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Pietro Verri: The History of Smallpox Vaccination Through His Pencil

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ABSTRACT

The last case of natural smallpox infection occurred in 1977, and the disease is considered eradicated since 1980. Throughout the history of medicine, early attempts to combat smallpox involved inoculation, a practice based on the observation that those who recovered from the disease became immune. The Lombard Enlightenment movement marked a period of intellectual flourishing in the 18th century, during which reason, science, and progress took center stage. Pietro Verri, a prominent intellectual, was a key figure in this movement on the Italian peninsula. Interestingly, he was deeply fascinated by medicine and what we now refer to as public health. His style was characterized by clarity, logic, and a profound understanding of human behavior. His writings are still influential today and could shed light on the history of variolation and smallpox vaccination. Pietro Verri practiced a form of proto-vaccination on his daughter even before Edward Jenner's experiment on his young son in 1790. Verri's figure could serve as an example of the promotion of vaccination both on a scientific and public level during an era characterized by a hesitant attitude towards such a practice.

Recent pandemics have intensified the global debate on vaccination as a preventive measure. Moreover, vaccine hesitancy and misinformation have reduced the effectiveness of herd immunity. Nevertheless, there was an era in which reason, science, and progress took centre stage. The Lombard Enlightenment marked such a period of intellectual flourishing in the 18th century, with Pietro Verri, a prominent intellectual, as a key figure in Italy. This manuscript aims to shed light on Pietro Verri's involvement in variolation and vaccination during the Lombard Enlightenment, showing how his courage remains relevant today and how his example may help mitigate current vaccine hesitancy. Scientific databases and historical records were reviewed.

Ancient Chinese and Indian manuscripts dating back to 3000 BC contain descriptions compatible with smallpox, while the last case of natural smallpox infection occurred in 1977. In 1980, the World Health Organization declared smallpox eradicated thanks to a global vaccination campaign [1]. It was long observed that smallpox survivors were resistant to subsequent infections and that infection through skin abrasions resulted in milder symptoms. This led to attempts to mitigate disease severity by administering fluid or powder from the pustular crusts of infected individuals to healthy subjects, a practice known as variolation. Although the smallpox virus was the active agent, severe systemic symptoms and even death were not uncommon. In the early 18th century Lady Mary Montagu, wife of the British ambassador to Constantinople, became an ardent champion of a form of variolation and worked actively to introduce it in Europe [2].

Edward Jenner (1749–1823; Figure 1A) paved the way for the eradication of smallpox by replacing the smallpox virus with the

FIGURE 1 | (A) Edward Jenner vaccinating his son, held by Mrs Jenner. A maid rolls up her sleeve, a man stands outside holding a cow. Coloured engraving by C. Manigaud after E Hamman. Wellcome Collection. *Source:* Wellcome Collection. Public Domain Mark. Available at: https://wellcomecollection.org/works/b7d6yvdr/images?id=np6gnqz2. (B) Engraving depicting Pietro Verri. Date: before 1843. *Source:* Wikimedia Commons. (C) 5 October 1779, 12th day after the graft [3]. For (C) to the best of our knowledge, no copyright restrictions apply as 100 years after the death of the author have passed. The original autograph image has been searched without results in the Archivio Verri—Fondazione Raffaele Mattioli—and in the Sommi Picenardi archive.

cowpox virus, maintaining the effectiveness of vaccination without the risks associated with variolation [4]. Jenner's conviction in his assumption was so strong that in December 1790 he had his ten-month-old infant son inoculated with pustular material by his nurse (the purulent material could have been swine/pig- or small-pox) [5]. In Italy since the 18th century, many physicians practiced the Jennerian vaccine, including Luigi Sacco (1769–1836) and Gennaro Galbiati (1776–1844).

The Lombard Enlightenment movement marked a period of intellectual flourishing in the 18th century that emphasized reason, science and progress. Pietro Verri (Figure 1B) was a key figure in this movement. Born in Milan in 1728, Verri was a prominent economist, philosopher and writer who played a key role in shaping the cultural landscape of Lombardy and the future Kingdom of Italy. He was a co-founder of the Società dei Pugni, a literary and scientific society that brought together some of the brightest minds of the time. Through this society, Verri and his colleagues promoted the dissemination of knowledge, the exchange of ideas and the advancement of the arts and sciences [6, 7]. Interestingly, he was deeply interested in medicine and what we now call public health. His style was characterized by clarity, logic and a deep understanding of human behaviour. This is why his writings are still influential today [8].

Pietro Verri promptly shows great interest in the new practice of smallpox inoculation, as evidenced primarily by his journalistic

interventions published in the last five issues of "Il Caffè" (1766), the journal of Lombard Enlightenment thinkers. In these articles, Verri effectively wages a scientific battle against the 18th-century epidemic, demonstrating a profound understanding of the subject and its health implications, advocating for inoculation based on converging testimonies favourable to the success of the procedure [9]. Here, Verri examines the various methods of introducing the disease (by contact or by incision), explains the entire inoculation procedure, describes the period of careful preparation that must precede the inoculation, traces the history of smallpox from its first appearances in Europe to contemporary experiments in Tuscany, inspired by the inoculation theories expounded by the Tuscan physician Angelo Gatti (1724–1798) [10]. Verri provides precise documentation of the observations conducted up to that point and presents a significant table with the overview of the results achieved, including the number of operations performed in Europe: out of more than twenty-four thousand inoculations (24,167) only nineteen resulted in death [9].

Verri promoted variolation as a practical intervention for the public good, aimed at preventing a nearly inevitable disease that killed a tenth of mankind through a relatively safe procedure. His reasoning was clear: given the high mortality of smallpox and the low probability of avoiding infection, it was preferable to undergo a controlled disease with a favourable outcome rather than risk natural infection. For Verri, this was essential to public well-being, although the greatest challenge was persuading parents to overcome their understandable reluctance to deliberately expose their children to a potentially fatal disease [9].

Even before Jenner's experiment on his young son in 1790, Pietro Verri practiced a similar inoculation on his daughter. Years later, Verri revisits the topic in a strictly private writing, recounting his experience as a father who has his daughter vaccinated. Though in line with the most advanced positions, Verri reveals the more fragile aspect of his personality when he anxiously observes the reactions of his 7-month-old daughter to the smallpox inoculation. Pietro diligently monitors its aftermath, even drawing a map indicating the location of each individual pustule on his daughter's face, fearing that traces may remain in the future (Figure 1C) [3].

The history of smallpox vaccination and eradication was long and troubled. Nevertheless, cross-reactivity between smallpox and related poxviruses has long benefited medicine. In the Democratic Republic of Congo, human monkeypox rates were 20 times higher decades after smallpox vaccination was discontinued than during its use. Thus, 18th-century discoveries not only led to smallpox eradication but also had unexpected benefits against emerging infections, with the Lombard Enlightenment contributing to this progress.

Pietro Verri deserves recognition in the history of preventive medicine for his knowledge of variolation and vaccination and his commitment to public well-being over individual opinions and political positions. His courage and trust in science anticipated Jenner in the experiment on his son. Although not a physician, Verri embraced medical innovation for prevention, making him a valuable example for promoting vaccination at both scientific and public levels.

Author Contributions

O.S., F.B. designed the study. O.S. conceived the manuscript. O.S., S.D.B. drafted the manuscript. O.S., A.M.S., V.Z., I.M.C., S.D.B., F.B. revised the manuscript. O.S., V.Z., I.M.C., S.D.B., F.B. performed a search of the literature. O.S., F.B. critically revised the manuscript, conceptualization, and methodology. O.S., F.B. supervised investigation and data curation. A.M.S. wrote the chapter "Public health in Pietro Verri's works". All authors have read and approved the latest version of the paper for publication.

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Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki (1975, last revised 2024) and was approved by the local Ethics Committee.

Patient Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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