

# LESSONS FROM SMALLPOX

Approximately 40 years ago, the World Health Assembly adopted a resolution declaring the accomplishment of a global goal. Smallpox had been eradicated. This was a significant achievement, as the disease had been a devastating part of our human experience for thousands of years.



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This achievement took place about 200 years after Edward Jenner's vaccine experiment, when the English doctor made discoveries that inoculation could provide protections from the illness. So, the discovery of a vaccine did not immediately result in defeating the disease. The journey from global pandemic to eradication offers some ethical lessons as we grapple with the current pandemic, COVID-19.

Most of us are familiar with the general story of Jenner's discovery of a vaccine. He knew that dairymaids who were infected by cowpox developed a natural immunity to smallpox. So, he found a young woman, Sarah Nelms, who had open lesions from cowpox and transmitted the pus in her wounds to his test subject. Although there were some reactions to the infection, these were short lived, and upon recovery the person was immune to smallpox.<sup>1</sup> Jenner is often understood to be the founder of immunology.

Medical historians, though, have a much more nuanced understanding of the origins of immunization and Jenner's role. He was not the first to note the connection between cowpox and smallpox, nor was he the first to deliberately inoculate in order to prevent smallpox.<sup>2</sup> In the century prior to Jenner's use of cowpox to inoculate against smallpox, physicians deliberately infected patients with smallpox to establish immunity. Jenner was himself inoculated with smallpox when he was eight years old and, by a contemporary's account, the experience was quite horrible.<sup>3</sup> Jenner's contribution was to make

the technique safer, to demonstrate its scientific effectiveness and to promote the technique, spreading its use.

There are some initial lessons that we can take from Jenner's work. Jenner experimented with injecting cowpox into a test subject, James Phipps, the 8-year old son of his gardener. One scholar Blake Edward DeLeon, has defended this action as being moral in the time that the decision was made, because inoculation, while not a common practice, was being used to develop immunity.<sup>4</sup>

From our perspective today, it is clear that we would not reach the same conclusion. It was common practice in Jenner's time to use slaves, children and prisoners as test subjects for medical experimentation. Among the developments in the ethical considerations of clinical trials in the past century, safeguards have been established to protect children and other vulnerable persons from any research that would not offer some expected tangible benefit to them. To be fair to DeLeon, he

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does argue that the second inoculation of smallpox was consistent with the accepted practice of trying to mitigate the disease. There is a confusion here between culpability and immorality. One can say that someone who acted immorally may not be morally responsible because of ignorance. But,

that will never make an immoral act good.

The initial injection of cowpox was experimental; it was not clear that it was for the good of the patient. There was a hope, certainly, but hopes and experiments are categorically different. To mistake the one for the other is to create the conditions for an abusive relationship between the researcher and the subject.

In short, in the past century, ethicists have rightly condemned the misuse of power by health care personnel toward patients and subjects who lack the ability to protect themselves. The Tuskegee Syphilis Trials, the Nazi medical experiments, and the Willowbrook Hepatitis Trials are representative of instances where experimental subjects were used as a means to an end, rather than being treated as persons with human dignity.

Of course, in judging the choices made over two centuries ago, there should be a measure of consideration given to the culture of the time. Nevertheless, from the contemporary vantage point, injecting the child of a servant with an experimental substance was immoral. We cannot let the hope of a reward lead down a path where we use others to achieve what is a worthy goal. So, we may say that this is an instance where there was no culpability, but certainly there was immorality.

Today, with the challenges of COVID-19, it is essential that we maintain ethical guidelines regarding testing. So far, pharmaceutical companies have issued broad appeals for test subjects. We must not place the burden of testing on disadvantaged persons or communities. We all might want to consider if we're able to volunteer, to ensure that a wide and equitable population of people are part of the trials.

Jenner did succeed in bringing the medical community together to support his research and program to inoculate cowpox to prevent smallpox. The challenge was to obtain enough of the vaccine derived from cowpox to inoculate. There was simply not enough of the vaccine available. He often mentioned his frustration at not being able to supply colleagues who asked him for the requisite vaccine.<sup>5</sup> Human to human transmission of cowpox came to be called the Jennerian technique, and it was used for the next 90 years.

However, over time, it lost its strength to create a lifelong immunity to smallpox. Another drawback was that this method sometimes also transmitted other diseases, like syphilis.

The next step to the eradication of smallpox was to develop a stable, effective and reproducible vaccine. In 1840, Giuseppe Negri of Naples, Italy, created larger and more effective quantities of the vaccine by infecting calves with cowpox. The technique became known as animal vaccination. It was used more widely after it was discussed at a medical congress in France in 1860.

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Eventually, “vaccination parks” in Europe, and “vaccine farms” in the U.S. produced sufficient quantities of the vaccine. These facilities were not regulated as was typical in medical practice at the time, and contaminated vaccines led to a number of deaths.<sup>6</sup> Some governments began vaccine safety and quality control measures in the early 20th century.

Wyeth Laboratories created the modern vaccine with Dryvax, a freeze-dried vaccine in the 1950s. This enabled the production of a heat-stable vaccine that could be stored without refrigeration. With that innovation, it became possible to begin to eradicate smallpox. The first goal was to eliminate the disease from the Americas. Then the World Health Organization called for a global program beginning in 1958.<sup>7</sup>

The eradication of smallpox would not have happened without the work of many people who perfected techniques and even instruments, like the bifurcated needle, that made mass immunizations possible. Medicine has often depended upon international cooperation and collaboration. It is essential to work together to control and eradicate a disease like COVID-19.<sup>8</sup> A global pandemic requires a global response that does not set one nation against another.

We also should not assume that speed to develop an effective COVID-19 vaccine or vaccines is the hallmark of an effective response to this pandemic. The talk of an effective and safe vaccine for the public in the relatively short time frame of one year may place short-term considerations over long-term benefit. Let's not place hubris above hope and safe scientific inquiry. To do so would be to ignore the lessons from the work of Edward Jenner, and the many, many people who have helped to eradicate one of the world's worst diseases.

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#### NOTES

1. Stefan Reidel, "Edward Jenner and the History of Smallpox and Vaccination," *Proceedings* 18, no. 1 (2005): 21-5, doi:10.1080/08998280.2005.11928028.
2. Lady Mary Wortley Montague brought the technique of immunization from Istanbul to the Western world.
3. Richard Fisher, *Edward Jenner 1749-1823* (St. Edmunds: St Edmundsbury Press, 1991), 14, as cited in Blake Edward De Leon, "The Perception of Medical Ethics within the Case Study and Campaign of Jennerian Vaccination, Harvard University thesis, November 2018, 8-9, <https://dash.harvard.edu/bitstream/handle/1/37945151/DELEON-DOCUMENT-2018.pdf?sequence=1&isAllowed=y>.
4. De Leon, 42-48.
5. A note on the word vaccine: Originally, the technique was termed "variolation," and it meant to be infected with a weakened form of the original disease. Vaccination is a term created by Jenner that refers to the Latin noun "vacca," or cow. So in his use of the term, he acknowledges his injection was derived from cows.
6. José Esparza et al., "Early Smallpox Vaccine Manufacturing in the United States: Introduction of the "Animal Vaccine" in 1870, Establishment of "Vaccine Farms", and the Beginnings of the Vaccine Industry." *Vaccine* 38, no. 30 (2020): 4773-79, doi:10.1016/j.vaccine.2020.05.037.
7. Edward A. Belongia and Allison L. Naleway, "Smallpox Vaccine: The Good, the Bad, and the Ugly," *Clinical Medicine & Research* 1, no. 2 (2003): 87-92, doi:10.3121/cmr.1.2.87.
8. Cary P. Gross and Kent A. Sepkowitz, "The Myth of the Medical Breakthrough: Smallpox, Vaccination, and Jenner Reconsidered," *International Journal of Infectious Diseases* 3, no. 1 (1998): 54-60, doi:10.1016/s1201-9712(98)90096-0.

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