280.2005.11928028. PMID: 16200144; PMCID: PMC1200696. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC1200696/>
- [19] Esparza J, Nitsche A, Damaso CR. Beyond the myths: Novel findings for old paradigms in the history of the smallpox vaccine. *PLoS Pathog*. 2018;14(7):e1007082. doi: 10.1371/journal.ppat.1007082. PMID: 30048524; PMCID: PMC6062137. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6062137/>
- [20] Esparza J, Schrick L, Damaso CR, Nitsche A. Equination (inoculation of horsepox): An early alternative to vaccination (inoculation of cowpox) and the potential role of horsepox virus in the origin of the smallpox vaccine. *Vaccine*. 2017;35(52):7222-7230. doi: 10.1016/j.vaccine.2017.11.003. Epub 2017 Nov 11. PMID: 29137821. Available from: <https://www.sciencedirect.com/science/article/pii/S0264410X17315451?via%3Dihub>
- [21] Blake J. B. Classics in infectious diseases, Benjamin Waterhouse and the Introduction of Vaccination; *Reviews of infectious diseases*, vol. 9, no.5. 1987. Available from: <https://sci-hub.se/10.1093/clinids/9.5.1044>
- [22] McIntyre JW, Houston CS. Smallpox and its control in Canada. *CMAJ*. 1999;161(12):1543-7. PMID: 10624414; PMCID: PMC1230874. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC1230874/>
- [23] Early vaccinations in British North America. *Can Med Assoc J*. 1938 ;39(4):385. Erratum for: *Can Med Assoc J*. 39:181. PMCID: PMC536768. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/instance/536768/pdf/canmedaj00197-0073b.pdf>
- [24] Pérez Pérez A, Vallejo JR. The Smallpox Vaccine in Latin America: A New Approach (1801-1804). *Medicina (Kaunas)*. 2023 ;59(6):1093. doi: 10.3390/medicina59061093. PMID: 37374296; PMCID: PMC10302900. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10302900/>
- [25] Vigezzi GP, Vecchio R, Barbati C, et al. Historical analysis of the first smallpox vaccination campaigns in early 19-century northern Italy: organisation and communication insights for contemporary epidemics’ prevention and control. *Vaccine*.

- 2025;49:126764. doi: 10.1016/j.vaccine.2025.126764. Available from: <https://www.sciencedirect.com/science/article/pii/S0264410X25000611>
- [26] Lanzarotta T, Ramos MA. Mistrust in Medicine: The Rise and Fall of America's First Vaccine Institute. *Am J Public Health*. 2018 ;108(6):741-747. doi: 10.2105/AJPH.2018.304348. PMID: 29741934; PMCID: PMC5944868. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5944868/>
- [27] Wolfe RM, Sharp LK. Anti-vaccinationists past and present. *BMJ*. 2002;325(7361):430-2. doi: 10.1136/bmj.325.7361.430. PMID: 12193361; PMCID: PMC1123944. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC1123944/#:~:text=The%20Vaccination%20Act%20of%201853,cumulative%20penalties%20for%20non%2Dcompliance>
- [28] Kopel J. An exploration of vaccination in the 19th century through the eyes of Dr. Albert Mackey. *Proc (Bayl Univ Med Cent)*. 2022;35(4):505-509. doi: 10.1080/08998280.2022.2052478. PMID: 35754572; PMCID: PMC9196845. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9196845/>
- [29] School Vaccine Mandates. *Encyclopedia Britannica*. Available from: <https://www.britannica.com/procon/school-vaccine-mandates-debate>
- [30] Fressoz, JB; The Vaccine and Its Simulacra: Agnotology, Ontology and Biopolitics in France, 1800–1865 *Journal for the history of public administration*, volume 1, 2016, page 173-192, doi: 10.2478/ADHI 2018-0010 Available from: https://www.researchgate.net/publication/326943810_The_Vaccine_and_Its_Simulacra_Agnotology_Ontology_and_Biopolitics_in_France_1800-1865
- [31] Hüntelmann A.C. Smallpox vaccination in the German Empire. Vaccination between biopolitics and moral economy. doi.org/10.3989/asclepio.2020.01 Available from: <https://asclepio.revistas.csic.es/index.php/asclepio/article/view/1000/1626>
- [32] Ukonaho S, Lummaa V, Briga M. The Long-Term Success of Mandatory Vaccination Laws After Implementing the First Vaccination Campaign in 19th Century Rural Finland ; *American Journal of Epidemiology*, Volume 191, 2022, Pages 1180–1189, doi.org/10.1093/aje/kwac048. Available from: <https://academic.oup.com/aje/article/191/7/1180/6549054>
- [33] Schwartz M. The Pasteurian contribution to the history of vaccines. *Comptes Rendus. Biologies, Pasteur, a visionary*, Volume 345 (2022) no. 3, pp. 93-107. doi: 10.5802/crbiol.83; Available from: <https://comptes-rendus.academie-sciences.fr/biologies/articles/en/10.5802/crbiol.83/>
- [34] Wolfe RM, Sharp LK. Anti-vaccinationists past and present. *BMJ*. 2002 ;325(7361):430-2. doi: 10.1136/bmj.325.7361.430. PMID: 12193361; PMCID: PMC1123944. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC1123944/>

ISTORIJSKI PRIKAZ RAZVOJA VAKCINACIJE DO KRAJA 19 VIJEKA

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Sažetak. *Imunizacija je proces kojim osoba, zahvaljujući primljenoj vakcini, postaje imuna ili otporna na zaraznu bolest. Priča o vakcinaciji ne počinje prvom medicinski formulisanom vakcinom Edwarda Jennera, već razumijevanjem rizika zaraznih bolesti kod ljudi u antici i pokušajima da se obezbijedi imunitet na tu bolest. Oko 1100. godine nove ere, u Turskoj, Kini, mnogim afričkim zemljama i nekim dijelovima Evrope razvijene su tehnike variolacije, koje su uključivale inokulaciju djece i odraslih osušenim materijalom krasta dobijenim od pacijenata oboljelih od malih boginja. Ovaj rad ima za cilj da sistematski predstavi događaje koji su uticali na razvoj procesa donošenja zakona ili propisa o obavezi masovne imunizacije ljudi do kraja 19. vijeka. Zahvaljujući svijesti istaknutih ljudi tog vremena o rizicima širenja epidemija ozbiljnih zaraznih bolesti, različite tehnike variolacije iz mnogih udaljenih zemalja Starog svijeta donesene su u Evropu i Ameriku. To je podstaklo rad na medicinskim tehnikama za sprječavanje pojave smrtonosnih zaraznih bolesti. Neke od ovih istaknutih osoba su: gospođa Mary Wortley Montagu, supruga engleskog ambasadora u Turskoj, engleski ljekar Charles Maitland, izumitelj iz 17. stoljeća Benjamin Franklin, škotski ljekar Francis Home, ruska carica Katarina Velika, engleski ljekar Thomas Dimsdale, kao i George Washington, tadašnji komandant Kontinentalne armije u Američkom građanskom ratu. Nakon 1888. godine i osnivanja Pasteurovog instituta u Parizu, započela je era uvođenja zakona o javnom zdravlju, koji su uključivali segment vezan za obaveznu, preporučenu ili apsolutno dobrovoljnu imunizaciju, čime je započela moderna era u imunizaciji ljudi.*

Ključne riječi: *zarazne bolesti, variolacija, Jenner, vakcinacija, zakoni*