Anthrax Vaccine Absorbed and the InterAgency Board's (IAB) Standardized Equipment List (SEL)

BACKGROUND

Some local public health and biosecurity advisors, supported by the manufacturer of anthrax vaccine, wish to include anthrax vaccine absorbed (AVA) on the Department of Homeland Security (DHS) Authorized Equipment List (AEL) and the IAB's SEL for prophylactic vaccination of civilian emergency responders in the United States.[1] This vaccine is the only Federal Drug Administration–approved anthrax vaccine and would protect immunized individuals from weaponized *Bacillus anthracis*. In addition to protecting local emergency responders from inhalational anthrax following an attack with this agent, expansion of the vaccine's market may improve its commercial viability and availability.

Several justifications have been cited for their position. First, post-exposure antibiotic prophylaxis (PEP) may not be effective in covert attacks or if the inhaled dose vastly exceeds the ID_{50}, thereby accelerating onset and acuity of the infection. Bioengineered strains not sensitive to antibiotics may also be used in an attack. The public health and point-of-distribution infrastructure may not be adequate to ensure timely PEP of all first responders following an attack. Finally, since "federal" responders were immunized against anthrax, failure to vaccinate local emergency responders represents unequal protection of the workforces and discrimination against first responders.

CURRENT RECOMMENDATIONS

In 2000, the Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination with AVA only for workers with substantial risk of occupational exposure.[2] Specifically, laboratory personnel involved in "production quantities or concentrations of *B. anthracis* spores" and those engaged in activities that are likely to aerosolize the spores should be vaccinated. The committee did not recommend vaccination of first responders as their risk of exposure to weaponized anthrax was not definable but considered to be small. The availability of effective antibiotics with or without vaccine for post-exposure prophylaxis was also mentioned as a mitigating circumstance for first responders. The panel did not comment on either a presumption or the effectiveness of personal protective equipment (PPE) for first responders in environments potentially contaminated with anthrax spores.

The ACIP released supplemental guidance on vaccination with AVA after the anthrax attacks of 2001.[3] Vaccination was recommended for those at risk for *repeated* exposure to spores, including workers doing environmental remediation of contaminated facilities and Laboratory Response Network personnel who were processing confirmatory samples. These supplemental recommendations were predicated on limited supplies of the vaccine and were actually presented

as priorities rather than as absolute indications. It is possible that groups such as first responders that were not named as priorities at that time might be appropriate candidates for immunization if vaccine supplies are not limited. These supplemental recommendations were also informed by the knowledge that 10,000 workers who were potentially exposed to the anthrax-contaminated mail took post-exposure antibiotic prophylaxis (with variable levels of compliance). There was a not single case of anthrax observed in this population. The existence of an efficacious alternative to prospective vaccination in preventing fatal inhalational anthrax allowed the ACIP to save immunization for those who were exposed.

In 2007, the ACIP was asked by the Health and Human Services Assistant Secretary for Preparedness and Response to update the recommendations for first responders in view of the expanding supply of AVA and the recent study demonstrating roughly equivalent protection but decreased adverse effects using a new route and regimen of vaccination with AVA.[4] Although its revised formal recommendations have not yet been released, it has been reported[5] that the ACIP approved the following language regarding local emergency responders:

> "Occupational groups engaged in response activities, including, but not limited to, police departments, fire departments, hazardous material units, government responders, and the National Guard, are not routinely recommended to receive anthrax vaccine due to lack of a calculable risk assessment. However, selected groups with potential engagement in response activities that may lead to exposure to aerosolized *B. anthracis* spores may choose to offer their workers pre-event vaccination on a voluntary basis and under the direction of a comprehensive occupational health and safety program."

RISK: BENEFIT CALCULUS

Since the vaccine is efficacious, the potential benefit can be assessed only if there is a quantifiable danger of exposure and subsequent illness. [6] The likelihood that local emergency responders will be occupationally exposed to anthrax derives from (1) the threat of a natural or intentional release of spores in a local area, (2) the nature of calls to which a particular emergency service may be dispatched and (3) the type(s) of PPE worn by responders on those calls. The risk of acquiring anthrax following exposure appears to vary individually but also depends on proximity to the source and the duration of exposure to the spores.[7] Since the targets of bioterrorism are seldom known ahead of time, the probability of a domestic attack over a given time interval is unknown, and post-attack functions of law enforcement, fire/rescue, and EMS personnel may vary, the probability of exposure and subsequent illness cannot be reliably quantified. [8]

"Risk" in the present risk:benefit calculus refers primarily to the probability of adverse effects from the vaccine. In Department of Defense experience, up to 35% of those receiving AVA suffered minor reactions at or near the injection sites that lasted for a few days. Minor reactions typically included localized pain, swelling, and redness at the injection site, and lasted for 24–72

hours. Fewer than 10% of those vaccinated reported systemic or severe local reactions.[9] Systemic reactions that were reported included fever, rashes (16%), headache (14%–25%), arthralgias (12%–15%), nausea, and allergic reactions, generally resolving within a few days. In 750 person-years following vaccination, there were 10 incidents of vaccine reactions requiring hospitalization.[10]

In one cohort of military personnel that was followed longitudinally through the six-injection immunization process, an average of 3.9% of males and 5.8% of females were temporarily unable to perform their normal duties due to pain, limited range of motion at the elbow, and upper extremity swelling following each injection. Interference with ability to work was highest after the initial dose (6.0% of males and 12.2% of females) and decreased after that.[11] The threshold for inability to work will likely be lower in some first responders than in military personnel and will result in considerable loss of wages as most are paid on an hourly basis. Firefighters will be at particular risk of temporary disqualification due to vaccine reactions. Their safety depends on their strength, agility, and ability to tolerate PPE as well as conditions that predispose them to uncompensable heat stress. The preliminary data on six months of experience with the IM regimen showed fewer minor, localized, adverse reactions such as arm swelling, nodule formation, and immediate injection site pain compared with the SQ regimen, although subsequent pain, stiffness, and systemic reactions were about the same and total incidence of adverse reactions still approaches 50%.[4]

From a policy perspective, the risk:benefit ratio might also be analyzed according to the benefits that would accrue to a community or even the nation rather than the individuals if first responders are vaccinated against anthrax. If most emergency responders were immune to anthrax, then they could continue their essential functions following an anthrax attack. Furthermore, they would not burden local pharmaceutical distribution systems following such an attack. In their studies modeling interventions that would mitigate the consequences of a large-scale anthrax attack, Wein et al.[12] reported that first responders must be prospectively vaccinated to ensure adequate staffing for time-critical distribution of countermeasures and medical care of symptomatic patients.

IAB ACTION PROPOSED BY MSG

The MSG of the IAB has considered addition of AVA to the SEL for use in voluntary, prophylactic immunization of first responders against anthrax and has declined to do so for a number of reasons:

1. None of the vaccines routinely recommended for health-care workers[13] as part of their occupational medical programs are included in the SEL.
2. No vaccines that address other biological threats, e.g., smallpox (vaccinia), are included in the SEL.
3. The ACIP apparently does not plan to recommend AVA for first responders in its updated guidelines. The information currently available indicates a permissive stance with respect to

response agencies whose occupational medical programs wish to purchase, administer, and monitor AVA for members who voluntarily request vaccination.

4. The MSG believes that inclusion of AVA on the SEL implies some endorsement of its use for voluntary, pre-event vaccination programs for local emergency responders that does not reflect its current position. It should be noted that addition of AVA to the SEL as part of a post-exposure regimen that also includes prophylactic antibiotics was not requested and was not considered by the MSG.
5. The MSG is concerned that marketing of AVA to occupational medical providers of first responder agencies will convey a level of threat that cannot be confirmed or refuted by reliable intelligence available to them.
6. The MSG believes it is the responsibility of Department of Homeland Security (DHS) to evaluate the threat of domestic anthrax attack through classified and other sources of intelligence. Further, it is the responsibility of the Centers for Disease Control and Prevention (CDC) to use the DHS threat assessment to make recommendations regarding whether or not local emergency responders should be vaccinated. This recommendation should be based on benefits to the personnel and/or to national preparedness that outweigh the risk and cost of vaccination.
7. The MSG believes that individual personnel should not be asked to decide for themselves whether to voluntarily receive AVA offered by their local occupational medical providers. If vaccination of certain subsets of first responders is justified by DHS and recommended by CDC, a program similar to that set up for smallpox vaccination in 2002–2003 (including surveillance and compensation of personnel suffering adverse effects) should be established.

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