Vector-Borne Diseases as Potential Agents of Bioterrorism

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What does bioterrorism have to do with vector control?

- Many of the “best” bioterrorism agents are vector-borne
- Surveillance of vector populations may be required to measure risk and detect spread, before or after an event
- An “event” may require emergency vector control measures to prevent further spread or to prevent the establishment of a local enzootic cycle where one did not exist before

A-List Bioterrorism Agents
- Definition -

- Can be easily disseminated or transmitted from person to person, good availability
- Can result in high mortality rates and have the potential for major public health impact
- Can cause public panic and social disruption
- Require special action for public health preparedness and control

A-List Bioterrorism Agents
- Anthrax (Bacillus anthracis)
- Plague (Yersinia pestis)
- Smallpox (variola major)
- Botulism (Clostridium botulinum toxin)
- Tularemia (Francisella tularensis)
- Viral Hemorrhagic Fevers (certain filoviruses and arenaviruses)
First Evidence

- Several diagnoses of an unusual disease
- Commonalities such as time, geography, demographics
  - Venues (i.e. airport, mall, govt building)
  - Events (i.e. religious holiday, sporting event)
  - Children (i.e. school, museum, campus)
- Additional cases and deaths

Confounding factors

- Multiple agents (same or diff locations)
- Multiple locations (same or diff agents)
- Drug resistant agents (abnormal deaths)
- Antigen deficient agents (false neg tests)
- Altered organisms (?)
- Coated organisms (prolonged survival)
- Multiple releases (different times)

Characteristics of a “Good” Bioterrorism Agent

- Easy to obtain
- Dissemination and production are within the capabilities of terrorists
- High mortality and panic (pain & suffering)
- Environmentally stable or high possibility for “escape” beyond initial dissemination
- Relatively difficult for authorities to control

Tularemia: Microbiological Aspects

- Small gram negative coccobacilli – more uniformly rod shaped during log growth phase (0.2 - 0.5 μ)
- Aerobic, slow growing, may take 2-4 days to achieve visible colonies
- Often stains bipolar with Grams or Giemsa stains
- Cysteine enriched media required (exceptions)

Tularemia: Microbiological Aspects

F. t. tularensis (Type A)

- North America
- ID₅₀ = 10¹ organisms
- More severe clinical illness, 5% ~ 15% fatality rate if untreated, >90% for pneumonic
- Ferments glycerol

F. Tularensis non-type A

- F.t. holarctica (Type B)
- F.t. philomiragia
- F.t. novicida
- others
### Tularemia: Clinical Aspects

**Six Clinical Syndromes**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulceroglandular</td>
<td>Most common form</td>
</tr>
<tr>
<td></td>
<td>Papule, ulcer at portal of entry, lymphadenopathy</td>
</tr>
<tr>
<td>Glandular</td>
<td>Regional lymphadenopathy</td>
</tr>
<tr>
<td></td>
<td>No sign of cutaneous lesion</td>
</tr>
<tr>
<td>Ocuglandular</td>
<td>Eyes and conjunctiva inflamed, lymphadenopathy</td>
</tr>
<tr>
<td></td>
<td>Nodules and ulcers on palpebral conjunctiva</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>Sore throat out of proportion to physical signs</td>
</tr>
<tr>
<td></td>
<td>Acute (exudative) tonsillitis with cervical adenitis</td>
</tr>
<tr>
<td>Typhoidal</td>
<td>Acute sepsisemia with no localizing signs</td>
</tr>
<tr>
<td></td>
<td>Secondary pleuropulmonary involvement</td>
</tr>
<tr>
<td>Pneumonic</td>
<td>Most severe and lethal form</td>
</tr>
<tr>
<td></td>
<td>May present as unresponsive community acquired pneumonia</td>
</tr>
</tbody>
</table>

### Tularemia: Clinical Aspects

- Abrupt onset of fever, chills, headache, myalgia, fatigue, sore throat, vomiting, diarrhea
- Lymphadenopathy (may suppurate), heptaosplenomegaly, pharyngitis (may include ulceration)

### Treatment

- Streptomycin or Gentamicin
- Chloramphenicol added for meningeal infection
- Doxycycline >14 days, relapses more frequent
- Universal precautions
- Person to person transmission NOT known to occur
- Laboratorian infection not uncommon BSL-3

### Zoonotic Aspects

**Most Important Vectors**

- *Deremacentor variabilis* (American Dog Tick)
- *Amblyomma americanum* (Lone Star Tick)
- *Dermacentor andersoni* (Rocky Mountain Wood Tick)
- Other ticks

**Other Important Vectors**

- Deerflies mechanically transmit, especially in the western US
- Mosquitoes likely mechanically transmit, especially in Scandinavian Countries (Type B)
Tularemia: Geographic Distribution

- F. holarctica (Type B)
- F. t. tularensis (Type A) and F. t. holarctica (Type B)
- F. novicida
- F. media asiatica

Tularemia: Distribution in the U.S. 1990-2000

Tularemia: Epidemiological Aspects

- Average annual incidence rates of tularemia, by sex and age group — United States, 1985-1994

Tularemia BT Vector-Borne Issues

- Many different species of mammals could become infected from a primary air, food or water dissemination
- Insect/Tick transmission cycles could develop in areas with appropriate host/vector populations outside normal enzootic regions
- Livestock could become infected (especially sheep)
- Environmental Health issues involving food/water

Tularemia BT Vector-Borne Issues

- BSL-3 necropsy and laboratory facilities needed for field investigation
- Need for host/vector collections, samples, identification (entomologists, mammalogists)
- Environmental risk assessment for public health (disease ecologists, epidemiologists)
- Emergency host/vector control issues (kill the vector first!)
Tularemia: Real Life Examples

- BioWatch is a system of monitors dispersed in a number of large cities
- Collects material on a filter media, analyzed daily by PCR
- Several large cities and sports venues have recorded false positive “hits”

- Several monitors tested positive for tularemia in Houston
- Reverse plume modeling implicated this site
- No animals tested positive, soil samples tested positive by PCR only
- F. t. novicida identified as the agent from BW monitor

Plague

“Plague has killed more people than the combined totals of every war man has ever fought.”

“Plague is the only disease to have ever legitimately threatened the survival of the human species.”

Alexander Yersin (circa 1899)

Plague was the catalyst for many public health concepts including quarantine and public health sanitation.

Plague: Microbiological Aspects

- Yersinia pestis, a small gram negative coccobacillus (0.5 - 2.0 μ)
- Facultative anaerobe, slow growing, may take 2-3 days to achieve visible colonies, optimum growth is 26-28°C
- Often stains bipolar with Grams or Giemsa stains
- Does not form a spore

- LD₅₀ = 1-10 organisms
- Requires a temperature specific bacteriophage lysis confirmation to differentiate from Y. pseudotuberculosis
- Three basic biovars
  – Y.p. orientalis
  – Y.p. mediaevalis
  – Y.p. antigua
Plague: Microbiological Aspects

- Frequently misidentified using automated lab software
- Frequently missed on culture due to overgrowth by faster growing bacteria when incubated at 37°C
- Rarely a critical danger to laboratorians, BSL-2

Plague: Clinical Aspects

Primary Clinical Syndromes

- Bubonic – original infection in the lymphatic system
- Septicemic – original infection in the blood
- Pneumonic – original infection in the lungs

Secondary Clinical Syndromes

- Septicemic – secondary to bubonic
- Pneumonic – secondary to septicemic
- Plague Meningitis
- Plague Gangrene
- Plague Pharyngitis

Sudden onset of high fever, painful localized lymphadenopathy, severe malaise, headache

Occasionally accompanied by diarrhea, vomiting

Rapid decline, untreated fatality rate 40-60% (if treated 10-15%)
Plague: Clinical Aspects
Primary Pneumonic
• Sudden onset of high fever, cough often with bloody sputum, severe malaise, headache
• Rapid progression with bacterial pneumonia and death as quickly as 24-36 hours from onset
• Fatality rate is 98-100% if untreated, 80-90% if treatment delayed more than 24 hours, and <50% if treated within 24 hours

Plague: Zoonotic Aspects
• Most important reservoirs are the various ground squirrels, commensal rats, and woodrats.
• Plague is found in many parts of the world and hundreds of species of rodents (and rabbits) are susceptible.
• Many species of fleas can transmit plague. *Xenopsylla cheopis* and *Xenopsylla brasiliensis* are the most important species worldwide.

Plague: Zoonotic Aspects
Other Important Modes of Transmission
• Primary septicemic plague is occasionally acquired by handling animal carcasses (hunting, cooking)
• Primary pneumonic plague is acquired through human or animal (esp cats) respiratory droplets

Plague: Enzootic and Epidemiological Aspects

Plague: Epidemiological Aspects
World Distribution of Plague, 1998

Plague Cases in the Western U.S., 1970 - 2005
Plague: Epidemiological Aspects

- movement is northward and upslope -

1947-1989

1990-1999

N = 327

N = 85

Plague: BT Vector-Borne Issues

- Many different species of mammals could become infected from a primary aerosol dissemination
- The development of a rat-flea cycle in a large city may occur and would require specialized emergency control measures
- Most city rodent control programs are not equipped to “kill the flea first”

Plague: Bioterrorism Concerns

- Wide-spread availability (natural and weaponized), relatively easy to grow (room temp)
- Potential changes to the organism
- Person-to-Person spread
- Secondary zoonotic spread
- Very limited expertise available
- In-appropriate “host” control (kill the fleas first!)
- International and travel concerns

Exercise Examples

Scenario 1: Anthrax
1,000 people initially infected
6 days to mass antibiotic prophylaxis

**Exercise Examples**

**Scenario 2: Plague**

1,000 people initially infected
6 days to mass antibiotic prophylaxis

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**Model by Giovachino M and Carey N: Center for Naval Analyses, US Navy, Alexandria, VA; 2001.**

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**CDC BT Response**

- Medical
  - Triage & primary medical care
  - Mortuary and burial
  - Prophylaxis of “at risk” population
- Epidemiology
  - ID source
  - ID additional cases and exposures
  - Containment
- Environmental
  - Identify agent
  - Genetic sequences
  - Antibiotic susceptibility patterns
  - Confirm cases, screen suspect cases
- Laboratory
  - Vaccine efficacy
  - Analyze environmental samples

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**Environmental Response**

- Develop/assess remediation efforts
- Assess risk of “new” reservoirs/vectors
- Assess veterinary risk/spread
- Assess ecological impact
- Assess long term environmental impacts

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**Deployment**

**Basic Environmental Field Response**

(180 persons for large)

- CDC / DVBID
- PHS / CCRF
- National Guard
- State/Local Health Department & Local Vector Control

**Augmented as needed**

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**Onsite – “Ground 0”**

- Operations Team
- Mammal/Insect Collection Teams (3)
- Environmental Sampling Teams (2)
- Necropsy Teams (2)
- Vector Control Team
- Veterinary Team
- Security Team
- Logistics Team
- Support Team
  - Station issues, occupational health & safety issues
- Laboratory Teams (2)
- Billeting & Mess Unit

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**Response Plans**

- Pre-identify National Responders
- Baseline Data for Most Likely Targets (Cities)
- Equipment & Supply Push-Packs
- Training & Exercises

**Issues from lessons learned**

- Who’s in charge?
What does it take to be a bio-terrorist?

1. One microbrewery

2. One pickup truck with a ULV sprayer