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A Mass Smallpox Vaccination Campaign: Reasonable or Irresponsible?

The global eradication of smallpox in the late 1970s stands as one of the great achievements of mankind, a testament to what is possible when there is a confluence of scientific knowledge, international public health vision, and political will. The deliberate reintroduction of smallpox would be an unthinkable crime against humanity, with the potential to spread disease well beyond the intended target population. However, the September 11, 2001, terrorist attacks and the clumsy attempt to foment civil disruption by the distribution of anthrax spores through the U.S. mail alert us that no crime is irrational to those intent on advancing their own contorted ideology.

The only certainty is that the last known repositories of smallpox virus are being maintained at the Institute of Virus Preparations in Moscow and the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. Beyond this, the information required for a reasonable assessment of risk does not exist. There are plausible allegations that "weapons grade" smallpox virus covertly produced by the Soviet Union and the technical expertise to adapt it for bioterrorism purposes may have found their way into the hands of rogue states,¹ but if the western intelligence community knows more, it has not been forthcoming with the information.

Nonetheless, even a risk of "close to zero" requires vigilance. While complete safety is not guaranteed, the responsibility lies with the federal government to do everything reasonable and possible to reduce the threat and the consequences of a smallpox reintroduction. Well before September 11, the CDC had a plan under development that relies on rapid response, isolation of small pox patients, vaccination of contacts of cases and the household members of contacts, vaccination of medical personnel and others at risk of exposure, and surveillance. These strategies were effective in eradicating smallpox throughout the developing world in the 1960s and 1970s, but they might be challenged by a large smallpox outbreak in a highly mobile western society. The CDC Advisory Committee on Immunization Practices has updated its recommendations for use of smallpox vaccine.² In addition, the National Institutes of Health has initiated a clinical trial to determine whether the 15 million doses of at least 20-year-old lyophilized calf lymph smallpox vaccine could be diluted to provide as many as 60 to 135 million additional doses. The terrorist events of the past fall have put these studies on a fast track and have led to the order of 210 million doses of cell culture-grown vaccine by the federal government.

The CDC plan includes pre-exposure vaccination of persons who would first respond to an outbreak, but it does not call for general immunization of the public as a preventive measure. This has engendered vocal criticism on the part of those who consider the CDC plan inadequate to contain a large-scale, multisite release of smallpox virus. These critics are calling for voluntary immunization of all U.S. residents once adequate supplies of smallpox vaccine and vaccinia immune globulin are available. Vaccinia immune globulin would be needed to modify the rare but sometimes fatal adverse reactions known to complicate smallpox vaccination. While the

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overall risk for severe complications is low, the absolute number could be substantial if vaccination recommendations are extended to the entire U.S. population.

The paper by Kemper and colleagues in the current issue³ attempts to estimate the number of serious adverse reactions and deaths that would result from a universal vaccination policy. This “back-of-the-envelope” calculation simply applies the rates of adverse reactions reported from a nationwide survey published in 1968 by epidemiologists at the CDC to the 2000 census data. By this method, Kemper and colleagues estimate that 4200 persons would have reactions serious enough to warrant vaccinia immune globulin treatment and 153 people would die among 178.5 million 1- to 65-year-old vaccine recipients, based on an overall vaccine coverage rate of 75%.

For several reasons, it is difficult to know whether these figures are even in the right ballpark. First, many more immunocompromised persons are living freely in society today than in the 1960s. The authors give U.S. denominators for some at-risk groups (recipients of solid-organ transplants, patients with HIV infection or AIDS) but do not include (perhaps larger) numbers for others at risk (patients receiving oral or inhaled corticosteroids for allergies, asthma, or rheumatic and vasculitic diseases; persons with inherited immunodeficiency syndromes or common variable immunodeficiency; and pregnant women). Furthermore, it is not clear that their estimates include the inevitable cases of progressive vaccinia that would result from inadvertent vaccination or exposure of an immunocompromised person to a vaccine recipient.

Second, as the authors acknowledge, age-specific data on the incidence of adverse reactions from an era in which many persons received smallpox vaccine in infancy does not apply to our current population. Third, the authors have erroneously assumed that persons vaccinated before 1972 (1 million persons) would have the same risk for adverse reactions as primary vaccine recipients. The best available information indicates substantial, but not complete, immunity to smallpox among persons vaccinated more than 50 years previously, and this immunity is likely to extend to vaccinia virus as

well.⁴ Finally, one must question the assumption that smallpox vaccine would be readily accepted by even 75% of the population once the inevitable reports of adverse reactions and deaths from vaccination begin to appear in the press. More precise estimates of vaccine-related morbidity and mortality are needed to inform the debate.

The proponents of universal immunization seem willing to accept a “moderate” number of vaccine-related deaths and permanent neurologic impairment to reduce the morbidity and mortality and the civil disruption that would result from a large-scale smallpox release.^{5, 6} While imperfect, Kemper and colleagues’ back-of-the-envelope calculations remind us of the serious downsides of a universal vaccination strategy. Physicians who have taken an oath to “first do no harm” will struggle with the idea of vaccinating their patients to ward off an ill-defined and seemingly remote threat. Policymakers will need to weigh the best available analyses of vaccine-related morbidity and costs against the best available assessment of risk for a smallpox release. This will be an arduous and contentious task but a necessary one.

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