

EDITORIALS

An Unfortunate Need to Revisit Smallpox Preparedness

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Often hailed as the single greatest accomplishment in modern health practice, the eradication of smallpox in 1980 ended its historic scourge of death and severe disease. (1): During the 39 years since smallpox eradication, for most of the world its historic human devastation has become but a distant memory. A concerted effort by the World Health Organization ensured that variola major, the virus responsible for smallpox, was no longer in existence in clinical research laboratories around the world. Today we believe that the virus is located in only two repository, high-security biosafety level 4 laboratories—in the United States and Russia.

The likelihood that the virus remains in yet unidentified laboratories throughout the world is, at best, a theoretical possibility. For this reason, despite a call by some to maintain preparedness for the possible return of smallpox, such preparedness remains a low priority for almost all countries in the world.

More recently, however, concern about the potential release of smallpox into the public grew when Canadian scientists synthesized a closely related orthopoxvirus, horsepox, using technology and resources that would be available to a number of laboratories throughout the world. This work remains controversial and raises serious ethical and scientific questions about whether it should even be done. Regardless, it is a stark reminder that someone with a similar capability as the Canadian scientists could synthesize variola major and, with the release of that virus into the public, begin the catastrophic return of smallpox. The world's population is now immunologically naïve to smallpox owing to the end of smallpox vaccination programs more than 40 years ago and waning vaccine immunity in older adults.

We must recognize the challenge that this situation presents to society. Most bioterrorism preparedness experts agree that the likelihood that smallpox could return and cause a devastating regional or even global outbreak remains very low. Nonetheless, because of the potential consequences of such an outbreak, I believe that society has no choice but to have at least a moderate level of preparedness, in both the availability of effective vaccines and in strategies for responding to outbreaks quickly and effectively.

It is for this reason that the inaugural papers in this new online journal, *Global Biosecurity*, deserve the attention of the world. Two of the papers are a result of a smallpox virus outbreak simulation exercise carried out

by C. Raina MacIntyre, MBBS, PhD, and her colleagues. The purpose of the exercise was to review preparedness for a smallpox bioterrorism attack in the Asian Pacific region and globally. The results of the exercise are sobering. The authors have provided us with substantial food for thought with regard to the speed at which a comprehensive outbreak response could be launched in one or more locations around the world and how the very limited supplies of our current smallpox vaccines will be most effectively deployed. While this work focuses on the Asian Pacific region, the results and lessons learned should be considered by every country in the world.

The two related papers in this issue also deserve close reading: "The current and future landscape of smallpox vaccines," by J. Michael Lane MD, and "Effectiveness of three key antiviral drugs used to treat orthopoxvirus infections: a systematic review" by Yu and Raj. First, a comprehensive and thoughtful review of the current and future landscape of smallpox vaccines by Lane serves as a primer on our current smallpox vaccine capability and potential for developing safer and possibly more effective smallpox vaccines for the future. As Lane points out, however, given the general sense by most countries that smallpox will not again be a serious public health challenge, it's unlikely that we will see much investment in developing and stockpiling these fourth-generation vaccines any time soon.

The systematic review of the effectiveness of three key antiviral drugs used to treat orthopoxvirus infections should also serve as a primer for biopreparedness experts considering use of such drugs in humans and their effect on disease progression. Not covered in this important paper—but nonetheless a critical factor in the potential use of these drugs in a smallpox outbreak—is the number of doses currently available in our government stockpiles.

How will those drugs be deployed in countries where a smallpox outbreak might emerge? There are still many challenges considering how the limited supplies of both vaccine and drugs would be distributed. An intentional attack launched simultaneously in multiple global regions would complicate the response still further.

I welcome this new publication and congratulate the authors for focusing on an often not-thought-about but nonetheless potentially catastrophic issue—the return of smallpox. Anyone considering such preparedness today should use these four papers to prepare for what could, and unfortunately one day might, happen.

How to cite this article: Osterholm MT. An Unfortunate Need to Revisit Smallpox Preparedness. *Global Biosecurity*, 2019; 1(1).

Published: February 2019

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