

The origins of vaccination: no inoculation, no vaccination

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This article is the second in a two part series. It is based on Chapter 25 ('The pretty milkmaids') in Boylston AW (2012). Defying Providence: Smallpox and the Forgotten 18th Century Medical Revolution.

Edward Jenner attempted to publish the Phipps experiment in a manuscript which was rejected by the Royal Society.¹ Why would this august body turn down what we now regard as one of the most important discoveries ever made? Actually, the manuscript was a mess. Although Jenner gave short details of 10 patients who had resisted inoculation several years after having cowpox, Phipps was the only patient he had immunized with cowpox.² One example was not enough to support replacing inoculation with smallpox with cowpox. When John Haygarth heard of the experiment he thought that it was potentially interesting but that one case provided insufficient evidence; 20 or 30 would be more convincing. The rest of Jenner's paper consisted of speculations on the animal origin of cowpox; he thought that it was derived from a horse disease called 'grease'. And he gave a rambling hypothesis that many human diseases were derived from animals and a very confusing observation that immunity seemed to work in only one direction. Cowpox prevented smallpox, but smallpox did not prevent cowpox. By rejecting the paper the Royal Society spared Jenner the criticism and derision that would have followed his weak evidence and unsupported ideas. They actually saved his reputation.

Undeterred by rejection, Jenner attempted to expand his experiment. He recognized that there were one or two problems that he needed to overcome before his idea became a useful treatment. He had shown that whatever cowpox was, it could make someone immune to smallpox. But was this a stable property of the cowpox, or would it only work when transmitted from someone who had been directly infected by a cow? In a world that had no idea what germs were, there was no way to be certain that an infection always produced the same result. Jenner believed that cowpox was derived from 'grease', an infection of horse's hooves, which acquired the properties of cowpox when it infected a different species,

the cow. Perhaps cowpox would also change when it was passed from person to person.

However, he could not perform any more immunizations because there was no cowpox in the neighbourhood. He had to wait until the Spring of 1798 when cowpox reappeared. This time he conducted a complicated experiment, first inoculating William Summers with cowpox, then 12 days later, using fluid from Summers's pustule to 'inoculate' William Paed. Eight days later he transferred fluid from Mary Paed to several children and adults, and, from one of them, Hannah Excell, he inoculated a further four children seven days after that. Finally, he used fluid from one of them, Paed, to inoculate a boy, J. Barge. Sometime later Jenner arranged for his nephew Henry to inoculate Summers and J. Barge with smallpox fluid, which, as he expected, resulted in no reaction.

Jenner's complicated passage of fluid from one child to another was important because it satisfied him that whatever was responsible for immunizing the children was stable and could be passed from one person to another without losing its potency. He once stated that it was the only original contribution that he made to the establishment of cowpox as a better form of inoculation.³ Now he was ready to publish his experiments.

Edward Jenner's first publication about cowpox, *An Inquiry into the Causes and Effects of the Variolae Vaccinae, or Cowpox*,⁴ did not arrive on a completely unsuspecting world. Jenner had discussed his ideas with many of his friends, including George Pearson, who had discussed the basic concepts with John Hunter as early as 1789. However, Jenner's paper was actually rather thin. He provided 16 case histories of individuals who had proved to be immune to smallpox following cowpox and he had 'cowpoxed' at least 10 others, but he had only performed a smallpox challenge on three of his subjects. Although they were immune, it was weak evidence at best.

William Woodville, physician to the Hospital for Smallpox and Inoculation, managed to find a cowpox-struck cow in London and collected material to perform his own trial assisted by George Pearson. From the beginning it was a disaster. Many of their patients developed pustules on their bodies, not just the solitary pustule at the inoculation site as Jenner had claimed. One of their 500 patients died, which was more than the one in 600–800 that Woodville expected from his many years at the inoculation hospital. Woodville concluded that there was little difference between inoculated cowpox and inoculated smallpox.⁵

Jenner refuted Woodville's claims at once. None of his patients had ever developed more than a single pustule. The problem lay in the Inoculation Hospital where the atmosphere, fixtures, and even Woodville himself, were so marinated in smallpox that he had accidentally contaminated his vaccine. When none of Woodville's private patients, who were vaccinated away from the hospital, developed any other sores he concluded that Jenner was correct.

Although Pearson had confirmed many of Jenner's claims about cowpox, relations between the two men soured, especially when Pearson founded a vaccination clinic in London and offered Jenner a subsidiary role in its management. The Vaccine Institute, Pearson's project, was intended to monopolize the vaccination trade in London and generate a large private practice in vaccination for its founder. Matters came to a head in 1802 when Jenner's friends petitioned Parliament to grant Jenner an honorarium of £10,000 to compensate him for the lost income he suffered while developing his innovation. But Jenner made a near fatal mistake. He opened his petition, claiming that he was the true discover of the benefits of cowpox.⁶ Later in the document, his nephew George corrected this, claiming instead that the person to person transmission was the original discovery which had established vaccination. Jenner's mis-statement opened the way for George Pearson. During the House of Commons investigation Pearson gave testimony that he had gathered a great deal of information implying that Jenner did not deserve the reward. His case was based on several features of Jenner's work. First, Jenner had not 'discovered' that cowpox prevented smallpox; this fact had been known for at least 30 years before Jenner's *The Inquiry* was published. Second, Jenner did not understand the basis of his 'discovery' since he believed that 'grease' was the source of cowpox and claimed that he had immunized with material taken from horses' hooves. Numerous attempts to confirm this observation had failed. A farmer named Jesty, and at least one other doctor, had inoculated with cowpox

material years before Jenner so he did not deserve to claim priority. Finally, Pearson and Dr William Woodville, physician to the Smallpox and Inoculation Hospital, had been the first to confirm Jenner's observations by initiating a large series of vaccinations, which were far superior in their value to the few cases Jenner had produced.

Most of Pearson's comments were fair; only the claims that he and Woodville had initiated trials confirming the findings were shown to be untrue. Another physician, Henry Cline, had begun before them. Indeed, Jenner had never claimed that he had discovered the value of cowpox, nor had he claimed that he was the first to vaccinate. His claim was based on his demonstration that the agent could be passed from person to person while retaining its protective properties. Parliament found in favour of Jenner and voted to give him £10,000.

Many medical innovations divide public opinion. Immunization has been opposed by some parts of society from its very beginnings. Opponents of vaccination (cowpox inoculation) used Pearson's arguments to denigrate Jenner and deprecate his discovery. Pearson went so far as to invite farmer Jesty to London where he had his portrait painted. This was hung in the Vaccine Establishment as a reminder of the view that Jenner's reputation was inflated.⁷

Much of the opposition to vaccination stemmed from the undoubted success of inoculation. Woodville admitted that the Smallpox Hospital had misled their patients into believing that they were being inoculated when they were being vaccinated because they would have refused 'cowpoxing'. Families all over Britain had been inoculated in the great expansion of the practice brought about by the Suttons.⁸ Now parents and grandparents wanted the same well-known and well-regarded treatment for their own children. Country doctors who had used inoculation with great success for the whole of their careers were reluctant to give up a practice that they trusted for a less well understood innovation.

Within a decade of Jenner's first publication it was clear that there was a major flaw in vaccination: it did not produce lifelong immunity to smallpox. Shortly after the new practice began to spread, cases of true smallpox in patients previously vaccinated appeared. At first Jenner tried to explain them away by claiming that the inoculator was an unskilled operator, or that he had used spurious cowpox to perform the operation. However, soon there were cases where there could be no explanation, other than a failure of vaccination to provide protection. Eventually even one of Jenner's patients developed severe confluent smallpox 10 years after the master had performed his

vaccination. Although none of these cases had been fatal, their existence raised the possibility of severe disease. Everyone knew that sometimes smallpox was discrete and other times confluent. Parents now faced the anxiety of what to do about their vaccinated children. Should they have them inoculated to be on the safe side? To many, such failures argued that Jenner had been wrong and that vaccination was a failed experiment that should be abandoned. Since the idea that 'grease' was the forerunner of cowpox had been proven false, perhaps the value of cowpox was also an illusion. Jenner's concept of 'spurious cowpox' was attacked. Nothing like spurious smallpox or spurious measles existed, so why believe in 'spurious cowpox'. If that idea was also false, then all of Jenner's arguments relying on it as the explanation for failed vaccinations were also false. Inoculators resorted to the timeless medical teaching 'never abandon experience for experiment'.

One of the first to notice that vaccination sometimes failed was Daniel Sutton.⁹ He replied to a Royal College of Physicians circular asking for information about the success of cowpox, giving a report of two patients that he had personally vaccinated with cowpox who had subsequently developed smallpox. He was livid when the College demanded that he attend in person and bring exact details of his cases. How dare they imply that he was lying? It would be Sutton's last public appearance where he defended what had become commonly known as 'the Suttonian method' in contradistinction to 'cowpoxing'. But his treatment was a symptom of another issue surrounding vaccination. Opponents of vaccination felt that the medical establishment had sold out to Jenner and were censoring all criticism. Eventually, it would become clear that vaccination 'wore off' after a few years and that it only provided complete protection for 3–5 years in some individuals. But to some even this was a nuisance since inoculation provided lifelong protection.

Because vaccination would eventually prove such a huge success and lead to the eradication of smallpox it can be difficult for modern observers to realize exactly how controversial vaccination was in the early 19th century. Jenner's reputation was under attack from several aspects. It becomes easier to understand why John Baron, Jenner's biographer deliberately misleads posterity by publishing a truncated version of Fewster's letter, which only included his comments that he did not think cowpox was better than smallpox.¹⁰ For years Jenner's opponents had argued that Fewster, not Jenner, was the true discoverer of inoculation and Baron wanted to stamp on this claim. Fewster himself never claimed that he was the originator and remained friends with Jenner, even sending

him occasional case reports to add to his collection. Yet Baron clearly took Fewster's letter seriously enough to misrepresent its contents and to belittle Fewster's subsequent lack of interest in cowpox when Jenner tried to raise the subject at their medical society meetings. He inadvertently confirms the likely accuracy of the account by trying to discredit it. Baron even suggests that the other members of the society threatened to banish Jenner if he did not stop his continual dialogue around cowpox. The effect of Baron's biography is to characterize Fewster and his colleagues as ignorant fools who were unable to appreciate the genius of Jenner. Whatever Fewster did, it was enough to upset John Baron. Yet, despite having ample opportunity for over 20 years, Edward Jenner never refuted Fewster's account of the discovery of the cowpox effect. Modern smallpox texts cite Fewster as an example of a discredited claim for priority and never publish the entire text of his letter. Further, some of them confuse the issue by stating that Fewster claimed to have reported his findings to a London medical society and that no published records of the event remained.¹¹

Quite where the various versions of Fewster's actions came from is difficult to track down. Certainly there could not have been a presentation to the London Medical Society in 1765 since that organisation was not founded until 1776, and Fewster could not have made his discovery in 1765, as some accounts claim, because he only moved to Thornbury in 1768. These versions appear to be attempts to defuse the claims of the importance of Fewster's role by reducing them to unpublished observations that had no impact on the subsequent development of vaccination. Baron's creation of the milkmaid myth serves a similar purpose. In the absence of any statement from Jenner about what had really happened the Fewster letter gained credence. By planting the milkmaid story, and claiming that Jenner had told it to him more than once, Baron provided an alternative version, which he strengthened by claiming that Jenner had repeated it on his death bed.

Baron's milkmaid fiction soon took on a life of its own. Subsequent authors attempted to explain how a milkmaid could have known that cowpox protected her from smallpox by inventing a tradition that milkmaids had singularly beautiful faces because they were not scarred by smallpox. However, no one ever commented on this at the time (the 1760s or before) and there are good reasons to believe that it was not so. For one thing boys as well as girls milked cows in England, and no one ever suggested that cowboys had smooth complexions. Furthermore, both smallpox and cowpox occurred sporadically and

there was no reason why a future milkmaid would get cowpox first. There should have been both scarred and smooth milkmaids and, again, no one noticed.

Smallpox was actually not very contagious so that during an outbreak at a farm or small farming village a few individuals would escape the infection by chance or because they were resistant to the virus.¹² There would be no way to connect their escape to a previous attack of cowpox until artificial infection – that is, inoculation – made the link obvious. There is a direct link between the introduction of inoculation in the West in the 1720s and the eradication of smallpox 250 years later.

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