HARVARD MEDICAL SCHOOL
BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL

CASES IN GLOBAL HEALTH DELIVERY

GHD-047
DECEMBER 2022

Eradicating Smallpox: Delivery Strategies to Reach the Last Mile

In early 2020, a new virus, SARS-CoV2 (COVID-19), was spreading across the globe. Governments were in panic mode. People everywhere faced uncertainties about what it would mean for them now and in the future. Dr. William Foege, former director of the US Centers for Disease Control and Prevention (CDC), who many had credited for the eradication of smallpox in India, received a request from the National Academies of Science, Engineering, and Medicine (NASEM) to chair one of the newly formed committees that would advise on COVID-19 strategy. Foege's committee was asked to "develop a model for allocating COVID-19 vaccine when it became available." Manufacturers would not be equipped to produce or distribute vaccines in large volumes for some time. Nations were figuring out how to manage the limited supply of vaccine in the midst of a global pandemic.

Foege was no stranger to this scenario. He had faced the issue of how best to use scarce vaccines while working on smallpox in Nigeria almost 50 years earlier. The strategy he deployed there was later instituted in India and ultimately led to the eradication of smallpox – the only time a human disease had ever been wiped off the face of the earth. Smallpox had once been the most feared disease on the planet, having killed more than half a billion people and disfiguring countless others.

Being called to serve NASEM as a global pandemic raged energized Foege. Foege reviewed his work on allocating the scarce smallpox vaccines and the efforts to detect, mitigate, and contain the infectious disease, particularly his experience on the ground in India. How could that experience and that of the colleagues who had aided in the smallpox fight, both globally and locally, help prepare leaders to respond to the COVID-19 pandemic?

Julie Rosenberg, Iman Ahmad, and Rebecca Weintraub prepared this teaching case with assistance from Mark Renella and Sara Pellegrom for the purpose of classroom discussion rather than to illustrate either effective or ineffective healthcare delivery practice.

Overview of India

India, bordering Burma and Pakistan on the east, China, Nepal, and Bhutan on the north, and Pakistan on the west, had the second-largest population and one of the highest population densities in the world.

India had not always been an independent country. The English East India Company controlled India for 100 years before the British monarchy took over in 1857. The British monarchy insisted that the British wanted to help India progress, but Indian leaders saw things differently. Millions of Indian soldiers had served in the British Indian Army during both world wars, and more than 1 million Indian soldiers died helping Britain. After World War I, Mohandas K. Gandhi began his passive-resistance campaigns to advocate for a peaceful and nonviolent end to British rule.

In 1947, 200 years of colonialism ended and resulted in two new nations: India, created as a Hindu nation, and Pakistan, created as a Muslim one. Initially seen as a political compromise, the partition led to the forced displacement of tens of millions of people, outbreaks of religious violence, and one of the largest human migrations in history. Hindus and Sikhs migrated from Pakistan to India, and Muslims migrated from India to Pakistan. The partition also disrupted trade patterns by drawing boundaries between formerly integrated regions.[1,2]

The newly independent India became a parliamentary democracy. The president was the head of state and was elected by an electoral college composed of the state assemblies and parliament. The prime minister was the head of government. The States Reorganization Act in 1956 turned the 550 states that had existed pre-independence into 14 states and six union territories, divided primarily along linguistic differences. The federal government had authority on issues like foreign policy, defense, currency, and taxation, while state governments had the power to legislate on public health, sanitation, and local government.

The 1960s were a time of upheaval for India. Wars with China, in 1962, and Pakistan, in 1965, diverted India's financial resources to the military and defense instead of industrialization or economic development. Droughts cut agricultural production by more than 16%, creating food shortages and inflation. In addition, the World Bank did not meet its promises of aid to India. In 1966, the government devalued the rupee by 57% to slow the soaring inflation. The move was very unpopular and led people to distrust the government.[3]

The 1970s were a time of continued concern about inflation. In the early 1970s, inflation exceeded 20% due to poor agricultural production and a surge in international oil prices, upon which India was dependent. Receiving 8 million East Pakistani refugees who were fleeing growing oppression from the army in their home country further strained India's resources. In December 1971, India fought a two-week war with Pakistan that led to the liberation of East Pakistan, which became the new nation of Bangladesh.[3,4] By 1971, the total number of states had risen to 21.

According to the 1971 Census, India's population was approximately 548 million, a nearly 25% increase since 1961. Population density varied from 549 persons per square km in Kerala to 6 persons per square km in Arunachal Pradesh.[5] The Census recorded approximately 580,000 villages and 2,628 towns. Of the villages, approximately 318,000 had a population of less than 500, while 6,332 had a population of 5,000 and over.[5]

There were 15 major languages and about 250 regional dialects in India. The most widespread language was Hindi, spoken by nearly half the population.[5] In 1971, the working population was approximately 180 million (33% of the total population; 149 million males and 31 million females), the majority of whom worked in agriculture and allied occupations.[5] The literacy rate in 1971 was 39.5% for males and 19.7% for females. However, 61% of children attended primary school,[6] compared to only 33% in 1951. Primary education was free in all the states.[5]

Transportation into and around the country was plentiful. India had four international and 84 domestic airports and 10 major and 160 intermediate ports. The Indian railway system was the largest in Asia and the fourth-largest in the world. In 1972–1973, India ran 10,800 trains daily, carrying over 730,000 passengers and 550,00 tons of freight.[5]

India's Health System

At the central level, the Minister of Health and Family Planning, Dr. Karan Singh, was responsible for all health matters. The Director-General of Health Services, Dr. J.B. Shrivastav, headed the technical arm of the Health Ministry and implemented health programs. The Ministry's Five-Year Plan (1974–75 to 1978–79) outlined national health objectives including the provision of basic public health facilities integrated with family planning and nutrition programs. It aimed to increase access to health services in rural areas; correct regional imbalances of care; intensify infectious disease programs, especially smallpox and malaria; improve the training of health personnel; and provide specialists in the upgraded primary health centers.[5]

The Constitution of India stated that "health is a state benefit." The state administrative structure was similar to that of the Central Health Ministry. In some states (i.e., Bihar, Madhya Pradesh, Maharashtra, Uttar Pradesh), there was a health organization at the divisional level. In each district, there was a district health organization headed by a Chief Medical Officer of Health, assisted by other officers. The basic health unit within the district was the primary health center, responsible for 80,000–150,000 people living in 150–350 villages.[5] The World Health Organization (WHO) South-East Asia Regional Office (SEARO), approved shortly after the WHO launched in 1948, operated with two staff members, including the regional director, from one small room of the Government of India in New Delhi.[7]

Smallpox

Smallpox as a disease was quite lethal and painful. Smallpox was caused by one of the two closely related strains: variola major and variola minor. Several variations or forms of variola major existed. The most common form had a case-fatality rate of about 30%. The less-common hemorrhagic form had a near 100% case-fatality rate. (See **Exhibit 1** for WHO classification of smallpox types.)

Before becoming a highly visible disease, smallpox cases commenced with an uneventful 10- to 14-day incubation period. After incubation, symptoms included high fever, fatigue, severe back pain, and (less often) vomiting and abdominal pain. Two to three days after these initial symptoms, the virus produced a recognizable rash with pustules full of a clear liquid (see **Exhibit 2** for photos of infected child). The pustules later developed a crust that dried and then fell off. The rash began on the face and hands, then spread to the rest of the body.[8] Survivors were left with pockmarks or deep scars.

Those infected with smallpox became contagious when sores appeared in the mouth and throat (the early rash stage). Droplets from coughing and sneezing, as well as contact with soiled items like clothes or rags, could spread the virus. Rarely, did smallpox spread through the air in enclosed settings, such as a building (airborne route) and not involve a nonhuman host.[9,10] A person remained contagious until the last scab fell off. Survivors would usually have lifelong immunity to the disease.

Early Epidemiological History

Up to 1960, smallpox was one of the three leading lethal diseases in the world, along with malaria and tuberculosis. The disease dates to 10,000 BCE in the northeastern part of Africa. From there, it was spread by

Egyptian traders to India[11] and was described in early Indian writings (1500 BCE). Through exploration, trade, conquest, inter-regional conflict, and emigration, it continued to spread across continents.[10]

Some historians attribute the decline of the Roman Empire to smallpox, which killed "a quarter to a third of the entire population."[12,13] Smallpox carried by Spanish conquistadores wiped out large swaths of the Inca and Aztec peoples, contributing to the fall of their empires.[11] Just a few hundred years later, (1754–1767), it is thought that the British intentionally spread smallpox to Native Americans[11] as a form of biological warfare.[14]

Centuries of Combatting Smallpox: From Variolation to Vaccines

Before the eighteenth century, "variolation" – derived from the term "variola" – was probably used in China, India, and Africa to combat the spread of smallpox. Variolation deliberately exposed people to material from actual smallpox pustules of infected persons either through inhalation or subcutaneously by scratching the skin.[10] Lady Mary Montagu was credited for bringing the idea of inoculation from the Ottoman Empire to Europe in 1721 (variolation and inoculation follow very similar procedures, but "variolation" refers only to the use of smallpox pustules).[15] About 2%–3% of people who underwent variolation had adverse outcomes, including death or spreading the virus to others, but it reduced the fatality rate of smallpox 10 times.[11] This success led to both large-scale variolation efforts by physicians and resistance by some skeptics who considered it dangerous.[11] These distinct views ultimately made inoculation a political issue.

Englishman Edward Jenner, who was inoculated as a boy in 1757, observed that people who had contracted cowpox (often women who milked cows) did not contract smallpox.[10] In 1801, Jenner suggested a new procedure he called vaccination, named for the Latin word for cow, *vacca*. Vaccination used material from cowpox lesions to inoculate people. Despite some opposition and its painful and scary-looking delivery mechanism, vaccination soon replaced the riskier variolation. In 1853, vaccination was a standard practice for preventing smallpox.[16] In the mid-twentieth century, liquid lymph , derived from the blood of infected cows, was being used as the vaccine. The vaccine was relatively inexpensive, but it was of low potency, temperature sensitive, and had high failure rates. Vaccinators administered six inoculations at once, using the rotary lancet and the scratch method, to overcome the relatively high failure rate of a single inoculation (see **Exhibit 3** for photos of vaccination tools). They dipped the metal tool with a ring of prongs in the vaccine, then drove it into patients' arms and rotated it to create a circular wound. Often, the rotary lancet was not sterilized between patients, leading to secondary infection.

In 1953, the first director of the WHO, Dr. Brock Chisholm, attempted to persuade the World Health Assembly (WHA) to work toward global smallpox eradication. Most WHA members dismissed the proposal as unrealistic. Failed efforts earlier in the twentieth century to eradicate hookworm, yellow fever, and malaria bolstered skepticism about smallpox eradication.[7] However, the Soviet Union, returning to the WHA in 1958 after an absence, believed that its support of a global smallpox eradication campaign could help reestablish the WHO's reputation.

The WHA passed a resolution by only two votes supporting smallpox eradication in 1959 (see **Exhibit 4** for WHA Resolution). At the time, 63 countries reported a total of 77,555 cases of smallpox. Smallpox was endemic in much of sub-Saharan Africa as well as Indonesia, Nepal, Pakistan, Afghanistan, India, and Brazil. Prevalence had fallen steadily in Europe and the Americas. However, the appearance of smallpox in New York City in 1947 (traced to an importer who had just traveled to Mexico) was a reminder that the disease could re-emerge anywhere.[7]

The WHA encouraged nations to work toward 80% vaccination coverage – considered essential to break the chain of transmission by achieving "herd immunity."[17] At about USD 0.10 per person, the total cost of

purchasing the vaccine would be USD 98 million.[18] The WHO urged nations to organize inter-regional conferences to coordinate efforts.[19]

New technology helped the fight against smallpox take a leap forward. First developed for medical use in the early 1960s, the "jet injector" used a high-pressure burst to plunge vaccine under the skin (see **Exhibit 3** for photo of a jet injector).[20] No needle was used, and the delivery was reliable and standardized, with good "take rates" of nearly 100% (takes were successful vaccinations that appeared in the form of a scar, crater, or blister several days after vaccination). Vaccination was protective for 10 years and could prevent symptoms even if given after exposure. The Ped-O-Jet, a foot-operated jet injector, could deliver up to 1,000 vaccinations per hour.[7] Foege recalled setting up the jet injector at various sites throughout Africa. "People often milled around the site watching the procedure before committing to participate. Even after their own vaccination, they would stay around to watch others …, pressing in to the point where we could no longer move people past the injector. Crowd control was essential."

Intensification of Global Efforts

In the first half of the 1960s, investments in smallpox eradication programs were minimal. The WHO budgeted around USD 0.5 million, 0.2% of its annual budget, for smallpox eradication. A medical officer and secretary were the only full-time employees working on the program, and five full-time employees were assigned to field programs. Other countries followed the WHO's lead and did not prioritize smallpox. In 1964, case reporting was at 1% or less of actual cases. No one knew where the cases were or if progress was being made.[18] The WHO recommended that the entire population in all affected countries be vaccinated to achieve eradication, and few believed the logistics were possible.

In 1965, US President Lyndon Johnson announced that the US supported global smallpox eradication, leading the way for international engagement. The next year, USD 2.4 million was allocated to the WHO for global eradication,[7] including efforts in central and western Africa to reach 100% vaccination coverage. A longtime proponent of smallpox eradication and former chief of the Epidemic Intelligence Service at the CDC, Dr. D.A. Henderson, was sent to lead the WHO's Smallpox Eradication unit. "I was reluctant to take on the job ... there wasn't a lot of money assigned to this – USD 2.4 million wasn't even enough to buy the vaccine we needed. Beyond that, nearly half the delegates in the World Health Assembly were doubtful about undertaking the programme in the first place."[7]

In 1967, the WHO launched its Intensified Smallpox Program to eliminate smallpox in 10 years. That year, the number of smallpox cases was an estimated 10 to 15 million, with about 2 million deaths.[21] (See **Exhibits 5a and 5b** for maps of countries where smallpox was endemic from 1967 to 1975.)

The WHO relied on donated vaccines from the US and the USSR, which had come together in the midst of the Cold War to support a shared cause.[22] Not all the vaccines met quality standards, however, so labs in the Netherlands and Canada helped to test vaccine samples. Some vaccine manufacturers began producing manuals that endemic countries could use to produce their own vaccines.

Further improvements in vaccine delivery aided progress. Jet injectors were hard to transport, required training, and needed frequent cleaning and maintenance. Around the end of the 1960s, the bifurcated needle became popular, bringing many advantages.[9] This needle was a steel rod with two tongs that held the right amount of vaccine for a single vaccination.[7] It required about 20% of the vaccine needed for other techniques, and the half-cent needles could be reused after sterilization. Field workers could be trained in 15 minutes and vaccinate up to 500 people a day.[7] Wyeth pharmaceuticals waived patent royalties to make it affordable.

With improved manufacturing processes and delivery methods and the elimination of the need for cold storage, mass vaccination programs became possible. The WHO strategy aimed to vaccinate everyone and,

after reaching a certain threshold, focused on vaccinating people near the cases. WHO deployed teams in the 31 endemic countries to aid its approach.

Scarcity Led to Innovation: Surveillance - Containment Strategy

Nigeria was one of the endemic countries. Dr. William Foege agreed to be a consultant to smallpox and measles efforts in the eastern region of Nigeria. Foege had been inspired by his uncle, a Lutheran missionary in New Guinea, and had served as an Epidemic Intelligence Service Officer for the CDC in the US.

When vaccine shipments were delayed and supplies were running low, Foege directed his team to reserve the limited supply for the people living in and immediately surrounding each house with an infection. "Runners" went to each village to check for smallpox. Foege explained, after vaccinating those in the immediate vicinity, they considered where it was likely to spread and used the rest of the vaccine on those areas, which turned out to be areas for commerce. There was little resistance to vaccination. "When there is smallpox in the area, that changes the minds of everyone. The vaccine deniers disappear." In just two to three weeks, they saw outbreaks diminish. "It got us thinking, 'Could this work?'" he said.

Similar findings were seen elsewhere when strong case surveillance and reporting were followed by vaccination. It became clearer that the vast majority of spread occurred with very close, prolonged face-to-face contact with visibly sick patients during the first five or six days of the rash.[23] The "surveillance-containment"[24] approach to vaccination, also termed "ring vaccination," started to become accepted as more effective than mass vaccination over the next two years. During that time, 17 of the 21 countries in western and central Africa became free of smallpox. A year and a half later, 20 of the countries were free of smallpox, ahead of schedule and under budget.

Foege was later named chief of the CDC's Smallpox Eradication Program.

Smallpox in India

Early Smallpox Vaccination Strategies

The British were responsible for the first vaccination campaigns in India and struggled with resistance. With the British 1880 Bengal Vaccination Act, public vaccination stations were established, vaccinators were appointed, and fines were imposed for adults who failed to vaccinate their children or resisted vaccination. By the early 1900s, many colonists supported vaccination; acceptance was lower in Indian villages. Chickenpox and smallpox were often considered the same disease in India (referred to by the same Hindi word, "chechak."[21] (See **Exhibit 6** for the poster on the differences between smallpox and chickenpox.)

Following independence in 1947 and reports of low vaccination, the new democratic government made smallpox vaccination a priority.[25] Major smallpox epidemics had been recorded approximately every five to seven years in India since 1900.[5] Due to the vaccine's low potency and because some people would rub cow dung on the new vaccination (risking tetanus), high failure rates and secondary infection were common. Compulsory mass vaccination plans and other strategies across states were inconsistent and often ended as soon as each smallpox epidemic waned.[25]

Smallpox vaccinations were not integrated into general immunization services. Even though smallpox vaccination was determined to be a priority, the 1950's campaigns were rife with challenges, including unreliable funding, competing health demands, and political opposition to vaccine mandates. There was a shortage of workers, and the workforce was underprepared. Higher wages and benefits for vaccinators created a stronger, unified workforce, but rural districts still lacked vaccinators. One vaccination inspector

explained, "it could take hours to persuade just one man to take his shot." Promising strategy reports included vaccinators jabbing themselves in front of the community to prove that there was nothing harmful in the process.[26]

In the late 1950s, India accounted for 60.3% of total global cases. This motivated the Ministry of Health to focus on eradicating smallpox through a Central Expert Committee. In 1959, the Central Expert Committee recommended that the entire population be vaccinated in three years through a National Smallpox Eradication Programme (NSEP). The WHO and the Government of India signed a joint commitment to eradicate smallpox.[24]

The eradication approach included multiple phases and strategies. The first phase of the vaccination campaign – the "attack" phase – aimed to vaccinate 80% of the people in each state. The next phase – "maintenance" – focused on vaccinating newborns and re-vaccinations, thought to be needed to correct decreased immunity. Other plans included shifting to freeze-dried vaccines with improvements to storage and distribution, adding 20,000 new vaccinators, and health education.

There was a shortage of epidemiologists who could help direct local efforts, assess progress, track cases, and use data to plan efforts. Under Shrivastav, two smallpox program officers and six government medical officers supported efforts. At the state level, the state program officer was responsible for coordinating and implementing the smallpox eradication program.

New resources added momentum. In January 1962, the Ministry of Health allocated USD 8,600,000 for the launch of a national program. The following month, the USSR donated 250 million doses of freeze-dried vaccine, with new installments every quarter. The relative scarcity of freeze-dried vaccines made refrigerators important for keeping liquid vaccines cold. UNICEF donated 200–300 refrigerators to district health offices with electricity. With assistance from WHO and UNICEF, two centers were developed to produce freeze-dried smallpox vaccine in India. (See **Exhibit 7** for production of freeze-dried vaccines.)

In October 1962, NSEP activities began, with 152 mobile units operating across the country. Vaccination units visited each village four times a year (see **Exhibit 8** for vaccinations by year). Despite administering 324 million vaccinations in two years, in 1963 the country saw 83,000 smallpox cases with 26,000 deaths—a more than 100% increase since the start of NSEP and the highest fatality rate ever in India. It was later revealed that accessible populations such as school children or industrial plant workers were being revaccinated while many less-accessible adults in urban slums and migrants in rural areas remained unvaccinated.

In January 1964, as a next step, the Government of India followed the advice of the WHO Expert Committee on Smallpox and committed to the goal of 100% vaccination of the Indian population. That year, two more manufacturing centers to produce freeze-dried smallpox vaccine were developed.

Smallpox Eradication in India, 1966–1973

While vaccine supply and administration improved and increased, there were many impediments to progress; case numbers remained steady, at around 80,000 annually (see **Exhibit 9** for cases by year). Impediments included a shortage of financial resources due to other national crises including the partition of India and Pakistan, inflation, currency devaluation, and drought. There was also inaccurate reporting. Surveillance had not been a priority. Families who did not want vaccinators to visit their homes concealed cases. During this time, a district-level population survey reported that 18% of the population resisted vaccination.[24] Vaccinators who feared being blamed for not attaining the 100% vaccination did not report progress accurately either. Finally, health care workers, who were supposed to make sure that each case was confined at home and to vaccinate known contacts, also underreported cases to make the job easier.

In October 1967, eight experts from the WHO joined representatives from the Indian government to assess vaccination efforts and determined that both the strategy and execution of efforts were flawed. Only four states (accounting for less than 1% of the population) were reported free of smallpox. They noted 14 Indian vaccine manufacturing plants still focused on making liquid vaccines, which were expensive, often contaminated, and had a shelf life of 48 hours without refrigeration. Refrigerators needed to store liquid vaccines were often faulty. The commission urged the manufacturing of more freeze-dried vaccines.

Several important Indian officials interpreted the commission's assessment to mean that smallpox was impossible to eliminate. Henderson approached the director-general of Indian Health Services and pressed India to maintain its commitment to eradication while suggesting that vaccination systems be reformed.

Relaunch of NSEP with International Support

The Indian government shifted the governance of NSEP back to national, centralized control. The WHO and Indian government signed another new operation plan in September of 1970. The government increased the number of vaccinators in urban and rural areas to one per 25,000 people and a supervisor for every four vaccinators.[9] While there was significant underreporting, weekly case reports were instituted to allocate and direct resources, including people, around India.[25]

To improve communication and cooperation, SEARO established a smallpox eradication unit, led by Nicole Grasset, a French-Swiss virologist and epidemiologist.[7] Indian government officials, including National Institute of Communicable Diseases Director Dr. M.I.D. Sharma joined the leadership team. As Foege described him, Sharma was "the wise person to whom everyone turned ... Scientific acumen, management savvy, and a rare sensitivity." During one meeting in which a foreign epidemiologist was condemning Indian health workers, Sharma calmly said, "Let me remind you that this is our country."[9]

Looking outside of India provided some inspiration, however. The WHO invited Dr. R.N. Basu, one of India's smallpox eradication program leaders, to visit Ethiopia's smallpox eradication program. He saw healthcare workers who "ceaselessly crisscrossed the countryside in jeeps looking for Agent Pox." The approach left an indelible mark on him and stood in sharp contrast to the bureaucratic system he knew in India.[27] The 1971 declaration that the Western Hemisphere was free of endemic smallpox also provided hope.

The NSEP took lessons from the surveillance-containment approach. It refocused its national strategy on active surveillance and on improved reporting and renewed its investment. Vaccination was prioritized for groups most likely to spread disease, especially children under 14 and those near an outbreak. Changes in reporting included establishing a weekly reporting network (see **Exhibit 10** for reporting structure). No one was allowed to skip reporting. The primary health centers and district and state health officers aggregating the reports were expected to send a "nil report" to differentiate between states "mistakenly forgetting" to send reports and those actually having zero cases to report The Government of India, the state governments, and the WHO (see **Exhibit 11** for map of collaboration model) increased funding by 23% to support personnel costs and vaccine procurement.

Despite the increased government and global resources, increased staff, sufficient vaccines, the improved vaccination method with bifurcated needles, timely reporting, and national coordination, smallpox cases increased. Between 1971 and 1972, the number of smallpox cases reported worldwide rose 69%; Indian cases made up 42% of the total and had increased 50% in just one year. The states of Bihar, Madhya Pradesh, Uttar Pradesh, and West Bengal reported over 79% of the Indian cases.

Many Indian participants became skeptical about the surveillance strategy after so much disappointment. "It's hard to get away from mass vaccination if people are comfortable with it," Foege explained. They were also concerned about diverting resources from other public health issues, such as family

planning.[24] "We don't need someone from outside telling us what to do. So many Indians know smallpox," the health minister said. "He was right," Foege said. He told the minister: "You have so many people who believe that eradication can happen. What you should question is *when* eradication will happen – under your watch or the next minister's?"

Grasset wrote a personal letter to Prime Minister Indira Gandhi, requesting her support:

> By your presence and words, you can bring better than anyone hope and conviction ... [You must] convince each of the participants that by ensuring complete and prompt notification of all cases and taking effective measures of control, eradication of smallpox is a realistic goal.[28]

Gandhi responded to this personal appeal and said she would support the eradication effort. At this time, Indian manufacturers had improved their vaccine quality and increased their output. The WHO and UNICEF had donated equipment, making India self-sufficient in vaccine production. The vaccine was stable at room temperature for two months.

Intensified Smallpox Campaign Begins, 1973

In 1973, the multinational group of smallpox program officers of the endemic states, the central government, and WHO staff were holding frequent meetings to review and revise their plan. Foege, then chief of the CDC Smallpox Eradication Program, joined Grasset at the SEARO Office in New Delhi. SEARO's assignment was to help the country rigorously implement the surveillance-containment method. India was responsible for nearly 64% of all cases around the world by this time. "The population density of India was overwhelming – everything was multiplied by 100," Foege said, comparing it to Nigeria. "And if we lost there, we lost everywhere."

The leadership team did not want to lose. They devised separate guides for endemic and non-endemic states. These documents outlined a three-month plan to find every hidden case of smallpox: 11 teams of WHO epidemiologists, primarily from the CDC, and another 11 teams of Indian epidemiologists (including some who came out of retirement) would work across the states. The short-term consultants were selected, trained and deployed quickly – within three weeks, compared to the regular six-month process. Each epidemiologist covered an average of five or six districts (occasionally more than 10 million people per zone), depending on the extent of the problem. They trained and collaborated with the special teams created at the block, district, and state levels. Each foreign epidemiologist was provided with a jeep, a driver, and a paramedical assistant. The paramedical assistants served as interpreters supporting all the field activities.

The number of teams and their placement were a moving target, increasing to 50 foreign and 50 Indian special epidemiologists by 1974. "It was always a matter of getting resources to the places with the biggest problems," Foege explained.

Foreigners were generally esteemed locally. Walter Orenstein, a CDC epidemic intelligence service officer deployed as a field epidemiologist in Uttar Pradesh, reflected on his experience:

> People [villagers, health workers] respected me, even though I was a foreigner. I felt I got more respect because I was coming from the CDC in the United States than the actual Indian people who deserved the respect. The words that would come out of my mouth, even if they were the same words that came out of a native Indian person, would be more effective in my opinion ... The paramedical assistants were extremely helpful because they had enough experience and recognized what kinds of strategies work or not even though I came out as the in-charge person, they really played a big role in guiding me in terms of what I would recommend, be done or require be done to terminate chains of transmission.

The first phase of the intensified campaign – July to August 1973 – focused on the main towns of heavily affected states to decrease the urban reservoir of infection. During the campaigns, a six-day, intensive search

would be held each month, involving every health worker available and additional day laborers to meet personnel needs.

During the six days, searchers were assigned a specific number of villages and/or municipal wards daily. They interviewed people at gathering places (e.g., schools and markets) while publicity was provided via radio announcements and parades featuring an elephant painted with slogans encouraging people to report smallpox. Efforts quickly resulted in increased case detection. Once cases were detected, medical teams were notified about possible chains of transmission (see **Exhibit 12** for smallpox cases by week**)**.

After the searches, health workers borrowed from other disease areas would return to their posts, and smallpox workers would focus on containment. All cases were rigidly confined to their own houses. "Watch guards" were posted at all doors to prevent infectious persons from leaving or unvaccinated contacts from entering. People making the customary visits to the sick were stopped and vaccinated on their way in. "You can't mess with culture," Foege said. A series of forms designed for identifying and tracking contacts and cases aided in containment and notification practices. Containment vaccination efforts then began, administered in 30–40 residences around the affected area. The team then looked for unreported cases in other parts of the affected village as well as adjacent villages.

The second phase – September to December 1973 – aimed at addressing smallpox in the entire country with a special focus on the four major endemic states. The Government of India established a state-level Indian epidemiologist and a state surveillance team for each of the four priority states. State surveillance teams, including an epidemiologist, a medical officer, a paramedical assistant, and a vehicle with a driver, were composed of state-salaried employees. The teams' responsibilities were to coordinate the smallpox eradication activities in their designated area; provide guidance to primary healthcare staff; strengthen the reporting system; actively participate in pre-search meetings at various levels; assess the active smallpox searchers; attend to any rumors of smallpox; and take responsibility for containment. Of the 63,890 health workers participating in the search weeks, 36,073 were in the four most endemic states.

Officials – including epidemiologists, divisional, state, central, and WHO officials – came together each month to review and adapt their strategies, renewing their commitment. "Setting goals, tracking progress, and shifting resources were the heart and soul of the monthly meetings," WHO state special epidemiologist J. Michael McGinnis stated. Orenstein further elaborated, "They were a morale-building exercise because they really gave us hope. And I would leave those meetings much more dedicated than when I came in because of the interactions I had with my colleagues … the coffee breaks or lunch breaks, dinners, where we could really talk about our day, what we had learned, and what we thought was important to implement in order to overcome things."

Each month the strategy improved until, ultimately, the primary search was to every house in a village. Secondary surveillance was done in markets, and tertiary searches were carried out in special populations such as brick kiln workers who moved from job to job and beggar groups. When searchers learned that people ran from government vehicles, they would visit houses at night to find people. Another change included separating the role of searchers and containment workers/vaccinators completely. "People are people. They never want more work, so finding something is less likely if it means more work," Foege explained. Forms and data were sent between cadres of workers to coordinate efforts.

One leader explained, "There is the argument that we or WHO will lose credibility by discussing new strategies, that we cast doubt on old strategies and that we could reduce the involvement of local health workers if we change approaches. The truth is that we lose credibility with an inferior strategy."

Intensified Campaign Expands, 1974

Investments in smallpox eradication continued to grow. The Government of India's USD 3.69 million investment in 1973 increased to USD 4.55 million in 1974. During this period, WHO expenditure increased correspondingly from USD 370,000 to USD 2.1 million, thanks to contributions from the Swedish International Development Authority (SIDA). Smallpox eradication had become a clear priority in India.

Prime Minister Gandhi endorsed WHO efforts while also periodically freezing the number of foreign staff members that it could hire. WHO officials accused many Indian state administrators of similar mixed signals. In a personal letter to Grasset, Henderson elaborated:

> The Government of India has not yet given the programme the priority which they had pledged in the WHO Assembly ... As time passes the situation will become increasingly embarrassing to them … and of course the organization will have no choice but to point out forcefully the gross failures in India ... I'm afraid it's still too early for them to appreciate this but I hope it will increasingly be obvious beginning this autumn. Let us do our best between now and then and pray that a real disaster does not overwhelm us.[28]

Senior WHO officials, including Grasset and Henderson, began to push the Government of India to convert the intensified program into a centralized program, supported by the Prime Minister's office and managed by the Federal Health Ministry's smallpox eradication department. Foege reflected on long train rides with Indian leaders to visit various states and forged indelible bonds with them. "We became a unit."

Bihar, the Most Challenging State

Bihar, a state in eastern India, faced the most difficult smallpox problem in India (see **Exhibit 13** for summary of Bihar search findings). It was bounded at the time by Nepal to the north and by the Indian states of West Bengal and Uttar Pradesh and was one of India's most densely populated states with a population of 62 million people.

The state faced nine major deficiencies, according to a confidential communication from American epidemiologist John M. Pifer, who had been working for SEARO in Bihar: a shortage of vaccinators, including more than 50% of positions being unfilled; a shortage of medical officers who were responsible for all health issues in the area; lack of funds for gas and transportation, which prevented health workers from investigating; and resistance from tribal villages to vaccination and to case reporting. He wrote: "[N]o effort is made in most outbreaks to find the source of the outbreak. It has been the experience of this observer that the source of outbreaks can easily be found … 80-90% of the time. Once the source is found, cross notification is absolutely necessary, but is rarely performed here."[28] (See **Exhibit 14** for full quote.) Pifer's insights had been important in promoting the intense program.

Early 1974 Tumult

Manmade and natural disasters and local and global crises further hindered Bihar's progress. In February 1974, Dhutta investigated 1,188 new outbreaks in Bihar and learned that the state's smallpox eradication officer was corrupt and had undermined eradication efforts. Simultaneously, Bihar faced drought in the south and flooding in the north. Famine stalked the entire population. Circumstances spurred migrations that could spread smallpox in adjacent regions. Simmering political unrest in response to corruption erupted into the student-led "Bihar Movement." Strikes made it impossible to ship vaccines or for the central team to move quickly between the capital and the states. Next, the railway workers went on strike. At about this same time, the global oil crisis began to be reflected in India as gasoline costs doubled and

inflation spread. Finally, half of the vaccinators in Bihar went on strike. The other half declared they would also go on strike.

In late April 1974, smallpox outbreaks in formerly smallpox-free areas in India (see **Exhibit 15** for state status) were traced to a town in southern Bihar, Jamshedpur that was home to the Tatanagar railway stations. The town, with a population of 800,000, was one of India's major steel-producing areas. It was home to Tata Industries, a heavy industrial manufacturing group. The relatively high average income of those working in private-sector industries in the town contrasted with that in poorer areas – southern Bihar and northern Orissa – luring many beggars and people looking for work into the Tatanagar stations. With 15 autonomous health units in this area, no single entity for public health existed; it was unclear who was responsible for reporting cases among the large mobile population. The area was ripe for the spread of smallpox.

Of 1,760 villages within a 45 km radius, 1,203 were searched, and 40% of all villages searched had active smallpox cases. From the railway epidemic alone, 300 additional outbreaks and 2,000 cases occurred in 11 states of India and Nepal. The worst exportation was to Bilaspur, Madhya Pradesh, where a single case from a Tatanagar railway station led to 464 additional cases and 76 deaths affecting 72 villages and 18 primary health centers within the district. According to the WHO, "this area was ranked the fourth most smallpox-affected district in the world, but probably ranked as the world's greatest exporter of smallpox."

The epidemics in Bihar made world headlines, much to the Indian government's dismay. SEARO sent Larry Brilliant, an American medical officer in West Bengal, and another medical officer to Jamshedpur in May 1974 to support an active search operation. There were 36,000 cases in India at the time. In one week, 11,000 cases were reported, resulting in 4,000 deaths. This smallpox news contrasted sharply with the news that India had tested its first atomic device, raising questions about priorities. The government was feeling pressure to improve its smallpox eradication program as Pakistan prepared to announce its last case.

Because intensive surveillance efforts in India effectively found many more cases, the minister of health for Bihar state interpreted this as meaning that the search and containment approach was making things worse. He was ready to give up on the surveillance-containment strategy and revert to mass vaccination. Shrivastav and others decided that the only way to bring smallpox under control was to cease all efforts directed toward surveillance and containment and to launch a "backlog fighting program," with the goal of 100% vaccination coverage.

Proponents of the surveillance-containment method were deeply concerned. Henderson reflected, "My feelings of despair during the first six months of 1974 are etched in memory."[29] Foege echoed, "May of 1974 was the only time I was concerned we could not finish the job … not because of the amount of smallpox but rather the impact of the railway strike to influence vaccinators and medical officers to go on strike, the impact of the embarrassment the government felt because of journalists saying they could conduct nuclear tests but they couldn't handle smallpox, and the push to return to mass vaccination. Those were the threats."

Finally, in one meeting about mass vaccination, an Indian physician was able to reverse the course. He stood up and recalled growing up in a poor village. "When there was a fire, the villagers poured water only on the burning hut, not on all the houses. This is the surveillance-containment strategy." he said. "I'll give you one more month," the minister replied.[9] There was great relief.

While the Government of India also accepted the proposal for the centralized program, new problems arose. There was tension between established state healthcare workers and newly hired smallpox workers with "special status." Additionally, some state administrators began to demand that their public health workers assigned to work on smallpox from other programs (i.e., malaria, family planning) return to their original duties rather than support the intensified central program.

New and Renewed Support Spurs Progress

Mr. J.R.D. Tata, chairman of the Tata Group, stepped in to help. Tata did not know the extent of the problem, but agreed to support the Smallpox Eradication Programme in southern Bihar. It was the second time that a corporation was making a major contribution to global health. The WHO and Tata Industries entered an agreement whereby the WHO would provide technical guidance and Tata would provide equipment, manpower, and funding valued at USD 550,000. Tata funds supported 40 vehicles, support for 72 medical officers, 308 paramedical staff, 63 drivers and mechanics, and 30 administrative staff. When containment efforts commenced, all bridges and major roads were barricaded, and trains were diverted to a checkpoint where compulsory vaccinations or scar checks were carried out. No one was permitted to enter or leave the epidemic area without an "on the spot" vaccination or proof of recent vaccination. It became evident that additional teams were needed to assist the epidemiologists. Shrivastav's office deputed approximately 400 recent medical graduates and senior medical students to lead special containment teams.

By June 1974, there were declines in smallpox cases. This allowed for greater investment in each outbreak. More than 75% of costs were borne by the Government of India with SIDA contributing an additional USD 2.8 million. Among the 150,000 workers, only 250 were international.[5]

Every house with a case would have 24-hour guards to keep patients from leaving the house and ensure that anyone who entered was vaccinated. All residents living within 500–1,000 houses of any case would be registered and vaccinated as well. Poor families received a stipend to cover food costs during the quarantine period. A public statement from the prime minister requested "the fullest cooperation of all citizens."

After two months of intensive activities in southern Bihar, the situation was contained. Eventually, the government and Tata Industries agreed that Tata personnel would assume responsibility for the program throughout southern Bihar. Tata's endorsement carried important political weight; he was a major supporter of the Congress Party and had personal access to Prime Minister Indira Gandhi. WHO officials leveraged their relationship with Tata to gain easier access to important government officials of the central government.

After a period of four to six weeks, if no cases were discovered, the episode was considered closed and removed from the "pending" list. If an area was still reporting cases 21 days after an initial outbreak, officials from the WHO and India would visit to assess what was happening. "When we saw the disease declining, we were able to use that to reinforce and reinvigorate our efforts," McGinnis said. "Some things have to be believed to be seen," Foege explained.

Continuing Efforts and Challenges

Challenges persisted in the tribal areas in Bihar. Dr. Shard Narvaker, a young official selected to work in the Santhal Parganas district of Bihar, wrote in a confidential letter,

> It pains me to report that even after my persistent efforts with my team, I am unable to bring down the number of outbreaks as per expectations in Jamtara block. It is mainly because of Dr. Suresh, Jamtara's block medical officer who: (1) Does not believe in WHO strategy of containment work to be carried out in affected villages. (2) Does not pay visits to the villages during search and containment. No checking and cross-checking. He visits the affected villages only either with me or my containment team and that too with reluctance. (3) He cannot extract work from his subordinates as he lacks leadership qualities. (4) He has not coordinated the activities of block level among the Block level officials, non-officials and elected levels of the public. Motivational part is nil ... (5) He is not constructive in nature. Always complaining type ... These points may be viewed seriously ... He may kindly be transferred from Jamtara immediately and an energetic medical officer may be posted who will assist me in controlling smallpox in Jamtara Block.[28]

Despite the increased investments in personnel and supplies, more qualified personnel were hard to come by. This shortage required Bihar to transfer district health officers from the states of Orissa, Madya Oradesh, Andhra Pradesh, and Maharashtra. The CDC had sent more workers to India than any other non-Indian institution. Together with the Indian epidemiologists, they received a three-day training at SEARO before going to the field. The central government added 25 additional personnel to assist in coordinating efforts. WHO was not readily accepting women into the program, and some suggested India was resisting the entry of women volunteers.

By August of 1974, 65 of the 84 epidemiologists assigned to the Indian smallpox eradication program, the majority of whom were assigned from the CDC, were working in Bihar. One epidemiologist reflected on his experience: "One of the civil servants I worked with felt very threatened because I had money, I had vehicles, I had command over the people who I worked with, and he didn't have that same ability, and so there was a great feeling of resentment."

New Outbreaks

The smallpox campaign saw a wave of new setbacks in late 1974. Flooding ravaged Bangladesh, leading to famine and tens of thousands of new refugees. Smallpox began spreading rapidly, especially along the border with India. Special surveillance teams repeatedly searched these areas, discovering 30 imported outbreaks. The smallpox eradication units in Geneva and New Delhi actively encouraged "border meetings" between both countries, which began to occur weekly.

Another outbreak occurred in Bihar after pilgrims gathered to recognize the 2,500 years since the death of the religious leader of the Jain sect at one of India's holiest sites, Bohd Gaya. Some sect members traditionally rejected vaccination. Soon after the pilgrimage, 40 households were diagnosed with smallpox. The principal religious leader reluctantly agreed to vaccination, and stringent containment measures followed for several months until the outbreak was contained.

Bihar remained the center of the epidemic and recognized the need to tighten screening efforts to ensure eradication. As a result, each outbreak spurred surveillance within a radius of 16 kilometers. Traditional village-to-village searches were replaced by house-to-house searches. If cases were found, workers would be immediately sent to that region to undertake containment efforts within 48 to 72 hours (see **Exhibit 16** for graph of weekly outbreaks in Bihar, 1974–1975, shared with health workers).

Monthly searches were conducted in Bihar and Uttar Pradesh, and a reward was offered to anyone reporting a case. In Bihar in 1974, an average of 57 outbreaks were investigated and contained each month in each of the 31 affected districts with a maximum of 134 outbreaks per district during the peak month of June. In total, 21,323 outbreaks were contained that year. In 1974, across India, 120 million households were visited by 135,000 health workers for vaccination, reaching a record-breaking number of 123 million people.

Operation Smallpox "Target Zero," 1975

After Pakistan accounted for its last case in October 1974, epidemiologists began a countdown to zero cases for India in their monthly surveillance letter. As cases decreased, the international workforce downsized rapidly; WHO short-term consultants' three-month contracts were not renewed. Health workers became slightly less vigilant.

New cases reported in the village of Pawa Puri in Bihar quickly demonstrated that eradication efforts needed to be maintained. "Target Zero" intensified efforts in areas where smallpox was still extant. Bihar's chief secretary, Sharan Singh, appointed Brilliant to coordinate activity in Pawa Puri following the media

attention Brilliant got for supporting the eradication in Jamshedpur. Singh urged other officials in the state to use government resources. Bihar used military police to protect staff and to help quarantine villages with active infections.

At this point, any signs of an outbreak were noted and specimens of every suspected index case of every outbreak were tested in a lab. Containment measures were promptly instituted whenever a smallpox case or suspected case was reported. Watch guards were posted in front of affected households, with the number of guards doubling from two to four. After areas surrounding an outbreak in a 16-kilometer radius were searched, vaccinations were given to everybody within a 1.6-mile radius. (This radius could contain 4–5,000 people in rural areas and as many as 80,000 in crowded cities). Vaccinating entire villages quickly helped to reduce resistance to vaccination. (See **Exhibit 16** on the estimated cost of containment of one smallpox outbreak in 1975.)

World Health Day on April 7, 1975, kicked off an all-India search for any remnants of the disease with the theme of "Smallpox – Point of No Return." An army of 115,000 health workers conducted a weeklong house-to-house search throughout India. With thousands of volunteers, workers from other health programs such as malaria, family planning, filariasis, leprosy, and basic medical care assisted the 25,000 NSEP vaccinators, supervisors, and paramedical assistants. Delhi's Medical Officer for Communicable Diseases reflected, "When we go into the fields, we're welcomed [unlike in 1958]." The massive search culminating on April 15 confirmed that smallpox was close to being officially eradicated.

Remaining Vigilant for the Final Mile

In May 1975, there were 25 pending outbreaks in India. On May 17, 1975, the last known indigenous smallpox case was recorded in Bihar. The last known case in India, imported from Bangladesh, occurred in the state of Assam on May 24, 1975.

The Minister of Health Karan Singh was excited to share the news around the world. On June 30, 1975, he announced that smallpox had been eradicated from India, making headlines. Henderson noted, "The minister was elated and could not resist announcing the news to the public ... However, our entire staff was deeply concerned that the announcement might be premature … calling into question the credibility of WHO."[29]

Measures were taken to ensure the news of eradication from India remained true. Because Bangladesh remained a possible source of new infections, 100 checkpoints at entries on the India-Bangladesh border were established. In addition, surveillance searches were conducted in some Indian villages within 16 kilometers of the border with Bangladesh. India was proclaimed non-endemic. As the prospect of eradication seemed closer, a three-part reward of Rs. 1,000 (USD 133.51) was announced, to be given to any member of the general public who reported a smallpox outbreak; to the health worker to whom information was given; and to the medical officer who verified the diagnosis.

On August 15, India celebrated its Independence Day along with "India's Freedom from Smallpox." Prime Minister Gandhi saluted the people of India on their 28th year of independence and proclaimed that India had won "freedom from smallpox." That same day, the president of Bangladesh was assassinated, raising alarms about a new influx of refugees. In October 1975, three all-India, house-to-house searches began. Soon after, in January 1976, a new surveillance practice developed: Fever-with-Rash Outbreak Surveillance. This required that each health worker report every fever-with-rash case to specific registers for careful evaluation. In 1976, 100 cases were reported, all of which were associated with chickenpox.

Additionally, starting January 1, 1976, the vaccination program policy was modified to prioritize: (1) containment vaccination near suspected cases; (2) primary vaccination of newborn infants; (3) vaccination

required under international health regulations; (4) vaccination of groups at risk due to the nature of their occupation; and (5) vaccination on request.

Surveillance and rapid reporting remained important. In February 1976, representatives from Bangladesh, India, and Nepal conducted an informal workshop in Kathmandu on smallpox surveillance. Soon afterward, an "All India Active Search Operations" team inspected 110 million households in urban and rural areas. A final search campaign took place in the fall of 1976. Employing 152,000 health workers, the campaign aimed to search 668,000 villages. Searchers detected 41,000 cases of chicken pox but no smallpox. Assessors followed up and they found that 97% of the villages had been searched correctly.

During the Intensified Campaign, 1974–1977, the Indian government contributed over USD 19,000,000 and the Indian states and union territories another USD 21,000,000. The WHO, mainly through SIDA, contributed USD 11,000,000. The total per capita expenditure was less than USD 0.12, while eradicating smallpox saved India USD 91 million in hospital facilities and drugs alone.[5]

End of an Era

A national commission including international members then created plans for final smallpox containment efforts over three months. The commission recommended continuous surveillance in all states in India from February to March of 1977. In April 1977, a Smallpox Assessment Commission with an international membership declared India free of smallpox.

Over the next few years, a few cases were detected in Ethiopia and Somalia (see **Exhibit 17** for timeline of eradication in India and globally). The last known person to naturally get smallpox was a hospital cook in Somalia in October 1977. The following year, a lab error at a medical school in England caused the death by smallpox of a medical photographer, who became the last person to die of the disease. The Global Commission for the Certification of Smallpox Eradication declared the smallpox era closed in 1979.[7,10,21]

Reflecting Back

On May 9, 2020, the world celebrated the 40th anniversary of the World Health Assembly's declaration that smallpox had been eradicated. Smallpox remained the only human disease to have ever been eradicated. It was estimated that the USD 300 million investments to eradicate smallpox saved the world more than USD 1 billion annually every year since 1980.

Sitting in Atlanta, Georgia, in the United States, Foege reviewed old notes and papers. The work he had done in India was the most productive and satisfying of his distinguished career and also some of the hardest. "People were looking to you for answers and you have no position here. I had to keep people inspired and believing this could be done."

In the midst of the COVID-19 pandemic, Foege was frustrated that the US administration declared its intention to withdraw from and to cease funding the WHO. It was a time to come together. He had seen that in India. The solidarity among leaders across sectors and institutions had been critical. What else could he learn from smallpox eradication that could inform how to manage the uncertainty of a new virus and plans for how to distribute a new vaccine to global populations?

Exhibit 1 *WHO Classification of Smallpox Types, India, 1972*

Type of variola major	Characteristics	Case-fatality rate
Ordinary	• Most common form • 90% of cases in unvaccinated persons	30%
Modified	• Milder form • Produced fewer, smaller, and more superficial lesions • 2% of cases in unvaccinated; 25% of cases in vaccinated persons	Cases of modified smallpox were rarely fatal.
Malignant or flat	• Lesions were flatter, evolved more slowly, and coalesced • 7% of cases in unvaccinated persons	97%
Hemorrhagic	• Difficult to diagnose • Rash accompanied by bleeding into mucous membranes and skin • Less than 3% of cases	Near 100%
Variola sine eruptione (without rash)	• Occurred in previously vaccinated contacts or in infants with maternal antibodies • Affected persons were asymptomatic or had a short-lived fever, headache, and influenza-like symptoms • Transmission of clinical smallpox had not been documented for variola sine eruptione	Not available; however, in cases of variola minor, death occurred in <1% of persons.

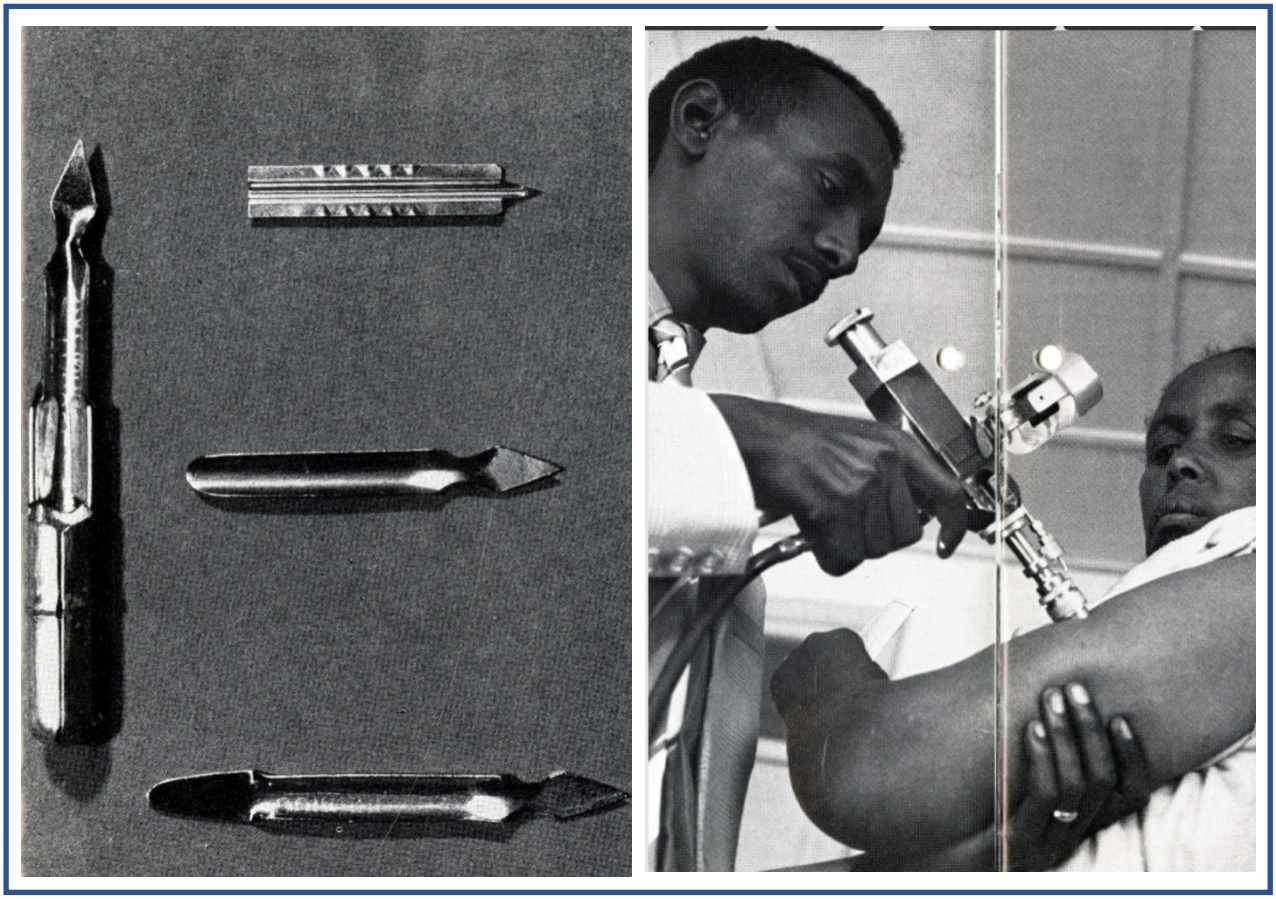
Source: Johns Hopkins Center for Health Security. Variola Virus (Smallpox) Fact Sheet. 2014. Available from: https://www.centerforhealthsecurity.org/our-work/publications/smallpox-fact-sheet. Derived from Fenner F, Henderson DA, Arita I, Ježek Z, and Ladnyi ID. Smallpox and Its Eradication. Geneva: World Health Organization; 1988, p. 4.

Exhibit 2 *Child with Smallpox, as Pictured on WHO Smallpox Recognition Card*

Note: Photos are of the front and back of the WHO smallpox recognition card. The card portrays a patient with relatively mild smallpox and was widely used from 1971 to facilitate case detection in endemic countries.

Source: World Health Organization. 1988. Available at: https://www.who.int/publications/m/item/who-smallpox-recognition-card

Exhibit 3 *Early Tools for Vaccination - vaccinostyle with needle tips used to administer smallpox vaccine using scratch technique and jet injector*



Source: World Health Magazine. October 1972, p. 10-11. Available from University of Michigan Gallery; https://apps.lib.umich.edu/online-exhibits/exhibits/show/smallpox-eradication-india/gallery

Exhibit 4 *World Health Assembly Resolution, 1959*

WHA12.54 Smallpox Eradication

The Twelfth World Health Assembly,

Having considered the report of the Director-General on smallpox eradication; [1]

Noting:

(1) that although great progress has been made in the eradication of the disease in some areas of the world, important endemic foci of smallpox still remain in other areas, especially in South-East Asia and Africa, from which the disease can be exported to countries already free of it;

(2) that eradication of smallpox from an endemic area can be accomplished by successfully vaccinating or revaccinating 80 per cent. of the population within a period of four to five years, as has been demonstrated in several countries;

(3) that sufficient scientific and technical information is available on the production of a suitable smallpox vaccine; and

(4) that although an eradication programme may require, for four or five years, an increase in the national efforts and financial obligations for the intensified campaign against smallpox, the heavy annual burden of continuing expenditure incurred for this purpose may be considerably lightened by increasing the interval between vaccinations once eradication may be considered to have been accomplished,

1. EMPHASIZES the urgency of achieving world-wide eradication;

2. RECOMMENDS to the health administrations of those countries where the disease is still present that they organize and conduct, as soon as possible, eradication programmes, making provision for the availability of a potent stable vaccine;

3. REQUESTS the Director-General:

(1) to urge health administrations of those countries where the disease is still present to develop eradication programmes and to offer them any necessary technical guidance and advice;

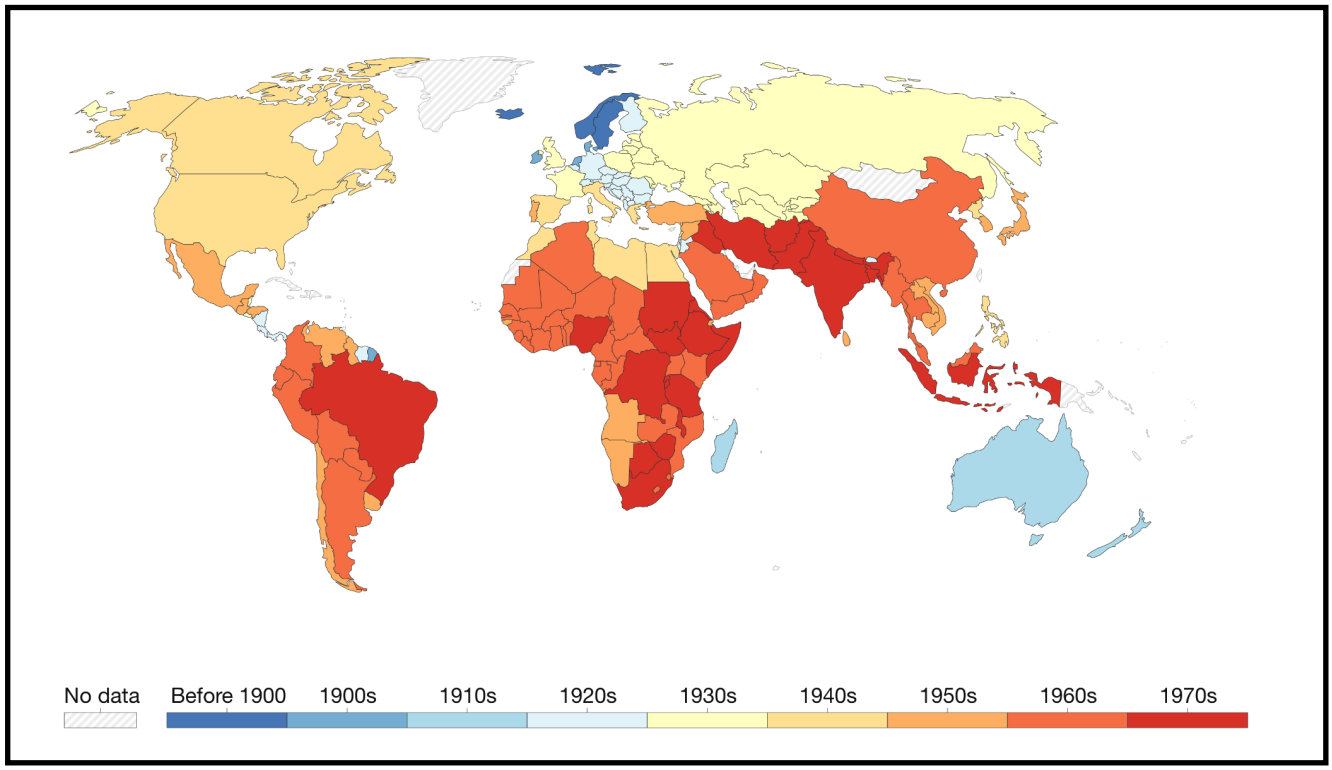
(2) to provide for the necessary activities to further smallpox eradication programmes and for the assistance requested by national health administrations for this purpose, in his programme and budget for future years; and

(3) to collect from the countries concerned information on the organization and progress of their respective eradication programmes and to report further to the Thirteenth World Health Assembly.

Twelfth plenary meeting, 29 May 1959 (section 1 of the fifth report of the Committee on Programme and Budget)

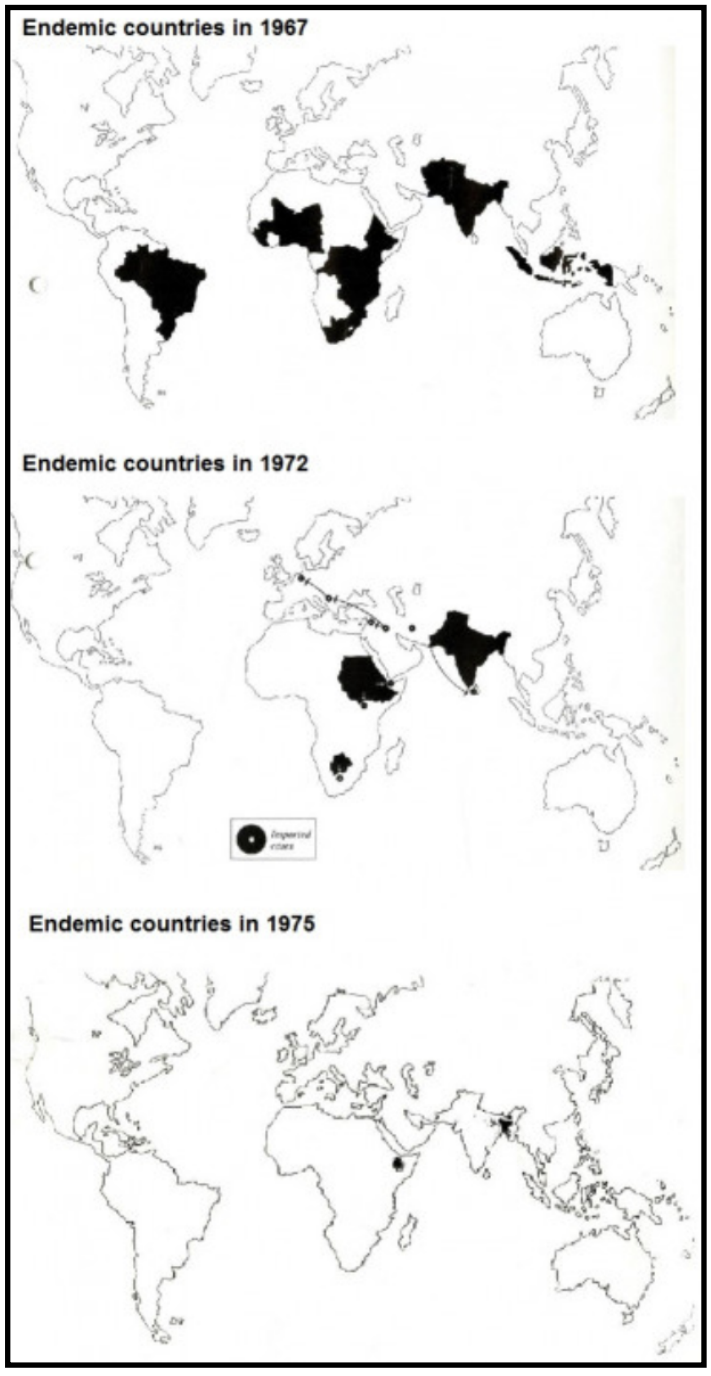
Source: World Health Assembly, 12. (1959). Twelfth World Health Assembly, Geneva, 12-19 May 1959: resolutions and decisions: plenary meetings: verbatim records: committees: minutes and reports: annexes. Retrieved from https://apps.who.int/iris/handle/10665/85719

Exhibit 5a *Decade in Which Smallpox Ceased to be Endemic by Country*



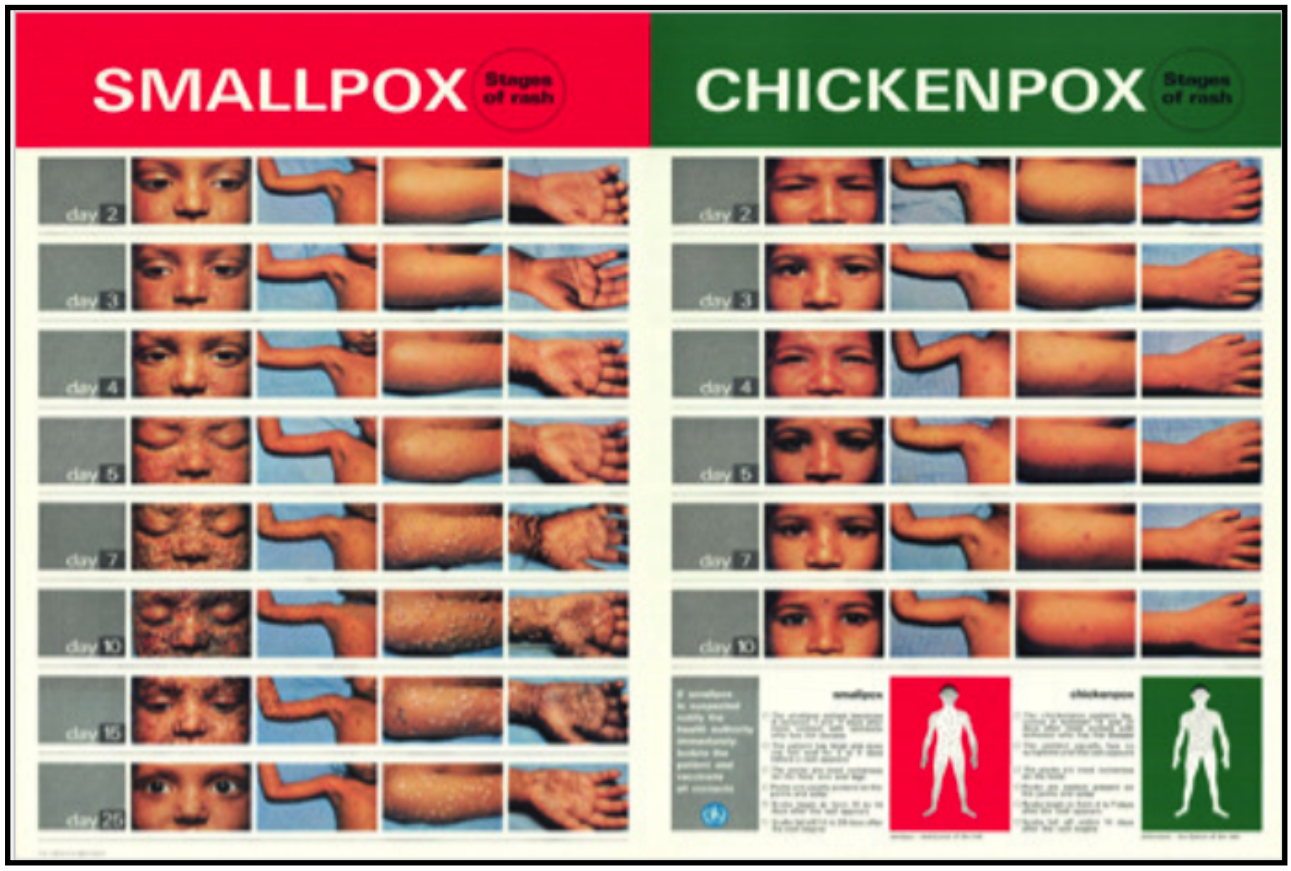
Source: F. Fenner, D. A. Henderson, I. Arita, Z. Jezek, I. D. Ladnyi (1988) – Smallpox and its Eradication. World Health Organization (WHO) 1988. https://ourworldindata.org/grapher/decade-in-which-smallpox-ceased-to-be-endemic-by-country.

Exhibit 5b *Map of Endemic Countries, 1967–1975*



Source: *World Health* [Magazine]. October 1975, p. 15.

Exhibit 6 *Smallpox and Chickenpox Rash Identification Poster*



Note: The poster was prepared in 1970 to help newly recruited staff recognize the differences between the rashes for each disease. The text and drawings at the bottom give simple guidance to distinguish the signs and symptoms of smallpox from those of chickenpox.

Source: World Health Organization, 1970. Retrieved from University of Michigan, https://apps.lib.umich.edu/online-exhibits/exhibits/show/smallpox-eradication-india/item/5366?exhibit=143&page=1219&return=2972.

Exhibit 7 *Production of Freeze-Dried Vaccine, 1962–1976*

Period	Patwadangar (Vials)*	Belgaum (Vials)*	Guindy (Vials)*	Hyderabad (Vials)*	Total
1962–63	38 368	–	–	–	38 368
1963–64	87 171	–	609	–	87 780
1964–65	480 208	–	5 418	–	485 626
1965–66	1 202 296	–	212 565	–	1 414 861
1966–67	858 889	172 000	380 639	–	1 411 528
1967–68	959 931	620 155	557 867	173 685	2 311 638
1968–69	1 188 680	1 123 031	852 667	401 827	3 566 205
1969–70	1 077 385	812 383	470 000	466 759	2 826 526
1970–71	829 054	498 337	1 114 000	244 657	2 686 048
1971–72	1 185 385	1 164 037	792 662	381 434	3 523 518
1972–73	2 765 181	1 447 573	1 204 684	442 398	5 859 836
1973–74	4 054 862	2 317 641	1 627 417	807 542	8 807 462
1974–75	3 298 075	3 174 857	1 886 277	1 065 035	9 424 244
1975–76	2 853 113	1 908 252	1 721 082	691 073	7 173 520
1976–77	1 545 918	1 888 716	1 628 057	569 657	5 632 348

* An ampoule or vial contained 12 or 15 doses upon manufacturer's recommendation. With the bifurcated needle 50 to 75 vaccinations could be given from 1 ampoule.

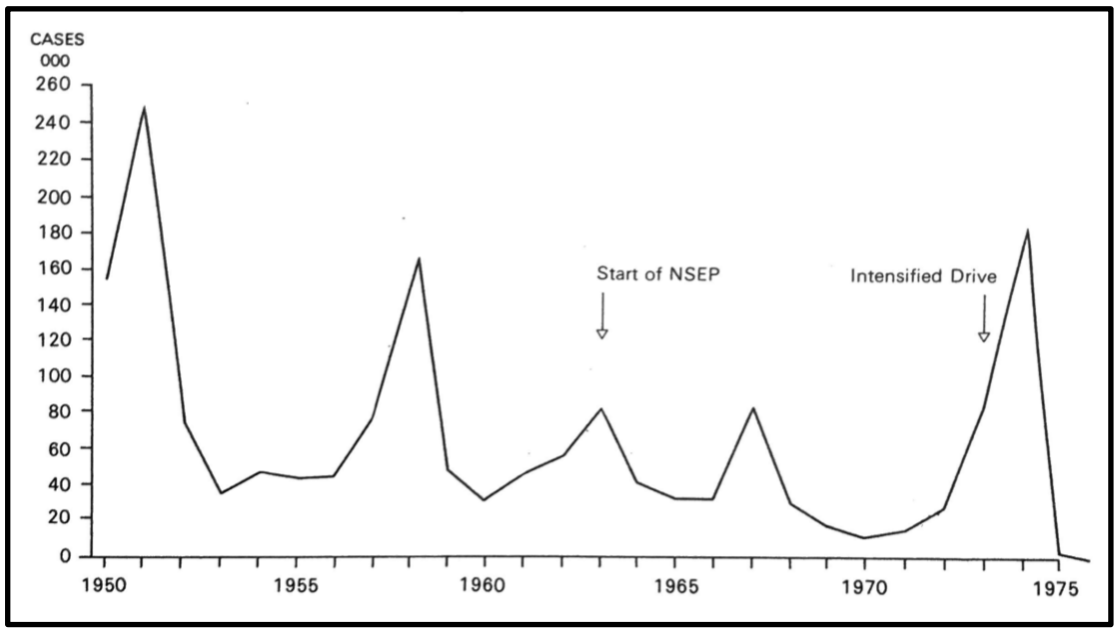
Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 8 *Primary Vaccination and Revaccination, 1962–1976*

Year	Primary Vaccination	Re-Vaccination	Vaccination Total	Percentage of Population Covered	
				Primary Vaccination	Re-Vaccination
1962	3 520 000	28 830 000	32 350 000	0.8	6.4
1963	16 350 000	122 370 000	138 720 000	3.6	26.6
1964	15 400 000	114 980 000	130 380 000	3.3	24.4
1965	17 390 000	92 450 000	109 840 000	3.6	19.2
1966	17 230 000	65 770 000	83 000 000	3.5	13.3
1967	18 560 000	77 890 000	96 450 000	3.7	15.5
1968	22 000 000	61 000 000	83 000 000	4.3	11.8
1969	22 700 000	54 170 000	76 870 000	4.3	10.3
1970	23 060 000	54 050 000	77 110 000	4.3	10.1
1971	24 190 000	67 490 000	91 680 000	4.4	12.3
1972	26 950 000	85 780 000	112 730 000	4.8	15.3
1973	24 840 000	87 500 000	112 340 000	4.4	15.4
1974	24 180 000	99 250 000	123 430 000	4.2	17.1
1975	19 025 474	67 693 160	86 718 634	3.2	11.4
1976	16 745 086	50 109 145	66 854 231	2.8	8.3

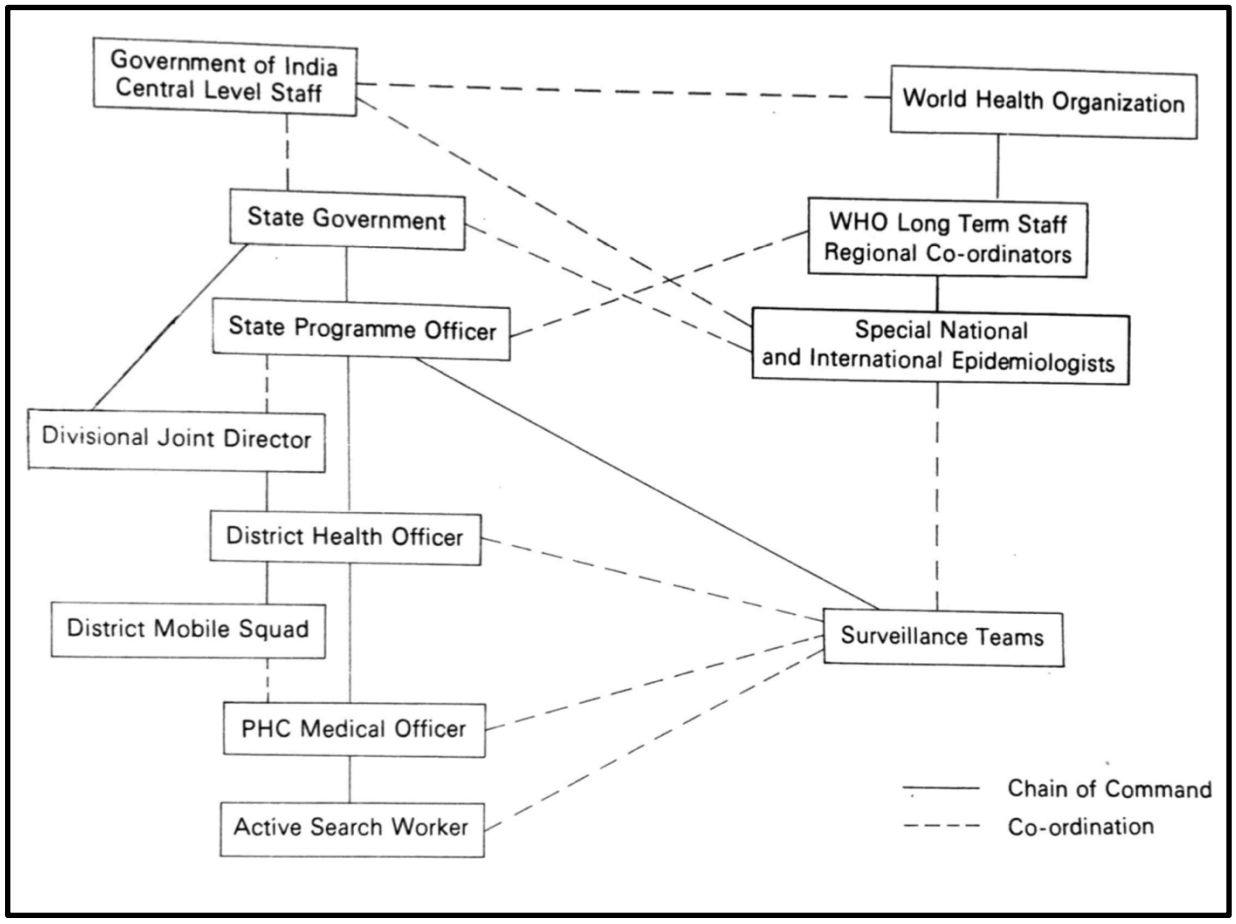
Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 9 *Smallpox Cases in India, 1950–1976*



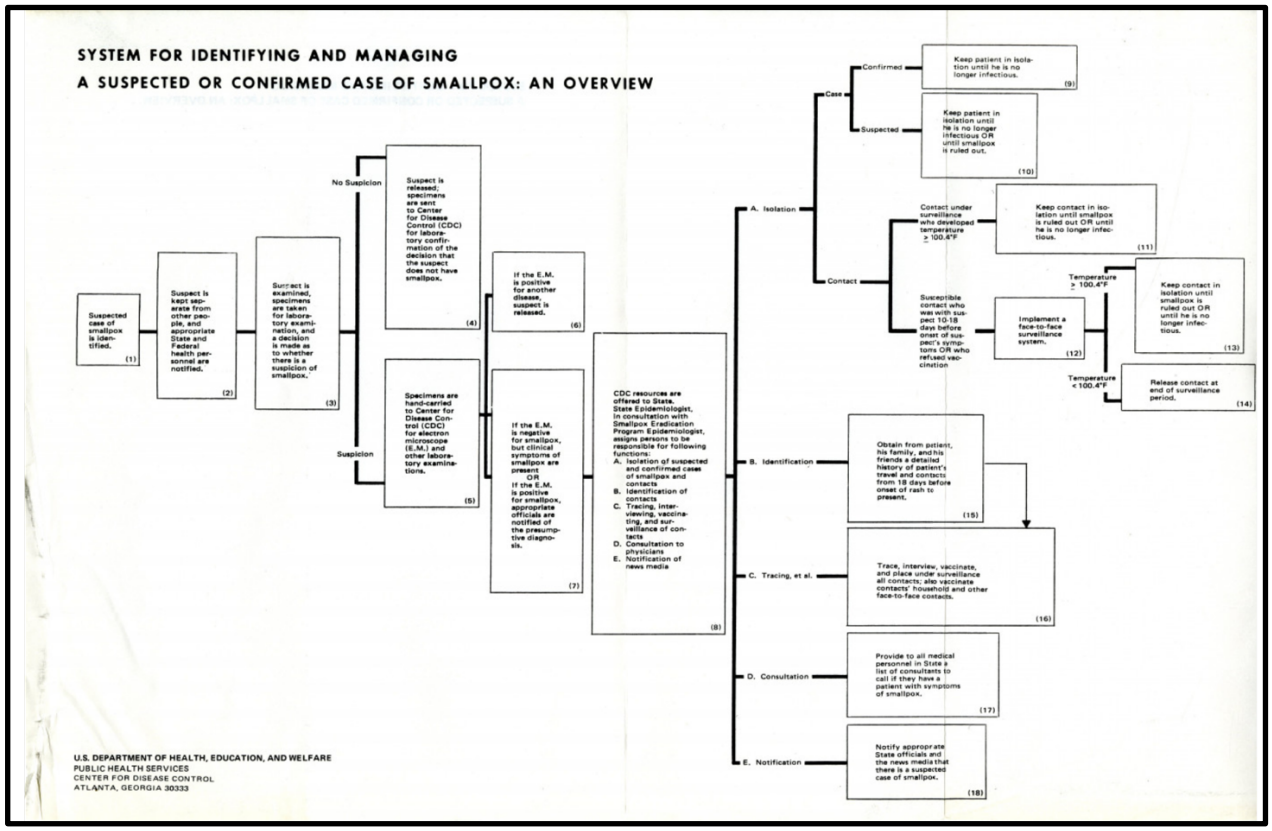
Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 10 *International Coordination for Smallpox Eradication*



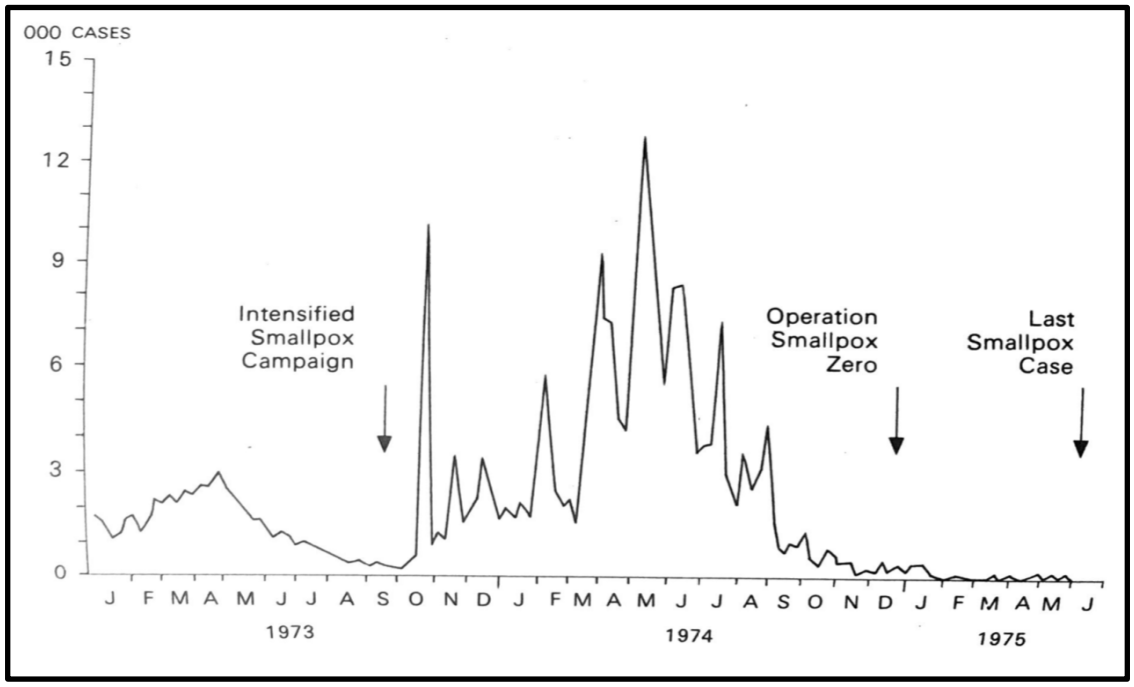
Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 11 *Reporting System for Suspected Smallpox Cases*



Source: U.S. Department of Health, Education and Welfare, Public Health Services, Center for Disease Control. Retrieved from Brilliant Collection, Taubman Health Sciences Library, University of Michigan, https://apps.lib.umich.edu/online-exhibits/exhibits/show/smallpox-eradication-india/item/5334?exhibit=143&page=1213&return=2972.

Exhibit 12 *Smallpox Cases by Week, January 1973–June 1975*



Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 13 *Bihar Searches in 1973*

	First search 15–20 October	Second search 12–17 November	Third search 10–15 December
PHCs with new outbreak	NR	166	157
Villages searched	50 426	68 806	74 160
Villages with new outbreaks	601	484	385
Percentage of villages searched having new outbreaks	1.2	0.7	0.5
Municipalities with new outbreaks	13	21	21
Total new outbreaks	614	505	405
Total new cases	3 826	2 459	2 619

NR = Not Reported

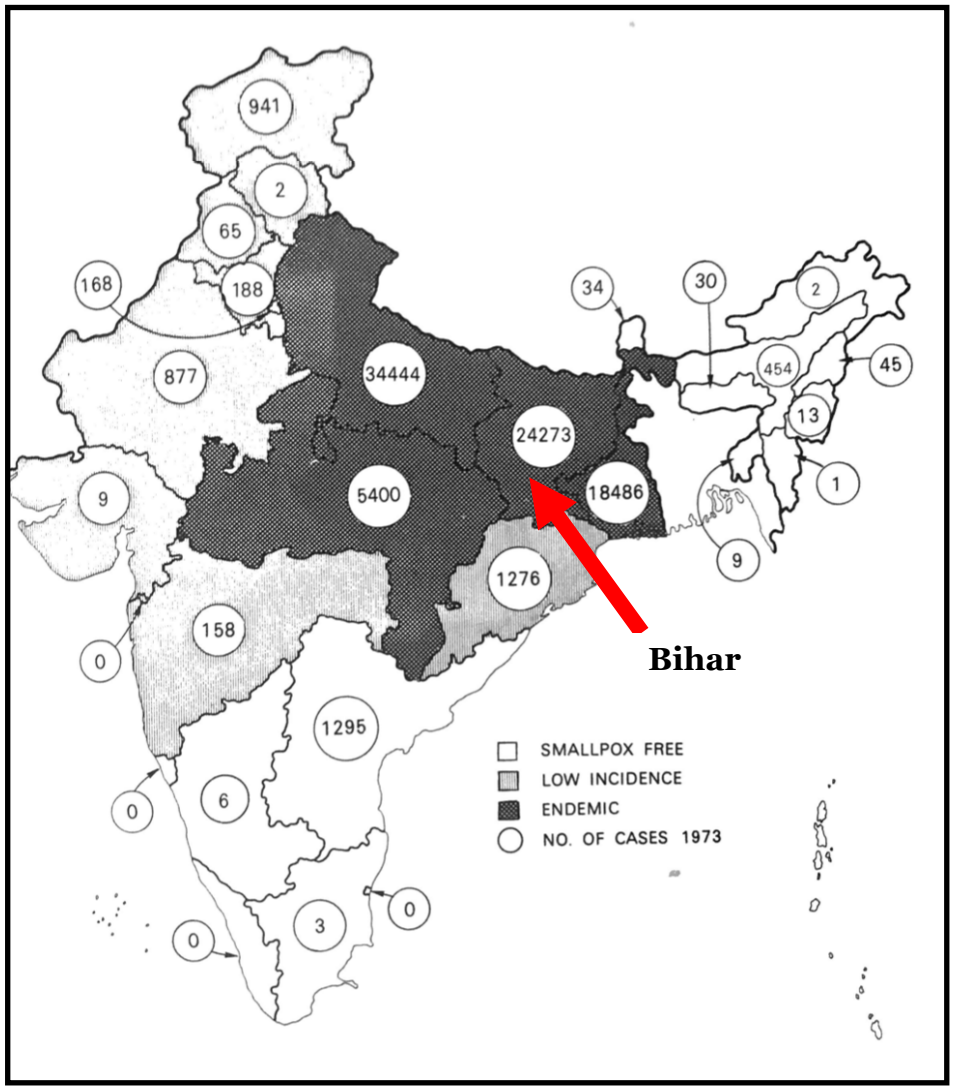
Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 14 Note *from the Field: Smallpox in Bihar State of India During 1971*

"Firstly, the district is greatly understaffed in terms of vaccinators. Out of a total of more than 75 vaccinators that are sanctioned for this district fully 37 of these posts are not filled. No relaibale estimate if the vaccination coverage in this district is available, but the age/sex distribution of smallpox cases indicated that it is certainly very poor and may be as low as 50-60%. An example of the poor staffing of blocks of Karen block, which has one permanent vaccinator for a population of 70,000. Secondly, most blocks in the district have only one medical officer who is responsible for family planning, the state dispensary and the block. These posts are normally filled by three medical officers. Thirdly, control measures taken in known smallpox outbreaks have been extremely slow with poor vaccination coverage, even several months after the outbreak was reported… Fourthly, no effort is made in most outbreaks to find the source of the outbreak. It has been the experience of this observer that the source of outbreaks can easily be found in Sant al Parganas district 80-90% of the time. Once the source is found, cross notification is absolutely necessary, but is rarely performed here. Fifthly, there is a lack of transportation at the block level… Sixthly, the district also has no funds for petrol since September 1971 so that the district NSEP vehicles have been severely limited in the amount of touring they can perform. Seventhly, the medical officers of smallpox have severe medical problems that restrict investigations of outbreaks. Eighthly, some of the staff have in the past been very poor… Lastly, there are many tribal villages that are quite resistant to smallpox vaccination even during smallpox epidemics. As these people also do not report smallpox cases this leads to a particularly difficult situation where small unvaccinated communities such as Ganchua in Jama block can sustain smallpox transmission for 6,7, or 8 months at a time."

Source: John M. Pifer "Confidential: Smallpox in Bihar State of India during 1971." Retrieved from *Expunging variola: the control and eradication of smallpox in India*, Bhattacharya 2006, p. 174.

Exhibit 15 *Incidence in States, 1973*



Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 16 *Cost of Containment for One Smallpox Outbreak in 1975*

(1) *Hiring of additional staff (not budgeted elsewhere)*

Watchguards (assume two infected houses) 8 workers at Rs. 5 per day for 42 days	Rs. 1 680
Search workers to search ten-mile radius (assume 500 villages in ten-mile radius) *300 search-days at Rs. 5 per day	Rs. 1 500
Search workers to do repeat search of ten-mile radius	Rs. 1 500
Vaccinators to vaccinate the village (assume 1000 population) 20 vaccinators for five days at Rs. 5 per day	Rs. 500
Vaccinators to vaccinate the 1-mile radius, 20 vaccinators for 15 days at Rs. 5 per day	Rs. 1 500
Supervising (at one supervisor to 5 worker-days)	
(a) for search of 10-mile radius, 60 supervisor-days at Rs. 10/- per day	Rs. 600
(b) for repeat search	Rs. 600
(c) for watchguards—1 supervisor for 42 days	Rs. 420
(d) for vaccinators of village, 4 supervisors for five days	Rs. 200
(e) for vaccination of 1-mile radius, 4 supervisors for 15 days	Rs. 600
Total	Rs. 9 100

* This estimate is based on the experience that 30 workers take about ten days to search 500 villages which works out roughly to 60 man-days per block. A block usually has about 100 villages.

2) *Petrol*—Usually, in a previously endemic area, each new outbreak is attended by several teams with jeeps for various periods of time. The jeeps are used in the outbreak area for supervision, search assessment and follow-up. The following is a reasonable jeep utilization schedule:

Days 1– 5	4 jeeps	or	20 jeep days
Days 6–21	3 jeeps	or	45 jeep days
Days 21–35	2 jeeps	or	30 jeep days
Days 36–42	1 jeep	or	7 jeep days
		Total	102 jeep days

Experience indicates that petrol costs an average of Rs. 80–100 per day of jeep use.

Personal costs of one outbreak (already budgeted elsewhere)

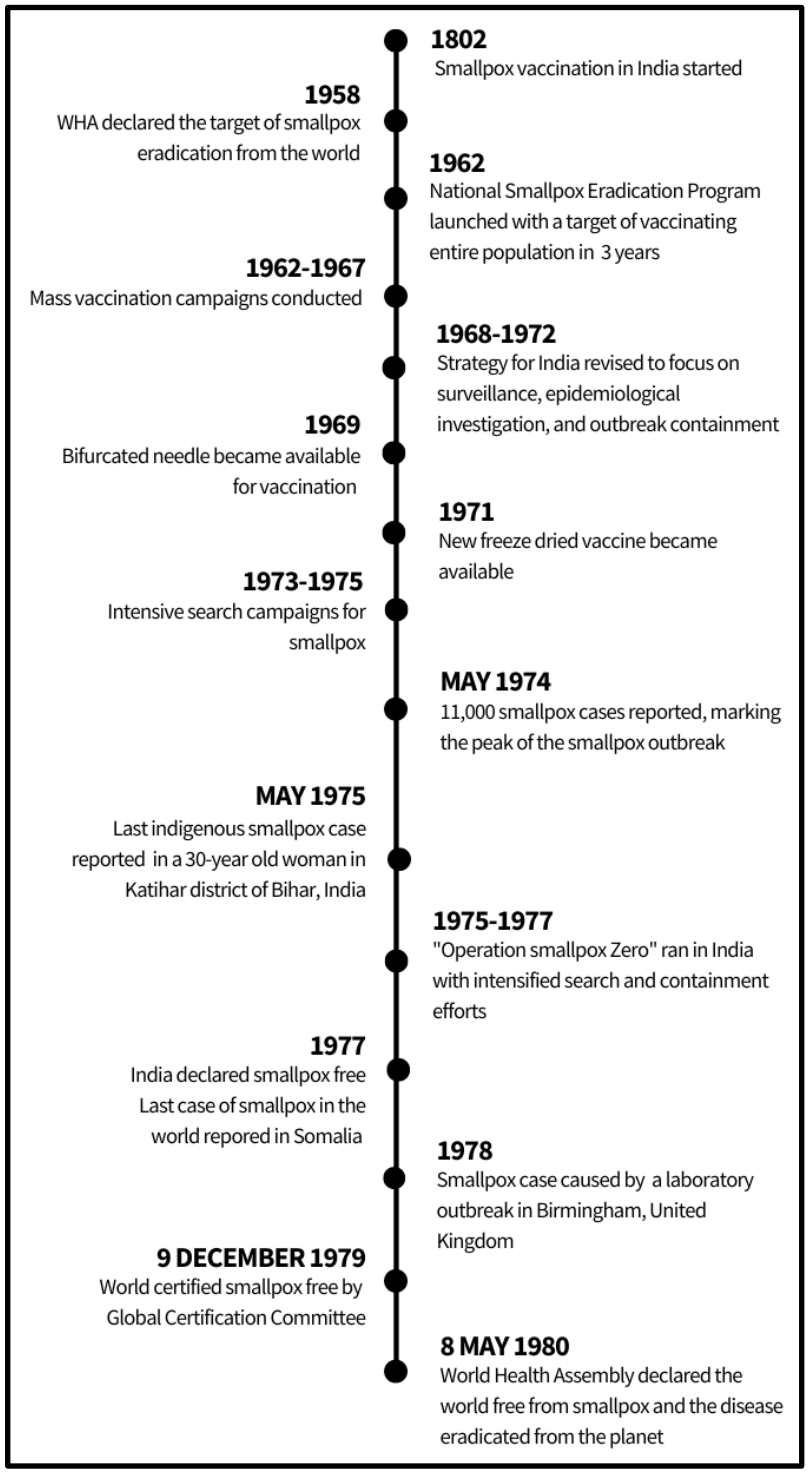
Epidemiologist, 21 days at Rs. 100	Rs. 2 100
JMO or SST MO, 42 days at Rs. 35–50	Rs. 1 764
PMA, 42 days at Rs. 15–30	Rs. 924
Driver, 102 days at Rs. 10–15	Rs. 1 224
Total	6 012

Total estimate Rs. 24 000 ($3 000)

Note: WHO medical officer's estimate of the cost of containment of one smallpox outbreak in 1975

Source: Basu RN, Jezek Z, Ward NA. The Eradication of Smallpox from India. World Health Organization, South East Asia Regional Office; 1979.

Exhibit 17 *Timeline of Smallpox Eradication in India and Globally*



Adapted from Lahariya C. A brief history of vaccines and vaccination in India. Indian J Med Res. 2014 Apr;139(4):491-511. PMID: 24927336; PMCID: PMC4078488.

References

1. Bharadwaj P, Khwaja AI, Mian AR. The partition of india: demographic consequences. *SSRN Journal* 2009. DOI:10.2139/ssrn.1294846.
2. Drawing the line: The short- and long-term consequences of partitioning India | VoxDev. https://voxdev.org/topic/institutions-political-economy/drawing-line-short-and-long-term-consequences-partitioning-india (accessed Sept 14, 2022).
3. Indian Experience of Inflation. *Economic and Political Weekly* 2015; published online June 5.
4. The Wire: The Wire News India, Latest News,News from India, Politics, External Affairs, Science, Economics, Gender and Culture. https://thewire.in/ (accessed Oct 17, 2022).
5. Basu RN, Jezek Z, Ward NA. The eradication of smallpox from India. New Delhi, India: World Health Organization, South East Asia Regional Office, 1979.
6. Children out of school (% of primary school age) - India | Data. https://data.worldbank.org/indicator/SE.PRM.UNER.ZS?locations=IN (accessed Oct 14, 2022).
7 World Health Organization. Bugs, drugs and smoke : stories from public health. Chapter 1 Smallpox. World Health Organization, 2012 https://www.who.int/about/bugs_drugs_smoke_chapter_1_smallpox.pdf (accessed March 3, 2022).
8. Smallpox. *Br Med J* 1971; 3: 323–4.
9. Foege WH. House on fire: the fight to eradicate smallpox. University of California Press, 2019 DOI:10.1525/9780520948891.
10. Centers for Disease Control and Prevention. Origin of Smallpox . Origin of Smallpox. https://www.cdc.gov/smallpox/history/history.html (accessed Feb 21, 2022).
11. Riedel S. Edward Jenner and the history of smallpox and vaccination. *Proc (Bayl Univ Med Cent)* 2005; 18: 21–5.
12. Duncan-Jones R. The Antonine Plague Revisited. *Arctos : acta philologica fennica* 2018; : 41.
13. Antonine Plague - World History Encyclopedia. https://www.worldhistory.org/Antonine_Plague/ (accessed Sept 14, 2022).
14. Fenn EA. Biological Warfare in Eighteenth-Century North America: Beyond Jeffery Amherst. *The Journal of American History* 2000; 86: 1552.
15. How Mary Wortley Montagu's bold experiment led to smallpox vaccine – 75 years before Jenner | Vaccines and immunisation | The Guardian. https://www.theguardian.com/society/2021/mar/28/how-mary-wortley-montagus-bold-experiment-led-to-smallpox-vaccine-75-years-before-jenner (accessed Oct 14, 2022).
16. Smallpox and the story of vaccination | Science Museum. https://www.sciencemuseum.org.uk/objects-and-stories/medicine/smallpox-and-story-vaccination#what-is-vaccination (accessed Sept 14, 2022).
17. Fenner F. Smallpox: emergence, global spread, and eradication. *Hist Philos Life Sci* 1993; 15: 397–420.
18. Center for Global Development. Case 1: Eradicating Smallpox. Center for Global Development, 2004.
19. Bhattacharya S, Campani CEDP. Re-assessing the Foundations: Worldwide Smallpox Eradication, 1957-67. *Med Hist* 2020; 64: 71–93.

20. Jet_injector. https://www.bionity.com/en/encyclopedia/Jet_injector.html (accessed Sept 14, 2022).

21. Lalla N, Boissiere M. Smallpox Eradication in India, 1972-1977. University of Michigan Online Exhibits. https://apps.lib.umich.edu/online-exhibits/exhibits/show/smallpox-eradication-india (accessed Feb 13, 2022).

22. At the height of the Cold War, the US and Soviet Union worked together to eradicate smallpox | World Economic Forum. https://www.weforum.org/agenda/2016/07/at-the-height-of-the-cold-war-the-us-and-soviet-union-worked-together-to-eradicate-smallpox/ (accessed Oct 14, 2022).

23. Lane JM. Mass vaccination and surveillance/containment in the eradication of smallpox. *Curr Top Microbiol Immunol* 2006; 304: 17–29.

24. Brilliant L. The Management of Smallpox Eradication in India . Ann Arbor, Michigan: The University of Michigan Press, 1985.

25. Bhattacharya S. Uncertain advances: a review of the final phases of the smallpox eradication program in India, 1960-1980. *Am J Public Health* 2004; 94: 1875–83.

26. Chacko A. A goddess defied . *World health Organization* 1980. http://apps.who.int/iris/bitstream/handle/10665/202493/WH_1980_May_p15-18_eng.pdf;jsessionid=217C5453EF981FA3569E80EA730A7D77?sequence=1 (accessed May 5, 2022).

27. Past and Present | The India Forum. https://www.theindiaforum.in/article/past-and-present (accessed Sept 14, 2022).

28. Bhattacharya S. Expunging variola: the control and eradication of smallpox in India, 1947-1977. Orient Blackswan, 2006.

29. Henderson DA. Smallpox: The Death of a Disease. Prometheus Books, 2009.