Anthrax

*(Bacillus anthracis)*

As a Bioterrorism Agent
Anthrax

- A zoonotic disease of cattle, sheep, and horses
- Human infection results from direct contact with infected animals or animal products
- Spores can survive in the soil for decades
- Most likely would be released as an aerosol
- May be sent as powder/slurry resulting in limited number of exposed
Anthrax (cont.)

- Weaponized by the U.S. in 1950's and 60's
- Major emphasis of U.S.S.R. and Iraq programs
- Accidental release in Sverdlovsk in 1979 (79 cases, at least 68 deaths)
- Aum Shinrikyo Cult in Japan tried to use several times
- Released via mail Fall 2001
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 Spores

- Bacilli form spores when nutrients are exhausted
- Anthrax spores germinate in an environment rich with amino-acids, nucleosides, and glucose
What is a micron?

- 1 micron = 1/1,000,000 meter
- 1 mil = 1/1000 inch
- 1 inch = 25,400 microns
- 1 mil = 25.4 microns

- Eye of needle 1,230 microns
- Beach sand 100 – 2000 microns
- Human hair 40 – 300 microns
Inhalational Anthrax

- Infectious dose - "conventional wisdom"
  8-50,000 spores
- Incubation period: 1-5 days (up to 60)
- Initial symptoms nonspecific (2-5 d)
  - fever, malaise, sweat/chills
  - non-productive cough, chest discomfort
  - nausea, vomiting
Inhalational Anthrax (Con’t.)

• Syndrome
  – hemorrhagic mediastinitis/pleural effusion
  – rapid progression to severe respiratory distress with dyspnea, diaphoresis, stridor, cyanosis
  – 50% of cases may rapidly develop concurrent hemorrhagic meningitis with bloody cerebral spinal fluid
  – septicemia, toxic shock/death occur within 24-36 hours after onset of respiratory distress
Inhalational Anthrax (Con’t.)

- Historically high mortality rate
- Mortality in 2001 attacks – 46%
- Data are insufficient to identify factors associated with survival
Chest radiograph of patient with anthrax.

*Taken from source (6).*
Diagnosis of Inhalational Anthrax

- Radiograph: widened mediastinum (WM)
  - (7/10 recent cases had WM; 7 had infiltrates, 8 had pleural effusion)
- Sputum may be helpful
- Blood cultures
- Nasal swabs have NO clinical utility
- Hemorrhagic pleural effusion or meningitis may develop
Inhalational Anthrax: Differential Diagnoses

- Community acquired pneumonia
  - *if* infiltrate (rare) or pleural effusion present
- Pneumonic tularemia or plague
  - *if* pleural effusion present
- Hantavirus pulmonary syndrome
- Bacterial/fungal/TB mediastinitis
- Fulminant mediastinal tumors
- Dissecting aortic aneurysm
  - widened mediastinum but usually *no* fever
## Anthrax, Influenza, or other Influenza-like Illness (ILI)?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Anthrax</th>
<th>Influenza</th>
<th>ILI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever/chills</td>
<td>100%</td>
<td>83-90%</td>
<td>75-89%</td>
</tr>
<tr>
<td>Fatigue/malaise</td>
<td>100%</td>
<td>75-94%</td>
<td>62-94%</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>80%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>60%</td>
<td>35%</td>
<td>23%</td>
</tr>
<tr>
<td>Myalagia</td>
<td>50%</td>
<td>67-94%</td>
<td>73-94%</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>10%</td>
<td>79%</td>
<td>68%</td>
</tr>
<tr>
<td>Sore throat</td>
<td>20%</td>
<td>64-84%</td>
<td>64-84%</td>
</tr>
</tbody>
</table>

MMWR
Inhalational Anthrax Victim
(view of chest cavity)
The Human Brain

Normal Brain

Brain of a person who died from inhalational anthrax
Inhalational Anthrax Treatment

• Early IV antibiotics and intensive care required
  – Mortality may still exceed 80%
• Current treatment of choice:
  – Ciprofloxacin 400 mg IV q 8-12 h
    or
  – Doxycycline 200 mg IV x 1 then 100 mg IV q 12
    and
  – one or two additional antimicrobials

MMWR October 26, 2001
Duration of Treatment

- Antibiotic treatment must be continued for 60 days as there is a high risk of recurrence due to delayed germination of spores.
- Once clinical condition improves, oral therapy can replace parental therapy.
Anthrax Post-Exposure Prophylaxis

- Starting antibiotics within 24 hours after aerosol exposure is expected to provide significant protection.
- Duration: 60 days with or without vaccine.
- Most effective when combined with vaccination.
- Antibiotics are still indicated even when fully immunized.
- Long-term antibiotics necessary because of spore persistence in lung/lymph node tissue.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Adults</th>
<th>Children (&lt; 9 yrs or age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Fluoroquinolones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>500 mg twice daily PO</td>
<td>10-15 mg per kg of body mass per day divided every 12 hours PO</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>400 mg twice daily PO</td>
<td>not recommended</td>
</tr>
<tr>
<td>Oral Tetracyclines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg twice daily PO</td>
<td>5 mg per kg per day divided every 12 hours PO</td>
</tr>
<tr>
<td>Oral Penicillins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin VK</td>
<td>7.5 mg/kg 4 x daily PO</td>
<td>50 mg/kg/day divided four times daily</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg 3 x daily PO</td>
<td>80 mg/kg/day divided into 2 or 3 doses daily</td>
</tr>
</tbody>
</table>
Cutaneous Anthrax

- Most common naturally occurring form (95% cases; 2000 worldwide)
- Deposition of spore into skin usually at site of cut or abrasion; papule forms
- Incubation period - 1-7 days
- Papule enlarges into a 1-3 mm vesicle by second day; progresses to a painless depressed black eschar in 3 to 7 days
- Patient may have fever, malaise, headache, and regional lymphadenopathy
Cutaneous Anthrax
Cutaneous Anthrax (cont.)
Cutaneous Anthrax (cont.)

- Diagnosis based on clinical findings and culture/direct smears and FA of fluid/lesions
- 20% case fatality w/o antibiotic treatment; rare with treatment
- Updated treatment for patients without systemic symptoms and lesion not on head or neck and not with extensive edema:
  - Ciprofloxacin 500 mg q 12 hrs
  - or Doxycycline 100 mg q 12 hrs
  - or Amoxicillin 500 mg q 8 hrs
Laboratory Response Network

• A national system to coordinate clinical diagnostic testing for bioterrorism events

• LRN is organized into four laboratory levels (A-D) with progressive levels of safety, containment and technical proficiency

• MDH laboratory, a Level C facility, has advanced capacity for rapid identification and can rule-in and refer
Anthrax Microbiology

*B. anthracis*

- Non-motile
- Non-hemolytic
- Encapsulated
- Gram-positive rod
Positive encapsulation test for *Bacillus anthracis*
Anthrax - Laboratory Diagnosis

- Gram positive bacilli on blood smear
- Blood culture growth of large gram-positive bacilli
- Growth on sheep’s blood agar cultures