

Montagu and Jenner: The Campaign Against Smallpox

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The smallpox (variola) virus has killed more people than any other microorganism. The virus probably evolved from an orthopox virus in Africa. The earliest records of smallpox are from Egypt and China in 1000 B.C. It is likely that Egyptian armies were responsible for moving the disease to the Middle East. In A.D. 166, Roman soldiers brought smallpox to Europe where it killed up to 200 people a day. The Persian physician Rhazes recognized smallpox and measles as two distinctly different diseases in A.D. 900. Over the centuries, smallpox became the leading infectious disease and epidemics ravaged the world.

European colonization brought smallpox to the Americas and to Africa south of the Sahara. Smallpox killed millions of Amerindians in the 16th century; the case fatality rate exceeded 50 percent in the new, nonimmune populations. The Spanish conquests of Amerindians in the 16th century coincided with epidemics of smallpox that reduced the Amerindian populations so they could not resist the armies of Hernando Cortés and Francisco Pizarro. In 1721, 5,759 cases of smallpox were reported in Boston (population, 10,700) and one out of every seven patients died. By the 18th century, smallpox was killing 200,000 to 600,000 people every year in Europe.

Smallpox was a frightening disease that lasted two weeks or longer. Transmitted through the respiratory route, the virus infected internal organs before being transported through the blood to the skin. Viral growth in the epidermis caused small bumps on the face, upper body, and arms. Over several days the bumps filled with fluid, became inflamed, broke, and formed a soft yellow crust. Those who recovered from the disease carried disfiguring scars.

In 1967, smallpox was endemic in 30 countries, infecting 10 to 15 million people with two million deaths annually and the World Health Organization initiated a campaign to eradicate the disease. The campaign was so successful that by 1971 the value of smallpox vaccination was being questioned. Between 1951 and 1970, 103 cases of smallpox with 37 deaths were reported

in Great Britain. During that period 100 people had died due to smallpox vaccination. The disease hadn't occurred in the United States in over 20 years so that the United States discontinued vaccination of children and only travelers to endemic countries had to show proof of immunizations—yet physicians used 2.5 million doses of the vaccine in 1978. The endemic countries in 1974 were Bangladesh, India, Pakistan, and Ethiopia and WHO predicted the last cases of smallpox would be seen in 1975. It didn't happen quite that fast, but the last 192 cases of smallpox in the wild occurred in a 1977 outbreak in Somalia.

The last case of smallpox resulted from an accident with a laboratory culture at the University of Birmingham Medical School in 1978. Nearly all laboratory cultures were destroyed after that. By 1995, the viral genome had been mapped so the remaining cultures in Moscow and Atlanta were scheduled to be destroyed in 1996.

Vacca is Latin for cow

Smallpox is the first disease we have eradicated. This was possible, in part, because humans are the only host for the virus. Smallpox virus was in a tenuous position for a parasite: if all its hosts are killed or if they developed immunity, the virus had no place to replicate. Since the virus didn't kill all of its hosts and new hosts are always born, evolution worked in favor of the virus—until human ingenuity provided another obstacle.

Lady Mary Wortley Montagu

Mary Wortley Montagu, a socialite and writer, was born Mary Pierrepont in London in 1689. She educated herself by reading from her father's library rather than learning the superstitions her governess was teaching her. In later years she described her governess's teachings as "the worst in the world." Her family belonged to British society and her father was proud of Mary's wit and beauty. She was elected reigning beauty at his Whig men's club when she was

eight years old. She began her writing career in her teens with poems and an autobiography. At the age of 23, to avoid an arranged marriage, Mary eloped with Edward Wortley Montagu.

Between 1717 and 1718, she was stationed in Turkey with her husband who was England's ambassador to Turkey. In Turkey, Montagu did not spend her time behind the embassy's shutters. Instead, she intended to see everything. She wrote letters back to England in which she described the beautiful Turkish women, the high moral conduct of the Turkish people, and gave her forthright and witty opinions on everything. Her "Turkish Letters" record political and social customs, including her admiration (or envy) that Turkish women are "the only free people in the Empire." In particular, she noted that married women had their own money and kept it after a divorce "with an addition which he is obliged to give them."

Montagu was keenly aware of the perniciousness of smallpox. Her brother died from the disease and she was left scarred from her battle with the virus in 1715. On April 1, 1717, she wrote that "Smallpox, so fatal and so general amongst [the English], is here [in Turkey] entirely harmless by the invention of ingrafting." In September, an old woman would bring pus collected from a victim of a mild case of smallpox in a nutshell. The woman would quickly and painlessly scratch open a vein on her patient, smear the pus in the vein four or five times, and cover the wounds with a piece of nutshell. After eight days, the patient developed a mild fever that lasted two days and a few pox. The patient recovered and was immune to smallpox. After describing the process in a letter, she vowed to tell doctors in England about it "if I knew any one of them that I thought had virtue enough to destroy such a considerable branch of their revenue for the good of mankind." She believed that the procedure was harmless and essential and had her six-year-old son engrafted in 1718 by the Embassy surgeon Charles Maitland. A Greek physician, Emanuel Timoni, practicing in Turkey was also employed to attend the Wortley Montagus. Timoni first described this procedure in the *Philosophical Transactions* of the Royal Society of London in 1714. James Pylarini again

described the process in the *Transactions* in 1716. The procedure was called variolation (*varus* = pimple) or inoculation (*inoculare* = to graft).

After returning to England she achieved notoriety as an intellectual when her writings were published and as a feminist when her picture in Turkish dress holding a book entitled "The Female Traveler" was published. In 1721, a smallpox epidemic struck England. To encourage people to have their children inoculated, Montagu had Maitland inoculate her three-year-old daughter in a well-publicized event.

Montagu then went to the Court of King George I, forming a friendship with Caroline, Princess of Wales. Caroline arranged for human testing of the smallpox inoculation. Seven condemned criminals from Newgate prison were given the option of the gallows or submitting to smallpox inoculation. The latter choice might have led to their freedom and immunity to smallpox. Or, it might have meant disfigurement or death from the disease. The prisoners chose inoculation. They survived with nothing worse than their inoculation scars—and gained their freedom. The experiment was repeated on half-dozen orphan children and, again, they all survived. In 1722, the King was sufficiently convinced to be persuaded to have two of his grandchildren inoculated. This was also successful. Inoculation for smallpox was becoming general practice when, unfortunately, Maitland inoculated another child. Six servants in the child's household contracted smallpox during the girl's illness and convalescence. Some clergymen then claimed it was against God's will and some physicians cited the danger of spreading the disease.

In response to attacks on the practice, she anonymously published "A Plain Account of the Inoculating of the Small Pox by a Turkey Merchant" in a London newspaper. The inoculation did gain general acceptance and in 1754 Montagu was prophetically eulogized for "bringing into her own country a practice, of which ages to come will enjoy the benefit." Lady Mary died on August 21, 1762 when a young man named Edward Jenner was a 13-year-old apprentice to Daniel Ludlow, a Bristol surgeon.

"to the merit and to the immense services rendered by one of the greatest of Englishmen"

Edward Jenner, M.D., F.R.S.

Edward Jenner was born on May 17, 1749 in Berkeley, England. His parents died before he was five years old. His brother, Reverend Stephen Jenner (Jr.), who inherited his father's position as an Anglican clergyman, raised him. At the age of eight years, like other English children, Jenner was inoculated with smallpox.

During his early schooling at Wotton-under-Edge, Jenner became proficient in the classics but his first love was natural history. When other boys were playing, young Jenner wandered in meadows looking for fossils and other natural objects.

Jenner apprenticed with Ludlow from 1762 to 1770. Between 1770 and 1773, Jenner worked with John Hunter, a surgeon at St. George's Hospital (London). Jenner helped Hunter arrange the zoological specimens collected by Joseph Banks during his voyage with Captain James Cook to the South Pacific (1768-1771).

In 1773, Jenner returned to Berkeley to practice medicine while maintaining his interest in zoology, especially ornithology. Like Montagu, Jenner was a poet but he wrote about nature instead of people. Two of his poems are "Address to Robin" and "The Signs of Rain."

While working with Ludlow, Jenner saw a dairymaid who was ill with what seemed to be smallpox. However, when Ludlow mentioned smallpox, the woman insisted that she had already had cowpox and "nobody caught smallpox after having cowpox." This idea intrigued Jenner but Ludlow said there was no truth to it.

Cowpox is characterized by pox similar to human smallpox on the teats and udders of infected cows. People milking cows picked up the Cow Pox and came down with a mild disease from which they recovered.

A smallpox epidemic struck England in 1778. People who had not been inoculated were afraid of getting sick. So Jenner was kept busy giving inoculations. Most of the people Jenner inoculated with smallpox developed a mild case, however, farmhands were not affected by the inoculation. When Jenner asked them if they had ever had smallpox, they always replied no but that they once had cowpox. After hearing this, Jenner thought of the dairymaid, from years before, who said cowpox protected people from

Smallpox is caused by an orthopoxvirus known as variola. The Orthopoxviridae are large, DNA-containing viruses. There are two basic forms of this disease: variola major, with a mortality rate of 20% or higher, and variola minor, with a mortality rate of less than 1%. Variola minor first appeared around 1900. A worrisome development is the recent appearance in the Democratic Republic of the Congo of at least 100 cases of monkeypox.

smallpox. One milker remained healthy while living in the same house with six family members who had smallpox.

Jenner began to find out all he could about cowpox. He learned to recognize the disease in cows. He observed all types of milkers' pustules and found that not all types conferred immunity; he learned to distinguish those that did. The fluid from the pustules on a cow's udder infected cuts on the hands of milkers, producing sores. Jenner found that these pox were most likely to result in immunity for the milker at about the eighth day of the disease. He coined the term "variolar vaccinae" to describe cowpox.

Cowpox was uncommon in England so Jenner could not immediately test his immunity hypothesis. In 1796, Jenner removed some of the fluid from a cowpox pustule on Sarah Nelmes, a dairymaid. On May 14, 1796, Jenner inoculated eight-year-old James Phipps with this cowpox matter. After seven days, James complained of a pain in his armpit. Two days later, he lost his appetite, ran a slight fever, and had a headache. He spent the night restlessly but the next morning he was well. Six weeks later, Jenner inoculated James with pustular material from a case of human smallpox. Every morning after the inoculation, Jenner went to James's home and every morning James ran out to greet him. There was no need to ask how James was because Jenner could see for himself: the boy remained well and was immune to smallpox.

In 1798, Jenner inoculated several children with cowpox again and challenged the inocula-

tion with smallpox. Every child was safe. He now had a study consisting of 23 cases, which he published, in the pamphlet “An Inquiry into the Causes and Effects of the Variolae Vaccinae” in 1798. Jenner’s report failed to arouse much interest among physicians or patients. Unfortunately, George Pearson, an advocate for the cowpox inoculation was using a preparation that was contaminated with smallpox and his patients were getting sick. Then Henry Cline, a surgeon with whom Jenner had left some dried cowpox, used a quill of Jenner’s cowpox preparation as a counter-irritant in treating another disease, and found that his patient had become immune to smallpox inoculation. Cline’s report confirmed Jenner’s and cowpox inoculation gained acceptance. Jenner must have realized the importance of his work when he wrote: “The joy I felt at the prospect before me of being the instrument destined to take away from the world one of its greatest calamities, blended with the fond hope of enjoying independent and domestic peace and happiness, was often so excessive, that in pursuing my favorite subject among the meadows, I have sometimes found myself in a kind of reverie.”

Jenner published two more pamphlets on vaccination: “Further Observation on the Variolae Vaccinae or Cowpox” (1799) and “A Continuation” (1800). In 1800, Jenner vaccinated the 85th regiment of the British Army. In July 1800, Thomas Jefferson, Vice-president of the United States, promoted cowpox inoculation in major cities in the United States.

In 1803, the Royal Jennerian Society was established in London to promote the proper use of cowpox. In an 18-month period, London’s annual smallpox mortality rate fell from 3,000 to 600. Parliament awarded Jenner £10,000 in 1802 and another £20,000, in 1806, which he used to vaccinate the poor.

Jenner continued to live humbly and practice medicine in Berkeley. Although Jenner had begun his practice of medicine in 1773, it was not until 1792 that he was granted an M.D. degree from St. Andrews University. He was elected a Fellow of the Royal Society of London in 1788. In 1813, Jenner was awarded an honorary Doctor of Medicine from Oxford University. In 1822, Jenner wrote “On the Influence of Artifi-

cial Eruptions in Certain Diseases” and in 1823, he presented a paper entitled, “On the Migration of Birds,” to the Royal Society.

On January 26, 1823, a cerebral hemorrhage killed Edward Jenner. Jenner’s cowpox inoculation contained live cowpox (vaccinia) virus and this live vaccinia preparation was used, with little modification, for the next 150 years. Jenner did not know that he did, in fact, provide the means to “take [smallpox] away from the world.” In 1881, at the International Medical Congress in London, Louis Pasteur coined the term *vaccination* “to the merit and to the immense services rendered by one of the greatest of Englishmen, Jenner.”

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