Ring vaccination versus mass vaccination in event of a smallpox attack

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Abstract

Since vaccination is critical in responding to smallpox exposure, vaccination strategies must be evaluated during bioterrorism preparedness. Information on historical factors, smallpox characteristics, public health capabilities and hypothetical attack scenarios was used to evaluate major vaccination strategies. In event of a smallpox attack, the optimal strategy is situational; mass vaccination may be best for dense island populations such as Oahu.

Introduction

Since the bombing of the World Trade Center on September 11, 2001 and the subsequent cases of anthrax, much concern has arisen regarding use of smallpox as a weapon of bioterror. Though smallpox officially exists in only two secure laboratories, one in the United States and one in Russia, other countries may harbor undocumented stores of the virus. It is feared that terrorists might use these illicit stores to generate biological weapons. Thus, plans for protecting the population in the event of a smallpox attack must be formulated.

Vaccination will play a central role in controlling the sequelae of a smallpox attack. The optimum strategy for immunization is unclear. Mass and ring vaccination are the two major tactics under consideration. In both, infected individuals would be isolated. However, mass vaccination would entail indiscriminate vaccination of the entire population while ring vaccination, also known as surveillance and containment, would involve targeted immunization of primary and secondary contacts. Which strategy would be most effective in preventing spread of smallpox, especially in island populations? What role does the risk of vaccination play in selecting a strategy? Given resource limitation, are both strategies equally feasible?

Methodology

Articles pertaining to smallpox vaccination policy were identified by searching PubMed. Keywords bioterror, bioterrorism, smallpox, vaccination and vaccine were used as the following string: (bioterror OR bioterrorism) AND (smallpox) AND (vaccine OR vaccination). All article types were considered. Language was limited to English. Information on historical factors, smallpox viral characteristics, public health capabilities and hypothetical attack scenarios was extracted from identified articles. Information was also obtained from the Centers for Disease Control website and textbooks. This information was used to evaluate major vaccination strategies.

Results

242 articles were identified using the delineated search strategy. Ring vaccination and mass vaccination were established as the major vaccination policies under consideration for responding to smallpox attacks. Based on titles and available abstracts, 32 articles were selected for use in further evaluation of vaccination strategies.

Pros and cons of each vaccination strategy are shown in Table 1. Discussion of these factors in light of historical experience and hypothetical scenarios follows below.

Discussion

Historical Lessons

History provides clues as to the effectiveness of both ring and mass vaccination. Though smallpox was declared eradicated in 1980, the struggle to reach that point was arduous. Smallpox had long been a deadly, feared disease, which killed in epidemic waves. During the late eighteenth century, Edward Jenner began promote vaccination with cowpox to prevent smallpox. His work eventually led to a vaccinia based smallpox vaccine. However, epidemics continued to decimate significant numbers of people.[1]

The first case of smallpox in Hawaii was diagnosed in 1853. It reportedly originated from a ship out of Boston. The subsequent epidemic afflicted 9,082 of Oahu's population of 19,126, with 5,748 deaths. Consequently, the legislature mandated mass vaccination for smallpox in 1854. Despite this measure, Hawaii

experienced three more smaller smallpox outbreaks in 1861, 1873, and 1882. These epidemics, with 282 additional deaths, were likely caused by failure to achieve a 100% vaccination rate.[2]

In 1967, the World Health Organization launched the Intensified Smallpox Eradication Program. The program initially also relied upon mass vaccination, which proved efficacious in Western countries. However, again, 100% vaccination rates were impossible to achieve and smallpox continued to plague developing nations, particularly those with dense populations. Meanwhile, events in Nigeria stimulated evolution of a new strategy. Though most of Nigeria's population had been vaccinated, a religious sect that had resisted vaccination developed an outbreak. Faced with limited resources and delivery delays, eradication campaign staff learned quickly to isolate infected individuals and vaccinate others to control disease spread. Within a few years, this method of surveillance and containment, known as ring vaccination, had successfully controlled several outbreaks in India and become a worldwide standard.[3,4]

With these two major vaccination strategies, smallpox was controlled over several decades. The last US case occurred in 1949.[5] Nonetheless, vaccine was still administered to all children, military recruits and tourists until 1972. Routine smallpox immunizations were subsequently discontinued in the US, as the risks of vaccine adverse reactions were felt to outweigh the risk of a future smallpox epidemic.[6] However, high-risk individuals continued to receive vaccine.[1] Worldwide, the last natural case occurred in Somalia in 1977. Successful smallpox management thus relied initially upon mass vaccination, and later ring vaccination strategies.

The Smallpox Threat

Though natural smallpox outbreaks are no longer a public health threat, officials fear that the virus may be employed as a weapon of bioterror. Given this scenario, selection of a vaccination strategy cannot be based solely upon historical factors. Smallpox was not traditionally considered a biological weapon; it didn't start from a point-source; and infectious characteristics were more predictable. At present, we do not know whether smallpox will be re-introduced to our now naïve population. If smallpox were re-introduced, would it be a mutated, more deadly form? Would it spread similarly to historical smallpox? And would it be suddenly introduced in one location or simultaneously in multiple locales? All of these issues influence decisions regarding a vaccine strategy.

Since the probability of a smallpox bioterrorist event is low, pre-event vaccination of the general population is not recommended. Only individuals likely to participate in an initial response to a smallpox event have been immunized.[7] Others will receive vaccination in response to a known exposure, rather than prophylactically.

Table 1.— Mass Vaccination Versus Ring Vaccination In the Event of a Smallpox Attack

MASS VACCINATION	RING VACCINATION
PROS:	PROS:
• Entire population is prepared	• Efficient use of resources
• Herd immunity	• Higher likelihood intended recipients are vaccinated
• Less intense surveillance required	• Effective up to 4 days post-exposure
• Public sense of security	• Incubation non-contagious; Prodrome sometimes contagious
• Special advantages to dense island populations such as on Oahu	• Likely effective for less populated Neighbor Islands, especially more geographically isolated communities such as Hana
CONS:	CONS:
• Resource requirements for administering vaccine	• Resource requirements for surveillance after attack
• Pockets of susceptibility may be overlooked	• Time required to trace primary / secondary contacts
• Everyone must consent	• Risk of overlooking high-risk individuals
• Adverse reactions / contraindications	• Public demand

Vaccination Strategies

Once a known smallpox event has occurred, agencies must be prepared to vaccinate at-risk individuals. This can be accomplished by either mass or ring vaccination. Each strategy has pros and cons.

Mass Vaccination

A mass vaccination response would ensure that the entire population is prepared for subsequent contact with infected individuals as well as for future attacks. Thus it would decrease the need for surveillance of contacts and reduce the extent of vigilance necessary. It would also provide herd immunity, reducing propagation of infection if contagious individuals did interact with the uninfected. Thus, this strategy would likely reduce the impact of future attacks. It might also give the public a sense of security, decreasing the probability of popular hysteria in response to perceived risk.

Nonetheless, mass vaccination has significant drawbacks. It requires tremendous resources. Not only would we need sufficient stocks of vaccine for an entire population, but also adequate trained personnel to administer it. The costs associated with such an undertaking would be staggering. Another problem with mass vaccination is its potential to inadvertently overlook certain groups of individuals, thus resulting in pockets of susceptibility. Along the same lines, at least 90% of individuals must submit to vaccination for this strategy to be effective. Mandatory vaccination may infringe on the individual's right to informed consent and to refuse medical care. Thus initiation of mass vaccination could be delayed by legal proceedings or formulation of guidelines.

Furthermore, the presently used vaccinia-based vaccine has side effects. Though rare, the risks associated with vaccination may outweigh potential benefits if the threat of smallpox exposure is low. Constitutional symptoms, eczema vaccinatum, myopericarditis, generalized vaccinia, progressive vaccinia and postvaccinial encephalitis are potential adverse reactions, but are more common among primary vaccinees than re-vaccinees.[8] In 450,293 healthy military vaccinees, one case of encephalitis and thirty-seven cases of acute myopericarditis developed after vac-

cination; there were no cases of eczema vaccinatum or progressive vaccinia.[9] However, adverse reactions may be more common in the general population. In a study on smallpox vaccine dilutions, fifteen of 148 vaccinees developed dermatologic reactions.[10]

Under normal circumstances, contraindications to smallpox (vaccinia) vaccine include dermatidities, immunodeficiency, immunosuppression, pregnancy, allergy to vaccine component, age under 18 years, concurrent illness, and breastfeeding. For pre-event prophylaxis, people with contraindications are not vaccinated because the risk of adverse reaction outweighs potential benefit. However, in the event of an actual attack, the benefits of vaccination outweigh the risks. Since there are no contraindications to post-exposure vaccination, the likelihood of adverse reactions increases. Mass vaccination could thus result in increased morbidity and mortality in people with pre-exposure contraindications.[11]

Ring Vaccination

Ring vaccination also has its pros and cons. On the positive side, ring vaccination strategy may utilize resources more efficiently. Because only primary and secondary contacts of infected individuals would be vaccinated, less vaccine and labor would be required to perform the actual immunizations. Focused surveillance with targeted vaccination would probably also increase the likelihood that intended recipients are vaccinated.

Were vaccination effective only if given prior to exposure, surveillance and containment might not be a prudent option. However vaccination is reportedly effective for four days post-exposure and can be supplemented with vaccinia immunoglobulin.[12] Although there are no FDA-approved antiviral medications indicated for smallpox at this time, the experimental compound hexadecyloxypropyl-cidofovir (HDP-cidofovir), has reportedly inhibited smallpox viral replication in early in vitro and mice studies.[13] Lastly, people are not infectious during the incubation period. Some become contagious when the prodromal symptoms begin, while others are non-contagious until the rash occurs. This course facilitates timely identification. Given these circumstances, at-risk individuals would still receive vaccination within a safe period. Thus surveillance and containment is a reasonable tactic.

On the other hand, there are drawbacks to ring vaccination. It requires rapid identification of exposed individuals, and thus more intense surveillance than mass vaccination once an attack is recognized. This sudden demand for labor and resources could become a serious problem in the event of multiple attacks within a brief period. Furthermore, ring vaccination would only protect primary and secondary contacts of known exposures. Given the possibility that some cases might not be detected in a timely manner, this could increase the risk of non-immunized individuals developing smallpox. Another problem is that members of the non-exposed general public would likely demand vaccination. Public opinion polls have suggested that approximately half of US adults would want to be vaccinated when the smallpox vaccine is available.[10] Such exigency would lead to deviations from protocol and confusion regarding vaccine administration.

Best of Both Worlds

Given the assumed characteristics of smallpox, the optimal method of vaccinating the general public would depend primarily upon the type of attack sustained. If an attack or few attacks were localized, ring vaccination would be a more reasonable strategy. It would facilitate efficient use of resources, appropriate protection and minimization of adverse reactions. However, in the event of multiple attacks or high risk of multiple subsequent attacks, mass vaccination would be more appropriate. Mass vaccination would provide protection to the large numbers at risk and reduce the need for intensive surveillance. This situation-based approach would maximize resource utilization while minimizing morbidity and mortality. Moreover, mass vaccination may be especially advantageous in dense island populations such as Oahu, to best avoid a reprisal of the devastating effect the virus had in Hawaii's smallpox- naïve population in the 19th century. In contrast, ring vaccination may be preferred on the less populous neighbor islands, especially in more geographically isolated communities such as Hana where surveillance may be conducted more readily and efficiently.

Mathematical models evaluating smallpox vaccination policy options are in agreement with this situational approach. Modeling takes into account several possible scenarios, characteristics of the virus, response logistics and varying probability of attack.[14,15] In general, models support a ring vaccination strategy so long as the probability of attack remains low. Once the probability of attack exceeds a particular threshold, which varies amongst models, mass vaccination may be more practical.

Regardless of vaccination strategy employed, education of the lay public must be addressed. The public should understand the mechanisms and implications of bioterror, specifically smallpox, before an event occurs. Studies have shown that the public is not knowledgeable about smallpox. In one survey, the majority of respondents believed there exists an effective treatment for smallpox, that there have been cases of smallpox within the past five years and that there is not enough vaccine for everybody in the US.[16] Such misconceptions could propagate in the community, contributing to inappropriate reactions, for example hysteria. Education would prepare the public to respond calmly and aptly.

Conclusion

In conclusion, mass vaccination and ring vaccination are the two major vaccination strategies that may be used in response to a smallpox bioterror event. Mass vaccination, which entails indiscriminate vaccination of the entire population, would be appropriate for multiple attacks, if risk of subsequent attacks is high, and in dense urban island populations such as Oahu. Ring vaccination, which entails surveillance with subsequent vaccination of high-risk individuals would be more appropriate for a localized smallpox attack and low risk for subsequent attack, such as on less populated, more geographically isolated communities on the Neighbor Islands. Thus, both ring and mass vaccination have a place in response to smallpox exposure. The choice between the two is situational.

Acknowledgements

The authors thank Dr. Robert Kim-Farley and Susan Foo, MAE for their invaluable feedback regarding this manuscript.

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In conclusion, the WWW can be used to facilitate the editing process of organizing a textbook. It is also a new medium for academic publishing, which can be used to facilitate the professional and academic development of faculty.

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