Operational Concerns during an Anthrax Mass Vaccination Campaign

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Advisory Committee for Immunization Practices
October 26, 2017
U.S. Licensed Anthrax Vaccine

- Anthrax Vaccine Adsorbed (AVA (BioThrax®))
  - Manufactured
    - Michigan Dept of Health until 1998
    - Currently Emergent BioSolutions
  - Sterile, cell-free filtrate made from microaerophilic cultures of avirulent, non-encapsulated *B. anthracis* V770-NP1-R

- Final product
  - 1.2 mg/mL aluminum (added as aluminum hydroxide in 0.85% sodium chloride)
  - Contains as preservatives: 25 µg/mL benzethonium chloride and 100 µg/mL formaldehyde
  - Primary immunogen is protective antigen (PA)
AVA Updates Since Last ACIP Recommendations in 2010

- **AVA Licensure Changes**
  - Change to IM administration for pre-exposure prophylaxis – 2008
  - Elimination of priming dose at week 2 for pre-exposure prophylaxis – 2008
  - 0-1-6 month priming schedule (3-IM) – 2012
    - Protection achieved at 6 months
  - First EU approval in Germany for pre-exposure prophylaxis – 2013
    - 3-IM priming, 3-year booster
  - PEP Licensure using SC administration – 2015

- **New Data**
  - Additional safety studies
  - Animal models supporting AVA PEP approval and planned BLA application for next generation anthrax vaccine (AVA plus CPG 7909 (NuThrax®))
  - Dose-sparing studies
Licensed Indications

- **Pre-Exposure Prophylaxis (PrEP)**
  - Intramuscular (IM) route
  - 3-dose priming series at 0, 1 and 6 months
  - Booster doses at 12 and 18 months, then annually

- **Post-Exposure Prophylaxis (PEP)**
  - Sub-cutaneous (SC) route
  - 3-dose series at 0, 2 and 4 weeks
  - Co-administration of antibiotics for 60 days
Bioterrorism

- *Bacillus anthracis* spores: the most likely bioweapon
  - Relatively easy and cheap to produce
  - Can be stored for a long time
  - Can be aerially dispersed a variety of ways
  - Odorless, colorless, tasteless
  - Inhalation anthrax is highly lethal
  - May survive > 40 yrs

- Can cause widespread illness and death among unprotected persons
  - Sverdlosk incident, 1979
  - US mail incident, 2001
Hypothetical Wide Area Outdoor Release

[Map showing infection risk by geographic area with color-coded risk levels and marked sites such as airports and features like Friendship Village and McLean.]
Federal Response to a Wide-area Release of *B. anthracis* Spores

- CDC stockpiles medical countermeasures
  - Oral antimicrobials and vaccine for PEP
  - Parenteral antimicrobials and antitoxin for treatment
  - Ancillary supplies

- Individuals exposed to aerosolized *B. anthracis* spores should receive 60 days of oral antimicrobial in conjunction with a three-dose course of anthrax vaccine

- PEP should be started as soon as possible
60-day Anthrax Response Timeline

**DAY 0-1**
Direction to Deploy SNS Assets
- 10 DAY unit of use (u/u) PEP oral antimicrobials
  - Doxycycline and Ciprofloxacin

**DAY 2-8**
- 50 DAY u/u PEP oral antimicrobials
  - Doxycycline
  - Ciprofloxacin
  - Amoxicillin
  - AVA Shipment 1 of 3

**DAY 3-10**
Equipment/Supplies
- Available Upon Request to Healthcare Facilities
  - IV Antimicrobials
  - Antitoxins

**WEEK 2**
AVA Shipment 2 of 3

**WEEK 4**
AVA Shipment 3 of 3
Operational Concerns

- Supplies for administering vaccine
  - CDC SNS does not stockpile sufficient numbers of 5/8” needles to administer stockpiled vaccine via SC route
  - Manufacturer supply chain does not have sufficient 5/8” needles either
  - 1” needles supplies are more available and come closer to meeting needs

- CDC SNS will start transitioning to AVA plus CPG 7909 (NuThrax®) in 2018
  - During the transition over next 4-5 years, SNS will have two vaccines with two different routes of administration

- In a large anthrax event, efficiency of administering vaccine to a large number of people is a major concern
  - IM administration could be technically easier and faster than SC
Approximately 10,000 persons were recommended for at least 60 days of antimicrobial prophylaxis to prevent inhalational anthrax.

Interviews on 6,178 persons recommended PEP
- Most of the respondents were 40–64 years of age
- 60% were men

Adherence to Antimicrobial PEP – Anthrax Event 2001

- 787 (13%) never started their antimicrobial prophylaxis

- 2712 (44%) persons reported taking antimicrobial prophylaxis for 60 days

- Reasons for stopping included
  - Adverse events (43%)
  - Perceived a low risk for anthrax (25%)
  - Identified fear of long-term side effects from antimicrobial PEP (7%)

Adherence to Antimicrobial PEP – Anthrax Event 2001

- Florida: 31%
- New Jersey: 61%
- Hart Senate Building: 58%
- Brentwood facility: 64%
- New York City: 21%
- Connecticut: 22%
PEP Following Laboratory Incident at CDC

- 42 individuals potential exposed to *B. anthracis* spores were recommended to receive 60 days of antimicrobials and AVA 3-dose series
- Information regarding antimicrobial adherence was available for
  - 29 (69%) at day 30 of PEP
  - 18 (43%) at day 60 of PEP
- Of the 29 individuals who responded to the survey
  - 28 (97%) started the antimicrobial PEP course
  - 15 (52%) reported discontinuation by day 30
- Of the 18 who responded at day 60, only 6 (33%) surveyed reported completion of the 60-day antimicrobial PEP
- Reasons for stopping antimicrobial PEP early
  - Low perceived risk (9/14 (64%))
  - Experiencing AEs (5/14 (35%))

Estimates of Adherence to Antimicrobial PEP

- 10% who get PEP will not take it
- 90% still take PEP at 1-15 days
- 75% still taking PEP at 15-30 days
- 50% still taking PEP at 30-45 days
- 25% still taking PEP at 45-60 days
Adherence to PEP Vaccine

- Little data on the effect of adverse events and vaccine adherence in emergency situations
- AVRP study evaluated an alternative administration route and a reduced priming and booster schedule
- Intramuscular administration results in a lower proportion of injection site adverse events compared to subcutaneous administration
- No association between drop-out rate and route of administration
Summary of Work Group Discussions

- **Operational Concerns**
  - Supplies to administer vaccine
  - Two vaccines with different routes of administration
  - Efficiency of response

- **Adherence to antimicrobial PEP**

- **Adherence to vaccine PEP**