Mass vaccination unnecessary in the event of a large bioterrorist US smallpox attack

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Mass vaccination would not be necessary in the event of a large-scale smallpox bioterrorist attack in the United States, according to a study led by researchers at Fred Hutchinson Cancer Research Center that appears online in the *International Journal of Infectious Diseases*.

Instead, the current U.S. government policy of post-release surveillance, prompt containment of victims and vaccination of hospital workers and close contacts would be sufficient to thwart an epidemic, according to lead author Ira M. Longini Jr., Ph.D., a world leader in using mathematical and statistical methods to study the natural course of infectious diseases.

"We found that a well-prepared response of surveillance and containment, if done quickly, within a day or two of detecting the first smallpox case, would contain a large attack if up to 500 people were infected," said Longini, a member of the Public Health Sciences Division at the Hutchinson Center and a professor of biostatistics at the University of Washington School of Public Health and Community Medicine. These results apply to scenarios involving even the most virulent, fatal forms of the virus.

However, Longini emphasizes, failure to quickly isolate known smallpox cases and vaccinate their close contacts could thwart the containment of an epidemic.

These findings emerge from a committee of smallpox experts –

including infectious-disease modelers, epidemiologists, statisticians and clinicians – who were commissioned by former Secretary of Health and Human Services Tommy Thompson to evaluate a variety of intervention strategies to determine whether the United States could contain a large-scale smallpox bioterrorist attack and, if so, how.

Specifically, the researchers were charged with determining whether surveillance and containment – isolation of detected smallpox cases and vaccination of their close contacts – would be sufficient to contain a large attack. They also wanted to find out whether other interventions, such as mass pre-vaccination of the general public, pre-vaccination of hospital personnel, vaccination of the target community and closure of schools after a smallpox release would help contain the spread of the disease.

Thompson's senior science adviser, Donald Ainslie (D.A.) Henderson, the physician and epidemiologist who oversaw the World Health Organization's successful campaign to eradicate smallpox from the world in the late 1970s, served as a consultant to the committee, known as the Smallpox Modeling Working Group. The group was convened by the Secretary's Advisory Council on Public Health Preparedness, a branch of the U.S. Department of Health and Human Services.

"Earlier studies recommended mass pre-vaccination of the general population to protect against a smallpox attack. None of us on the committee believed this was necessary, including D.A. Henderson, who intimately understands the natural history of the virus," Longini said. "The secretary of Health and Human Services wanted to settle such issues regarding smallpox containment once and for all, and this was our charge."

While the researchers did find that mass vaccination would slightly reduce the number of deaths from smallpox, they also found that the rate

of severe illness and death caused by the vaccine itself would cancel out any benefit from mass vaccination. One person in 10,000 will have a severe reaction and one in a million will die from the vaccine, Longini said.

"Precautionary vaccination of hospital personnel and post-release vaccination of the target population would further contain the spread of smallpox, but at a cost of many more people being vaccinated," said co-author and Hutchinson Center biostatistician M. Elizabeth (Betz) Halloran, M.D., D.Sc. "The financial cost and potential illness and death related to vaccination must be weighed against the potential benefits in the event of an attack. In our opinion, pre-vaccination of the population at large is unnecessary," she said. Longini, Halloran and colleagues also found that closure of schools after a smallpox attack would have a minimal effect in preventing transmission of the disease, and that any delay in quarantining infected individuals would take a much greater toll on the community than failing to pre-vaccinate potential cases.

To conduct the study, Longini and colleagues created a computer model that calculated the spread of smallpox via aerosol dissemination – the most likely choice of terrorists – within a community of 50,000. Members of this virtual community interacted the way people normally do: within households, neighborhoods, preschool groups, schools, a community hospital and the community at large. The age distribution and household sizes were based on the U.S. census for 2000.

Predicting the spread of an infectious disease such as smallpox requires much more than simply connecting dots on a map. Instead Longini and colleagues rely on a tool called stochastic modeling to take into account real-world unpredictability, as well as many factors about the disease and the affected population. In constructing these models, Longini and colleagues begin with assumptions about how people interact and how the virus spreads. They also introduce and evaluate the effectiveness of

various intervention strategies.

The study represents the first attempt to integrate what science knows about the natural history of smallpox – how various forms of the disease manifest over time – with human patterns of behavior to construct the most-comprehensive model of a smallpox epidemic to date.

"If smallpox appeared in Seattle tomorrow, which it could do, I'm absolutely confident that we could contain it if our recommendations for surveillance and containment were put into practice. I rest easier now that we've done this study," Longini said. "The process was kind of like unveiling the enemy to the point where we really understood it. This research has helped us demystify the threat a bit."

Although smallpox has been eliminated as a naturally-occurring disease, the virus still exists in two approved laboratories in the United States and Russia. The Centers for Disease Control and Prevention classifies it as a "Category A" agent, presenting the greatest potential threat for harming public health if developed and used as a bioterrorist agent.

Smallpox is caused by the variola virus, which emerged thousands of years ago. Variola major, the most common form of the virus, is divided into four subcategories: ordinary (which accounts for about 90 percent of cases and has a fatality rate of about 30 percent), modified (which occurs in people who have been vaccinated and has a death rate of about 10 percent), and flat and hemorrhagic (both very rare and uniformly fatal).

According to the CDC, exposure to the variola virus is followed by an incubation period of seven to 17 days, during which people are not contagious and feel fine. The first symptoms emerge during what is called the prodrome phase, and they include head and body aches, fatigue, a high fever and, sometimes, vomiting. This phase lasts two to

four days and at this point people may or may not be contagious. Then a rash emerges all over the body and grows increasingly severe over the next 20 or so days, eventually forming scabs; during this period people are contagious, particularly during the first seven to 10 days of the rash. The disease eventually resolves and contagion ends after all of the scabs have fallen off. People who survive are then considered to be immune from smallpox.

A person can become infected by prolonged, face-to-face exposure with someone who is contagious, direct contact with infected bodily fluids or a contaminated object, such as bedding or clothing, and exposure to an aerosol release.

Routine smallpox vaccination ended in 1972, which leaves at least 43 percent of the U.S. population unvaccinated, Longini said. Research suggests that those previously vaccinated may still have substantial residual immunity although, if infected, they could still transmit the virus to others. Those most vulnerable to the virus are the very young and those whose immune systems are compromised due to HIV/AIDS, cancer or some other medical condition. An estimated 50 million Americans fall into this category, Longini said.

Source: Fred Hutchinson Cancer Research Center