Successful smallpox eradication: what can we learn to control COVID-19?

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On 8 May 2020, the World Health Organization (WHO) celebrated the land mark milestone of the declaration of smallpox eradication exactly 40 years ago. The declaration marked the end of a disease that had plagued humanity for at least 3000 years, killing an estimated 300 million people during the 20th century alone.[1] As recently as 1967, the year in which eradication efforts were intensified, an estimated 2.7 million deaths were attributed to smallpox.

Smallpox was eradicated thanks to a global effort that began in 1959 spearheaded by WHO, further intensified in 1967. It involved ten-thousands of health workers around the world who administered an estimated half a billion vaccinations. The cost of the intensified effort, led by WHO, was estimated to be 300 million USD in cash by global donors in addition to countries` contributions. Those investments were well spent as they now save the world far more than US$ 1 billion every year since 1980. Speaking at a virtual event hosted at WHO-HQ to celebrate the 40 year anniversary of smallpox eradication, WHO Director-General Dr Tedros Adhanom Ghebreyesus said, "As the world confronts the COVID-19 pandemic, humanity's victory over smallpox is a reminder of what is possible when nations come together to fight a common health threat."[2]

Some of the lessons learned from the eradication of smallpox could be essential in helping us now tackle the COVID-19 pandemic.

What are the characteristics of smallpox? Smallpox is an acute febrile viral disease characterized by a distinct pustular-vesicular rash. The incubation time is approximately 12 days.[3] Transmission results from droplets expressed from the oral, nasal, or pharyngeal mucosa of an overtly ill patient that are inhaled by susceptible persons in close contact with the patient. Variola major, the only known variety until the end of the 19th century, resulted in case fatality rates of 30% or more, whilst Variola minor became the prevalent variety throughout the United States, parts of South America, Europe, and southern and eastern Africa from the 19th century onward, and has a case fatality of 1%. The impact of smallpox on human civilization cannot be overstated as it posed a risk to the entire world. During the 18th century, five reigning European monarchs died of smallpox, and the Austrian Habsburg line of succession shifted four times in four generations because of smallpox.[4]

Most estimates for the R_0 (the average number of unvaccinated secondary cases infected by each primary case) of smallpox are between 3 and 6, similar or even higher to that currently estimated for SARS-CoV-2.[5] It spread less widely and rapidly compared to diseases such as measles associated with an even higher reproduction number.[6] Transmission of variola virus sometimes occurred 2-3 days after the onset of fever, but most times it occurred at a time when patients were already sick and unable to circulate widely. For this reason, smallpox outbreaks tended to be clustered in a segment of a town or village and in localized areas of a province or district. Transmission from persons who were still mobile when infectious occurred if they attended social events, such as the congregation of large numbers of people at festivals and weddings, or the seasonal movement of nomads. The incidence of smallpox was highest during winter and spring. High-risk groups were health care workers.

Countries had substantial expenditures to control smallpox, care for its victims and operate quarantine programs to prevent the importation of disease. [4] In 1967, India estimated the cost of smallpox at USD 722 million, of which 10 million USD was for vaccination, 12 million USD to care for sick patients, and 700 million USD indirect costs from loss of economic productivity from morbidity and mortality. In the United States, even in the absence of endemic disease by 1968, the estimated cost associated with smallpox protection was 150 million USD due to the cost of vaccination and of death and disability associated with the vaccine, and 14 million USD for international traffic surveillance including costs related to delays in clearance of vessels.[4] Other countries, such as the United Kingdom and Germany, maintained special hospitals to be opened to admit patients when imported cases of smallpox occurred. [4]

Smallpox eradication

Various processes including variolation were used to prevent smallpox, and in 1796 Jenner introduced the smallpox vaccine. As a result, the disease rapidly declined in most of the Western world. However, the vaccine was not equitably distributed throughout the world, and it was only when a global effort to eradicate smallpox began in 1967 that all countries had access to vaccine leading to the eradication of smallpox by 1980. Eradication required cooperation and support that was for long difficult to build. For instance, a plan to eradicate smallpox was launched by WHO in 1959. Those efforts were stymied by a lack of funds, vaccine access and cooperation from countries. A new effort was launched in 1967 under the umbrella of WHO: the Intensified Eradication Program. By this point, the disease had been eliminated in North America and Europe, but outbreaks still plagued parts of South America, Africa and Asia. A turning point came during the Cold War when the Soviet Union and the United States came together to help eliminate disease by coordinating on strategy, logistics and vaccine donations despite major geopolitical political tensions at the time.[7]

These coordinating strategies included ramping up vaccine production and access in affected countries, training health-care staff and developing clear public health messages so that people could better protect themselves and their communities. The effort also leveraged targeted techniques like “ring vaccination” whereby only those who had been in contact with an infected person were monitored and vaccinated, a technique also successfully now used during Ebola outbreaks. During the early eradication efforts, mass vaccination campaigns aimed at reaching 80% or more of the population, as it was thought that a herd immunity level of 80% and above was necessary to stop transmission. Later, it transpired that surveillance combined with targeted vaccination of primary contacts for each case was equally effective at containing outbreaks. In fact, the special programs to detect and isolate cases, and contain outbreaks, called “surveillance and containment”, was thought to be one of the key components of smallpox eradication.[4] It required an effective case detection and notification system and focused attention on measures to reduce incidence. One reason for its success is the fact that all infections were clinically expressed with the same characteristic distribution of rash; case detection was therefore relatively easy and diagnosis did not require laboratory confirmation. Therefore the visible characteristic rash enabled rapid isolation, contact tracing and vaccination of contacts. There were several generations of smallpox vaccines, all very efficacious but also with substantial safety concerns. One dose of vaccine provided long-lasting immunity. An added

advantage of the smallpox vaccine was its benefit even as post-exposure prophylaxis: due to the long incubation time of smallpox, the vaccine was effective in preventing illness or modifying its course even if given within four days after infection.[7] With increasingly greater emphasis on surveillance-containment activities, endemic smallpox steadily receded. It was eliminated from 20 countries in Africa by 1979, from Brazil in 1971, and the entire African continent in 1975. The last naturally occurring case of smallpox developed less than 1 year after the originally projected 10 year target date, on October 26, 1977, in Somalia.[4] Two further cases were a result of laboratory infection in England in 1978 and these two cases were the last known human infections.

Learning from smallpox for COVID-19

The smallpox eradication effort required widespread cooperation, said the Director-General on 8 May during the celebrations, and was a first-of-its-kind global effort. “Viruses do not respect nations or ideologies," he added. “Although a vaccine was crucial for ending smallpox, it was not enough on its own”.[1]

Many of smallpox` characteristics are similar to COVID-19: high reproduction number, clustering effects with superspreading events, with social gatherings as amplifiers. Control of COVID-19 is however more challenging than that of smallpox because of some dissimilarities. Infections with SARS-CoV-2 are not all expressed in the same manner, and many infections result only in mild disease that resembles other respiratory infections – identification and diagnosis therefore requires laboratory testing and is not as rapid as for smallpox. Transmission can occur from pre-symptomatic or mildly symptomatic infections, and possibly from those that are asymptomatic, and therefore transmission is stealth-like.[8] Nevertheless, containment by maintaining a very low reproductive number was shown to be feasible in China and many other Asian countries with stringent public health measures[9], in particular South Korea, Taiwan, Hong Kong and Vietnam.[10]

By May 2020, the COVID-19 epicentres of fatal disease are now in the United States, Europe, Brazil and Russia. Although the global scientific community is accelerating the development of vaccines and therapeutics, there are diagnostic tests available to combat COVID-19, and the focus must be to increase access to these tests within countries despite health disparities[11] and also to low and middle income countries. All countries need to use enhanced testing to identify cases, test contacts who are identified during contact tracing and become sick within the period of surveillance, and isolate all those who are infected. Such focused public health measures were also successful for smallpox. It all boils down to disease surveillance, prompt patient identification, diagnosis and isolation of all cases, contact tracing and surveillance of contacts. The public health community needs to learn from history and needs to regain its ability to do shoe-leather public health. If we come together collectively and use the public health tools that we have at hand, enhanced by vaccination, we will be successful in containing COVID-19 despite geopolitical tensions, just as we were successful in eradicating smallpox despite the Cold War at the time. To this end, WHO is facilitating a Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 diagnostics, therapeutics and vaccines, called the “ ACT Accelerator”.

"….that same solidarity that we had for smallpox," said the Director-General, "is needed now more than ever to defeat COVID-19."[2]

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