Anthrax: Vaccine, Antitoxin, Chest Tubes

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Anthrax Vaccine in the USA: Approved for Use Before & After Exposure

- Different vaccines in different countries.
- In the USA only one vaccine ("BioThrax") is licensed (since 1970) by the Food and Drug Administration (FDA).
- This US vaccine does not have live bacteria.
- It is based on the "Protective Antigen (PA)" of *Bacillus anthracis,* and uses alum as an adjuvant.
- Thus, immunity is mostly antibody-based (not cellular).

Anthrax Vaccine BEFORE Exposure: 5 doses (IM) and Yearly Boosters

- For pre-exposure protection 5 doses of vaccine intramuscularly (IM) should be given at time zero, then at 1 , 6, 12, and 18 months.
- Yearly boosters recommended for ongoing protection
- The vaccine is commercially available in the US.
- (I have received >8 doses of vaccine, including in 2017)

Anthrax Vaccine AFTER Known or Suspected Anthrax Exposure Approved in 2015

- 23 November 2015, the US FDA approved use of the same “BioThrax” vaccine for post-exposure prophylaxis (PEP), along with recommended antibiotics (for 60 days)

- When the vaccine is used in this way as PEP after exposure to anthrax, only 3 doses (not 5) are given, and the vaccine is given subcutaneously (not IM) at time zero, 2 weeks and 4 weeks.

- Rationale: Immunity due to the vaccine will persist long after post-exposure prophylaxis of the antibiotic ends.

“Protective Antigen (PA)”:
An Essential Part of Both Anthrax Toxins

Lethal Toxin

- Protective antigen plus Lethal Factor

Edema Toxin

- Protective Antigen plus Edema Factor

3 Anthrax Antitoxins Approved in the USA: Focus on Antibody against Protective Antigen

- Much of the pathogenesis of anthrax is attributed to its two toxins: Lethal Toxin and Edema Toxin.

- Three antitoxins are approved by the US FDA:
- 1) Raxibacumab (2012): Monoclonal antibody to PA

- 2) AIGIV (2015): Polyclonal antibody from vaccines

- 3) Obiltoxaximab (2016): Monoclonal antibody to PA

- All are given intravenously.

Current US CDC Guidance on Anthrax Antitoxin

- CDC. Clinical Framework and Medical Countermeasures Use During an Anthrax Mass-Casualty Incident. 2015 (Dec. 4) MMWR Recomm Reports 64 (4):1-22.

- Two situations: Conventional Care and Mass Casualty

- Conventional Care: “An antitoxin should be added to the combination antimicrobial treatment for patients for whom there is a high level of clinical suspicion for systemic anthrax”. (above ref. page 15. Box 5)..

Current US CDC Guidance on Anthrax Antitoxin:
Mass Casualty with Potential Shortage of Antitoxin

- Emphasis placed on "…clinical judgment of the local triage team" as to if and when to give antitoxin, except:

- "Patients with probable, confirmed, or suspected meningitis should receive combination parenteral antimicrobial therapy plus antitoxin without delay" (p.15).

- NO specific preference given for any 1 of the 3 antitoxins

Combination IV Antibiotics Always Given with or without Antitoxin

- When meningitis excluded then one bactericidal* antibiotic PLUS one protein synthesis inhibitor**

- ***Ciprofloxacin** (preferred), levofloxacin, moxifloxacin, meropenem, imipenem, doripenem, or vancomycin
- Or for penicillin-susceptible strains: PCN G or Ampicillin

- **Clindamycin or Linezolid (either is equally preferred), or doxycycline, or rifampin (not a protein synthesis inhibitor but based on in vitro synergy).

- Same Ref (Dec 4. 2015 MMWR Recomm Rep) p.14

If Meningitis is even Suspected then give BOTH Fluoroquinolone and Beta-lactam

- **Ciprofloxacin** (or Levofloxacin or Moxifloxacin), PLUS
- **Meropenem** (or Imipenem or Doripenem),* PLUS
- **Linezolid** (or Clindamycin, rifampin, or chloramphenicol)

- (*Or for PCN-susceptible strains: PCN G, Ampicillin).

Pleural Fluid and Drainage in the 11 US Patients with Inhalation Anthrax in 2001

- (1) No drainage: > 1,000 cc at autopsy
- (2) Two thoracenteses, then chest tube
- (3) Three thoracenteses
- (4) Two thoracenteses
- (5) No drainage: 1,300 + 700 cc at autopsy
- (6) No drainage: 500 + 250 cc at autopsy
- (7) Chest tube drainage with 900 cc

2001 Cases Pleural Fluid Data (cont.)

- (8) Two thoracenteses then chest tube on right side; chest tube on left side.
- (9): Two thoracenteses
- (10): Two chest tubes (2,500 cc/ 1,000 cc)
- (11) One thoracentesis, then chest tube on left side; At autopsy rights side had 1,000 cc (newly developed in hospital, not drained).

Pleural Fluids in 2001: Large Amounts of Bacteria* and Blood

- "The characteristics of the pleural fluid in all patients were similar: hemorrhagic, with a high protein concentration and relatively few WBCs. Immunohistochemistry demonstrated large quantities of B. *anthracis* capsule and cell-wall antigens in pleural tissue or pleural fluid cell blocks." Jernigan et al. Emerg Infect Dis 2001; Nov-Dec

- *Note: Higher levels of lethal factor (from lethal TOXIN) would be found in the pleural fluid (compared with the serum) of a patient in 2006. Ref. Walsh JJ et al. Clin Infect Dis 2007; 44:968-71. thus, pleural fluid might be a reservoir for anthrax toxin.

Pleural Drainage Required for Anthrax Effusions: Infectious Diseases Text (Mandell et al.) 2005

- The “intermediate-progressive” stage of inhalational anthrax has “pleural effusions that are often large, hemorrhagic, and require repeated drainage”.

- Lucey D*. Anthrax. Principles and Practice of Infectious Diseases. 6th Ed. 2005. Mandell, Bennett, Dolin. p. 3618-3624.

- *In May 2006, initially advocated for use of chest tube drainage rather than thoracentesis.

Review of Inhalational Anthrax 1900-2005: Pleural Drainage Increases Survival

- Holty et al. Annals Internal Medicine 2006; 144:270-280.
- Total of 82 patients: 12 survived/ 70 died.
  (did *not* include patients from 1979 outbreak in Russia)
- 83% of survivors vs 9% of non-survivors had pleural fluid drainage ($p < 0.001$).
- Pleural drainage: “Bioterrorism response plans should consider the capacity to perform this invasive but potentially important procedure”.

2011 Visit to Russia to Discuss Pleural Fluid Drainage During 1979 Outbreak

- Meeting with Dr. Faina Abramova: who first diagnosed the 1979 outbreak as Anthrax, and

- Professor Dr. Lev Grinberg: who performed autopsies during the outbreak with Dr. Abramova, and published much research on anthrax in Russian & English literature

Faina A. Abramova
Doctor D.Lucey
November 2011, Yekaterinburg

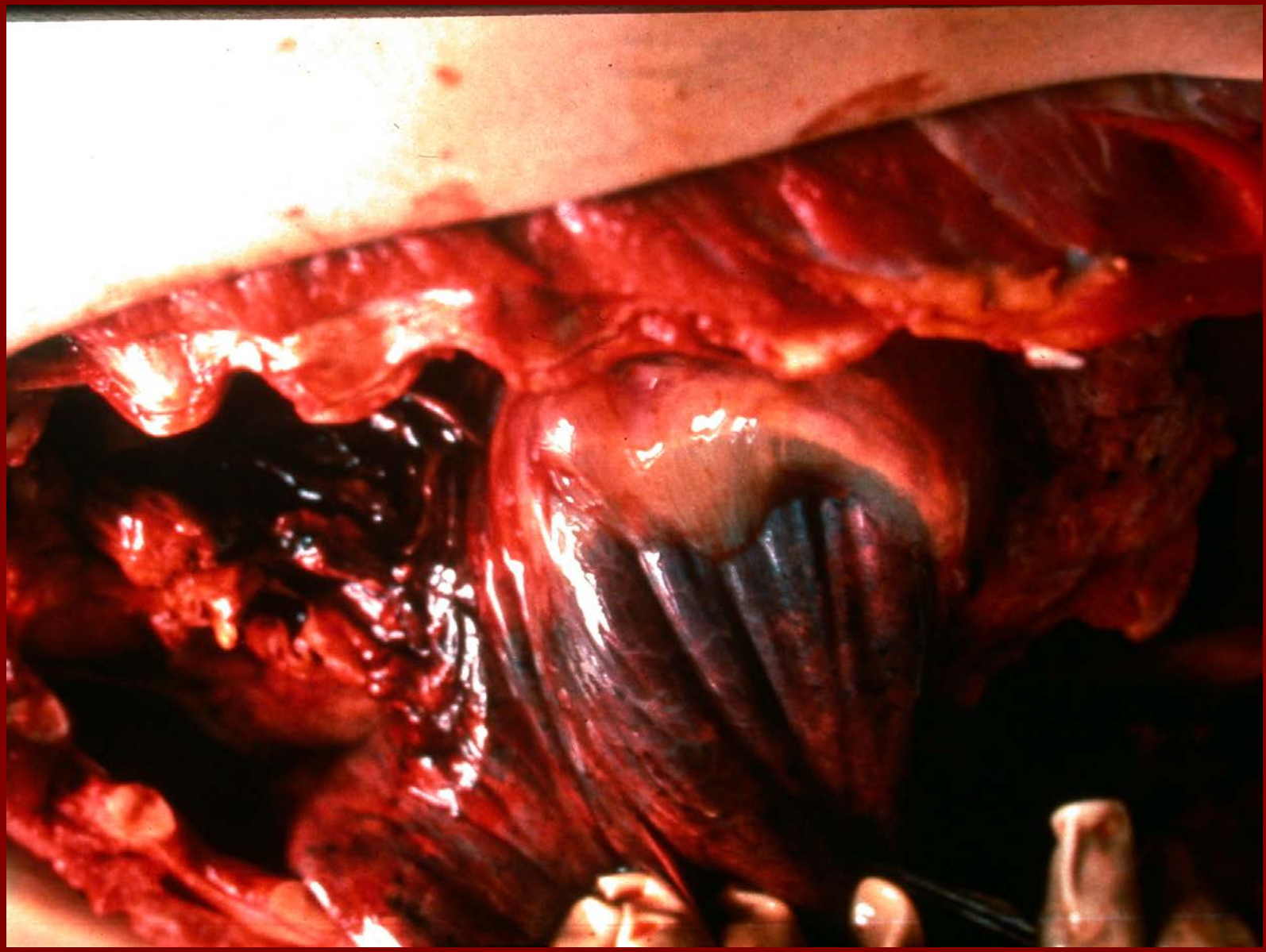
Large Pleural Effusions in 1979 Russian Outbreak

- 41 autopsies* on patients who died of inhalational anthrax in Russia (Sverdlovsk) in 1979 showed that the average volume of bilateral pleural fluid was **1,776 cc.**
- Apparent compression of lung tissue by effusions, contributing to respiratory compromise and then failure

- *Ginsberg LM et al. Quantitative Pathology of inhalational anthrax. Modern Pathology 2001;14:482-95

Pleural Gelatinous Edema

Photo courtesy of Prof. Dr. Lev Grinberg



Current US CDC Guidance on Pleural Effusions: CHEST TUBE Drainage preferred over Thoracentesis

- Conventional setting: “Early and aggressive drainage is recommended for any clinically/radiographically apparent pleural effusion.”

- “Chest tube drainage is recommended over thoracentesis because of high reaccumulation rates.

- Thoracotomy or video assisted thoracic surgery (VATS) might be required to remove gelatinous or loculated collections”.

- Ref. CDC. 2015 (Dec 4) MMWR Recomm Rep. p. 17.

Thank You

- Questions and Comments
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