History of Medicine and Ethics

The history of smallpox vaccination in Italy: the vaccination campaign in the Ligurian Republic between the end of the Ancien Régime and the advent of the Napoleonic period (1797-1805)

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Keywords

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Summary

In 1798, Edward Jenner publicized his technique of smallpox vaccination, thus making obsolete what had been for centuries the most effective weapon against smallpox: variolation. News of this sensational breakthrough spread quickly throughout Europe, reaching Italy, and particularly Genoa, then the capital of the Ligurian Republic (1797-1805).
Indeed, the first vaccinations in Italy were carried out in Genoa, and several doctors there, first individually and then collectively (within the "Medical Emulation Society"), went on to implement and spread the practice of vaccination.
Although it was only with the annexation of Liguria to the French Empire that the practice became more structured and more widely implemented, this period still marked an extremely prolific time for medical science in the Genoa area.

Introduction

Human beings have always sought to defend themselves against pathogens by exploiting whatever knowledge of hygiene and sanitation was available to them. Of the many diseases that afflicted humans for millennia, one of the most noteworthy is smallpox [1, 2]. However, unlike other diseases, such as plague or cholera, smallpox has been less intensively studied by scholars.
According to the historian Alberto Tanturri [3], this relative disinterest has been due to the modest impact that smallpox had at the demographic level [4-8], to the less systematic nature of the measures implemented in order to combat it [9-15] and the limited impact that the disease had on social behaviour [16, 17].
The pathway leading up to the definitive eradication of smallpox was very long (starting more than two centuries ago), and it was only in 1980 that the World Health Organization declared the disease to be extinct [18].

From variolation to Jenner's vaccination

Smallpox (term formed by combining the words small and pox used to distinguish it from the great pox or syphilis) is a highly contagious disease and is fatal in nearly 50% of cases. Caused by a virus belonging to the Variola family, it can be contracted by inhaling the air exhaled by an infected person (while coughing or simply breathing).
The initial symptoms of the disease are fever, malaise, headache and coughing, while the more distinctive skin lesions develop within 12-15 days.
These lesions are initially papular, but subsequently transform into vesicles and then into pustules, which leave permanent scars. For the first 7-10 days after being infected, the person is particularly contagious and therefore at high risk of transmitting the disease to others [19].
Since ancient times, people have always tried to limit the complications of smallpox by implementing a series of measures.
The oldest technique that we know of, and which proved quite effective [1], originated in Asia and in some parts of Africa around the 2nd century BC [20], and is known as 'variolation' or 'inoculation'. Indeed, this approach involved inoculating a healthy individual with material taken from the pustules of a subject infected with a mild form of smallpox (Variola minor).
In this way, a less dangerous (and therefore less lethal) form of the disease was deliberately caused, which rendered the person immune to the more lethal form.
This practice, however, made the "variolated" subject a vehicle for the spread of the disease and, furthermore, exposed him/her to the risk of contracting other diseases, such as tuberculosis [21] and syphilis, or of developing bacterial infections such as septicaemia [1].
Although variolation can be considered completely obsolete today, it nevertheless remained for a long time

the only way to prevent the disastrous and lethal effects of smallpox.

The first news regarding the practice of variolation reached Europe only at the beginning of the 18th century through the reports of some physicians from Istanbul [22] such as Emanuel Timoni (1670-1718) and Jacopo Pylarini (1659-1718) [1]. It was, however, the determination of a woman, Lady Mary Wortley Montagu (1689-1762), that brought this practice to the attention of European medicine.

In 1717, a few weeks after arriving in Istanbul with her husband, who had been appointed the new ambassador of the United Kingdom, she wrote to a friend telling of this method of preventing the disastrous, if not lethal, effects of smallpox. Remembering her own terrible experience of smallpox, Lady Montagu had her son inoculated in March 1718. The outcome was successful and, on returning to London in April 1721, she also had the procedure performed on her daughter, who was just 3 years old [1, 23].

Having been convinced of the effectiveness of this practice, the Princess of Wales, Caroline of Brandenburg-Ansbach, had her two daughters "variolated" in 1722.

From then on, variolation began to spread throughout the European courts. It was especially in the 1750s, following a spate of smallpox deaths among royal families, that the practice spread rapidly, even reaching the American continent.

Among those who underwent variolation were: the Empress Maria Theresa, Frederick II of Prussia (who also ordered his soldiers to undergo the same treatment) [24], Louis XVI of France, Catherine II of Russia and, finally, all the soldiers of the Continental Army led by George Washington [1].

The practice also spread to Italy, particularly the Republic of Venice [25-29], the Kingdom of Naples [3, 30, 31, 32, 33], the Grand Duchy of Tuscany [22, 28, 34] and Austrian Lombardy [28].

In this latter region, the spread of variolation was celebrated by two great intellectuals of the time:

- in 1765, Giuseppe Parini wrote an ode entitled "L'innesto del vaiuolo" ("The inoculation of smallpox") [35] and
- the following year Pietro Verri published an article entitled "Sull'innesto del Vaiuolo" ("On the inoculation of smallpox") in the periodical "Il Caffè" [36].

A more effective method of preventing smallpox was developed only in 1796 by the English physician and naturalist Edward Jenner (Berkeley 1749-1823). Jenner's method of immunization, which he called vaccination, involved inoculating healthy individuals with pus taken from skin lesions on cows or humans affected by cowpox, a disease that was much less dangerous than human smallpox.

In this way, the individual would also develop immunity to the much more dangerous and lethal form of smallpox.

Today, we know that Jenner was not actually the first to use vaccine material to immunize people against smallpox; indeed, many English doctors in rural areas were aware of this approach [1].

Nevertheless, Jenner had the undisputed merit of conferring scientific status on this practice (by empirically demonstrating that vaccination elicited immunity to smallpox) and of spreading it systematically through the publication of his pamphlet "An Inquiry into the Causes and Effects of the Variolae Vaccinae, [...]" in 1798 [37].

This innovative technique soon spread from England to European countries, including Italy. Among the Italian pioneers of Jenner's method, we may mention:

- the Ligurian physician Onofrio Scassi (Cogoleto 1768 - Genoa 1836), who is deemed to have been the first to practise smallpox vaccination in Italy [38], and
- the Lombard Luigi Sacco (Varese 1769 - Milan 1836), the first doctor to use vaccine material harvested in Italy [30]. Although recent studies have focused primarily on these and other prominent figures in the medical field, less well-known participants in the first vaccination campaigns in Italy also deserve attention.

The present article will therefore attempt to shed light on the work of a small group of doctors who worked to spread vaccination in the area of Genoa between 1797 and 1805.

The spread of vaccination in the Ligurian Republic

With the fall of the Republic of Genoa, on June 1797, the aristocratic government that had ruled Liguria since the 16th century came to an end, being replaced by the Ligurian Republic (1797-1805) (Fig. 1).

On paper at least, this latter professed to be more democratic, more representative and based on the sovereignty of the people [39, 40]. It was precisely within the brief and fragile political-institutional reality of this government that several doctors undertook the first smallpox vaccinations.

News of the first vaccination campaigns launched in European countries reached Genoa in October 1800, when an article in the local Gazzetta reported that 30,000 people in Vienna, Hanover, Paris and Geneva had already been vaccinated with 'cowpox pus' from England [41].

On 1st November, this first article was followed by the publication of a letter from the Genoese doctor Onofrio Scassi [42]. In it, the illustrious doctor praised Dr Jenner for his sensational discovery and reported that, since the previous April, he had managed (with the help of William Batt and the Genevan doctor Odier [43, 44]) to obtain some vials of 'vaccine pus' from Geneva, which he had used to vaccinate 10 children.

He concluded by asserting that "those who have had the vaccine can rest assured that they will not get smallpox", and adding (probably to rebut some false rumours that were circulating) that "the vaccine is not [...] contagious" [30, 41].

A few months later, on March 5, 1801, a small pamphlet entitled "Sulla Vaccina di Jenner" (On Jenner's Vaccine) was published by the doctor William Batt (originally from the United Kingdom but resident in Genoa since 1771) [45]. In its eight pages, Batt launched into a long

Fig. 1. Map of the Ligurian Republic and Northern Italy in 1799: taken from The Cambridge Modern History Atlas, Cambridge University Press, London, 1912.

dissertation on the efficacy of vaccination to protect people "in the future against smallpox infection" [45] and recounted his own experience as a vaccinator.

He ended by inviting "Doctors and other persons who are able to inform themselves of the truth on this matter", to spread the practice of vaccination, and assured them that "inoculation of the Vaccine confers perfect lifelong protection against Smallpox" [45].

Regarding the advantages of undertaking vaccination campaigns, he also mentioned, as a virtuous example to be followed, the decision of the Government of the Ligurian Republic to carry out vaccination in the Pammatone Hospital [45].

Probably as a result of this invitation to spread the practice of vaccination and the government's decision to implement vaccination campaigns at the Pammatone Hospital, about 20 Genoese doctors (including W. Batt, L. Marchelli, B. and G. Mojon [46], A. Mongiardini, O. Scassi and D. Viviani [47, 48]) [49] founded the Società Medica di Emulazione ("Medical Emulation Society") in May of the same year [39, 50].

The newly formed association was "composed of Professors dedicated to the health arts"; it was intended to serve as a place where men involved in the health field could "communicate to each other their insights and the felicitous results of their observations" and also spread the practice of smallpox vaccination [51].

Within a few months, the Society was already in the news; on July 11, an article in the "Gazzetta Nazionale" reported that the Society had sent a long letter to the Government Commission "presenting a sample of its early works" [52] and shortly afterwards, at a Society meeting on July 23, 1801, the work of a member, the surgeon Luigi Marchelli, on the inoculation of the vaccine was approved.

Luigi Marchelli had already declared himself a supporter of vaccination in a short article in the "Gazzetta Nazionale" on July 11, 1801. In the article, in addition to refuting some false rumours regarding the efficacy and safety of vaccination, he passionately appealed to "Parents who are still hesitant" to have their young children vaccinated [52].

That article was followed, on July 23, by the presentation and publication of a "Memoir on the Inoculation of the Vaccine" [53]. In it, Marchelli compared the impact of smallpox to that of the plagues of the past [54] and embarked on a long narrative on the origins of the disease and the remedies used over the centuries to combat it, finally arriving at the method devised by Jenner, "a man forever worthy of humanity's esteem" [53].

After this extensive historical preamble, Marchelli went on to provide a detailed description of the two main ways of inoculating the vaccine material ("with fresh pus, that is to say from arm to arm" or "by threads" [53]) and the instruments required, all accompanied by four very detailed illustrative plates (Figs. 2-5).

Finally, he analysed some clinical cases that had particularly intrigued him among the 132 subjects he had vaccinated from March 27, 1801 until that time.

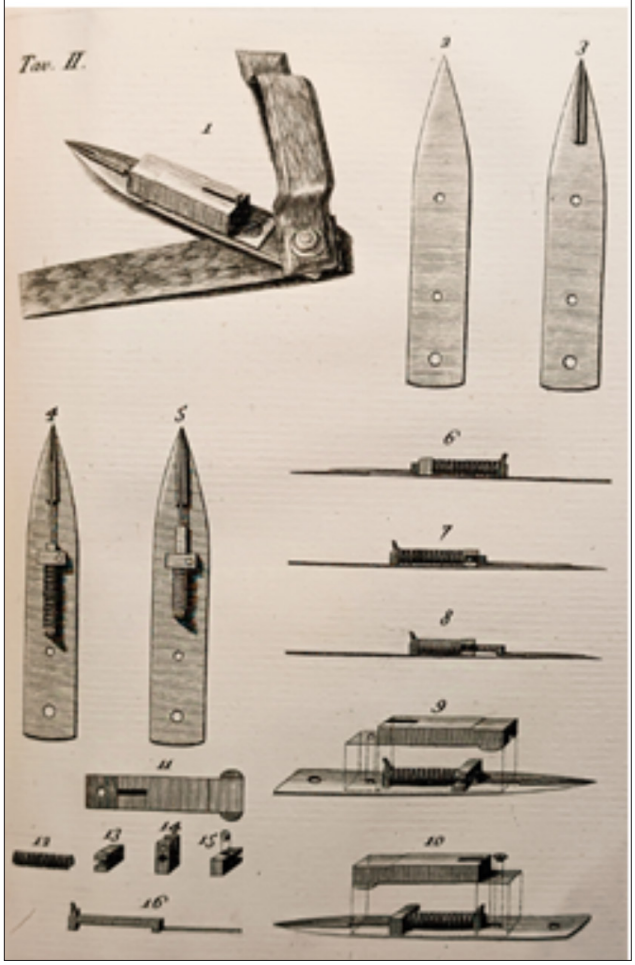
The work of spreading the practice of vaccination continued in August 1801. Indeed, on August 15, the "Gazzetta Nazionale" carried a new article, which reported that the vaccine was making "further progress every day in Liguria: indeed, we are counting many hundreds of vaccinated people in a short time" thanks also to the fact that "Jenner's work on the vaccine has been known in Genoa for three years" [55].

However, one should not think that vaccination was supported by all the doctors in Genoa, then the capital of the Ligurian Republic. Indeed, an article dated September 19, 1801, which was also published in the "Gazzetta Nazionale", mentioned "doctors who do not believe in the effectiveness of vaccination, and who arouse fears that it has harmful consequences", the aim of the article being to encourage parents to have their children vaccinated before it was too late.

Moreover, the various medical societies throughout Europe rebutted all the theses of these "opposition doctors", affirming that:

Fig. 2. Plate I illustrated the point at which to inoculate the vaccine.

Fig. 3. Plate II illustrated all the characteristics of the instrument with which inoculation was performed.



1. The true vaccine protects against smallpox;
2. The vaccine is not at all contagious;
3. The vaccine does not have any bad consequences" [56].

Unfortunately, however, the article did not have the desired effect; just over two months later, smallpox broke out in Genoa and some areas of Liguria, causing "considerable slaughter" [57].

Fig. 4. Plates III showed the evolution of the disease.

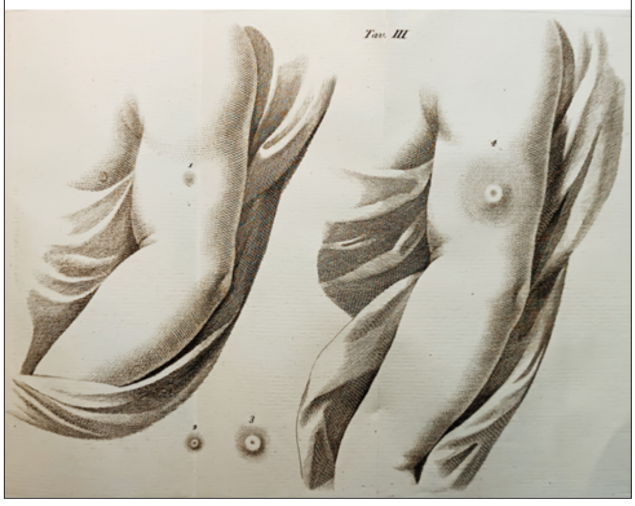


Fig. 5. Plate IV showed the evolution of the disease.

It was during that terrible health crisis that the Medical Emulation Society held its first meeting, directed by President Mongiardini and Secretary Marchelli. In his introductory speech, the President explained that the Society had been founded to emulate other medical societies scattered throughout Europe.

Among the Society's objectives, he also cited that of "especially encouraging Ligurians to take advantage of Jenner's discovery and protect themselves from the all-too-deadly smallpox" [51]. Precisely for this purpose, the Society used its own funds to finance the publication of several works in favour of vaccination until 1814, the year of its dissolution.

With the arrival of the new year, 1802, publications in favour of Jenner's method continued to proliferate.

On June 12, an article entitled "To the detractors of vaccination" appeared in the local Gazette. Signed by two illustrious Genoese scientists, B. Mojon and Dr. M. Covercelli, it aimed to "demonstrate the usefulness and safety of the procedure" [46].

On August 24, William Batt published, at the Medical Society's printing house, a short pamphlet entitled "The necessary distinction between vaccination and the errors or negligence of those who practise it" [58].

In this pamphlet, in addition to pointing the finger at some detractors of the innovative method [58], Batt described in detail all the steps (as they had been explained by

Jenner) to be carried out in order to correctly immunize the patient and the symptoms that the patient should develop in the days following inoculation.
Batt again took up the same arguments in another publication on September 15, less than a month later. In his memoir "On the origin of Vaccine inoculation" [59], he reiterated once again "the preservative efficacy of the vaccine" and then went on to translate into Italian the first part of Jenner's work entitled "On the origin of the inoculation of the vaccine".
And not even a month later, on October 13, 1802, Batt again intervened on the public scene with a short piece entitled "To the editors of the Osservatore", in which he gave the lie to some fake news on vaccination that had been printed in that newspaper by an "anonymous slanderer" [60].
This time, however, a reply to the frontal attack by the doctor of English origin came from a Genoese doctor, Giuseppe Pedemonte, who maintained "the inefficacy of the vaccine in protecting against smallpox" [61].
Notwithstanding the opponents of Jenner's method, however, the practice of vaccination spread to the neighbouring areas of the Ligurian Republic (albeit with greater difficulty) thanks to a few far-sighted doctors.
A perfect example of such commendable figures was Francesco Buffa, a doctor working in Ovada (today a small town near Alessandria in Piedmont, but at that time a territory of the Republic); between 1802 and 1807, he successfully vaccinated 72 young girls and boys between 4 months and 10 years of age [62].
Despite the harsh temperatures that characterized the winter of 1803, Genoa was spared a new smallpox epidemic, but still had to face an "epidemic of catarrhal disease", which caused several deaths in the city; this episode was narrated in a memoir written by the doctors De Ferrari, Landò and Mojon in June of the same year and presented publicly on August 11 of the following year during an open session of the Society [63].
On that occasion, the introductory speech was given by President Mongiardini, who mentioned the numerous "enemies" and "obstacles" that the Society had encountered in those two years of activity.
It had, nevertheless, always remained faithful to its objectives, namely "to fight [...] diseases, to alleviate the discomforts of old age and of civil life itself" by devoting to its homeland, the Ligurian Republic, "its vigils, its efforts, its very thoughts" [64].
In September of that same year, the Gazzetta Nazionale printed an article concerning a possible miraculous and involuntary effect of smallpox vaccination.
According to the Italian doctor Eusebio Valli [65], since smallpox had replaced bubonic plague as the deadly disease of the time, he resolved to discover whether smallpox vaccination would also be effective against the plague. He therefore set out to demonstrate that "the vaccine virus also protects against the plague, as it does against smallpox, both because the vaccinated person becomes unassailable, and because the plague loses much of its strength and its malignity in a vaccinated body" [66].
Unfortunately, however, as we know today, this is far from true: first of all because the plague is not caused by a virus, but by a bacterium (Yersinia Pestis), which was discovered in 1894 by the doctor Alexandre Yersin (1863-1943).
While the Ligurian capital was spared by smallpox in the freezing winter of 1803, this was not the case in the following winter, that of 1804.
Indeed, on that occasion, in addition to the more common "intermittent fevers", "sthenic diseases [...] some coughs, rheumatism and [...] measles", smallpox also appeared.
Fortunately, as narrated in the report drawn up – again – by doctors De Ferrari, Landò and Mojon, "the epidemic that reigned was one of the most benign, and few fell victim to that disease" [67].
One of the reasons for the low number of deaths was, undoubtedly, the result of the vaccination campaign that was implemented in Genoa as early as 1800. In this regard, an article published in the "Gazzetta Nazionale" on July 14 did not fail to underline that the epidemic provided overwhelming and definitive proof of the "preserving virtue of the vaccine, since none of the vaccinated individuals were attacked" [68].
Until 1805, smallpox vaccination continued to be – albeit in an increasingly "disorderly" manner [69] – the fruit of individual action taken by some far-sighted doctors, who read about, appreciated and put into practice Jenner's sensational discovery. Indeed, vaccinations were never directly managed by the local health administration [70], the Central Health Commission, which had been established in 1799 [71].
Only after the fall of the Ligurian Republic in June 1805 and the subsequent annexation of Liguria to the French Empire of Napoleon Bonaparte (1805-1814) was the practice of vaccination more widely implemented and structured [72].
Indeed, the implementation of smallpox vaccination constituted the most significant health policy undertaken by the Napoleonic authorities, both in the Empire and in all the other states under its influence [73].
In each of the newly established departments of Liguria, vaccination committees were created (in constant communication with the central committee in Paris) thanks to the participation of many of the Genoese doctors of the Medical Emulation Society [74].
However, despite the enormous efforts made by the Society and the French administration to spread vaccination even in the most rural areas of Liguria, "the war against smallpox was, at least temporarily, won by the disease", as demonstrated by the very severe smallpox epidemic that struck Genoa in 1829 [39].

Conclusion

While veritable vaccination commissions were created in some European countries, such as France [75, 76], Germany [77, 78] and Denmark [79], as early as the early 19th century [80, 81], the government of the Ligurian Republic almost entirely abandoned this task to

the free initiative of some far-sighted doctors, who, first individually and then collectively (within the Medical Emulation Society), devoted themselves to vaccinating as many people as possible.
It is difficult to quantify the work of these few doctors in terms of precise numbers and during the entire period of the Ligurian Republic:

- firstly, because it is unlikely that the lists of vaccinees drawn up by individual doctors (a practice, moreover, not obligatory) have come down to us;
- secondly, because the documents drawn up by the Society itself (which monitored vaccination developments) have reached us in a fragmentary manner.

Nevertheless, the huge number of printed documents produced in those years in the Ligurian capital enable us to appreciate and admire the commitment and energy that this small group of doctors – united by their love of science and their homeland – devoted to spreading smallpox vaccination in Genoa during the years of the Ligurian Republic.

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The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Not applicable.

Informed consent statement

Not applicable.

Authors' contributions

EB: conceived the study. EB, MM: designed the study; drafted the manuscript; performed a search of the literature; revised the manuscript; conceptualization and methodology; investigation and data curation; original draft preparation; review; editing. All authors have read and approved the latest version of the paper for publication.

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