

# The origins of vaccination: myths and reality

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In 1796, 75 years after Lady Mary Wortley Montague and Charles Maitland introduced inoculation into England,<sup>1,2</sup> Edward Jenner performed an experiment that would eventually lead to the eradication of smallpox and the end of inoculation. (NB: in this article, inoculation refers to immunization with smallpox virus and vaccination refers to immunization with cowpox virus.) He inoculated a child with material from a cowpox pustule just as he would have done from a smallpox pustule. About six weeks later, he performed a conventional inoculation on the same child using smallpox material. When there was no reaction to the inoculation, Jenner believed that he had demonstrated that cowpox could produce immunity to smallpox just like the real smallpox virus. His experiment had worked. But how did Edward Jenner get to this point, where had the ideas come from, and what lay behind his seemingly audacious practice on a defenceless child?

History texts and children’s stories all focus on the supposed role of milkmaids in guiding Jenner to cowpox. Even the most recent histories of smallpox eradication say that he learned of cowpox’s benefits from a milkmaid. In many cases, the milkmaid is beautiful because she cannot catch smallpox. In some versions of this story, the fabled beauty of the unscarred milkmaids is widely known and gives Jenner his first clue. Occasionally, other names pop up but are quickly dispatched as not really significant and home in on Jenner as the man who realized why the milkmaids were so beautiful.

Sadly the milkmaid story is a lie invented by John Baron, Jenner’s friend and first biographer.<sup>3</sup> Jenner himself never claimed to have discovered the value of cowpox, nor did he ever say, despite a huge volume of correspondence, how he first came across the idea. The myths of the milkmaids are just that, myths. To modern eyes, Jenner is revered for eradicating smallpox by using cowpox; in his lifetime, however, Edward Jenner faced severe criticism

from jealous competitors and from many ordinary doctors who did not trust his method because, unlike inoculation, it did not give permanent immunity to smallpox. John Baron invented the milkmaid story to counteract these criticisms.

What really happened is more prosaic although no less fascinating.

The Suttons’ improved method of inoculating<sup>4,5</sup> spread rapidly through England. By 1768, a country surgeon, John Fewster, and his colleague, Mr. Grove, had become partners with them. Years later, in response to the renowned chemist George Pearson’s inquiries, Fewster wrote:

In the spring of the year 1768 I came to live at Thornbury, where I have resided ever since. In that very year, from the following occurrence, I became well acquainted with the disease called Cow Pox. The late Mr. Grove and myself formed a connection with Mr. Sutton, the celebrated inoculator; and to inoculate for the smallpox we took a house in Buckover. We found in this practice that a great number of patients could not be infected with Small Pox poison, notwithstanding repeated exposure under most favourable circumstances for taking the disease. At length the cause of the failure was discovered from the case of a farmer who was inoculated several times ineffectually, yet he assured us that he had never suffered the Small Pox, but, says he, “I have had the Cow Pox lately to a violent degree, if that’s any odds.” We took the hint, and, on enquiry, found that those who were uninfected had undergone the Cow Pox. I communicated this fact to a medical society of which I was then a member, and ever afterwards paid particular attention to determine the fact.<sup>6</sup>

Thornbury is a town near Bristol on the river Severn. About six miles north is the town of Berkeley, and about seven miles inland is the market town of Chipping Sodbury. The events which led to

vaccination evolved over a 30-year span in the rough triangle formed by these three Gloucestershire towns.

In 1768, 19-year-old Edward Jenner was apprenticed to Daniel Ludlow, a surgeon, based in Chipping Sodbury.<sup>3</sup> Daniel and his apothecary brother Edward were members of a medical society which met at The Ship, an inn at Alveston near Thornbury.<sup>3</sup> This was Fewster's local medical society, referred to in his letter. At one of their meetings, Fewster reported his conversation with the old farmer and his subsequent inquiries, so there is a potential direct connection between Fewster and Jenner through the Ludlow brothers. Fewster's information probably spread through the West Country by word of mouth. It is just the sort of lightbulb moment that changes human knowledge forever. Before, the fact that some individuals resisted all attempts to inoculate them was a mystery and a considerable problem for doctors, since they were obliged to reinoculate their patients who had not had a smallpox pustule in response to their inoculation. Now that they had heard of cowpox on the grapevine they knew to ask their patients about cowpox, and if they did not respond to the operation there was a good explanation. The effects of cowpox would also have been of great interest to dairy workers who would have spread the information among their colleagues at fairs and market days. Within a few years, the news had spread around the West Country so that most doctors and many farm workers would have heard of the phenomenon.<sup>6</sup>

On one of the few occasions when Jenner discussed farmers' knowledge of cowpox he wrote:

... it appeared that it (cowpox) had been known from time immemorial, and that a vague opinion prevailed that it was a preventive of the smallpox. This opinion I found was, comparatively, new among them; for all the older farmers declared they had no such idea in their early days - a circumstance that seemed easily to be accounted for, from my knowing that the common people were very rarely inoculated for the smallpox, till that practice was rendered general by the improved method introduced by the Suttons: so that the working people in the dairies were seldom put to the test of the preventive powers of the cow pox.<sup>7</sup>

Here, Jenner himself draws the link between inoculations with smallpox and the discovery of the effects of prior cowpox. Many years later, a friend of his confirmed that Jenner once said that he first heard of cowpox in 1768.<sup>8</sup>

By 1769, Jenner was in London working as a house surgeon to the famed experimental surgeon

John Hunter at St. George's Hospital. Since he discussed the cowpox effect with Hunter, Jenner must have known about the discovery before leaving Gloucestershire. But the Suttonian method only became widely available after 1766–1767<sup>5</sup> so that the discovery could only have been made in a narrow window between 1767 and 1769, while Jenner was still apprenticed to Ludlow. Whether Jenner was actually present at the dinner where Fewster discussed his findings is not clear; apprentices were probably not invited) but it seems likely that he would have heard about Fewster's observations from his boss soon afterwards.

The advantages of cowpox could not have been discovered before general inoculation became a feature of country life, because only when large numbers of people were inoculated at the same time could the existence of several resistant individuals become apparent. Smallpox epidemics often smouldered rather than exploded and it could take months or years for the disease to leave a particular area. The few who escaped might have had previous mild smallpox and have been rendered immune by the undetected infection, something that was particularly likely to happen when the individual was an orphan because the parents, who might have remembered the early childhood infection, were dead; or they might just have been lucky and avoided exposure to the virus. John Haygarth had shown that direct contact with a smallpox patient or their possessions was necessary to contract the infection.<sup>8</sup> A few individuals, thought to be about one in 20, seemed to be naturally resistant to smallpox and never caught the disease. Inoculation itself was also not 100% effective; individuals sometimes had no response to the operation and it was common practice to reinoculate them to test whether they were resistant, immune, or whether, for unknown reasons, the first procedure had failed but the second was effective. If an individual failed to respond to inoculation after several attempts, it was usually assumed that they had had smallpox before. There was no way to link cowpox infection, which might have occurred years before and been forgotten, with inoculation resistance. However, once a large number of farmers and dairymaids were identified who resisted attempts to inoculate them, it became possible to question them closely until, as Fewster relates, one of them provided the crucial piece of information. Only cowpox infection shortly before inoculation could provide the clue required, and only when a large group of individuals were inoculated together would the necessary individual turn up. Cowpox itself was a sporadic illness found mostly in the south and west of England, so finding an individual with the right sequence of

infections would only happen when large group of dairymen was inoculated at one time.

Edward Jenner left his country apprenticeship for London where he had the good fortune to be the first pupil of John Hunter, who is widely credited with developing scientific surgery. Hunter had an obsessive interest in experimentation – his most famous aphorism, which Jenner would have heard frequently, was ‘*why think, do the experiment*’. Master and student became close friends and remained in correspondence for the rest of Hunter’s life. When Jenner returned home to Berkeley, he took the habits of observation and experimentation gained from his mentor with him. The country physician shared some of his ideas about cowpox with his former superior who was intensely interested in the concept since he was also an inoculator.

Back home in Berkeley, Edward Jenner settled into the routine of a country doctor. He joined two local medical societies; one of them the group that met at *The Ship* where Fewster and the Ludlows still participated in the discussions. Why didn’t cowpox fascinate them in the way that it became an obsession for Jenner?

Fewster’s lack of interest was based on his long experience of country medicine, which had convinced him that cowpox was actually a more serious disease than inoculated smallpox. The cowpox virus was transmitted by contact, and probably could only infect through cuts or scratches in the skin. If there was only a tiny scratch then there would only be a single ‘pock’, but if there were numerous scratches all over the arms, or extensively chapped skin from continuous outdoor work, then there would be many more pustules and the patient would have a fever and pronounced systemic symptoms. Sometimes the infection even spread to the face, transferred by scratching or licking a sore finger. A few patients who had widespread skin problems might have cowpox over their whole body, much like children with eczema following vaccination in the 20th century. Suttonian inoculation was actually milder than natural cowpox in most cases. Fewster wrote:

I think that it (cowpox) is a much more severe disease in general than the inoculated smallpox. I do not see any great advantage from the inoculation for the Cow Pox. Inoculation of the Small Pox seems to be so well understood that there is little need of a substitute. It is curious, however, and may lead to other improvements.<sup>6</sup>

In experienced hands, the death rate after inoculation was less than one in 500, and about 20% of patients had only a single pock at the inoculation site.

Although there was the risk of starting an epidemic, by then doctors knew how to prevent one, either by isolation or general inoculation. In contrast to inoculated smallpox, a cowpox pustule often matured into an intensely painful ulcer on the hand or fingers, which left the sufferer unable to work for several days. On balance, inoculation was less troublesome for the patient than having cowpox.

There was a second, and more compelling, reason why country doctors were not impressed by cowpox. It did not always protect against smallpox. Many individuals who said that they had had the cowpox before had perfectly normal inoculation smallpox. There were also cases of natural smallpox among individuals who had thought that they were immune from a previous infection caught from cows. While immunity always implied prior cowpox, previous cowpox did not always imply immunity. What would be the point of investigating the potential benefits of something that simply was not as effective as current practice? It is easy to see why Jenner’s colleagues found him tedious, and even he acknowledged that the imperfect protection problem was a major setback, noting that the term ‘cowpox’ was also applied to conditions – ‘spurious cowpox’ – which were not infections with vaccinia.<sup>9</sup>

It took Edward Jenner 25 years to unravel the mess. The problem lay in the definition of ‘cowpox’. There were at least three diseases that produced ulcers on the teats of cows<sup>10</sup> and only one of these was caused by the cowpox virus: ‘*this for a while damped, but did not extinguish my ardour*’. Jenner’s remarkable achievement is that he spent all that time untangling true cowpox from spurious cowpox and defining its unequivocal appearances. He learned how to recognize ‘milker’s nodes’ a painful bacterial infection on the fingers, which lacked the typical erosive ulcer of cowpox, and he could differentiate between cowpox and staphylococcal infections of the udder because the damage caused by staphylococcal bacteria spread beyond the teats. Eventually he learned how to recognize cases of true cowpox and could confirm that they really were resistant to inoculation. Jenner had also had a second insight that his colleagues had not appreciated. Inoculated cowpox would be much less severe than natural cowpox, just as inoculated smallpox was less dangerous than naturally acquired disease.

In May 1796, Jenner was asked to inoculate an 8-year-old pauper child named James Phipps. At the same time, there was a local outbreak of cowpox, something that only occurred every few years. Sarah Nelmes, a dairymaid, was infected with cowpox from her employer’s cows and had developed a large pustule where she had been scratched by a thorn.

...matter was taken from a sore on the hand of a dairymaid, ... and it was inserted, on the 14th of May 1796, into the arm of the boy by means of two superficial incisions, barely penetrating the cutis, each about half an inch long.

In order to ascertain whether the boy, after feeling so slight an affection of the system from the cow-pox virus was secure from the contagion of the smallpox, he was inoculated on July 1 following with variolous matter. The appearances were observable on the arms as we commonly see when a patient has had variolous matter applied, after having either the cow-pox or smallpox. Several months afterwards he was again inoculated with variolous matter, but no sensible effect was produced.<sup>11</sup>

Had Jenner done something unethical? In medical circles it is fashionable to claim that his first experiment would never have been approved by a modern ethics committee. Some writers even claim that the boy was an unwilling victim of Jenner's ego and he would never have 'volunteered' for the experiment. In reality, Jenner was acting in a completely acceptable way and actually giving Phipps, son of a poor labourer, protection against a feared disease. A child who had not had smallpox was almost unemployable because no one would take on a boy who might bring smallpox into the household and whose care and burial expenses would be charged to his employer if he did come down with the disease. If he caught smallpox before he was employed, his care would have been charged to his labourer father, who could not afford it, or to the parish overseers as his father was a pauper. Inoculation was the standard way to give the child immunity and protect him from the consequences of the infection. Although Jenner had never 'vaccinated' anyone before he had good reason to believe that the procedure might work, based on numerous patients of his who had proved resistant to inoculation after having cowpox. All he was doing was attempting to see whether artificial cowpox worked as well as natural cowpox, just as artificial inoculated smallpox protected against natural smallpox. After vaccinating Phipps, he was inoculated in the usual way. If cowpox had failed, he would just have a normal mild inoculation response; if it worked nothing would happen. Jenner was following up his experimental treatment with the 'gold standard' method of protecting the child. Since inoculation was a well-established and largely safe procedure that was widely used in England, there was no ethical issue with that part of the experiment. Inoculation would have been viewed as a necessary part of growing up for a child receiving parish support. Since cowpox was never

fatal and had few systemic effects, there were unlikely to be any unexpected complications apart from failure to immunize. Even in the hyper health-and-safety health- and safety-conscious 21st century, this experiment would have been given ethical approval.

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