May 2010 marked the 30th anniversary of the World Health Organization’s declaration that the world had won freedom from smallpox. An intensive two-year search had discovered no evidence of the disease since the last case on 26 October 1977. It was a historic moment — no disease had ever before been eradicated. Smallpox had terrorized humans for more than 3,500 years and in the 20th century alone had been responsible for 300 million deaths.

The success of the effort stands as an exemplar of the potential of public health and medicine when countries work together to achieve common goals and when research and technology play an ongoing, integral role. A professional staff of more than 70 nationalities worked across international borders to find cases and stop outbreaks. Even during the Cold War years, collaboration replaced confrontation.

**Eradication Timeline:** Why did eradication take so long? Smallpox vaccine was the world’s first vaccine. It was developed 180 years before eradication was achieved. One vaccination provided protection for five to 10 years. However, as we all know, many steps are needed between discovery and practical application in the field.

Smallpox vaccine is a classic example. Nearly 60 years elapsed before large-scale production became practical. This entailed culturing virus on the flank of a calf. Problems of sterility and packaging had to be overcome. Vaccine stability, especially in tropical countries, challenged most programs. In the mid-1950s, scientists perfected a method for producing commercial quantities of a heat-stable, freeze-dried product.

In 1966, the World Health Assembly set a goal of eradicating smallpox worldwide by December 1976. The target was missed by only nine months and 26 days.

Many people assumed that with a suitable product in hand, stopping smallpox could be achieved simply by mass vaccination. There were many obstacles, however. Large quantities of vaccine were required, but production capacity was limited. It was necessary to draw on laboratories in developing countries, but they would first need to be better equipped. Vaccine strains differed in their ability to protect and in the likelihood that they might cause serious adverse reactions. Comparative trials were selected, and production method details in each laboratory were harmonized. Quality control required establishing international standards and independent, international testing facilities.

Some vaccination techniques produced severe cutaneous reactions and secondary infections. Other techniques led to frequent unsuccessful vaccinations. Research led to development of hydraulic-activated, piston-powered jet injectors, but the guns needed frequent repairs and proved difficult to maintain. One manufacturer perfected a very simple needle inoculation device that was used in a new “multiple puncture” technique. Health staff could be trained in minutes, and successful vaccination rates rose from ~70% to 95%. Needles replaced guns.

But mass vaccination alone was seldom effective. The eradication of smallpox was the objective, and this meant knowing where, when, and why cases were occurring. Systems were established whereby all health units reported every week about smallpox cases, and small teams quickly investigated the cases and vaccinated all contacts and neighbors. This provided a protective barrier to prevent the disease from spreading. Epidemiological studies of all cases identified high-risk groups as well as failure of vaccination performance and containment.

Program strategy steadily evolved and changed as a result of definitive research and development activities. The program was never stagnant. Overall, its secret for success related closely to having the downstream components of operations in close contact with those engaged in upstream research and development.

**National Security:** As of 2001, smallpox was at the top of the list of threat agents of national concern. It had been the organism given highest priority for development in the Soviet secret biological weapons program. It presented special problems because of its capability to spread. We needed vaccines to stop outbreaks, but vaccine production had stopped worldwide. Priority efforts with tough time tables and broad cooperative efforts between government and industry resulted in acquiring sufficient vaccine within two years to meet national needs. With present reserves, there is sufficient vaccine to vaccinate everyone in the US if necessary and to deal with outbreaks wherever else they might occur. It was apparent that with clear goals, determined leadership, and good working relationships between government and industry, a great deal could be achieved and achieved rapidly.

Since 2001, other biological agents have emerged as potential serious threats, and there will be others beyond the ones we know. It is important today that we bear in mind that an attack using anthrax, smallpox, or other agents could come tomorrow. More than eight years have elapsed since the 2001 anthrax attacks. Some progress has been made, but much remains to be done before there is even a coherent national strategy, let alone a clear identification of needed measures. Especially alarming is that the urgency and concern that we all lived with in 2001–2002 has faded so markedly that most provisional planning documents seem to be regularly consigned to a big black box marked “difficult, tackle it tomorrow (whenever tomorrow comes).”

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