Bioterrorism

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Biological warfare

- “the employment of biological agents to produce casualties in man or animals or damage to plants,” (Takami, RM, 1951)
History

- **1346: Kaffa (Feodossia, Ukraine)**
  - Bodies of Tartar soldiers who died of plague thrown over walls of city

- **1710: Russia vs. Sweden (war)**
  - Russian troops used cadavers of plague victims to start epidemic in enemy camp

- **1767: French and Indian war**
  - Sir Jeffrey Amherst gave blankets infected with smallpox to Indians loyal to the French
  - Indians were decimated by the epidemic

- **1917: WWI**
  - Germans inoculated horses sent to France with glanders
History

- **1937-1945: Japanese program (WWII)**
  - Lab in Manchuria called Unit 731
  - Almost 1000 human autopsies of individuals exposed to aerosolized anthrax
  - >11 Chinese cities attacked with anthrax, cholera, shigellosis, salmonella
    - >10,000 persons died from “experiment”
  - 1940: epidemic of bubonic plague in China and Manchuria following flyover by Japanese planes
    - Infected fleas + grain to attract rats were dropped

- **1975-83: Laos and Kampuchea**
  - Soviet allies used clouds of aerosols called “yellow rain” believed to be composed of trichothecene toxins (mycotoxins)
  - Also used in Afghanistan
History

- 1978: Georgi Markov
  - Bulgarian exile died in London after being stabbed with steel ball containing ricin attached to the end of an umbrella
- 1979: Sverdlovsk (Ekaterinberg)
  - Accident at BW plant in Russia releases aerosolized anthrax resulting in death of >68 people living downwind from plant.
Iraq

- Evidence in 1991-2 of developing offensive biological weapons program
- Weaponized anthrax, botulinum toxin, and aflatoxin by 1991
- Plant was destroyed by UN in 1996
US Bioweapons program (1943-1969)

Eight ball

USAMRIID

Welcome to Fort Detrick
USAMRIID

- United States Army Medical Research Institute in Infectious Diseases
- Program was originally offensive
  - US weaponized anthrax, botulism, tularemia, brucellosis, VEE, and Q fever
- Defensive program started in 1953
- US has vowed never to use a biological weapon under any circumstances
- Current BW work limited to defensive measures such as developing vaccines, detection methods, personal protective equipment, decontamination, rapid diagnostic tests and treatment
- No classified work is done
“Advantages and disadvantages”

- Cause large number of casualties with minimum logistical requirements
- Perpetrators can escape before results are apparent
- Agents are easy to obtain
- Aerosol generating devices are available
- Widespread panic

- Hazardous to the user
- Dependence on optimal weather conditions
- Possible inactivation by solar radiation and other climactic conditions
- Long term effects
- Ethics??????
1984, USA

- Bhagwan Shree Rajneesh in Wasco County Oregon
- Zoning conflict with the local officials
- Inoculated salad bars of 10 restaurants with *Salmonella typhimurium*
- 752 people diagnosed with salmonellosis
- 9 of 10 restaurants closed permanently
Cyanide-laced Tylenol

- Appeared on store shelves in 1982 and 1986
- 1982 Chicago
  - 7 people died
    - 12 year old with a cold
    - New Mom just home from the hospital
- Johnson & Johnson (makers of Tylenol) lost $1billion
Aum Shinrikyo, Japan: 1990-1995

- Tried unsuccessfully to release anthrax and botulinum toxin
- March 20, 1995
  - Successful release of sarin, an organophosphate nerve gas
  - Tokyo subway system during rush hour
  - 5,500 people injured, 11 killed
Aum Shinrikyo and release of sarin gas, Tokyo, Japan
Anthrax Mail Attacks - 2001
Intentional release of anthrax in US

- 23 cases with 11 confirmed cases of inhalation anthrax
  - 5 deaths
    - 63 year-old male photo editor (index)
    - Two male postal workers (55 & 47 years old)
    - 61 year-old female health care worker
    - 94 year-old female Connecticut
- 13 cases of cutaneous anthrax
  - 8 confirmed
  - 5 suspected
- Majority associated with postal facility in New Jersey and District of Columbia or media companies in Florida and NYC where letters were handled
Who did this? Dr. Bruce Ivins, suspected anthrax bioterrorist, committed suicide on July 25, 2008
Biological agents

- Category A
- Category B
- Category C
Category A

- Anthrax
- Smallpox
- Plague
- Tularemia
- Botulism
- Viral hemorrhagic fevers
Category B + Category C

- Category B
  - Q fever
  - Brucellosis
  - Glanders
  - *Clostridium perfringens*

- Category C
  - Nipah virus
Anthrax: *Bacillus anthracis*

- Primarily disease of cattle and sheep
- **Organism:**
  - Model for study of infectious disease because relatively large (5-10μm)
  - Forms spores that can persist in the soil and animal products for years
- **Pathogenesis**
  - Enters through skin abrasions, inhalation, ingestion
Anthrax: 3 forms

- **Cutaneous**
  - Most common, spores enter tissues through abrasions or lesions
  - Infection on exposed skin surfaces
  - Swollen lesions develop and form black scab = eschar
  - Low mortality if localized, If spreads to blood (5%) often fatal

- **Pulmonary**
  - Inhalation of spores usually by person handling contaminated animals (wool sorters disease)
  - High fever, respiratory distress, pneumonia, sepsis, death in untreated cases

- **Intestinal**
  - Eating contaminated meat
  - Severe enteritis, high mortality
  - Very rare
Inhalational Anthrax

- Infective dose = 8,000-15,000 spores
- Incubation period = 1-6 days
- Illness duration – 3-5 days
- Clinical course usually includes a short period of improvement (up to 2 days) followed by abrupt respiratory distress and death in less than 24 hours
Why anthrax?

- Spore former
- Can be aerosolized
- High mortality rate from untreated inhalation or ingestion anthrax
  - Estimate that intentional release of 100kg over Washington DC would result in 130,000 to 3 million deaths
- Vaccine available, limited efficacy
- New vaccines in developmental stages
Anthrax
Smallpox: Variola virus

- Jenner and cowpox (1796)
- Campaign to eradicate smallpox began in 1967 & succeeded by 1977
  - WHO recommended that vaccinations cease in 1980
- Stocks of virus transferred to two reference labs
  - Institute of Virus Preparations in Moscow
  - CDC in Atlanta, Georgia
  - Controversy over WHO recommendation for all countries to destroy stocks
Smallpox

- Why is it a “good” weapon?
  - Aerosol release can disseminate widely
  - Low infectious dose
  - Highly contagious, many secondary cases
  - 30% mortality rate among unvaccinated

- 2 forms of disease
  - Variola major and Variola minor

- Transmission
  - Droplet nuclei, aerosols from oropharynx, contaminated clothing or bed linens

- Infectiousness
  - Onset of rash through first 7-10 days of rash
Smallpox: Variola major
Plague: *Yersinia pestis*

- **Bubonic plague**
  - Flea bite usually in leg with spread to lymph nodes
  - Multiplication and swelling in lymph node = buboes
  - Fever, chills, nausea, malaise,
  - Aerosolized from pain, bacteremia

- **Septicemic plague**
  - Spreads into blood resulting in purple lesions due to leaking blood (black death)
  - Bacterial emboli trapped in lungs

- **Pneumonic plague**
  - emboli
  - Death within 2 to 3 days

- **Mortality**
  - Untreated bubonic and septicemic = 50-75%
  - Pneumonic = 100%
Incidence in US

- Approximately 13 cases are reported per year
- Most of the cases occur in the Southwest among Native Americans

Specimens in BHI
Why plague?

- Can be aerosolized = pneumonic plague
- Widely available
- Very lethal, potentially contagious
  - 50kg of *Y. pestis* distributed by aerosol over a city of 5 million = 150,000 cases of pneumonic plague, 80-100,000 hospitalized, 36,000 deaths
- Causes widespread panic
- Vaccine is available, but has very little efficacy against pneumonic disease
Plague
Tularemia: *Francisella tularensis*

- Zoonoses with wild animal reservoir
- Transmission
  - Direct contact
  - Ingestion of contaminated food/water
  - Insect vector (ticks with transovarial passage and deerflies)
  - Associated with hunters, usual source rabbits or rodents
Tularemia

- **Pathogenesis**
  - Ulcer-like lesion at site of inoculation or bite
  - Spreads to regional lymph nodes = swelling, pain

- **Systemic symptoms**
  - Dizziness, headache, chills, fever, sweating, prostration, GI symptoms, pneumonia

- **Course**
  - Heals in 4-6 weeks
  - Complete resolution in 3-6 months
  - Some relapse (sequestered in host cells)
  - Mortality = 10% in untreated cases
Reported cases of tularemia in US 1990-8
Why tularemia?

- *F. tularensis* very infectious
- Low dose required = 10 or more organisms
- Easily disseminated
- Hardy
  - Can survive for weeks at low temperatures in water, moist soil, hay, straw, or decaying carcasses
  - Short incubation period
- Vaccine is available, but in low supply
Botulism: *Clostridium botulinum*

- **Organism**
  - Produces endotoxin causing food poisoning
  - 1-2µg produces illness/death in humans
    - Infective dose = 0.001 µg/kg
  - Very heat resistant spores
    - Can survive in temperatures >100°C for several hours

- **Pathogenesis**
  - Ingestion of preformed toxin produced during growth in food
  - Toxin absorbed in small intestines, into blood, into peripheral nerves
  - Prevents release of ACh from motor neurons
  - Paralysis of respiratory functions
Botulism

- Incubation: 1-5 days
- Symptoms
  - Blocks cholinergic synapses
  - Dry mouth, blurred/diplopia, muscle weakness, dysphagia
  - Descending flaccid paralysis can last for weeks to months
- Diagnosis
  - Clinical
    - A few labs can do serum toxin assay
- Death from respiratory failure
Why botulism?

- Very potent and lethal
  - Most poisonous substance known
- Easily produced and transported
- 7 antigenic types of toxin are produced (A-G)
- Antitoxin is available from CDC
- Toxoid used for laboratory workers, limited supply
  - Immunity for several months
  - Post-exposure prophylaxis
Viral Hemorrhagic Fevers

Ebola
Marburg
Lassa Fever
Viral hemorrhagic fevers

- Contagious = moderately
- Infective dose = 1-10 viral particles
- Incubation period = 4-21 days
- Duration of illness = 7-16 days
- Mortality = variable
- Non-endemic in US
- No vaccine
<table>
<thead>
<tr>
<th>Agent</th>
<th>BSL</th>
<th>Lab Risk</th>
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<tbody>
<tr>
<td><em>B. anthracis</em></td>
<td>2</td>
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<tr>
<td><em>Y. pestis</em></td>
<td>2</td>
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<tr>
<td><em>Brucella spp.</em></td>
<td>2/3</td>
<td>high</td>
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<tr>
<td><em>F. tularensis</em></td>
<td>2/3</td>
<td>high</td>
</tr>
<tr>
<td>Botulinum toxin</td>
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<td>medium</td>
</tr>
<tr>
<td>Smallpox</td>
<td>4</td>
<td>high</td>
</tr>
<tr>
<td>VHF</td>
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What can we do?
Support public health infrastructure

- We must have a strong public health system with well-trained personnel
- Service coverage should include evenings and weekends
- We must have a clear cut plan of action
  - Who do you call?
    - One phone call should be sufficient to activate the system
  - When do you need to call?
Support development of vaccines and new anti-infectives

- New vaccines and anti-infectives are needed for naturally occurring diseases
- Vaccine development and approval can take up to 17 years!
- Fewer companies are producing vaccines and pharmaceuticals
  - Only two companies manufacture “flu shots” each year
  - Only one company manufactures penicillin

We need more research...trained scientists...adequate facilities (BSL4)
Encourage more efficient surveillance and disease reporting

- We need surveillance and reporting to connect the dots
  - Local medical facilities and individual physicians must report disease occurrence in their area and among their patients so that unusual patterns of disease can be detected
Key Indicators of a BT Event

- Sudden increase in severity or incidence of illness
- Appearance of unusual (non-endemic) illness or syndrome in your community
- Geographic and/or temporal pattern of illness
- Occurrence of vector-borne disease where there is no vector
- Cluster of sick or dead animals
- Atypical seasonality
- Unusual expression of endemic disease
- Multi drug-resistant pathogens

You MUST have surveillance to be able to detect these things!