Smallpox is the most devastating contagious disease ever to strike the human race. The average mortality over time was 30%. On the other hand, the great pox was syphilis, or the French disease, and it is due to *T. pallidum*, a bacterium, not a virus.

Smallpox is part of the family of Orthopoxviruses which includes: *Variola major*, *Variola minor*, *Vaccinia* and Cowpox. Humans are the only species affected. The incubation period is 10-14 days. Characteristic symptoms include: fever, rash, headache, backache, and malaise. The skin rash can proceed to pustules and then "pocks" or scars. The virus is thought to have come from a rodent around 10,000 BC in northeast Africa. It remained in humans and did not transfer back to rodents. The disease is especially serious in the old and the young; and Native Americans.

Smallpox is highly contagious, mostly through the respiratory system. However, for a few weeks, it can live outside the body, and be attached to clothing, etc. The virus replicates in the cytoplasm, which is unusual, as most viruses replicate in the nucleus. There is no treatment for smallpox. Prevention is the only mechanism of control. Smallpox has been found in Egyptian mummies, in China and in India in the third century BC. It spread from Africa to Asia and then to Europe. Spanish and Portuguese explorers spread the disease to the New World. As mentioned, the natives were highly susceptible to smallpox, with some communities suffering an 80-90 % death rate.

Evidence of variolation, or preventive smallpox inoculation, (taking a small part of the material from one person’s arm to another) is known to have occurred in China and India in the 10th century (and Persia later). In the 17th century, the Turks heard that the Circassian people used inoculation. Those people lived in present-day Georgia, on the east side of the Black Sea. At that time, older Greek women administered inoculations every fall. Thousand had been inoculated with no deaths. Dr. James Pylarino (Univ. of Padua, Royal Society) heard of the procedure. In 1701, he inoculated a nobleman and his two sons. In 1714, Dr. Emmanuel Timoni (Univ. of Padua, Royal Society) performed an inoculation and wrote a paper. Pylarino’s paper was not published until 1715.

Greek citizens of Constantinople (Orthodox Christians) practiced inoculation but the Turks (Muslims) in the same city usually did not. In 1717, Lady Mary Wortley Montague, the wife of the British ambassador to Turkey, arrived in Constantinople. She had heard of the inoculation procedure performed by the Greek women. She had been afflicted by smallpox and wished to get involved in the prevention of the disease. After witnessing the inoculations of the women, Dr. Charles Maitland inoculated Lady Mary’s son, the first English person to have the procedure. When she returned to England in 1718, she pursued inoculation. Her education with texts and speeches led Princess Caroline and her father King George I to have inoculation performed on six prisoners. When they survived, they were freed. Inoculation spread among royalty and to other countries in Europe.

Inoculation in the U.S. happened n 1721. Cotton Mather’s slave, Oneimus, told Mather in 1716 that he had been inoculated in Africa. He was a member of the Akan people of Ghana and Ivory Coast. During an epidemic, Mather persuaded Dr. Zabdiel Boylston to perform inoculations. Inoculated persons had a 2% death rate, while uninoculated people suffered a 14% death rate. Inoculation was
later performed during the Revolutionary War on the order of Gen. Washington, himself a smallpox survivor.

Now the story of Edward Jenner must be told. He had heard of the stories of dairy maids’ immunity to smallpox. This was because they acquired immunity from Cowpox, a relative of Variola. Most country physicians knew that fact. Jenner performed inoculation with Cowpox on James Phipps, who survived. Jenner’s paper to the Royal Society in 1796 was returned. However, after he added a few more cases in 1798, the paper was accepted. His name is famous because he used cowpox scabs for inoculation. This is now known as vaccination (vacca is Latin for cow), because he brought it to the world’s attention. This is felt to represent the dawn of Immunology.

In the early 1900’s in the U.S. there were court cases against vaccination. The Supreme Court upheld a Massachusetts law requiring vaccination. Worldwide prevention came about because of the U.S. Public Service and the World Health Organization efforts to vaccinate everyone. Victory over smallpox was declared in 1980.

Two labs – one in Russia and one at the CDC in Atlanta, GA, retain the smallpox virus. A new smallpox virus could be created from Variola DNA segments inserted into a horsepox virus. A Canadian laboratory is working on that option in case a new vaccine is needed.