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Will Smallpox Vaccinations Save Lives?

Smallpox, one of the most feared pestilences in human history, is at the center of a national and international debate. To prevent significant loss of life in the event of a smallpox bioterrorist attack, should smallpox vaccination be reintroduced?

Smallpox kills up to 30 percent of those infected and disfigures many survivors. It is infectious and contagious. There is no known cure, but there is a preventive measure: vaccination. Vaccination has been so effective that smallpox, as a naturally occurring disease, has been completely eradicated. But the vaccine itself can be dangerous. It is made with a live virus that can cause illness and even death in a small percentage of people vaccinated. The risk of a bioterrorist attack must therefore be carefully weighed against the risk of the vaccine.

To help policymakers determine an appropriate course of action, a RAND Corporation team led by infectious disease specialist Sam Bozzette developed and analyzed six plausible smallpox attack scenarios, together with a variety of possible control strategies.

Is a Smallpox Attack Likely?

A detailed analysis of the likelihood that terrorists might obtain and use the smallpox virus as a weapon is beyond the scope of this study. However, in developing the smallpox attack scenarios, the RAND team took into account factors that a policymaker would

Key findings:

- The risk of a smallpox bioterrorist attack must be balanced against the risk of the vaccine.
- For most scenarios, vaccinating health care workers will probably save lives.
- But vaccinating the general public will probably not save lives.

need to weigh when determining whether a smallpox attack is likely.

Factors that make a smallpox attack less likely include the fact that the smallpox virus (variola) is difficult to obtain. There are known stocks only in Moscow and Atlanta. “Weaponizing” the virus is difficult and requires specialized equipment and knowledge. The effects of using smallpox as a weapon are unpredictable. For example, the disease could boomerang to affect the bioterrorists’ homeland countries. And there is considerable risk of a complete and devastating U.S. reaction, including military action.

On the other hand, factors that might make an attack more likely include the possibility that unknown stocks exist, that part of the U.S. or Russian stocks has been stolen or sold, that the virus can in fact be grown

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This Highlight summarizes RAND research reported in the following publication:

Bozzette SA, Boer R, Bhatnagar V, Brower JL, Keeler EB, Morton SC, Stoto MA. A Model for a Smallpox-Vaccination Policy, *New England Journal of Medicine*, Vol. 348, No. 5, January 30, 2003, pp. 416–425. (Published online at www.nejm.org, December 19, 2002.)

Facts About Smallpox	Facts About Smallpox Vaccination
<ul style="list-style-type: none"> • Disfiguring and often fatal disease, once widespread • Infectious and contagious • Fatal in up to 30 percent of cases • Caused by variola virus • No known cure, but can be prevented by vaccination • Last naturally occurring case in Somalia in 1977; declared eradicated by the World Health Organization in 1980 • Four stages (approximate durations): <ul style="list-style-type: none"> - Incubation: 12 days - Fever: 4 days (may be contagious in last days) - Rash: 8 days (contagious period) - Scab: 5 days (contagious period) 	<ul style="list-style-type: none"> • Effective preventive measure, especially when combined with isolation of infected person and contacts • Vaccine effective if given within 4 days of exposure • Vaccine contains live vaccinia virus • Vaccine does not cause smallpox • In a small number of people, vaccine can cause illness and even death • Vulnerable populations likely to be adversely affected by the vaccine include pregnant women, babies younger than 1 year, and immunocompromised individuals • Most Americans routinely vaccinated prior to 1972 • Effects of vaccine wear off over time; those who were vaccinated prior to 1972 probably have limited immunity

and weaponized, and that terrorists might find unpredictable or devastating effects to be acceptable. Terrorist groups might count on a vigorous U.S. response to increase the general level of havoc, and a rogue government under attack may feel that it has nothing to lose. The use of smallpox as a weapon may be influenced by U.S. military engagements abroad, and by the level of preparedness at home.

**Attack Scenarios and Control Strategies:
How Many Would Die?**

The team developed six plausible attack scenarios, ranging in severity from a hoax to a highly coordinated attack. The scenarios take into account the tendencies of terrorists to be members of loosely affiliated organizations and to target clinics, government offices, and airplanes or airports. The six attack scenarios are as follows:

- 1. Hoax:** An activist mails a “hoax” virus to a clinic, along with a threatening letter.
- 2. Laboratory release:** As a result of accident or sabotage, a previously vaccinated technician is exposed to smallpox virus that is being stored in his lab. He suffers a mild case, but his two children become quite ill and infect others.
- 3. Human vectors:** Three U.S. residents deliberately infect themselves with smallpox virus provided by fellow terrorists from abroad. After becoming ill, they use a mass transit system, coming into contact with many others.
- 4. Building attack:** Aerosolized smallpox virus is sprayed into the ventilation system of a large office building. Hundreds of workers are exposed.
- 5. Airport attack, low impact:** In a coordinated attack, terrorists go to the 10 largest U.S. airports and distribute the virus using portable nebulizers. 5,000 persons are infected.
- 6. Airport attack, high impact:** Same as above, except that 100,000 persons are infected.

For each of the attack scenarios, the research team modeled six control strategies:

- contact vaccination and isolation alone (e.g., vaccination of the persons known to be in contact with the infected individual, and isolation of the infected individual and his or her contacts as soon as the disease is diagnosed)
- post-attack vaccination of health care workers
- post-attack vaccination of health care workers and the public
- prior vaccination of health care workers
- prior vaccination of health care workers and post-attack vaccination of the public
- prior vaccination of health care workers and the public.

Contact vaccination and isolation are generally quite effective and are therefore part of all of the above control strategies. However, the research team noted that these control techniques depend on a high level of preparedness, including education to ensure early recognition of the disease, a system for delivering the vaccine efficiently, and isolation of the contacts of infected individuals.

Health care workers are defined as doctors, nurses, and others working in and around health care facilities, including paramedics, ambulance drivers, and hospital security guards.

The table shows estimated deaths for each of the six attack scenarios and control strategies. In all scenarios, the most extreme control strategy—prior vaccination of health care workers and the public—resulted in approximately 485 deaths from the vaccine. (This scenario assumes that most of the nation’s 10 million health care workers and approximately 60 percent of the general public would be vaccinated.) In the event of an airport attack, this strategy would save lives. For a high-impact airport attack, this strategy would save thousands of lives. But for less severe attacks (hoax, labora-

Estimated Deaths Due to Smallpox and Vaccination, Listed by Attack Scenario and Control Strategy

Control Strategy	Hoax	Laboratory Release	Human Vectors	Building Attack	Airport Attack—Low Impact	Airport Attack—High Impact
Contact vaccination and isolation alone						
Smallpox deaths	0	7	19	300	2,733	54,691
Vaccination deaths	0	0	0	0	2	37
Total	0	7	19	300	2,735	54,728
Post-attack vaccination of health care workers						
Smallpox deaths	0	7	18	298	2,731	54,643
Vaccination deaths	0	0	1	1	26	55
Total	0	7	19	299	2,757	54,698
Post-attack vaccination of health care workers and the public						
Smallpox deaths	0	6	18	286	2,631	52,541
Vaccination deaths	0	7	8	10	482	496
Total	0	13	26	296	3,113	53,037
Prior vaccination of health care workers						
Smallpox deaths	0	3	12	188	2,192	43,852
Vaccination deaths	25	25	25	25	26	49
Total	25	28	37	213	2,218	43,901
Prior vaccination of health care workers and post-attack vaccination of the public						
Smallpox deaths	0	3	11	181	2,114	42,320
Vaccination deaths	25	31	33	34	482	493
Total	25	34	44	215	2,596	42,813
Prior vaccination of health care workers and the public						
Smallpox deaths	0	2	2	53	641	12,857
Vaccination deaths	482	482	482	482	482	485
Total	482	484	484	535	1,123	13,342

Note: The number of vaccination deaths increases in the airport attacks because it is likely that more people (especially those in contact with an infected person) will get vaccinated after the attack, and, therefore, that more people will suffer adverse reactions to the vaccine.

tory release, human vectors, and building attack), prior vaccination of health care workers and the general public would merely add to the number of lives lost.

In all scenarios, health care workers (who are necessarily in frequent contact with infected individuals) are at greater risk. They account for 19 percent of all infected persons in the airport attacks and for 57 percent of those infected in the laboratory release scenario. Prior vaccination of health care workers greatly reduced the number of smallpox cases in this group (a median reduction of 85 percent as compared with contact vaccination and isolation alone). Since health care workers keep our hospitals open and our health care system running, prior protective measures for this group are especially important.

When Does Vaccination Make Sense?

Smallpox vaccination makes sense when lives saved exceed lives lost. This requires a “best guess” as to (1) the proba-

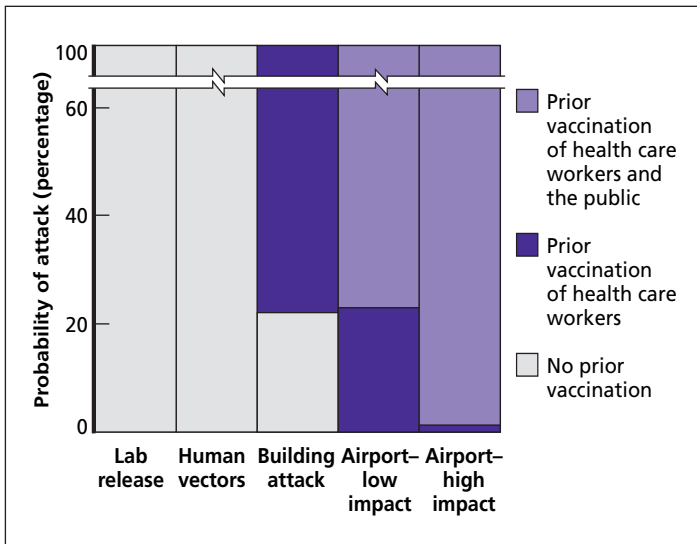
bility of a bioterrorist attack, and (2) the type and severity of the attack. The figure on the back page is designed to help policymakers decide when prior vaccinations would save lives.

How to Use the Figure

Suppose you’re a policymaker, and you judge that a bioterrorist attack is likely to take the form of a laboratory release or human vectors. If you use the research depicted in the figure, you would not recommend prior vaccination for anyone. Even if the attack were certain, expected lives lost from vaccination would exceed lives saved.

If you judge that the probability of a building attack is, say, 10 percent, you would again not recommend prior vaccination for anyone. Here again, expected lives lost from vaccination would exceed lives saved. But if you judge the probability of a building attack to be 20 percent or more, then you would recommend prior vaccination of health care

**Threshold Analysis for Policymakers:
When Would Vaccinations Save Lives?**



workers only. For this scenario, prior vaccination of health care workers at the 20 percent threshold would save lives. But prior vaccination of the public would not result in a net saving of lives, even if this type of attack were certain.

If you judge that bioterrorists might attack an airport, then you would recommend prior vaccination of health care workers. This type of attack is potentially so severe that prior vaccination of health care workers would save lives, even if the probability of an attack is very low.

If you judge that the probability of a low-impact airport attack is 20 percent or greater, or that the probability of a

high-impact airport attack is 2 percent or greater, then you would recommend prior vaccination of both health care workers and the general public.

What Happens If There Are Multiple Attacks?

The impact of smallpox bioterrorism would be greatly increased by multiple attacks at several locations. The research team developed models to evaluate the effects of combining one or more of the attack scenario probabilities, including the possibility that all six attack scenarios might occur simultaneously. For most attack probabilities, prior vaccination of health care workers results in the fewest deaths and is therefore the favored strategy.

Conclusions and Recommendations

Early recognition of the disease, efficient delivery of vaccine, and effective isolation substantially decrease the burden of an attack. Therefore, the team recommends that federal and local health care agencies and organizations maintain a high level of planning and preparedness for a bioterrorist attack.

Mass prior vaccination of the public will save lives if terrorists mount a coordinated multisite attack but will result in a net loss of life under most attack probabilities. Therefore, at this time, the team recommends that the general public not be vaccinated.

One of the team’s most important findings is that prior vaccination of health care workers would save lives even if the probability of attack is low. Therefore, the team endorses the policy of vaccinating eligible health care workers and first responders now. ■



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