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The social, political, ethical, and economic aspects of biodefense vaccines

Gregory A. Poland[a,b,c,*], Robert M. Jacobson[a,b,d], Jon Tilburt[c,e], Kristin Nichol[f]

[a] Mayo Vaccine Research Group, Mayo Clinic, Rochester, MN 55905, United States of America
[b] Program in Immunovirology and Biodefense, Mayo Clinic, Rochester, MN 55905, United States of America
[c] Department of Internal Medicine, Mayo Clinic, Rochester, MN 55905, United States of America
[d] Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN 55905, United States of America
[e] Division of General Internal Medicine, Mayo Clinic, Rochester, MN 55905, United States of America
[f] University of Minnesota, Minneapolis VA Medical Center, United States of America

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ABSTRACT

Besides natural disasters and naturally occurring novel infectious diseases, nothing potentially threatens the health and stability of nations and health systems as much as the devastating threat and unfathomability of bioterrorism. Other than attempts at political solutions and interdictive attempts, only antimicrobials and vaccines offer possible means for protection. Of these, vaccines offer the most immediate and definitive of preventive solutions. Limiting the development and use of vaccines however are social, political, ethical, and economic considerations, and this article will provide a brief exploration of each of these issues and the intersection with the need for such vaccines. In this article we define bioterrorism as the deliberate use of naturally occurring or bioengineered microorganisms in order to cause harm to people, animals, or plants.

1. What is the concern?

History informs valid concerns regarding bioterrorism. While a thorough discussion is beyond the scope and intent of this paper, it is clear that States, lone individuals, and political/terrorist groups have and mean to acquire and use biologic weapons in order to achieve a variety of political ends. In addition, widespread population susceptibility to these agents exists, placing the sustainability of nations at risk should a widespread bioterrorism event occur. In 2001, within the United States 22 cases of inhalational anthrax resulted from weapons-grade anthrax powder sent through the US postal system, resulting in 5 deaths. These attacks resulted in disruption of the postal system, the Senate and Senate buildings, airlines, and multiple other entities important to national economy and political life.

Similarly, an outbreak of monkeypox in the US and concerns over use of smallpox as a weapon resulted in large scale vaccination programs against smallpox in US military forces, and attempts at implementing a similar program among civilian health care workers and first responders [1,2]. In combination with increasing global political instability and radical fundamentalism, valid concerns over the ability to protect the civilian population against agents of bioterrorism remain widespread. Recognition of this threat, and methods with which to mitigate the threat, remains at the highest levels and with much public debate.

2. Current vaccines

At the current time only a limited number of FDA-licensed vaccines against bioterrorism agents exist in the US. These are vaccines against smallpox and anthrax. A number of biodefense vaccines in IND (investigational new drug) status exist, but are only used in extremely limited, special circumstances, and are neither suitable for nor available for widespread use in the civilian populations. In addition, passive immunization utilizing hyper-immune globulin is available for smallpox. Thus, for the majority of infectious disease bioterrorism threats, we, in fact, have no useful vaccine countermeasures. The Centers for Disease Control and Prevention (CDC) lists many infectious agents of concern (Category A–C agents) that could be used as agents of bioterrorism. This, of course, does not include the possibility of bioengineered agents.

A variety of issues conspire to make the use of the currently licensed vaccines among the general public not feasible. Chief among these are cost, limited vaccine availability, and reactogenicity/adverse events. Smallpox vaccine is a live virus vaccine, and as such a large number of contraindications exist such that an estimated 30–50% of the general public would be ineligible to receive the vaccine absent a high risk of exposure or actual exposure. For

* Corresponding author at: Mayo Vaccine Research Group, Mayo Clinic and Foundation, 611C Guggenheim Building, 200 First Street SW, Rochester, MN 55905, United States of America. Tel.: +1 507 284 4968; fax: +1 507 266 4716.
E-mail address: poland.gregory@mayo.edu (G.A. Poland).

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example, smallpox vaccine is the most reactogenic of all currently licensed US vaccines, and can lead to death (rare) and serious or life-threatening adverse reactions [1]. An additional concern for smallpox vaccine is that of human-to-human transmission of the vaccine virus to others.

As another example, at the current time anthrax vaccine requires a series of 6 injections over 18 months, followed by yearly boosters, making administration among the public impractical, absent a quantifiable risk of exposure. While some members of the US military receive this vaccine, limited availability of the vaccine is an issue, and the vaccine is not available to citizens on a routine basis.

3. Political concerns

Political concerns play an important decision-making role in both the decision to develop and the decision to use biodefense vaccines. Due to the sizeable time and monetary costs incurred, embarking on a vaccine development program must be informed by evidence of a credible threat. The decision by one country to develop a vaccine against a bioagent implies knowledge that another country has weaponized such an agent and has the intent, will, and means to use the agent as a bioweapon. The sudden resumption of use of smallpox vaccine among one nation's military, prompts concern and use in other countries. Politically this sends an important message to neighboring or other nations. Within domestic politics concerns also exist. The development of new vaccines is expensive, and funding such a program means diverting funds from other needs. This complicates decision-making and introduces a variety of considerations difficult to reconcile among the public.

4. Ethical concerns

Bioterrorism poses real dangers and societies possess a moral obligation to mitigate that risk [3–5]. Nevertheless, discussions of biodefense preparedness can lead to political battles, involve serious questions of research ethics, challenge the boundaries of professional obligation, and require important value judgments once ready for implementation. Mistakes in any of these sensitive areas can jeopardize the integrity of healthcare professionals and public health officials and their established bond of trust with the public.

As history teaches, when war, terrorism and fear mix, decision makers are susceptible to the influences of bias and political interests. King has argued that by framing risks of emerging very large public health problems in terms that make particular interventions (vaccines) appear necessary, logical, or practical; scientists and politicians build alliances and thereby acquire power and resources [6].

On a practical level, biodefense vaccine development and implementation raise several ethical challenges most notably in three areas: establishing informed consent during clinical testing, defining professional obligations of healthcare workers to participate in vaccine development research and fairly allocating vaccines once developed. Ethical standards of informed consent require autonomous authorization from participants with decision-making capacity informed of the risks and benefits of the research [7]. In particular, this principle must extend to all members of society and participation in studies of or receipt of experimental vaccines must not be presumed or forced upon anyone—absent exceptions codified in just law. As one challenging example, the development of biodefense vaccines could require development and testing of novel methods of delivery whose risks and benefits are largely unknown, making informed consent difficult or impossible.

Risk is the product of probability of an event multiplied by the severity of the event. For biodefense vaccines, there is considerable uncertainty about how to determine the probability of adverse events, as well as the probability of benefit, absent defined or known risks of exposure. Thus, disclosing the risks and benefits of participation in vaccine trials absent a current and tangible bioterrorism threat may be especially difficult. It is hard to image how, for instance, a healthcare worker should think about the personal risks and potential benefits of participating in a trial of a novel smallpox vaccine—the frequency and severity of a future attack is virtually incalculable, and the marginal benefits therefore are hard to conceptualize. Thus, often the risks as well as the benefits of biodefense vaccines are and will remain unknown until after their implementation. For this reason, research participation in the case of biodefense vaccines exacerbates the general challenges in research ethics related to informed consent. In such cases, we especially need to acknowledge the limitations of informed consent and insure that additional ethical safeguards beyond informed consent are in place such as the use of "best interest" standards, extensive community involvement, or additional layers of independent oversight. Each of these has been used in other circumstances where obtaining consent is not possible.

Establishing a strong professional obligation of healthcare workers to participate in vaccine development activities is also a challenging task. The fledgling attempts to get healthcare workers to accept smallpox vaccination as part of the 2002–2003 Federal plan to create smallpox response teams illustrated this struggle. The plan faced stiff opposition from individuals, institutions, and professional organizations. Even after legislation clarified liability concerns, health care professionals responded meagerly. While healthcare professionals clearly have an obligation to subject their interests and needs to that of the patients they serve, absent an actual outbreak, it is difficult to see why healthcare workers have a special duty to participate in vaccine development research. Thus, a well-founded case establishing a professional obligation for healthcare workers to participate in such research based on national security interests has not yet been developed, given that healthcare workers signed up for patient care, not national defense. Unlike the case of routine seasonal influenza where the risks are clear and moral obligations of the healthcare provider unambiguous [8], in the setting of bioterrorism, at best professions have a general, collective responsibility to promote public health preparedness but not necessarily a specific individual obligation [9].

Once vaccines are developed, tested and are ready for implementation other tough ethical choices will need to be made [10,11]. These include deciding who gets priority in receiving first dosing of vaccines, and what freedoms can be limited for the sake of the public good. These choices may well raise serious questions about where our personal and civic obligations lay in the setting of pandemic or bioterrorism conditions [12].

It is important to notice that under conditions of scarcity, either we will make deliberate allocation decisions based on sound principles, or expedience, self-interest, and serendipity will prevail. In the case of pandemic influenza preparedness, Persad et al. have proposed a "fair lifespan" model of rationally allocating scarce vaccines. They propose that those whom families and society have invested most in should be given the greatest priority to live a full life [13]. Others would resist such a consequentialist rationale; but regardless of ones final judgment about specific allocation proposals, we must admit that without defensible and proactive allocation principles biodefense vaccine implementation is likely to exacerbate existing inequities in public health.

We would argue that these and other ethical decisions must involve public, truthful, and balanced deliberations to insure long-term public trust and sustainability of the public health objectives of biodefense preparedness. However, achieving such a standard will be no small task.