

OVERVIEW

Anti-rabies vaccination between the 18th and 19th centuries and its pioneer Eusebio Giacinto Valli (1755-1816)

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Summary

An eclectic, versatile Tuscan doctor, Eusebio Giacinto Valli (1755-1816) was a scholar of several branches of medicine, particularly public health, preventive medicine and epidemiology. His brilliant and wide-ranging education, and his intense passion for physics and chemistry, as applied to the human body, enabled him to conduct numerous studies in the field of vaccinology.

He travelled to the Middle East in order to study the epidemiology of the plague and carried out experiments aimed at discovering a cure and a prophylaxis for rabies, succeeding in attenuating the

rabies virus by inoculating a mixture of saliva from rabid dogs and gastric juice from frogs.

Having travelled to Spain and then to Cuba, where he undertook the study of yellow fever, he died in Havana in September 1816, after injecting attenuated germs of the disease into his own body.

He was buried in the great Monumental Cemetery “Cristobal Colon”, where his tomb bears the epigraph: “victima de su amor à la humanidad (“a victim of his love for humanity”).

The life of Eusebio Giacinto Valli

Born in Casciana Alta di Lari (Pisa) on 16 December 1755, Eusebio Giacinto Valli was the son of a local doctor, Giuseppe Valli (from the family once known as Valle, Valla, della Valle, and today Valli) and Anna Maria Iacononi, both of whom originally came from Ponsacco. He was a multifaceted, eclectic physician, whose interests included pathophysiology, internal medicine, public health and preventive medicine, epidemiology and vaccinology, though his greatest passions were physics and chemistry, especially as applied to the human body. In September 1816, he died in Havana, Cuba, where he is buried in the great Monumental Cemetery “Cristobal Colon”, a “*victima de su amor à la humanidad*” [1].

After completing his high-school studies in Florence, where he studied classical languages and a few modern languages (English and French), and also dabbled in poetry, Valli took a degree in philosophy and medicine, after his elder brother, Jacopo, had graduated in canon and civil law.

In 1776, when Valli was in the second year of his degree course, his father died. The following year, his mother also died. Despite his restricted financial circumstances (he lodged at the house of one Domenico Cola in via Santa Maria, in the historical centre of Pisa), he managed to win a place at the Collegio della Sapienza di Pisa (which later became today’s Scuola Normale di Pisa); his uncle Michelangelo Valli acted as his guarantor.

Having graduated in philosophy and medicine, he moved to Turkey (Izmir, Constantinople), and then to Greece and the Aegean islands (1783-1785). Here, he became friends with the Greek physician, scientist and theologian, Angelo Kalogerà (1699-1768), author of a “Collection of Scientific and Philological Pamphlets” [2, 3]. During his stay on the islands, Valli visited “*in 1784, the beautiful, picturesque, rocky Island of Chios, Homer’s native land*”, which was at that time in the grip of the plague. He probably wrote a brief tract on the epidemic that afflicted the Island of Chios, but this has, unfortunately, been lost to us.

He subsequently travelled to Paris (1785-1786), where he served as a doctor in the Cablys’ regiment, then to Hindustan (today Pakistan, in 1786-1788), and finally to Egypt, to study the epidemiology of the plague, of smallpox, and of certain “malignant putrid fevers” (probably outbreaks of malaria).

Eusebio Valli’s scientific discoveries

In 1781, he discovered the anti-fermentation action of the red precipitate in wine preparation.

During his stays in the Middle East and Asia Minor, Valli worked out a theory according to which the etiopathogenetic development of the plague required the so-called “principle of affinity”, that is to say, a sort of predisposition to the disease. “*The forces that it deploys in the*

various subjects depend more on the constitution of each individual than on the character of the miasma".

In France, he took part in the debate between the humoral theory and solidism, embracing the latter; solidism was expounded in the principal work, "*Elementa medicinae*", of the Scottish physician John Brown (1735-1788), which was published in 1780 and translated into Italian by the clinician Pietro Moscati (1739-1824) [4]. In his "*Discorso sopra il sangue considerato in stato di sanità e di malattia*" (*Discourse on blood in the state of health and of disease*), Valli claimed that alterations in haematological parameters were due to the influence not of humoral agents, but of solid agents, or bodily organs. "*The blood is never altered by the germ of any disease whatever, nor by the forces of diseases themselves; on the contrary, it is the most resistant fluid, even to the action of poisons*" [5].

In the spring of 1789, at the outbreak of the French Revolution, he returned to Italy and settled in Pavia, where he met Francesco Volta. Despite the friendship and the excellent relations between the two, Valli took the side of Luigi Aloisio Galvani (1737-1798) in the dispute over the origin of animal electricity or bio-electricity, calling Volta's electricity of metals "*imaginary*" [6-8].

Valli repeated Volta's experiments meticulously, in an attempt to reproduce the results. In 1797, the German scientist and naturalist Alexander von Humboldt (1769-1859) would also try to reproduce these experiments [9]. Valli subsequently became the head of a hospital department in Mantua, and in 1802 returned to Turkey to experiment with the inoculation of smallpox vaccine to protect against the plague [10].

Indeed, over the years, Valli had elaborated the theory that infection by smallpox excluded infection by the plague, and vice versa. "*Those who have had smallpox either do not contract the plague or, if they do, they do not risk death. The plague becomes a benign disease, or fades out as soon as a smallpox epidemic arises*".

Thus, he held, there were two "poisonous pura", one produced by the plague and the other by smallpox, and contamination between the two would give rise to a "good pus", which was potentially curative. Valli's experimentation, which was dubbed "*hazardous but fascinating*" by Pietro Moscati, a doctor and minister of the Cisalpine Republic, received a sort of scientific endorsement from this latter. Indeed, on 31 May 1792, Valli became a corresponding member of the Academy of Sciences in Turin. In 1799, in Livorno, Valli partly reproduced experiments conducted by the French abbot, mathematician and physician Robert Rimbaud Deidier (1670-1746). Since 1772, he had succeeded in immunising "*several animals by inoculating saliva taken from a hydrophobic dog. None of the animals inoculated with the saliva, to which gastric juice from frogs had been added, contracted rabies*". With this preparation, Valli succeeded in treating a certain Pisan lady named Rosermini and her maidservant, achieving a very good result [11].

In 1802 and in 1818-1819, these experiments would be repeated by the French military doctor René-Nicolas Dufriche Desgenettes (1762-1837) and by the Spanish

doctor Serafin Sola in Tangier (Marocco), as reported by the Swedish consul Jacob Graf Graberg Hemsö [12]. Valli subsequently travelled to Dalmatia as a military doctor with the Franco-Italian army. There, he treated an officer's wife, who had been bitten by a rabid dog; she did not contract rabies.

In June 1809, he went to Spain to serve on a military medical commission [13].

Following his return to Italy, he was appointed in 1811 by the Italian government to examine the thermal waters of Monte Ortone, south-west of Padua, in the Euganei hills. In 1815, he briefly stayed in Milan, but then returned to Mantua, a city he loved and regarded as his "*second home*".

Finally, he travelled to Cuba, arriving there from New York in September 1816. Accompanied by Dr. Antonio Mendoza, he visited San Juan de Dios Hospital, where he studied the epidemiology of yellow fever.

"*At that time, Havana had a sad appearance: the streets were mostly narrow, winding and unpaved, which, together with the lack of gutters, contributing to maintaining the dirt, and also the unwholesomeness, which was exacerbated by the nearby swamps; consequently, diseases were common, and yellow fever raged more vigorously than in other parts of America. In the months of August and September, mortality was very high, and during that time the death rate was 25 per day on a population of about 130,000 inhabitants*". While attempting to find a remedy for yellow fever, Valli died, struck down by the germs of the terrible disease, which he had inoculated into himself, a "*voluntary martyr to an overarching boldness in his art*" [14].

Eusebio Valli and his scientific legacy

Valli was criticised by several academics. For example, Professor Giovanni Pietro Frank (1745-1821) said of him: "How could this young man have been able to write about chronic diseases, when I myself would perhaps be scarcely able to do so after practising medicine for more than 40 years?".

Instead Prof. Ulrico di Aichelburg, who taught microbiology at the University of Turin, described some of Dr Valli's important professional characteristics, including his particular interest and competence in the field of vaccinology:

"And it must be remembered... that Eusebio Valli strove to prevent disease by inoculating an attenuated form of its infectious principle (which, please note, was unknown in those days: this was in the 18th century) [...]. By mixing gastric juice with pus from plague and smallpox lesions, and with saliva from rabid dogs, and injecting these relatively innocuous mixtures into healthy persons, Valli claimed to have elicited immunity to the plague, smallpox and rabies [...].

We may doubt the results of Valli's claims, but we cannot doubt that he had inferred that scientific principle which Pasteur would later apply successfully: the principle of vaccination" [15].

Valli's studies and his various manuscripts, including the original copy of his death certificate, written by the Holy Guardian of the Church of the Angel in Havana, are now conserved in a room of the Istituto di Storia della Medicina (Institute of the History of Medicine) in Rome.

In the year in which a relative, the lawyer Giuseppe Valli, authorised the biography of Eusebio, Louis Pasteur devoted himself to developing an anti-rabies vaccine. On 6 July 1885, after four years of study, Pasteur succeeded in treating Joseph Meister (1876-1940), who survived [16, 17].

In both Casciana and Ponsacco, streets and plaques have been dedicated to Valli.

Conclusions

Eusebio Valli was a great physician and a pioneer of modern vaccinology: a personage who deserves to stand alongside Edward Jenner, whose work Valli greatly contributed to publicising. He blended observation and experimentation, being well aware that, without these, even the most fascinating hypotheses and theories “*are worth nothing*”. He possessed both courage and ambition: “*the man who is gnawed by the ambition of glory can overcome any obstacle*”. Moreover, he had to fight against “*the charlatans... the physicians who are ignorant or in bad faith, who... have discredited the greatest discovery of the century, shamelessly preaching the heresy that vaccination does not prevent and cannot protect against smallpox*” and, in doing so, he did not hesitate to boldly try his own remedies on himself.

Valli can be regarded as one of the first physicians, or perhaps the very first, to take up and publicise Edward Jenner's discovery of an anti-smallpox vaccination. Indeed, he formulated the principle according to which immunity to a contagious disease could be elicited by injecting the same, appropriately attenuated, “material” responsible for the infection. In this way, a mild form of the disease would be caused, which would be memorised by the immune system, thereby eliciting protection against more severe forms.

Moreover, Valli was the first vaccinator to operate in several countries in the world. In a sense, therefore, alone and as far as was possible at that time, he anticipated the activity, and to some extent also the philosophy, of *Médecins sans Frontières* [10].

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Conflict of interest statement

None declared.

Authors' contributions

MM and NB conceived the study, MM, NB drafted the manuscript, MM and BC revised the manuscript. NB, MM and BC performed a search of the literature. MM and BC revised critically the manuscript. All authors read and approved the last version of the manuscript.

References

- [1] Valli G. Cenni biografici sul Dottore Eusebio Valli da Ponsacco (Pisa). Pontedera: M. Ristori 1886.
- [2] Valli E. Sulla peste di Costantinopoli del 1803. Mantova: Soc Tipografica All' Apollo 1805.
- [3] Valli E. Memoria sulla peste di Smirne del 1784. Losanna: F. Grasset 1788.
- [4] Valli E. Saggio sopra diverse malattie croniche. Pavia: Eredi di P. Galeazzi 1792.
- [5] Valli E. Discorso sopra il sangue considerato in stato di sanità e di malattia. Mondovì: A. Rossi 1789.
- [6] Piccolino M, Bresadola M. Shocking frogs: Galvani, Volta, and the electric origins of neuroscience. Oxford: University Press 2013.
- [7] Valli E. Opuscolo sopra nuove e interessanti esperienze sul sistema di elettricità organica ideata dal valente fisico e Prof. d'Anatomia Dott. Luigi Galvani. 1794. Available at https://archive.org/stream/gliscienziatiita01mieluoft/gliscienziatiita-01mieluoft_djvu.txt.
- [8] Valli E. Experiments on animal electricity, with their application to physiology. And some pathological and medical observations. London: J. Johnson 1793.
- [9] Valli E. Lettera del dottore Eusebio Valli sull' elettricità animale ad un suo amico. Mantova: G. Braglia 1794.
- [10] Volpi R. L'uomo che inventò i vaccini, storia di Eusebio Valli, avventuroso inventore e sperimentatore di vaccini a cavallo tra Sette e Ottocento. Torino: Lindau 2017.
- [11] Castiglioni A. Valli, Eusebio. Encicl Ital Sci Lett ed Arti 1937.
- [12] Graberg d'Hemsö JG. Specchio geografico, e statistico dell' impero di Marocco. Genève: Pellas 1834.
- [13] Romay Chacón T, González del Valle F. Elogio del Dr. D. Eusebio Valli, medico ordinario del Hospital Militar de Dijon, individuo de la Academia Virgiliana de Mantua, de la Sociedad de Medicina de Venecia, del colegio medico de Edimburgo. Habana: Oficina de Arazona y Soler 1816.
- [14] Picaza S, Villaverde M. Mysterious Deaths in History Eusebio Valli's case. Bulletin of the History of Medicine Vol. 19, No. 4 (April, 1946), pp. 455-458.
- [15] Ulrico di Aichelburg. Vita e morte dei microbi. Milano; Mondadori 1977.
- [16] Spina G. Eusebio Valli. Sci Med Ital 1959;7(3):393-409.
- [17] Mieli A. Gli Scienziati italiani dall' inizio del medio evo al nostri giorni. Roma: A. Nardecchia 1921.