Anthrax Vaccine Immunization Program

Health-Care Provider's Briefing

Key Messages

- **Your health & safety are our #1 concerns**
- **Anthrax vaccine is safe and effective**
- **The threat of anthrax is deadly and real**
- **Vaccination offers a layer of protection, in addition to antibiotics and other measures, needed for certain members of the Armed Forces**

History of AVIP

- **Secretary of Defense ordered the AVIP in Dec 97**
- **Vaccinations began in Southwest Asia in Mar 98**
- **Vaccinations began in Korea in Aug 98**
- **Vaccine shortage caused slowdowns in 2000-2001**
- **AVIP resumed in 2002, after supply of FDA-licensed anthrax vaccine restored**
- **Injunction imposed, then lifted:**
  - **Federal Judge ordered injunction 22 Dec 03**
  - **FDA ruled anthrax vaccine effective regardless of route of exposure on 30 Dec 03**
  - **Judge lifted injunction on 7 Jan 04; DoD resumed AVIP**

Status of AVIP

- **Status:**
  - **FDA ruled anthrax vaccine is safe and effective regardless of route of anthrax exposure**
  - **Mar 98 to Jan 04: Over 3.7 million doses to over 1 million people**
  - **18 human safety studies**
  - **7 reviews by independent panels of civilian physicians, each affirming safety and effectiveness of the vaccine**

Independent Scientific Reviews

- **Food & Drug Administration (*Federal Register* 2004; 69: 255-67**
- **Armed Forces Epidemiological Board (AFEB), advising DoD, 1994 to present**
- **Cochrane Collaboration, Oxford, *Vaccine* 1998; 16: 880-884**
- **Working Group on Civilian Biodefense, *JAMA* 1999; 281: 1735-1745**
- **CDC's Advisory Committee on Immunization Practices (ACIP) (*MMWR* 2000; 49 (RR-15): 1-20)**
- **Anthrax Vaccine Expert Committee (AVEC), 1998 to present (*Pharmacoepid Drug Safety* 2002; 11: 189-202)**
- **National Academy of Sciences (IOM), Mar 2002**

AVIP Lessons Learned

- **We must ensure a continuous supply of vaccine**
- **We must educate all stakeholders early: patients, family members, health-care professionals, general public**
- **Our patients perceive the risk-benefit ratio from BW vaccines differently that other "routine" vaccines**
- **A strong foundation of research-based, third-party endorsed, published science is critical to credibility**
- **Health care provider involvement is the key to success**

Background: Anthrax Infections

- **Recognized as an illness for centuries**
- **Spores can survive in soil for decades**
- **Once common where livestock were raised**
- **Animal anthrax controlled using vaccine for livestock**
- **Human infection may result from direct contact with infected animals or animal products or anthrax spores**

Anthrax

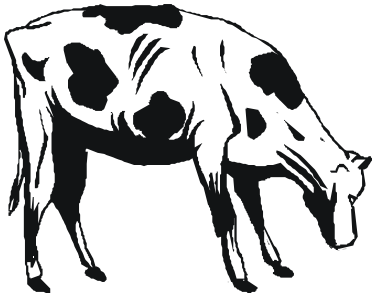
- **Anthrax can be loaded into shells, missiles, bombs, and other weapons.**
- **Inhalational anthrax is highly lethal.**
- **Vaccination is critical for <u>your</u> protection.**
- **This vaccination program is required, except for legitimate medical exemptions.**
- **Anthrax vaccine is safe and effective, according to FDA, CDC, and National Academy of Sciences.**

Threat

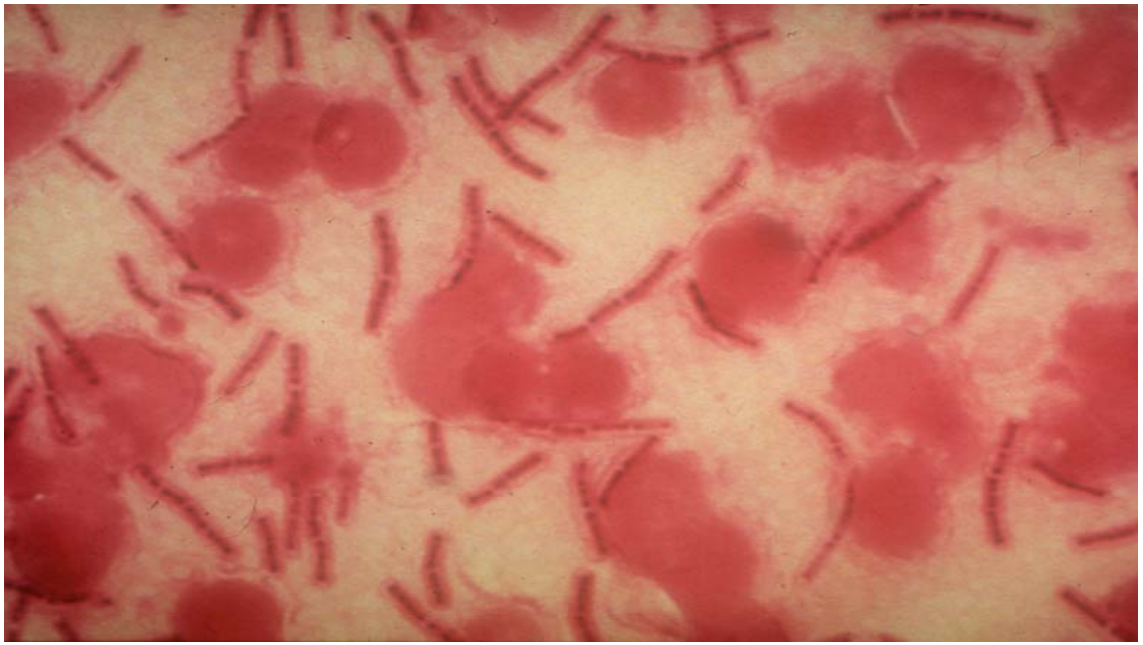
- **Anthrax: the most likely Bio-Warfare agent:**
  - **Relatively easy and cheap to produce**
  - **Can be stored for a long time**
  - **Can be dispersed in air in a variety of ways**
  - **Odorless, colorless, tasteless, difficult to detect**
  - **Inhalational anthrax is highly lethal**
- **Anthrax can cause widespread illness and death among unprotected people.**

Epidemiology of Anthrax

- **Disease of herbivores**
- **Humans infected via animal products**
- **Dramatic reduction in U.S. since early 1900s**
- **Still a problem in Asia and Africa**
- **Terror attacks via U.S. mail in Fall 2001**



Microbiology of Anthrax

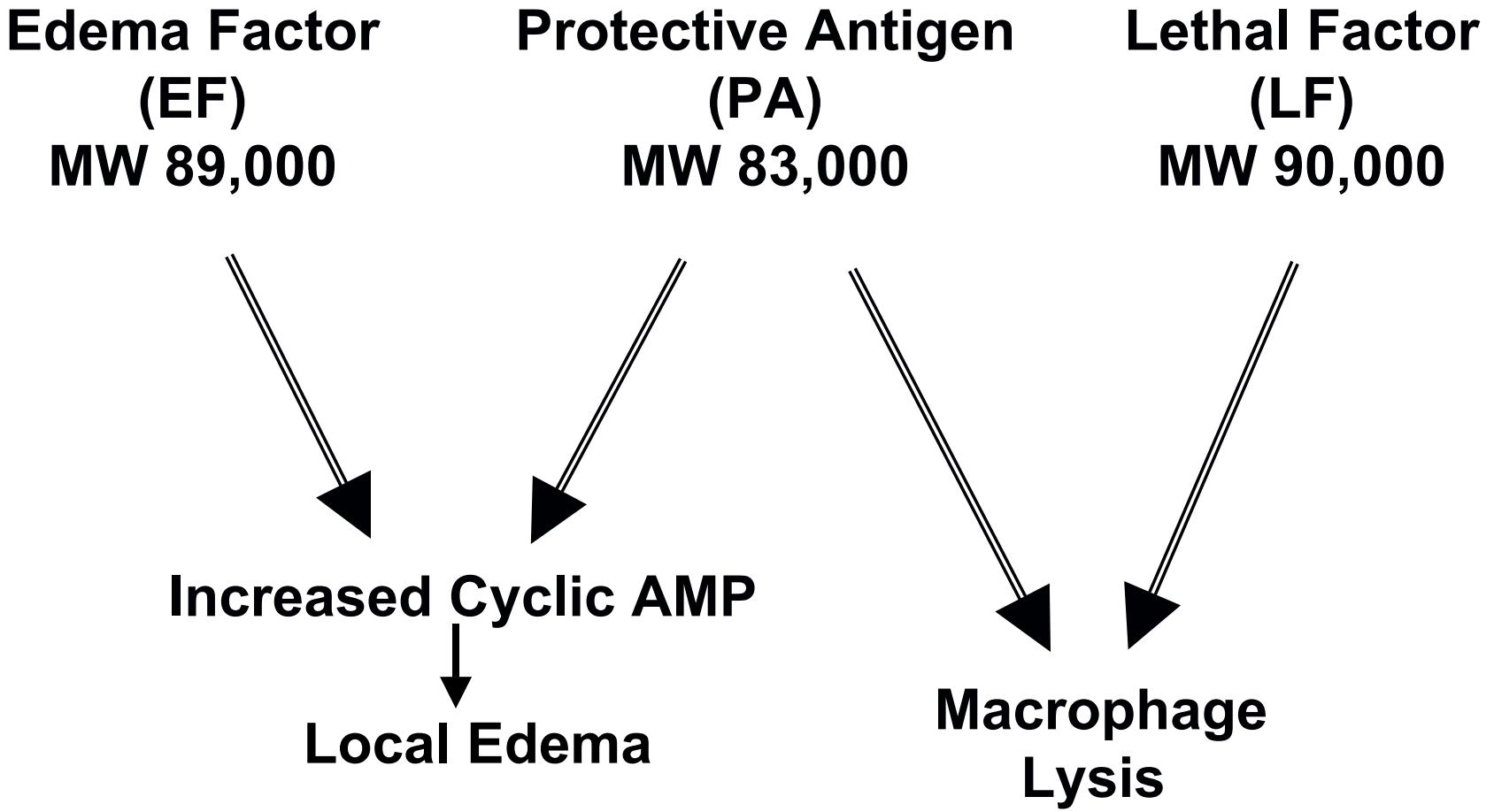


Gram-positive spore-forming rod

Pathogenesis

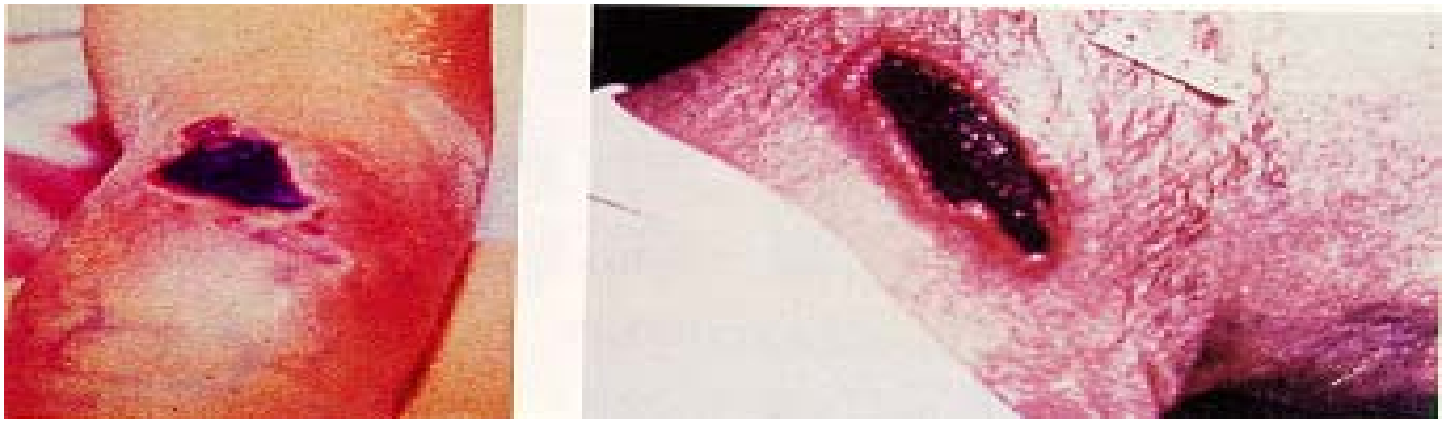
- **Spore enters skin, GI tract or lung**
- **Ingested by macrophages**
- **Transported to regional lymph nodes**
- **Germinate in regional nodes, mediastinum (inhalational)**
- **Local production of toxins**
- **Edema & necrosis**
- **Bacteremia & toxemia**
- **Seeding of other organ systems**

Anthrax Toxin Production & Effects



Cutaneous Anthrax

- **Greater than 95% of naturally occurring cases**
- **Spores enter breaks in skin after contact with contaminated animal products**
- **Within a few days, bump (papule) turns into blister (vesicle), then ulcer with black area in center (eschar)**
- **5% to 20% case-fatality rate if untreated**
- **Mortality with treatment < 1%**



Gastrointestinal Anthrax

- **Ingestion of insufficiently cooked meat from infected animals**
- **Symptoms include nausea, vomiting, fever and severe abdominal pain**
- **Lethality rate is 50% despite treatment**

Inhalational Anthrax

- **Inhalational anthrax occurs when spores enter the body through the lungs**
- **Not transmitted person to person**
- **Spores migrate to lymph nodes where bacteria multiply and produce lethal toxins**
- **Toxins cause bleeding and destruction of the brain or vital organs in the chest, resulting in death**

Diagnosis of Inhalational Anthrax

- **Initial symptoms nonspecific**
- **Development of respiratory distress**
  - **Chest X-ray with widened mediastinum**
  - **Usually no infiltrates**
- **Sputum not helpful**
- **Nasal swabs not individually meaningful (www.bt.cdc.gov/DocumentsApp/faqanthrax.asp#Q500)**
- **Blood cultures - positive late in course of illness**
- **Hemorrhagic pleural effusion or meningitis**

Chest X-Ray of Inhalational Anthrax

Inhalational Anthrax Treatment

- **Early IV antibiotics and intensive care required**
  - **Mortality may still reach 50%**
  - **Penicillin - historical treatment**
- **Current treatment of choice:**
  - **Ciprofloxacin 400 mg IV q 8-12 h**
  - **Doxycycline 200 mg IV x 1,**
    then 100 mg IV q 12 h
- **Disease not spread by respiratory secretions**
  - **Use 'Standard Precautions'**

Post-Exposure Prophylaxis

- **Starting antibiotics within 24 hours after aerosol exposure should provide significant protection**
  - **Ciprofloxacin 500 mg po BID**
  - **Doxycyline 100 mg po BID**
- **Most effective when combined with vaccination**
- **Antibiotics are still indicated even when fully immunized, to achieve survival as close to 100% as possible**

Anthrax Vaccine Facts

- **Vaccine primes body's natural defense system to fight anthrax**
- **Anthrax vaccine cannot cause anthrax**
- **Licensed by the FDA since 1970**
  - **Safely administered in the U.S. to at-risk veterinarians, laboratory workers, and livestock handlers**
  - **Over 3.7 million doses to over 1 million personnel between Mar 98 and Jan 04**
- **Manufactured in U.S. by BioPort Corporation**
  - **Lansing, Michigan**

Vaccine Quality Control

- **Each lot of each vaccine manufactured in the U.S. must meet FDA specifications and prescribed standards per 21 CFR 610, before release into interstate commerce**
  - **Potency, Sterility, Purity, General Safety**
- **Testing on each lot done by manufacturer; results submitted to and audited by the FDA**

Handling Anthrax Vaccine

- **Vaccine must be refrigerated**
  - **Store and maintain between 36 and 46 degrees Fahrenheit (2 – 8° C)**
- **DO NOT FREEZE**
- **Once vial opened, use until expired**
  - **Discard if contaminated**
- **Go to USAMMA web site for guidance on vaccine temperature, storage and handling:**
  - **http://www.usamma.army.mil/anthrax/antxhome.htm**

Vaccine Efficacy in Humans

- **Brachman et al. *Am J Public Health* 1962;52:432-45**
  - **Efficacy: 92.5% (95% CI: 65-100%), jointly against cutaneous and inhalational anthrax**
  - **Inhalational anthrax:**
    - **5 cases / 448 unvaccinated people**
    - **0 cases / 149 vaccinated people**
  - **Manufacturing improvements, 1960s CDC study**
    - **Microaerophilic, more PA, less EF and LF**
  - **Safety and efficacy reaffirmed by FDA advisory panel, Federal Register 1985; 50:51002-117**
  - **Final Rule by FDA 30 Dec 03; published in *Federal Register* on 5 Jan 04, vol 69: pages 255-67**

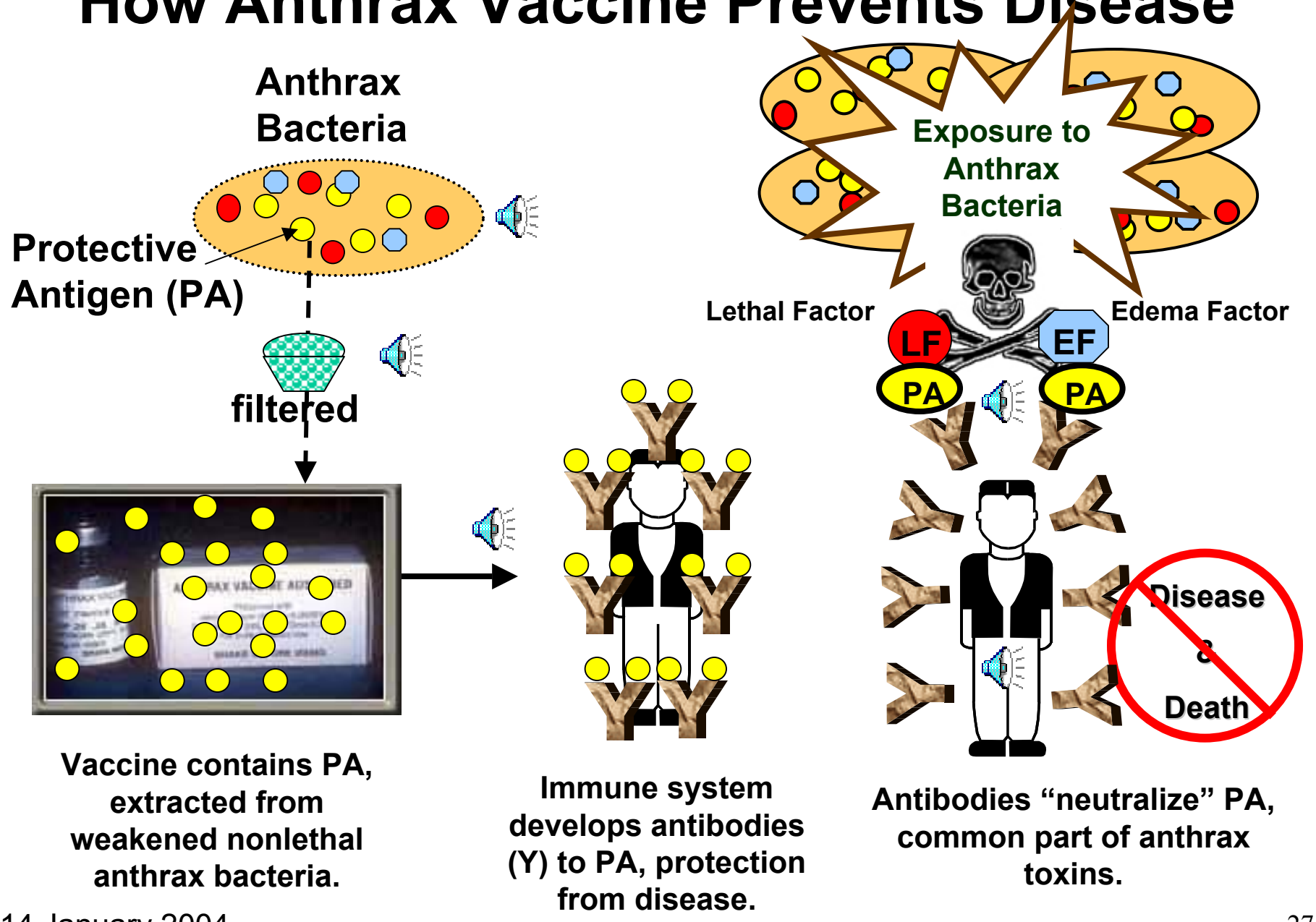
Inhalational Anthrax: Vaccine Efficacy in Non-Human Primates

- **55 monkeys vaccinated twice**
  - **Challenged with spore aerosol of dozens to thousands of times the median lethal dose, 8, 16, 38, or 100 weeks later**
  - **52 survived**
- **10 monkeys vaccinated once**
  - **Challenged with aerosol 6 weeks later**
  - **All survived**
- **Overall, 62 of 65 survived, 95% vaccine protective efficacy against inhaled anthrax spore challenge**

Response to Vaccination

- **Anthrax vaccine, like other vaccines, stimulates your body to produce protective antibodies**
- **Each dose of vaccine adds to protection, like walking up a set of stairs**
- **The full series is needed to obtain maximum and on-going protection.**

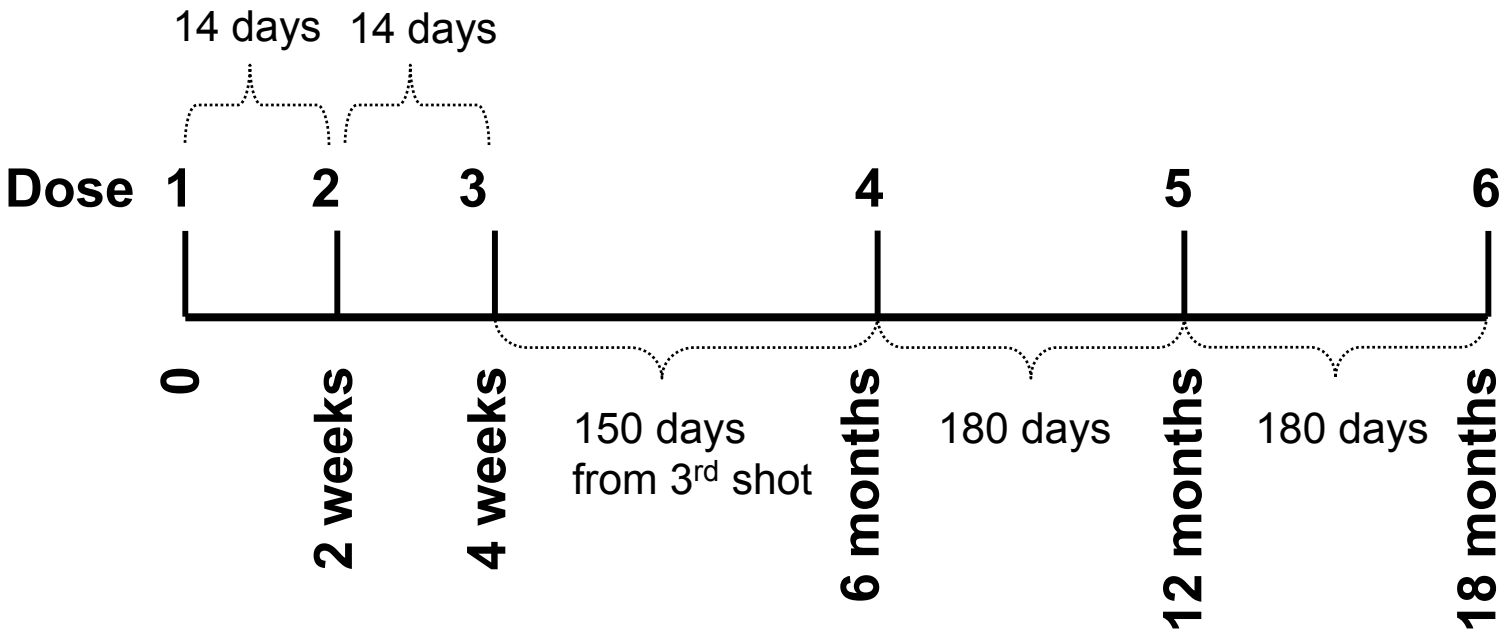
How Anthrax Vaccine Prevents Disease



Vaccine Protection Against Different Strains

- **Vaccine efficacy demonstrated against numerous anthrax strains (types) in various animal studies**
- **Protective antigen (PA) is the common disease-causing protein in all anthrax strains**
- **Blocking PA blocks the disease**
- **National Academy of Sciences: Anthrax vaccine is "an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by all known or plausible engineered strains"**

Vaccine Schedule

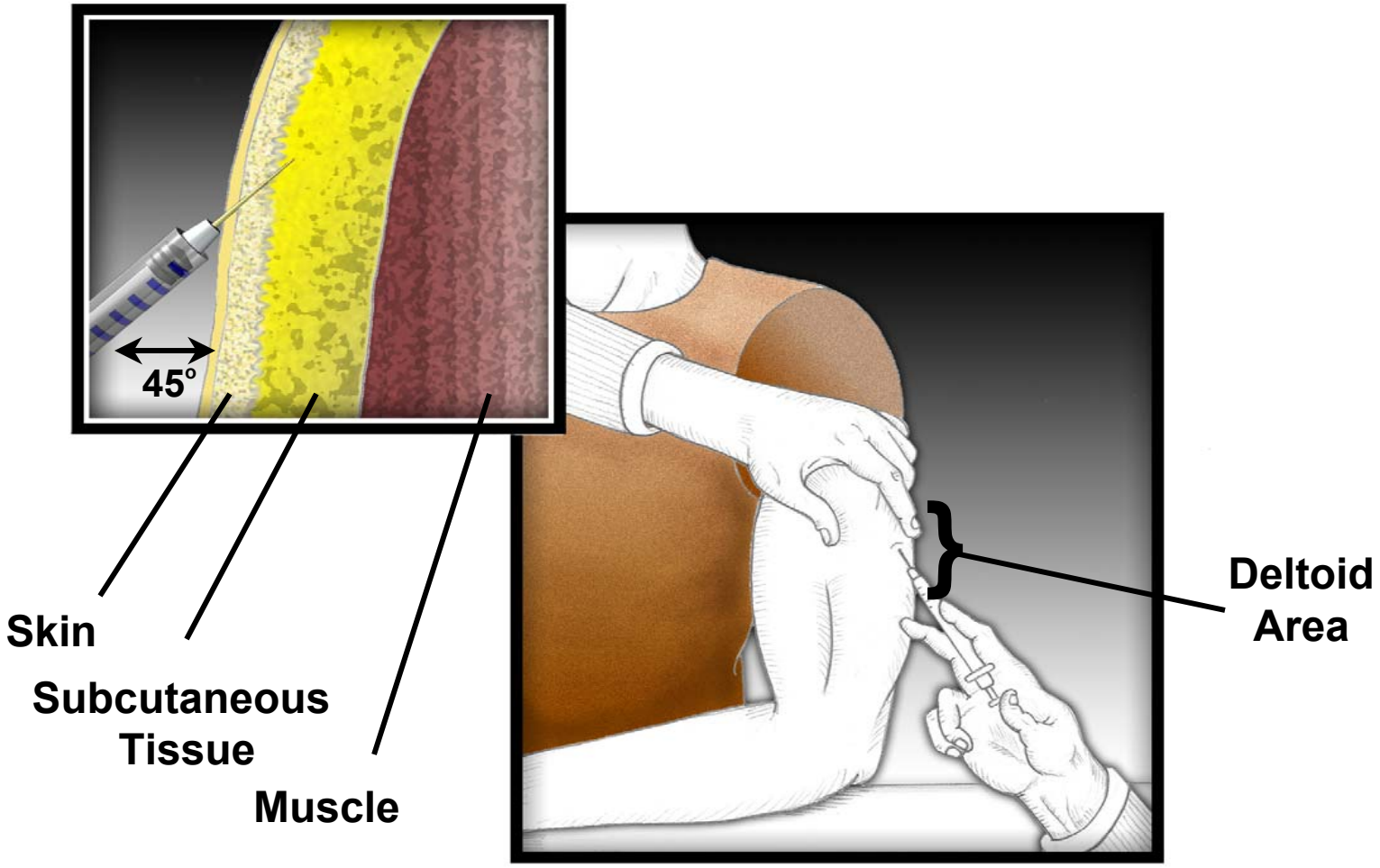


- **Six shots over 18 months, plus annual boosters**
- **Do not compress the schedule**
- **Adjust schedule for individual delays**

Anthrax Vaccination Schedule

- **DoD policy is to adhere to FDA-licensed vaccination schedule.**
- **Do NOT compress dosing schedule.**
- **Give late doses ASAP - adjust timing of later doses according to standard schedule.**
- **Use clinical judgment when managing individual cases.**
- **Seek subspecialty consultation as warranted.**

Vaccination



Pregnancy

- **Vaccinations routinely deferred during pregnancy**
- **Before vaccination, ask each woman if menses normal and on time. Postpone, if pregnancy possible.**
- **No reason to delay conception after vaccination:**
  - **Anthrax-vaccinated & unvaccinated women at Fort Stewart (*JAMA*, 2002):**
    - **same rates of conception**
    - **same rates of delivery**
- **Vaccination <u>during</u> pregnancy: Rates of birth defects under study. Rates before & after pregnancy are same as for unvaccinated women.**
- **Encourage pregnancy testing.**
- **Details at www.anthrax.mil**

Contraindications

- **Hypersensitivity reaction to a previous dose of anthrax vaccine or vaccine component**
- **Younger than 18 or older than 65 (pending further study)**
- **HIV positive**
- **Temporary deferral**
  - **Pregnancy, suspected pregnancy**
  - **Active infection/illness with fever**
  - **Depressed immune response, including corticosteroid or other immunosuppressive treatment**

Injection-Site Reactions After Anthrax Vaccination

- **For both genders, most injection-site reactions last 1 to 3 days and go away on their own**
- **From Hawaii, Korea, Ft. Bragg, Ft. Detrick, 1993-2000: Redness, itching, swelling (lasting a few days)**
  - **Less than 1 inch: men up to 30%, women up to 60%**
  - **1 to 5 inches: 1% to 5%**
  - **Greater than 5 inches: 1%**
  - **Swelling may extend below elbow**
  - **Soreness or local pain in 8% to 19%**
  - **Lump: 30% to 90% (may persist a few weeks)**

Systemic Events (Events Away from Injection Site)

- **From 5% to 35% will notice:**
  - **Muscle aches, joint aches, chills, low-grade fever, no appetite, headaches, nausea, malaise, related symptoms**
  - **Women experience these symptoms more often than men**
  - **These symptoms usually go away in a few days, less than a week**
- **Acute allergic reactions occur after any vaccine, about once per 100,000 doses**
- **Deaths have been reported rarely after any vaccination**

Injection-Site Reactions and Systemic Events

- **Screen for previous adverse reactions**
- **Treat and pre-treat adverse events**

  See clinical guidelines at www.vhcinfo.org
- **Do not give next dose if side effects persist from previous vaccination**
- **Issue temporary exemption if symptoms persist**
- **Consult provider skilled in diagnosis and management of vaccine adverse events for permanent exemption**

Long-Term Studies

- **Anthrax-Vaccine Recipients Followed for Years**
  - **TAMC-600 Survey (Tripler Army Medical Center)**
  - **Defense Medical Surveillance System (inpatient and outpatient visit surveillance)**
  - **Naval Health Research Center (inpatient and outpatient visit surveillance)**

- **Anthrax-Vaccine Recipients Followed for Decades**
  - **Fort Detrick Multi-Dose, Multi-Vaccine Safety Studies (1940s to 1970s)**
  - **Fort Detrick Special Immunization Program (1970s to present)**

Adverse Event Reporting

- **Vaccine Adverse Event Reporting System (VAERS)**
  - **FDA reviews 100% of adverse-event reports submitted to either FDA or DoD**
  - **Reviewed by independent panel of civilian physicians for 4 years**
  - **Anyone can submit a VAERS Form**
- **DoD requires a VAERS Form submission for:**
  - **Loss of duty 24 hours or longer (≥ 1 duty day)**
  - **Hospitalization**
  - **Suspected vaccine vial contamination**
- **Other submissions encouraged**
- **VAERS Form may be obtained from:**
  - **Your clinic, 1-800-822-7967, or www.vaers.org**

Reserve Component Adverse-Event Guidance

- **Someone with an adverse event in a non-duty status possibly associated to any vaccination:**
  - **Seek medical evaluation at a DoD, USCG, or civilian medical treatment facility, if necessary**
  - **Must report the event to your unit commander or designated representative as soon as possible**
  - **See local medical department or squadron for guidance**
- **Commander will determine Line of Duty and/or Notice of Eligibility status, if required**

Access to DoD Military Treatment Facility (MTF)

- **Once designated to receive anthrax vaccine, the following personnel may receive any dose at any MTF:**
  - **Active component**
  - **Reserve component (Must be in a duty status)**
  - **Emergency essential DoD civilian and contract personnel**
  - **U.S. Coast Guard as applicable**
- **Mass immunizations require prior coordination with MTF.**

Record Keeping

- **Automated immunization tracking**
  - **Service systems and DEERS central repository**
- **Written entries:**
  - **Health record**
  - **Adult Preventive and Chronic Care Flowsheet (DD form 2766 or DD form 2766C)**
  - **Yellow Shot Card (PHS-731)**
- **Required documentation:**
  - **Date immunized, name of vaccine, manufacturer, lot number, series number, dosage, provider name and MTF address**

What Troops Deserve From Their Health-Care Providers

- **Care, concern, and support**
  - **Q&A page at www.anthrax.mil explains many things of interest to your patients**
- **Quality health care, quality vaccine delivery**
- **Effective solutions to health-care needs**
- **Open communication and advice**
- **Compassion in dealing with adverse events**
- **Assistance in reporting adverse events**

Conclusions

- **Anthrax is a lethal threat to our forces.**
- **The anthrax vaccine is safe and effective.**
- **Personal protective measures are important**
- **The life-saving benefits of anthrax vaccine make this an essential immunization program.**
- **Health-care providers are key to Service Member understanding of the value of anthrax vaccination**

For Program or General Scientific Information:

- **Chain of Command**
- **AVIP Agency**
  - **Website: www.anthrax.mil**
  - **Customized answers to your individual questions via E-Mail: vaccines@amedd.army.mil**
  - **Toll-Free: 877.GETVACC**
- **CDC National Immunization Hotline: 800.232.2522**
- **www.bt.cdc.gov**
- **www.aviationmedicine.com**

For Medical Information:

If a Reserve Component or Active Duty member of the Armed Forces presents at your office for a condition they believe may be an adverse event caused by a vaccination, please provide care appropriate to their condition and contact the following as soon as possible for coordination and payment:

- **Walter Reed Vaccine Healthcare Center: 202.782.0411 (www.vhcinfo.org)**

- **Information for Civilian Healthcare Providers: Call the Military Treatment Facility (MTF) where the member is enrolled –OR– contact the Military Medical Support Office (MMSO): 888-647-6676 if the member is not enrolled to an MTF.**