What was the role of Gloucestershire in vaccination?

Gloucestershire's role in vaccination was huge. It was the home of Edward Jenner who pioneered the concept of vaccination and Berkeley is where he conducted his experiments. His work not only benefited the local area, but had a great impact globally. Although Jenner's work is internationally known, the principles of his discovery can also be traced back to Thornbury itself. Even with a historical event as well known as the discovery of the smallpox vaccination, there are still conflicting versions of this story. But by all accounts, Gloucestershire supplied the doctors, the patients, and even the cows.

Cowpox is an infection caused by the *Vaccinia* virus, which usually affects cows. It is from the genus *Orthopoxvirus* within the family *Poxviridae*. ⁶ When cowpox affects an unfamiliar host- a human- it is less virulent. The highly infectious smallpox virus, which was introduced to Europe between the 5th and 6th centuries, is also associated with this genus.¹³

Edward Jenner (1749-1823) was an English physician who is known as the 'Father of Immunology' owing to his contribution to immunisation and the ultimate eradication of smallpox. However, it is important to note that Jenner did not discover vaccination nor was he the first to propose that an exposure to cowpox would cure smallpox.¹² He lived in Berkeley, Gloucestershire and was the son of the vicar of Berkeley, Reverend Stephen Jenner, which allowed him to receive a strong basic education. He attended school in Wotton-under-Edge, Katharine Lady Berkeley's School, as well as Cirencester Grammar School and had a strong interest in science and nature.¹ During this time, he was inoculated for the smallpox virus and it is thought that his experience influenced him, as he was psychologically scarred by it,⁹ into his attempt to find a better method to prevent smallpox. Inoculation is the process of inserting a hollow needle full of fresh matter from a causative agent of a disease into the subcutaneous layer of the skin of someone unexposed to the disease. It was an unsafe way to attempt to combat smallpox, and was only successful if done very carefully.

When Jenner was fourteen years old, he went to Chipping Sodbury to be an apprentice to the surgeon and apothecary, Mr Daniel Ludlow. He was apprenticed there for seven years and this was where he gained most of his experience. Mr Daniel Ludlow was a member of a medical society which met at the Ship, an inn in Alveston.¹ This medical society (Convivio-Medical Society)¹⁴ is the cause of some of the conflicting views of Jenner's later discoveries. A common misconception is that Jenner had overheard a dairymaid say 'I shall never have smallpox, for I have had cowpox' when he was apprenticed to Mr Daniel Ludlow and this is what inspired him to conduct his famous experiment. However, Dr Arthur Boylston said that "the idea that cowpox could prevent smallpox infection came from Fewster's observations in 1768. There was no milkmaid." John Baron, Jenner's friend, was the first and only person to write about this milkmaid story; this was in a biography about Jenner written several years after his death. Boylston explains Baron was trying to protect Jenner's reputation. It is likely Baron invented this story to show how Jenner had come across this idea.²

Jenner continued his training at St George's Hospital in London but returned to Berkeley in 1772, where he became the local practitioner and surgeon. He inoculated his patients to protect them against smallpox.

He developed a hypothesis that cowpox could protect against smallpox.¹

In May 1796, Jenner diagnosed a patient, Sarah Nelmes, with cowpox rather than smallpox. She had a rash on her hand and told him that Blossom, one of her Gloucester breed of cows, had recently been infected with cowpox. He decided this was the perfect time to test his hypothesis and test the protective properties of cowpox by giving it to someone who had not suffered from smallpox. On 14 May 1796, Jenner inoculated an eight year old boy, James Phipps, with matter taken from Sarah Nelmes' sore. Phipps was Jenner's gardener's son and Jenner observed Phipps after he had been inoculated. A few days after the inoculation, James became mildly ill.¹ An article in the New York Medical Journal (1902) quotes Jenner's first publication: *An Inquiry into the Causes and Effects of the*

Variolae Vaccinae (1798). 'On the seventh day the boy complained of uneasiness in the axilla and on the ninth he became a little chilly, lost his appetite, and had a slight headache.'⁴ (Axilla is the technical name for the armpit.)⁷ On the tenth day, Phipps was well and had recovered. However, Jenner did note that 'the only difference... perceived was in the state of the limpid fluid, which assumed rather a darker hue, and in the efflorescence around the incisions, which had more of an erysipelas look than usual after variolous inoculation'. Jenner was comparing the appearance of cowpox inoculation with the standard smallpox inoculation. On 1st July, Jenner variolated Phipps and he was refractory- he did not develop smallpox, and therefore Jenner concluded that protection was complete.⁴ Phipps was inoculated many times after and was never infected with smallpox.¹ Thus, the experiment was an overwhelming success.

Erysipelas: An infection, usually of the face, caused by streptococcal bacteria, which are thought to enter the skin through a small wound or sore. ¹³

The ethics of experimenting on the child could be challenged on the grounds of consent, however Jenner would not have perceived much danger - he had never known of cowpox being fatal, even when acquired under the most unfavourable circumstances. Also, the exposure to smallpox was through the existing variolation.⁴



Hand of Sarah Nelmes from Edward Jenner's Inquiry (© The Jenner Trust) <u>https://jennermuseum.com/learning/collection</u>

In 1798, Edward Jenner published all of his research into smallpox into a book: An Inquiry into the Causes and Effects of the Variolae Vaccinae and it became one of the most important documents in the history of medicine.¹⁴ In the following two years, he published the results of further experiments which also confirmed his theory that cowpox could be used to protect against smallpox. However, the immediate reception was not favourable. The objections were natural.⁴ Firstly, cowpox was only in certain locations so doctors who wanted to test the new process needed to obtain cowpox matter from Edward Jenner. This led to the cowpox matter being contaminated with smallpox when the cowpox samples were handled by people working in smallpox hospitals or carrying out variolation. Many people who were administering the vaccination did not always follow the correct procedures that Jenner had recommended. Because of the cross-contamination, people were led to believe that this new process was no safer than the existing method to combat smallpox (smallpox inoculation). There was also opposition from people who were fearful of the vaccine. They were worried about any possible consequences, as the matter originated from cows, and also were opposed to it because of religious reasons.¹ Furthermore, there were many surgeons who unfortunately did not want to see Jenner succeed. Some of the earliest opposition was from professional inoculators of variola, who saw a lucrative industry threatened. Jenner received a letter from Dr. Jan Ingenhousz which set out the facts against the new process.⁴ Now most famous as the discoverer of photosynthesis, Dr Ingenhousz then had a reputation for inoculating.⁶ In response, Jenner published his side of the correspondence into a pamphlet called Further Observations on the Variolae Vaccinae or Cowpox (April, 1799). In

this pamphlet, Jenner explained that he was unable to extend the inquiry much further than the original because the supply of the vaccine virus was exhausted.⁴

Although Edward Jenner is known as the 'Father of Immunology', he was actually not the only local doctor linked to this discovery. John Fewster (1738-1824) was an apothecary and surgeon in Thornbury.¹⁰ ¹⁴ He was also Mayor of Thornbury from 1776-1777 and from 1811-1812. Fewster's involvement in vaccination was because of his findings on how to prevent smallpox epidemics. He ran a lucrative variolation practice, which included inoculating healthy children with cowpox just a few months before Jenner conducted his experiment with Phipps and Nelmes. The Convivio-Medical Society in Alveston, which Mr Daniel Ludlow attended, was Fewster's local medical society, and there is a potential direct connection between Fewster and Jenner through Ludlow and his brother, Edward.¹⁰ Fewster had inoculated and treated farmers in Thornbury, and some of these farmers that had been exposed to smallpox were already immune to the disease. He is the "Fewster" named in Dr Arthur Boyston's repudiation of the milkmaid story. In his letter to Mr Rolph, a former surgeon from Thornbury, 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... I became well acquainted with the disease called Cow Pox... a great number of patients could not be infected with Small Pox poison, not withstanding repeated exposure under most favourable circumstances for taking the disease. a farmer who was inoculated several times ineffectually, yet he assured us that he had never suffered the Small Pox. We took the hint, and, on enquiry, found that those who were uninfectable had undergone the Cow Pox. I communicated this fact to a medical society.' ¹⁴

In 1763, Fewster noted that two brothers had been variolated in Buckover, near Thornbury, but one did not react. When questioned, the brother that did not react said that he had previously contracted cowpox, but had never been infected with smallpox. Fewster then realised that there may be a possibility that cowpox could protect against smallpox. It has been reported that he discussed this possibility with members of his medical society at a dinner which included Mr Daniel Ludlow and the apprentice Edward Jenner. Thus Fewster reported the theory that cowpox could be used as a protective against smallpox 21 years before Jenner conducted his experiment with Nelmes and Phipps, but never published it. He did this in a paper entitled: *Cowpox and its ability to prevent smallpox*.¹⁰



The Ship Inn, Alveston - Holly Nicholas

In 1796, Fewster was called to visit a boy who had an early case of smallpox. The young boy's uncle, John Player, asked Fewster if he would consider inoculating the boy with cowpox so that he could be saved from smallpox. Player has said that Fewster had replied saying that he had considered inoculation, but believed that variolation was already successful and therefore another solution seemed superfluous. Although Fewster had decided against it, according to Player Fewster went on to inoculate three children in Thornbury with cowpox during the spring of 1796.¹⁰ Fewster's

involvement raises the question of who should be recognised for this discovery. If Fewster had told his friends about his theory, then he may have given Jenner the idea. However, there is some conflicting information about Fewster. One example of this is the date of Fewster's arrival in Thornbury. In his brief autobiography, Fewster states that he came to Thornbury 'soon after the peace', which refers to the Seven Years War (1756-1763). Player reports that 1763 was also the year Fewster noted that the two brothers had been variolated and one did not react. However in the letter written to Mr Rolph, Fewster says that he moved to Thornbury in the spring of 1768. If this account is true, then Fewster could not have made the discovery of the brothers in 1763. The original letter has been lost, so we cannot be sure of a mistranscription.¹⁴ Therefore, we cannot fully rely on the letter as evidence. To conclude, Jenner is not the only person that should be recognised and praised for his achievements.

Edward Jenner's work did not only have an impact on the local area, but became the foundation for modern day discoveries in immunology. As a result of the observations and experimentations carried out in Gloucestershire, smallpox has been globally eradicated and was declared extinct by the World Health Organisation in 1980.^{1 13} For centuries, smallpox devastated mankind and in 18th Century Europe, 400,000 people died each year. Three in ten people died from the virus.⁵ A UK Act of Parliament in 1840 banned variolation and made vaccination with cowpox compulsory.¹ Jenner's work is still relevant today: vaccinations save 2-3 million lives per year.¹¹ Currently, vaccines are being developed to combat the COVID-19 pandemic. The Moderna and Pfizer vaccines, like Jenner's smallpox vaccine, are incapable of causing the disease they are meant to prevent and under-eighteen year olds are now being invited to take part in vaccine trials.³

"No human being who has ever lived has saved more lives in history than the simple country doctor from Gloucestershire." - Andrew Marr (2012)⁸

Holly Nicholas

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