The threat of terrorism has raised the spectre of the use of biological agents as weapons. One of the possible agents is the variola virus, the cause of smallpox. On October 26, 1977, Ali Maow Maalin came down with smallpox in the town of Merka in Somalia. Within a few weeks he was fully recovered. Since that time, not a case of smallpox (except as a result of one laboratory accident) has been discovered anywhere in the world. By May of 1980, the World Health Organization (WHO) felt that it could confidently announce that smallpox had been completely eradicated. The WHO also asked that all countries with any stocks of variola virus in their laboratories either destroy them or transfer them to one of two secure laboratories (at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia or a state lab in Koltsovo in Russia). Although 74 countries did so, the fear remains that some countries may have retained stocks of the virus. Even before the complete eradication of smallpox, routine vaccination against the disease was halted in most Western countries. So today anyone under 30 years of age is fully susceptible and even those older may have lost protection against the disease.

A Little History

Smallpox certainly qualified as one of the greatest scourges of humanity. It regularly killed 25% and sometimes as many as 50% of its victims. Introduced into Europe around the sixth century A.D., smallpox rivaled plague in its ability to decimate entire populations. Introduced into the New World in the sixteenth century, smallpox devastated the native populations and played a far greater role than weaponry in the Spanish Conquest.

How was such a pestilence eradicated? Four factors were decisive:

1. The variola virus, which causes the disease, attacks only humans; no animal reservoirs have been found (as they have for the yellow fever virus, the rabies virus, and the plague bacillus).
2. If the victim recovers, the virus is completely eliminated from the body. There are no smallpox "carriers" as there are for such diseases as typhoid fever and malaria.
3. An effective vaccine was available. The vaccine could quickly establish a strong (and reasonably long-lasting) immunity. Thus the chain of contagion could be quickly broken by vaccinating all possible contacts associated with a new case.

4. The WHO and the countries involved provided personnel, money, and the determination to do the job. An effective vaccine had, as we shall see, been available since 1796 and had already rendered many parts of the world free of the disease during the first half of the 20th century. But still the disease smoldered in Asia, Indonesia, Brazil, and Africa. Only a heroic public health effort — a campaign that began in 1967 — finally eliminated it worldwide.

### Variolation

The first effective attempts to cope with smallpox were made in some of the same regions - Asia, India, Africa - that were the last to be freed of the disease. The technique was deliberately to inoculate susceptible individuals (i.e., those with no pockmarks to indicate that they had survived an earlier epidemic) with material taken from the pustules of people with a mild case of the disease. This practice, called variolation, induced an active case in the recipient, but usually the case was less severe than if the disease had been contracted in the normal way (by inhalation as it turned out).

Variolation was introduced into England and the American colonies early in the 18th century. The practice was often accompanied by violent controversy. It was not entirely safe. The variolated person often became quite ill and the mortality rate, although only a fraction of that for people who contracted the disease in the normal way, was nonetheless appreciable. But far more significant in terms of public acceptance was the fact that variolated people were fully contagious to others during the period of their brief, hopefully mild, illness. Thus a family electing variolation could start a fresh smallpox epidemic. Nonetheless, the practice gradually gained favor until it was replaced by vaccination. This table (from J. B. Blake, *Public Health in the Town of Boston, 1630-1832*. Harvard University Press, 1959) shows the effect of variolation on the death rate from smallpox during three epidemics in Boston.

<table>
<thead>
<tr>
<th>Year</th>
<th>1721</th>
<th>1764</th>
<th>1792</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>10,700</td>
<td>15,500</td>
<td>19,300</td>
</tr>
</tbody>
</table>

#### Natural Smallpox

- Cases: 5,759, 699, 232
- Deaths: 842, 124, 69
- Deaths/1000 cases: 146, 177, 298

#### Smallpox Caused by Variolation

- Cases: 130, 4,977, 9,152
- Deaths: 2, 46, 179
- Deaths/1000 cases: 15, 9, 20
Vaccination

Edward Jenner was a Gloucestershire physician who introduced the practice that led to the elimination of smallpox. Jenner's success was grounded on two observations:

1. The regional folk belief that if a milkmaid had ever contracted cowpox, she would never contract smallpox.
2. The inability to variolate successfully those who had an earlier case of cowpox. Cowpox is a disease that produces pustules on the teats and udders of cows. Persons in close contact with cows frequently contracted the disease and suffered a mild and transient infection.

Jenner systematically exploited these observations.

- First he deliberately induced cowpox in his human subjects by inoculating them with material from cowpox pustules.
- Then he showed that these individuals could NOT be variolated.

Jenner's procedure, which we call vaccination, (L. vacca, cow) quickly replaced variolation as a public health measure because:

- Any reaction it induced was far milder than the disease induced by variolation.
- The vaccinated subject was not contagious to others.

Jenner's was the first safe and successful attempt to artificially induce an active immunity. Many successful attempts have followed since Jenner's day, but the principles that guided him are still followed:

- Develop a harmless (or as harmless as possible) preparation that will, upon introduction into the body, induce a response that will protect the individual from a harmful pathogen.

Because of Jenner's priority and his success, the term vaccine is used today for all such preparations. The administration of a vaccine is called immunization. The virus used in today's smallpox vaccine is called vaccinia virus. Possibly it is a relative of cowpox virus, but when the switch occurred is lost in the obscurity of the years since Jenner's day.

What's Next?

Jenner himself was so confident of the efficacy of vaccination that he wrote:

"The annihilation of smallpox must be the final result of this practice".

In 1980, his prediction seemed to have been fulfilled. Today we are not so confident. What should we do now? Return to universal vaccination or use the vaccine only for emergency and medical people who might be exposed as they responded to a terrorist attack and those people in a "ring" around any person who comes down with the disease.

The argument against universal vaccination is that present vaccines are not 100% safe. There is a small, but definite, risk of serious complications from the vaccine itself, especially in people who have an immunodeficiency (e.g., from AIDS or taking immunosuppressant drugs). Such problems can be avoided by not giving the vaccine to people at risk. It
can also be avoided by having Vaccinia Immune Globulin (VIG) available to treat any cases of a bad response to the vaccine.

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