Learning Objectives

1. Define Bioterrorism
2. Identify the biological agents and products in bioterrorism
3. Explain the process of early detection and prevention using the Anthrax and smallpox as examples

Acknowledgement

A few slides are included from the University of Pittsburgh ID Epidemiology lecture series and the CDC website.

What is Bioterrorism?

- A bioterrorism attack is the deliberate release of viruses, bacteria, or other germs (agents) used to cause illness or death in people, animals, or plants.
- Although these agents are typically found in nature, they could be changed to increase their pathogenicity, make them resistant to treatment, or increase their ability to be spread in the environment.
- The act is intended to create fear and/or intimidate governments or societies in pursuit of political, religious, or ideological goals.


History of Biological Warfare

- 6th Century BC – Assyrians poison the wells of their enemies with rye ergot
- 6th Century BC – Solon of Athens poisons the water supply with hellebore (skunk cabbage) an herb purgative, during the siege of Krissa
- 184 BC – Hannibal forces hurled earthen pots filled with serpents upon enemy
- 1346 AD – Tatar army hurls its plague ridden dead over the walls of the city
History of Biological Warfare/…2
- 1422 – Battle of Carolstein, bodies of plague ridden soldiers plus 2000 cartloads of excrement are hurled into the enemy ranks
- 15th Century – Pizarrio’s army presented South American natives clothing laden with the variolola virus
- 1710 – Russian troops hurl the corpses of plague victims over the city wall (Russian – Sweden war)
- During Revolutionary War in America, Indians were repeatedly given blankets intentionally contaminated with smallpox scab

History of Biological Warfare/…3
- 18th Century: Smallpox Blankets

History of Biological Warfare/…4
- 20th Century:
  - 1943: USA bio weapon program launched
  - 1953: Bio Defensive program established
  - 1969: Bio Offensive program disbanded
History of Biological Warfare – Global Efforts

- 1925: Geneva Protocol
- 1972: Biological Weapons Convention
  - Accord signed by 103 nations
- 1975: Geneva Conventions Ratified

Bioterrorism—A New Trend

- 1978: Bulgarian exile injected with ricin, London
- 1979: Sverdlovsk, USSR – accidental anthrax released = 40 fatalities
- 1984: Oregon, Salmonella – Rajneesh cult
- 1991: Minnesota, ricin toxin
- 1994: Tokyo, Sarin and biological attacks
- 1995: Arkansas, ricin toxin
- 1995: Indiana, Y. pestis purchase
- 1998: Nevada, nonlethal strain of B. anthracis
- 1998-9: Multiple ‘Anthrax’ hoaxes
- 2001: Anthrax Outbreak USA
- 2017: VX (Nerve agent) to assassinate Kim Jong-Nam

Bioterrorism Basics

What makes the use of biological agents so attractive to the terrorist?

- Ease of Acquisition
  - Information readily accessible on World Wide Web
  - Ingredients are not difficult to attain

- Ease and Economy of Production
  - Only basic microbiology equipment necessary
  - Small labs require no special licensing
  - Investment to cause 50% casualty rate per sq. km:
    (Conventional weapon $2000, nuclear $800, anthrax $1)

- Lethality
  - 50 kg aerosolized anthrax = 100,000 mortality
  - Sverdlovsk experience, former USSR, April 2, 1979
What makes the use of biological agents so attractive to the terrorist? (...continued)

- Stability
- Infectivity
  - Weaponized agents may be easily spread
  - Clinical symptoms days to weeks after release
- Low Visibility
- Ease and Stealth of Delivery
  - Remote, delayed, undetectable release
  - Difficult/impossible to trace origin of agent

Routes of Delivery of Biological Agents

1. Aerosol is most likely method of dissemination
   - Easy, silent dispersal
   - Maximum number of victims exposed
   - Inhalation is most efficient portal of an infectious agent

2. Food/Water-borne dispersal less likely
   - Less stable, ineffective for some agents
   - Inefficient compared to aerosol

Events Suggesting Release of a Bio weapon

- Multiple people ill at the same time (epidemic)
- Previously healthy persons affected
- High morbidity and mortality among affected individuals
- Identification of diseases and pathogens unusual to a particular region
- Recent terrorist claims or activity
- Unexplained epizootic of sick or dead animals
Events Suggesting Release of a Bio weapon

- Severe respiratory disease in a healthy person
- An epidemic curve rising and falling rapidly
- Increase in fever, respiratory, and GI symptoms
- Lower attack rates in people working indoors vs. outdoors
- Seasonal disease during a different time of year
- Known pathogen with unusual antimicrobial resistance pattern
- Genetically-identical pathogen in different areas

CDC has defined and categorized bioterrorism agents into three categories

- **Category A**: agents with both a high potential for adverse public health impact and that also have a serious potential for large-scale dissemination
- **Category B**: Agents are moderately easy to disseminate and have low mortality rates.
- **Category C**: Pathogens that might be engineered for mass dissemination because they are easy to produce and have potential for high morbidity or mortality (examples: nipah virus, hanta virus, and multi-drug resistant Tuberculosis (MTB)).

Further Reading: [http://www.bt.cdc.gov/bioterrorism/overview.asp](http://www.bt.cdc.gov/bioterrorism/overview.asp)
[http://emergency.cdc.gov/agent/agentlist.asp#r](http://emergency.cdc.gov/agent/agentlist.asp#r)

### Bacterial Agents

1. *Bacillus anthracis* (**Anthrax**)
2. *Yersinia pestis* (**Plague**)
3. *Francisella tularensis* (**Tularemia**)
4. *Brucella spp.* (**Brucellosis**)
5. *Coxiella burnetii* (**Q Fever**)
6. *Burkholderia mallei* (**Glanders**)
7. *Vibrio cholerae* (**Cholera**)

### Agents of Bioterrorism
**Agents of Bioterrorism**

**Viral Agents**
1. Variola virus (Smallpox)
2. Venezuelan Equine Encephalitis Virus (VEE)
3. Hemorrhagic Fever Viruses: Ebola, Marburg, Lassa
4. Argentine and Bolivian Hemorrhagic Fever Viruses
5. Hantavirus
6. Congo-Crimean Virus
7. Rift Valley Fever Virus
8. Yellow Fever Virus
9. Dengue Virus

**Agents of Bioterrorism**

**Biological Toxins**
1. Botulinum Toxins
2. Staphylococcal Enterotoxin B
4. Mycotoxins (T2)—ergot, aflatoxin

**Characteristics of BT Agents**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type</th>
<th>Minimum Dose</th>
<th>Incubation period</th>
<th>Initial Symptoms</th>
<th>Duration of Illness</th>
<th>Lethality</th>
<th>Animal Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>Bacteria</td>
<td>0-10,000</td>
<td>1-6 days</td>
<td>Flu-like</td>
<td>3-5 days</td>
<td>High 95%</td>
<td>Yes</td>
</tr>
<tr>
<td>Plague</td>
<td>Bacteria</td>
<td>100 organs</td>
<td>2-3 days</td>
<td>Pneumonia</td>
<td>1-6 days</td>
<td>High 95-100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Tulara</td>
<td>Bacteria</td>
<td>10 organs</td>
<td>2-10 days</td>
<td>Flu-like</td>
<td>&gt;2 weeks</td>
<td>Moderate</td>
<td>Yes</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>Bacteria</td>
<td>5-60 days</td>
<td>Flu-like</td>
<td>Weeks to months</td>
<td>Low 2-15%</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Q Fever</td>
<td>Rickettsia</td>
<td>1 organism</td>
<td>10-40 days</td>
<td>Flu-like</td>
<td>2-14 days</td>
<td>Low 4%</td>
<td>Yes</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Virus</td>
<td>10 organisms</td>
<td>1-7 days</td>
<td>Flu-like</td>
<td>4 weeks</td>
<td>High 95%</td>
<td>Yes</td>
</tr>
<tr>
<td>Encephalitides</td>
<td>VEE, EEE, WEE</td>
<td>10 organs</td>
<td>2-6 days</td>
<td>Flu-like</td>
<td>days to weeks</td>
<td>Low 95%</td>
<td>Yes</td>
</tr>
<tr>
<td>Hemorrhagic Fevers</td>
<td>Ebo, Marburg Virus</td>
<td>1 organism</td>
<td>4-21 days</td>
<td>Flu-like</td>
<td>7-16 days</td>
<td>Marburg 25%</td>
<td>Yes</td>
</tr>
<tr>
<td>Botulinum</td>
<td>Toxin</td>
<td>100 ng</td>
<td>1-5 days</td>
<td>Muscle weakness</td>
<td>24-72 hours</td>
<td>High 95%</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Anthrax

- Caused by contact with spores of Bacillus anthracis, a spore-forming, gram-positive rod
- Three distinct forms of clinical illness:
  - **Cutaneous** by inoculation of skin lesions with spores; common, easily recognized and treated
  - **Inhalation** by inhalation of spores into the lower respiratory tract; rare, difficult to recognize, > 80% mortality (classic description = Woolsorter’s disease)
  - **Gastrointestinal** by ingestion of spores in contaminated meat; rarely encountered but highly lethal

**Cutaneous Anthrax**

- A nondescript, painless, pruritic papule develops 3 to 5 days after introduction of B. anthracis endospores
- In 24 to 36 hours, the lesion forms a vesicle that undergoes central necrosis and drying, leaving a characteristic black eschar surrounded by edema and a number of purplish vesicles: resolves without scarring
- 80-90% resolve without treatment, but mortality can approach 20%, so cases usually treated

**Anthrax: Cutaneous**

- Vesicle development
- Eschar formation

Day 2

Day 4

Day 6

Day 10
Left, Forearm lesion on day 7—vesiculation and ulceration of initial macular or papular anthrax skin lesion. Right, Eschar of the neck on day 15 of illness, typical of the last stage of the lesion.


Anthrax: Cutaneous

Healing after treatment
Anthrax: Cutaneous

Cutaneous Anthrax: Diagnosis

- Gram stain, polymerase chain reaction (PCR), or culture of vesicular fluid, exudate, or eschar
- Blood culture if systemic symptoms present
- Biopsy for immunohistochemistry, especially if person taking antimicrobials

Differential Diagnosis of Cutaneous Anthrax

- Spider bite
- Ecthyma gangrenosum
- Ulceroglandular tularemia
- Plague
- Staphylococcal or streptococcal cellulitis
- Herpes simplex virus
Inhalation Anthrax

Pathogenesis
- 1-5 micron *Anthrax* spore size is optimal for deposition into alveoli
- Inhaled spores are ingested by alveolar macrophages and transported to mediastinal and peribronchial lymph nodes, spores germinating en route
- *Anthrax* bacilli multiply in lymph nodes, causing hemorrhagic mediastinitis, and spread throughout the body in the blood

Clinical Presentation
- 10 days to 6 weeks after inhalation of spores, infected patients develop fever, non-productive cough, myalgia and malaise
- Early in the course of the disease, chest radiographs show a widened mediastinum, which is evidence of hemorrhagic mediastinitis, and marked pleural effusions
- After 1-3 days, the disease takes a fulminant course with dyspnea, strident cough, and chills, culminating in hypotension, shock, and death
Mediastinal widening & Pleural Effusion on Chest X-Ray in Inhalational Anthrax

Mediastinal widening

Mediastinal widening & Pleural Effusion on Chest X-Ray in Inhalational Anthrax

Inhalation Anthrax: Diagnosis

- Chest X-ray—widened mediastinum, pleural effusions, infiltrates, pulmonary congestion
- Affected tissue biopsy for immunohistochemistry
- Any available sterile site fluid for Gram stain, PCR, or culture
- Pleural fluid cell block for immunohistochemistry
Epidemic curve for 22 cases of bioterrorism-related anthrax, United States, 2001.

- Mycoplasmal pneumonia
- Legionnaires’ disease
- Psittacosis
- Tularemia
- Q fever
- Viral pneumonia
- Histoplasmosis (fibrous mediastinitis)
- Coccidioidomycosis
- Malignancy

Differential Diagnosis of Inhalational Anthrax

Gastrointestinal Anthrax

- Fever and diffuse abdominal pain with rebound tenderness develop 2-5 days after ingestion of spores in contaminated meat
- Melenic or blood-tinged stools, blood-tinged or coffee-ground emesis, and ascites develop
- Death results from fluid and electrolyte imbalances, blood loss, shock, intestinal perforation or anthrax toxemia
Gastrointestinal Anthrax

Gastrointestinal Anthrax: Diagnosis

- Blood cultures
- Oropharyngeal (OP) swab collection

Smallpox
Smallpox

- Worst-case scenario biological agent
  - Highly contagious once rash present (not before)
  - World’s population is largely susceptible
  - Up to 30% case fatality rate in non-immune
  - Secondary attack rate of 25-40% (10-20 secondary cases can be expected per index case)
  - No specific treatment available
- Globally very few physicians currently practicing have seen actual cases
- Virus has been weaponized by Soviets, uncertain who exactly owns viable stocks

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Smallpox

- Caused by Variola virus (Orthopox virus)
- Virus is stable in environment
- Spread primarily by respiratory droplets, also by contact, fomites
- Two distinct types of smallpox:
  - Variola Minor (Alastrim): diminutive lesions and mild systemic toxicity
  - Variola Major: Ordinary (subtypes discrete, semi-confluent, confluent), Modified, Flat, Hemorrhagic

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Smallpox

Clinical Presentation

- 7-17 day incubation period
- Prodromal phase: 2-4 days of malaise, fever, rigors, headache, backache, delirium
- Rash then develops on face, hands, forearms and legs, including palms and soles (centrifugal distribution is important distinguishing feature).
- Initial rash is maculopapular. In 1-2 days, lesions become vesicular, then evolve into round, tense pustules deeply imbedded in the dermis. Crusts form on 8th to 9th day of rash
- Crusts separate to form depressed, hypopigmented scars
Smallpox

Bioterrorism Basics
What we do as Healthcare Professionals

- Maintain a high index of suspicion by including biological agents in differential diagnoses
- Learn to recognize historical and physical examination findings suggestive of bioweapon exposure
- Stay informed of local, regional and national epidemiologic trends
- Be knowledgeable about treatment and prophylaxis of patients exposed to biological agents
- Know whom to report suspected biological agent exposures and illnesses to (Police, State Intelligence agency, Infectious Disease Specialists, Local and State Health Officials)