RECOGNITION AND MANAGEMENT OF AGENTS OF BIOTHREATS AND HIGHLY COMMUNICABLE INFECTIONS

David J. Weber, M.D., M.P.H.
Professor of Medicine, Pediatrics, & Epidemiology
Associate Chief Medical Officer
University of North Carolina at Chapel Hill, NC, US
TERRORISM TODAY

New York, September 11, 2001  Time, Special Edition
LECTURE TOPICS

- Potential exposures to rare and exotic diseases
- Major biologic warfare agents
- For most likely BW agents (anthrax, smallpox): Pre-exposure prophylaxis, post-exposure prophylaxis, therapy
- Recognizing a biologic warfare attack
- Review of anthrax and smallpox
Emerging infectious diseases can be defined as infections that have newly appeared in the population, or have existed but are rapidly increasing in incidence or geographic range.
SOURCES OF EXOTIC DISEASES

- Travel
- Animal exposure (zoonotic diseases)
  - Exposure via travel, leisure pursuits (hunting, camping, fishing), occupation (farming), pets
- Bioterrorist agents
- Research
  - Exposure via laboratory work or animal care
Speed of Global Travel in Relation to World Population Growth
# Visitors to the US, 2016

<table>
<thead>
<tr>
<th>Country</th>
<th>Visitors (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>19.3</td>
</tr>
<tr>
<td>Mexico</td>
<td>19.0</td>
</tr>
<tr>
<td>UK</td>
<td>4.6</td>
</tr>
<tr>
<td>Japan</td>
<td>3.6</td>
</tr>
<tr>
<td>China</td>
<td>3.0</td>
</tr>
<tr>
<td>Germany</td>
<td>2.1</td>
</tr>
<tr>
<td>S. Korea</td>
<td>2.0</td>
</tr>
<tr>
<td>Brazil</td>
<td>1.7</td>
</tr>
<tr>
<td>France</td>
<td>1.6</td>
</tr>
<tr>
<td>Australia</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>75.9</strong></td>
</tr>
</tbody>
</table>

OUTBREAKS AND EPIDEMICS IN AFRICA, WHO, 1970-2016

Figure 1 A graph of all the outbreak and epidemic events by disease in the countries of the WHO African region.
Since ~1950, an accelerating pattern of emerging pathogens has been observed, with over 300 new or re-emerging diseases identified. Key developments facilitating the spread of these pathogens include commercial air travel, global trade, urbanization, unchecked population growth, and climate change. Advances in controlling these emerging threats include genome sequencing for identifying new viruses, enhanced global communication networks, rapid diagnostics, and new approaches to vaccine and therapeutics.
EMERGING ZOONOSES

FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003

1 Health-care workers.
2 All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.
3 Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.
EMERGING DISEASES IN THE US

<table>
<thead>
<tr>
<th>DISEASE (source)</th>
<th>CASES</th>
<th>OUTCOME</th>
<th>YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Nile virus (Israel)</td>
<td>Thousands</td>
<td>Endemic (US)</td>
<td>1999</td>
</tr>
<tr>
<td>SARS (China)</td>
<td>8096 (8 US, 1 UNC)</td>
<td>Controlled</td>
<td>2003</td>
</tr>
<tr>
<td>Monkeypox (Africa)</td>
<td>71</td>
<td>Controlled</td>
<td>2003</td>
</tr>
<tr>
<td>Novel flu, H1N1 (Mexico)</td>
<td>Thousands</td>
<td>Endemic (Worldwide)</td>
<td>2009</td>
</tr>
<tr>
<td>MERS-CoV (Arabian Peninsula)</td>
<td>Hundreds</td>
<td>Epidemic (Arabian area)</td>
<td>2014</td>
</tr>
<tr>
<td>Enterovirus D68</td>
<td>Hundreds (13 UNC)</td>
<td>Epidemic (US)</td>
<td>2014</td>
</tr>
<tr>
<td>Ebola</td>
<td>Thousands (1 US)</td>
<td>Epidemic (West Africa)</td>
<td>2014-15</td>
</tr>
</tbody>
</table>
WHO LIST OF PRIORITY DISEASES, 2015

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS))
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika
UNC HOSPITAL PREPAREDNESS: HIGHLY COMMUNICABLE DISEASES

- Critical issues
  - Surge capacity
  - Maintaining adequate staffing
  - Provision of essential services/supplies

- Additional issues
  - Surveillance
  - Diagnosis
  - Protecting personnel
  - Occupational health
  - Stockpiling PPE
  - Triage of limited supplies/beds
  - Security
SPECIAL AIRBORNE/CONTACT PRECAUTIONS

- New outpatient clinic constructed to see patients with highly contagious diseases
  - Direct entry from outside
  - All rooms have airborne isolation
- Representative pathogens
  - Monkeypox
  - SARS Co-V
  - Smallpox
  - Ebola
Emerging infectious diseases: Focus on infection control issues for novel coronaviruses (Severe Acute Respiratory Syndrome-CoV and Middle East Respiratory Syndrome-CoV), hemorrhagic fever viruses (Lassa and Ebola), and highly pathogenic avian influenza viruses, A(H5N1) and A(H7N9)

David J. Weber MD, MPH a,b,*, William A. Rutala PhD, MPH a,b, William A. Fischer MD c, Hajime Kanamori MD, PhD, MPH a,b, Emily E. Sickbert-Bennett PhD, MS a,b

a Department of Hospital Epidemiology, University of North Carolina Health Care, Chapel Hill, NC
b Division of Infectious Diseases, University of North Carolina School of Medicine, Chapel Hill, NC
c Division of Pulmonary and Critical Care Medicine, University of North Carolina School of Medicine, Chapel Hill, NC
### Selected emerging diseases of infection control importance

<table>
<thead>
<tr>
<th>Disease (initial location)</th>
<th>Cases (United States)</th>
<th>Outcome</th>
<th>Person-to-person transmission</th>
<th>Patient-to-HCP transmission</th>
<th>Infection control risk</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legionnaires' disease</td>
<td>Unknown (thousands)</td>
<td>Endemic</td>
<td>No</td>
<td>No</td>
<td>High</td>
<td>1976-potential</td>
</tr>
<tr>
<td>HIV (Africa)</td>
<td>Millions (thousands)</td>
<td>Epidemic</td>
<td>Yes (blood exposure, organ transplantation, vertical, sexual)</td>
<td>Yes (blood exposure)</td>
<td>Moderate</td>
<td>1978-present</td>
</tr>
<tr>
<td>vCJD</td>
<td>Hundreds</td>
<td>Controlled</td>
<td>Yes (blood, theoretically via contaminated medical instruments)</td>
<td>No</td>
<td>Low</td>
<td>1996</td>
</tr>
<tr>
<td>West Nile fever</td>
<td>(Thousands)</td>
<td>Endemic</td>
<td>Yes (blood transfusions, vertical, organ transplantation)</td>
<td>No'</td>
<td>Low</td>
<td>1999</td>
</tr>
<tr>
<td>SARS (China)</td>
<td>~8,000 (8) (37 confirmed, 10 probable)</td>
<td>Controlled</td>
<td>Yes (droplet, contact, airborne?)</td>
<td>Yes</td>
<td>High</td>
<td>2003</td>
</tr>
<tr>
<td>Monkeypox (Africa)</td>
<td></td>
<td>Eliminated in United States</td>
<td>Yes (droplet, contact)</td>
<td>Yes'</td>
<td>High</td>
<td>2003</td>
</tr>
<tr>
<td>MERS (Middle East)</td>
<td>Thousands (2)</td>
<td>Controlled</td>
<td>Yes (droplet, contact)</td>
<td>Yes</td>
<td>High</td>
<td>2014-present</td>
</tr>
<tr>
<td>Ebola (West Africa)</td>
<td>Thousands (4)</td>
<td>Controlled United States, reduced Africa</td>
<td>Yes (contact, sexual)</td>
<td>Yes</td>
<td>High</td>
<td>2014-present</td>
</tr>
</tbody>
</table>

HCP, health care personnel; MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome; vCJD, variant Creutzfeldt-Jakob disease.

*Infection via a needlestick theoretically possible.

†No HCP developed infection during the U.S. outbreak but patient-to-HCP transmission described in Africa.
### Key infection control information for selected highly communicable emerging infectious diseases

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lassa fever</th>
<th>Ebola virus disease</th>
<th>MERS</th>
<th>SARS</th>
<th>Novel influenza A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Virus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year identified</td>
<td>1969</td>
<td>1976</td>
<td>2012</td>
<td>2003</td>
<td>Orthomyxoviridae</td>
</tr>
<tr>
<td>Family</td>
<td>Arenaviridae</td>
<td>Filoviridae</td>
<td>Coronaviridae</td>
<td>Coronaviridae</td>
<td>RNA Enveloped</td>
</tr>
<tr>
<td>Genome</td>
<td>RNA</td>
<td>RNA</td>
<td>RNA</td>
<td>RNA</td>
<td>RNA</td>
</tr>
<tr>
<td>Coat</td>
<td>Enveloped</td>
<td>Enveloped</td>
<td>Enveloped</td>
<td>Enveloped</td>
<td>Enveloped</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endemic location</td>
<td>West Africa</td>
<td>West and Central Africa</td>
<td>Middle East</td>
<td>China</td>
<td>Worldwide (location varies with strain)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>100,000-300,000 cases per year</td>
<td></td>
<td></td>
<td></td>
<td>No recent human cases</td>
</tr>
<tr>
<td>Reservoir</td>
<td>Rodent (rat)</td>
<td>Bats (fruit)</td>
<td>Bats, camels (intermediate host)</td>
<td>Bats, palm civet</td>
<td>Migratory birds, pigs</td>
</tr>
<tr>
<td>Transmission</td>
<td>Inhalation, ingestion, contact (nonintact skin)</td>
<td>Contact (nonintact skin, mucous membranes, sexual)</td>
<td>Droplet, contact, airborne</td>
<td>Inhalation, contact</td>
<td></td>
</tr>
<tr>
<td>Incubation period (d)</td>
<td>10 (range, 6-21)</td>
<td>6-12 (range, 2-21)</td>
<td>2-15</td>
<td>2-14 (range, 2-21)</td>
<td>Varies by strain</td>
</tr>
<tr>
<td>Infectivity, Rho</td>
<td>Not determined</td>
<td>1.5-2.0</td>
<td>0.3-1.3</td>
<td>2.2-3.7 (range, 0.3-4.1)</td>
<td>Varies by strain</td>
</tr>
<tr>
<td>Duration, maximum (d)</td>
<td>28</td>
<td>21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case fatality rate</td>
<td>15%-20%, hospitalized patients</td>
<td>-50% (range, 25%-90%)</td>
<td>&gt;35%</td>
<td>~10%</td>
<td></td>
</tr>
<tr>
<td><strong>Biologic safety</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biothreat level</td>
<td>▲</td>
<td>▲</td>
<td>Not specified</td>
<td>C</td>
<td>C (some strains)</td>
</tr>
<tr>
<td>Biosafety level</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>2-3</td>
</tr>
<tr>
<td>Clinical Therapy</td>
<td>Ribavirin</td>
<td>Supportive</td>
<td>Supportive</td>
<td>Supportive</td>
<td>Supportive</td>
</tr>
<tr>
<td>Infection control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation</td>
<td>Contact, droplet, airborne for aerosol-generating procedures</td>
<td>Contact, droplet, airborne for aerosol-generating procedures</td>
<td>Contact, airborne</td>
<td>Contact, airborne</td>
<td>Droplet, airborne for aerosol-generating procedures</td>
</tr>
<tr>
<td>Pre-exposure prophylaxis, vaccine</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes (some strains)</td>
</tr>
<tr>
<td>Postexposure prophylaxis</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes (antivirals)</td>
</tr>
</tbody>
</table>
KEY CONSIDERATIONS IN ASSESSING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- **Pathogen**
  - Taxonomy (provides clues regarding transmission routes, environmental stability, germicide susceptibility)
  - Host

- **Epidemiology**
  - Locations of endemicity (ie, locations in the world where sources or reservoirs reside)
  - Incubation period
  - Transmission routes
  - Infectivity (ie, communicability)
  - Duration of infectivity
KEY CONSIDERATIONS IN ASSESSING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Clinical
  - Symptoms
  - Signs
  - Risk factors for acquisition of infection
  - Morbidity
  - Mortality
  - Risk factors for morbidity and mortality
  - Diagnostic methods (sensitivity, specificity, biosafety)
  - Therapy (availability, efficacy, safety)
KEY CONSIDERATIONS IN ASSESSING THE THREAT OF AN EMERGING INFECTIOUS DISEASE

- Infection control
  - Environmental survival
  - Germicide susceptibility
  - Isolation recommendations
  - Recommended personal protective equipment
  - Pre-exposure prophylaxis (availability, efficacy, safety)
  - Postexposure prophylaxis (availability, efficacy, safety)
  - Recommended biosafety level in the laboratory
  - Recommended waste disposal (liquids and solids)
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

• General
  ■ Have a comprehensive facility plan for managing a highly communicable emerging infectious disease.
  ■ Nestle the plan for emerging infectious diseases within the general disaster plan.
  ■ Base the plan on the route(s) of transmission for the infectious agent.
  ■ Incorporate the incident command structure in the plan.
  ■ Periodically train key personnel on the plan.
  ■ The plan should include care of single patients (eg, Ebola) and managing large number of patients in an epidemic (eg, novel influenza).
  ■ Incorporate communications with local and state health department officials.
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

- Screening and signage (when appropriate based on the threat of a highly communicable disease)
  - Place signs at every entrance to the hospital and clinics that includes the following: epidemiologic clues to possible disease exposure (ie, travel locations), signs and symptoms of infection, and who to notify if the patient or visitor has both exposure and appropriate signs or symptoms.
  - Include messaging about the signs and symptoms of the concerning disease in all telephone contacts with the patient (eg, reminders about appointments) and who to contact prior to arrival at the health care facility.
  - Screen all patients immediately at the time of all health care visits.
  - Include screening in the electronic medical record (also have alerts in the medical record that require screening).
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

- Screening and signage (when appropriate based on the threat of a highly communicable disease)
  - Place an appropriate isolation sign on the door of all patients being isolated because of the possibility of a highly communicable disease.
  - For diseases transmitted via the droplet or airborne routes emphasize respiratory hygiene (ie, immediate use of a mask and proper disposal of tissues).
  - Emphasize the need for proper hand hygiene.
  - All messaging should be in appropriate languages for the region.
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

- Triage
  - Train frontline person in all clinics and the emergency department in appropriate use of personal protective equipment.
  - Have appropriate personal protective equipment available.
  - Have a designated location in the emergency department and all clinics in which to immediately place the patient (a private room; ideally with access to a sink and toilet, and if possible, one that meets standards for a disease transmitted by the airborne route (ie, negative pressure, out-exhausted air, >12 air exchanges per hour) if applicable.
  - For diseases transmitted by the airborne route and when an airborne isolation room is not available, ideally place a portable high-efficiency particulate air purifier in the room.
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

- Triage
  - Have a well-defined process for alerting key health care facility officials about the presence of a patient with a possible highly communicative disease (eg, disaster manager, infection preventionist).
  - Avoid blood tests or other procedures that may place the laboratory staff or other health care personnel at risk.
  - Have a well-defined and safe method for transporting a patient either to a properly equipped emergency department or hospital facility able to safely care for a patient.
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

• Inpatient care
  ▶ Have a well-defined plan for the inpatient location that will provide care to a patient with a highly communicative disease (or a plan for transporting such a patient to facility that can provide such care).
  ▶ In the inpatient care unit designate areas that are hot (ie, potentially contaminated) and cold (ie, areas that are not contaminated).
  ▶ Have a well-trained medical care team. For highly communicable diseases (eg, Lassa, Ebola), ideally provide 3-step training: (1) basic individual training on personal protective equipment donning and doffing (and including how to manage contamination of the environment from a spill and breach of the personal protective equipment. Such training should be individualized to the specialty of the health care providers [ie, physician, nurse, respiratory therapist]); (2) team training using mannequins; and (3) team training in the designated containment unit.
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTIOUS DISEASE

- Inpatient care
  - Train team personnel on donning and doffing using an explicit written list of all donning and doffing steps.
  - Screen and exclude health care personnel unable to wear the proper personal protective equipment. Consider excluding from the care team personnel at high risk for disease acquisition or more severe illness, such as persons with nonintact skin, pregnancy, and immunocompromised persons. Consider excluding trainees from providing care.
  - Store an adequate supply of personal protective equipment.
  - If needed, have dedicated point of care laboratory equipment.
  - Develop a method to safely dispose of solid and liquid wastes.
  - Restrict visitors (if indicated) and maintain a log of all visitors.
PREPAREDNESS FOR A HIGHLY COMMUNICABLE INFECTION DISEASE

• Inpatient care
  ■ Maintain a log of all health care personnel providing care.
  ■ Develop a plan for managing health care personnel with unprotected exposure to the infectious agent (eg, needlestick).
  ■ Assure that care team members receive proper rest.
BIOLOGIC WARFARE: HISTORY

- 300 BC: Greeks pollute wells and drinking water with animal corpses
- 1346, Kaffa: Attacking Tatar force catapulted cadavers of plague victims into city – outbreak of plague led to defeat
- 1763, Fort Pitt, North America: Blankets from smallpox hospital provided to Native Americans – resulted in epidemic of smallpox among tribes in Ohio River valley
- 1932-45, Manchuria: Japanese military physicians infected 10,000 prisoners with biological agents (B. anthracis, Y. pestis, V. cholerae, Salmonella spp., Shigella spp.) – 11 Chinese cities attacked via food/water contamination, spraying via aircraft
Attack in Northern Iraq by former Government using nerve and mustard gas

Sarin gas attack in Tokyo subway
USE OF BIOLOGICAL AGENTS: US

- Site: The Dalles, Oregon, 1984
- Agent: *Salmonella typhimurium*
- Method of transmission: Restaurant salad bars
- Number ill: 751 (45 hospitalized)
- Responsible party: Members of a religious community had deliberately contaminated the salad bars on multiple occasions (goal to incapacitate voters to prevent them from voting and thus influence the outcome of the election)

The cultists

Oregon, 1984. For months, the free-love commune of guru Bhagwan Shree Rajneesh had been at odds with its neighbors. As a critical town vote neared over land use affecting the cult, two members cultured salmonella in a secret lab. They dumped the bacteria into salad bars and coffee creamers at 11 restaurants. Supermarket produce was also contaminated, and plans were made to poison the city water supply. At least 751 people fell ill. It took investigators a year to link the attack to the sect. Two cult members pleaded guilty to conspiring to tamper with consumer products.

Photograph by Peter Liedtke. SPA PRESS GMBH. D.R. Tony Swaim. SPA PRESS. SHAKTI. MEENA. "Salmonella bacteria. Tom Reck. SPA PRESS. BHAGWAN SHREE RAJNEESH. STOCK. PETER SWAIM. ENVIRON."
USE OF BIOLOGICAL AGENTS: US

- Site: Large medical center, Texas, 1997
- Agent: *Shigella dysenteriae*
- Method of transmission: Ingestion of muffins/doughnuts
- Number ill: 45 (4 hospitalized)
- Responsible party: Disgruntled lab employee? *S. dysenteriae* identical by PFGE from stock culture stored in laboratory

BIOTERRORISM: WHY NOW?

- SecDef William Cohen, March 1998, Heritage Foundation
  - Our American military superiority presents a paradox...because our potential adversaries know they can’t win in a conventional challenge to the U.S. forces, they’re much more likely to try unconventional or asymmetrical methods, such as biologic or chemical weapons

- Richard Betts, Council on Foreign Relations
  - Nuclear arms have great killing capacity but are hard to get; chemical weapons are easy to get but lack such killing capacity; biological agents have both qualities.
TRENDS FAVORING BIOLOGICAL WEAPONS

- Biological weapons have an unmatched destructive potential
- Technology for dispersing biologic agents is becoming more sophisticated
- The lag time between infection and appearance of symptoms generally is longer for biological agents than with chemical exposures
- Lethal biological agents can be produced easily and cheaply
- Biological agents are easier to produce clandestinely than are either chemical or nuclear weapons

Heritage Foundation
TRENDS FAVORING BIOLOGICAL WEAPONS

- Global transportation links facilitate the potential for biological terrorist strikes to inflict mass casualties
- Urbanization provides terrorists with a wide array of lucrative targets
- The Diaspora of Russian scientists has increased the danger that rogue states or terrorist groups will accrue the biological expertise needed to mount catastrophic terrorist attacks
- The emergence of global, real-time media coverage increases the likelihood that a major biological incident will induce panic
Figure 1: Stages and Obstacles for Chemical and Biological Terrorism

Possess requisite technical skills

Acquire basic chemicals or infective biological seed cultures

Conduct testing procedures

Synthesize chemical agents or grow biological agents (unnecessary for toxic industrial chemicals)

Avoid detection by authorities

Process the chemical or biological agents into a form that can be effectively delivered (unnecessary for some chemical agents)

Recognize environmental and meteorological conditions

Assume personal risk where no vaccines or antidotes available

Improvise an agent delivery device

Release chemical or biological agents to cause mass casualties

Source: GAO, on the basis of analysis of technical data and discussions with chemical and biological warfare experts.
**CENTERS FOR DISEASE CONTROL**

**BIOTERRORIST AGENTS: CATEGORY A**

- Easily disseminated or transmitted person-to-person
- High mortality, with potential for major public health impact
- Might cause public panic and social disruption
- Require special action for public health preparedness

**Viruses**: Variola major (smallpox), filoviruses (e.g., Ebola, Marburg), arenaviruses (e.g., Lassa, Machupo)

**Bacteria**: *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)

**Toxins**: *Clostridium botulinum* toxin (botulism)

http://emergency.cdc.gov/agent/agentlist-category.asp
### CLASS A AGENTS OF BIOTERRORISM

<table>
<thead>
<tr>
<th>Disease</th>
<th>Agent</th>
<th>Incubation period</th>
<th>Transmission</th>
<th>Clinical symptoms and signs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td><em>Bacillus anthracis</em></td>
<td>2–4 d</td>
<td>Direct contact, inhalation, or ingestion</td>
<td>Cutaneous eschar, fever, mediastinitis with widened mediastinum on chest radiograph</td>
<td>Doxycycline or ciprofloxacin plus one or two other agents (see text)</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Smallpox virus</td>
<td>10–12 d</td>
<td>Airborne droplets and direct contact</td>
<td>Fever followed by vesicular rash in centrifugal distribution</td>
<td>Supportive treatment, consider early vaccination</td>
</tr>
<tr>
<td>Hemorrhagic fever viruses</td>
<td>Four families of viruses</td>
<td>2–21 d</td>
<td>Airborne droplets, bite of infected carrier, or direct contact</td>
<td>Virus dependent (see Table 2); fever, petechiae, bleeding, disseminated intravascular coagulation</td>
<td>Consider ribavirin</td>
</tr>
<tr>
<td>Plague</td>
<td><em>Yersinia pestis</em></td>
<td>2–4 d</td>
<td>Flea bite (most common), airborne droplet, and direct contact</td>
<td>Buboes, fever, pneumonia, acute respiratory distress syndrome, sepsis</td>
<td>Streptomycin or gentamicin</td>
</tr>
<tr>
<td>Botulism</td>
<td><em>Clostridium botulinum</em></td>
<td>12–36 h</td>
<td>Airborne droplet, ingestion, or contaminated wound</td>
<td>Descending paralysis with diplopia, dysphagia, dysarthria, and dysphonia</td>
<td>Supportive treatment and botulinum antitoxin</td>
</tr>
<tr>
<td>Tularemia</td>
<td><em>Francisella tularensis</em></td>
<td>3–5 d</td>
<td>Arthropod bite, airborne droplets, or ingestion</td>
<td>Fever, dry cough, pneumonia, pulse-temperature dissociation</td>
<td>Streptomycin, gentamicin, ciprofloxacin, doxycycline</td>
</tr>
</tbody>
</table>

CENTERS FOR DISEASE CONTROL
BIOTERRORIST AGENTS: CATEGORY B

- Moderately easy to disseminate
- Moderate morbidity and low mortality
- Require improved diagnostic capacity & enhanced surveillance.
- **Viruses**: Alphaviruses (VEE, EEE, WEE)
- **Bacteria**: Coxiella burnetii (Q fever), Brucella spp. (brucellosis), Burkholderia mallei (glanders), B. pseudomallei (melioidosis), Rickettsia prowazekii (typhus fever), Chlamydia psittaci (psittacosis)
- **Toxins**: Ricinus communis (caster beans) ricin toxin, Clostridium perfringens epsilon toxin, Staphylococcus enterotoxin B
- **Food/waterborne pathogens**: Salmonella spp., Vibrio cholerae, Shigella dysenteriae, E. coli O157:H7, Cryptosporidium parvum, etc.
CENTERS FOR DISEASE CONTROL

BIOTERRORIST AGENTS: CATEGORY C

- Availability
- Ease of production and dissemination
- Potential for high morbidity and mortality and major public health impact
- Emerging agents such as Nipah virus and hantavirus
CDC FACT SHEETS AVAILABILITY

- Anthrax
- Botulism
- Brucellosis
- Plague
- Smallpox
- Tularemia
- Viral hemorrhagic fevers

http://emergency.cdc.gov/bioterrorism/factsheets.asp
CHARACTERISTICS* OF PRIORITY AGENTS

- Infectious via aerosol
- Organisms fairly stable in aerosol
- Susceptible civilian populations
- High morbidity and mortality
- Person-to-person transmission
- Difficult to diagnose and/or treat
- Previous development for BW

* Priority agents may exhibit all or some of the above characteristics
# Sample Biological Agent Ratings

<table>
<thead>
<tr>
<th>Disease</th>
<th>Public Health Impact</th>
<th>Dissemination Potential</th>
<th>Special Preparedness</th>
<th>Public Perception</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morbidity Mortality</td>
<td>Stable/Produce/Distribute Transmissable</td>
<td>Preparedness</td>
<td>Perception</td>
</tr>
<tr>
<td>Smallpox</td>
<td>+ ++</td>
<td>++ + +</td>
<td>++ + +</td>
<td>+ + +</td>
</tr>
<tr>
<td>Inhalational anthrax</td>
<td>++ +++</td>
<td>+++ +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Pneumonic plague</td>
<td>++ +++</td>
<td>++ +</td>
<td>+ + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Tularemia</td>
<td>++ +</td>
<td>++</td>
<td>+ + +</td>
<td>+ +</td>
</tr>
<tr>
<td>Botulism</td>
<td>++ +++</td>
<td>++</td>
<td>+ + +</td>
<td>+ +</td>
</tr>
<tr>
<td>VHF</td>
<td>++ +++</td>
<td>+</td>
<td>+ + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Glanders</td>
<td>++ +++</td>
<td>++</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>VE</td>
<td>++ +</td>
<td>++</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Q fever</td>
<td>+ +</td>
<td>++</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>+ +</td>
<td>++</td>
<td>+ +</td>
<td>+</td>
</tr>
<tr>
<td>Toxins</td>
<td>++ ++</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>HPS</td>
<td>++ ++</td>
<td>+</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Nipah encephalitis</td>
<td>++ ++</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
CHEMICAL AGENTS

- Biotoxins
  - Abrin
  - Brevetoxin
  - Colchicine
  - Digitalis
  - Nicotine
  - Ricin
  - Saxitoxin
  - Tetrodotoxin
  - Trichotecene

- Blood agents
  - Arsine (SA)
  - Carbon monoxide
  - Cyanogen chloride (CK)
  - Hydrogen cyanide (AC)
  - Potassium cyanide (KCN)
  - Sodium cyanide (NaCN)
  - Sodium monofluoracetate
CHEMICAL AGENTS

- Blister agents/vesicants
  - Mustards
  - Phosgene (CX)

- Caustics (acids)
  - Hydrofluoric acid

- Incapacitating agents
  - BZ
  - Fentanyl & other opioids

- Choking/lung agents
  - Ammonia
  - Bromine, Chlorine
  - Hydrogen chloride
  - Methyl bromide
  - Methyl isocynante
  - Osmium tetroxide
  - Phosgene, Disphosgene
  - Phosphine, Phosphorus
  - Sulfuryl fluoride
CHEMICAL AGENTS

- Riot control agents
  - Bromobenzylcyanide
  - Chloracetophenone
  - Chlorobenzylidenemalononitrile
  - Debenzoxazepine

- Nerve agents
  - G agents
  - Sarin (GB)
  - Soman (GD)
  - Tabun (GA)
  - VX

- Metals
  - Arsenic
  - Barium
  - Mercury
  - Thallium
Exposure via:
- Inhalation
- Ingestion
- Transdermal
- Exposure of fetus via mother

WMD-specific tissue and organ damage may cause prolonged illness and long term risks for:
- Psychiatric or neurological problems
- Eye and skin disorders
- Recurrent infection, pulmonary fibrosis
- Cardiac arrhythmias, heart failure

WMD damage to bone marrow, DNA, and germ cells may increase risks for:
- Leukaemia, immune dysfunction, infertility, pregnancy loss, birth defects, cancers

Key:
- Mustard gas
- Nerve agent
- Radiation
- Mycotoxin

WMD agents spread from initial points of entry, accumulate in different tissues, and disrupt many biochemical pathways.
SOURCES OF BIOTERRORISM

- Biological warfare
- State sponsored terrorism
- International terrorist groups
- National cults
- The deranged “Ioner”
government try
capital defend-
15, Attorney
decided to
ity. "I must
decision’s deci-
penalty for
s me,”
ates.

If the def-
the jury of
it will be Da
position to
ence insta-

TOM ROSKE—POOL/AP
Kaczynski's mailbox near Lincoln, Mont. Says one trial expert: "He was never able to have any social interaction except through the mail."
The Next Unabomber

As accused murderer Theodore Kaczynski goes on trial, the FBI is investigating more than 50 cases of terrorists suspected of plotting attacks here. Their tools are easy-to-make chemical and biological weapons.
BIOTERRORISM: IMPACT

- Direct infection: Mortality, morbidity
- Indirect infection: Person-to-person transmission, fomite transmission
- Environmental impact: Environmental survival, animal infection
- Other: Social, political, economic
EFFECTS OF A NUCLEAR WEAPONS RELEASE

Casualties from Nuclear Release
(Either a small (10 kiloton) bomb or destruction of a nuclear reactor)

Prompt Effects
- 98% Dead
- 50% Dead
- Incapacitated
- Irritant
- Primarily Ecological Effects

Siegrist, Emerging Infectious Diseases 1999
EFFECTS OF A BIOLOGICAL WEAPONS RELEASE

Casualties from Biological Weapons Release
(10kg viable Anthrax) Maximum Value=0.00657
% Fatality

40 km

Source: Robert M. Cox, NDU and Richard Fry, DoD.

Siegrist, Emerging Infectious Diseases 1999
**BIOLOGICAL WARFARE: IMPACT**

[release of 50 kg agent by aircraft along a 2 km line upwind of a population center of 500,000 – Christopher et al., JAMA 278;1997:412]

<table>
<thead>
<tr>
<th>Agent</th>
<th>Downwind reach, km</th>
<th>No. dead</th>
<th>No. incapacitated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rift Valley fever</td>
<td>1</td>
<td>400</td>
<td>35,000</td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>1</td>
<td>9,500</td>
<td>35,000</td>
</tr>
<tr>
<td>Typhus</td>
<td>5</td>
<td>19,000</td>
<td>85,000</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>10</td>
<td>500</td>
<td>125,000</td>
</tr>
<tr>
<td>Q fever</td>
<td>&gt;20</td>
<td>150</td>
<td>125,000</td>
</tr>
<tr>
<td>Tularemia</td>
<td>&gt;20</td>
<td>30,000</td>
<td>125,000</td>
</tr>
<tr>
<td>Anthrax</td>
<td>&gt;20</td>
<td>95,000</td>
<td>125,000</td>
</tr>
</tbody>
</table>
CHARACTERISTICS OF BIOWARFARE

- Potential for massive numbers of casualties
- Ability to produce lengthy illnesses requiring prolonged and intensive care
- Ability of certain agents to spread via contagion
- Paucity of adequate detection systems
- Presence of an incubation period, enabling victims to disperse widely
- Ability to produce non-specific symptoms, complicating diagnosis
- Ability to mimic endemic infectious diseases, further complicating diagnosis

STEPS IN MANAGEMENT

1. Maintain an index of suspicion
2. Protect thyself
3. Assess the patient
4. Decontaminate as appropriate
5. Establish a diagnosis
6. Render prompt therapy
7. Practice good infection control
8. Alert the proper authorities
9. Assist in the epidemiologic investigation
10. Maintain proficiency and spread the gospel

## Infection Control Issues for Selected Agents of Bioterrorism

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incubation period (days)</th>
<th>Person-to-person transmission</th>
<th>Infection control precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalational anthrax (see Chapter 185)</td>
<td>2–43*</td>
<td>No</td>
<td>Standard</td>
</tr>
<tr>
<td>Botulism (see Chapter 25)</td>
<td>12–72 hours</td>
<td>No</td>
<td>Standard</td>
</tr>
<tr>
<td>Primary pneumonic plague (see Chapter 176)</td>
<td>1–6</td>
<td>Yes</td>
<td>Droplet</td>
</tr>
<tr>
<td>Smallpox (see Chapter 151)</td>
<td>7–17</td>
<td>Yes</td>
<td>Contact and airborne</td>
</tr>
<tr>
<td>Tularemia (see Chapter 177)</td>
<td>1–14</td>
<td>No</td>
<td>Standard</td>
</tr>
<tr>
<td>Viral hemorrhagic fevers (see Chapter 183)</td>
<td>2–21</td>
<td>Yes</td>
<td>Contact and airborne</td>
</tr>
<tr>
<td>Viral encephalitides (see Chapter 23)</td>
<td>2–14</td>
<td>No</td>
<td>Standard</td>
</tr>
<tr>
<td>Q fever (see Chapter 235)</td>
<td>2–14</td>
<td>No</td>
<td>Standard</td>
</tr>
<tr>
<td>Brucellosis (see Chapter 180)</td>
<td>5–60</td>
<td>No</td>
<td>Standard</td>
</tr>
<tr>
<td>Glanders</td>
<td>10–14</td>
<td>No</td>
<td>Standard</td>
</tr>
</tbody>
</table>

* Based on limited data from human outbreaks; experimental animal data support clinical latency periods of up to 100 days
### Table 2. Selected Features of the Conditions Discussed.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Contagious</th>
<th>Clinical Form or Forms</th>
<th>Vaccine Available</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>No</td>
<td>Three primary forms: cutaneous, inhalational, and gastrointestinal</td>
<td>Yes</td>
<td>Combination antimicrobials, effusion drainage, monoclonal antibody</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Yes</td>
<td>Centrifugal rash with same-stage lesions</td>
<td>Yes</td>
<td>Supportive treatment</td>
</tr>
<tr>
<td>Plague</td>
<td>Yes</td>
<td>Pneumonic or bubonic</td>
<td>No</td>
<td>Antimicrobials</td>
</tr>
<tr>
<td>Botulism</td>
<td>No</td>
<td>Inhalational or gastrointestinal</td>
<td>No</td>
<td>Antitoxin</td>
</tr>
<tr>
<td>Tularemia</td>
<td>No</td>
<td>Inhalational or ulceroglandular</td>
<td>No</td>
<td>Antimicrobials</td>
</tr>
</tbody>
</table>

Fomite Acquisition

- Agents acquired from contaminated clothes
  - Variola major (smallpox)
  - *Bacillus anthracis* (anthrax)
  - *Coxiella burnetii* (Q fever)
  - *Yersinia pestis* (plague)

- Management
  - Remove clothing, have patient shower
  - Place contaminated clothes in impervious bag, wear PPE
  - Decontaminate environmental surfaces with EPA approved germicidal agent or 0.5% bleach (1:10 dilution)
DETECTION OF OUTBREAKS

- Epidemiologic clues
- Medical clues
- Syndromic surveillance
- Other
  - Intelligence reports
  - Claims of release
  - Discovery of munitions or tampering
  - Increased numbers of pharmacy orders for antibiotics
  - Increased number of 911 calls

ID Clinics NA 2006;20:179-211
DETECTION OF BT OUTBREAKS:
EPIDEMIOLOGIC CLUES

- A rapidly increasing disease incidence
- Unusual clustering of disease for the geographic area
- Disease occurrence outside of the normal transmission season
- Simultaneous outbreaks of different infectious diseases
- Disease outbreak in humans after recognition of disease in animals
- Unexplained number dead animals or birds
- Disease requiring for transmission a vector previously not seen in the area
- Rapid emergence of genetically identical pathogens from different geographic areas
DETECTION OF BT OUTBREAKS: MEDICAL CLUES

- Unusual route of infection
- Unusual age distribution or clinical presentation of common disease
- More severe disease and higher fatality rate than expected
- Unusual variants of organisms
- Unusual antimicrobial susceptibility patterns
- Any patient presenting with a disease that is relatively uncommon and has bioterrorism potential
THE PROBLEM OF NEEDLES IN HAYSTACKS

- Outbreak severe acute respiratory infections
  - MERS, SARS, H5N1, H7N9, HxNy...

- Viral hemorrhagic fevers (VHF)
  - Ebola, Marburg, Lassa fever, Rift Valley, CCHF, bunyavirus

- Intentional release
  - Anthrax, smallpox, ricin

- Naturally occurring severe infections
  - Bacterial: Plague, tularemia, melioidosis
  - Viral: Adenovirus, parainfluenza, RSV
DEVELOPING A BT PLAN

- Recognition of infection
- Incident command system
- Communication with public health
- Triage of patients
- Decontamination of patients
- Maintaining clean and contaminated areas
- Proper patient isolation
- Post-exposure prophylaxis
- Treatment
- Control/screening of visitors
- Immunization of HCWs
- Internal communications
- Availability of diagnostic tests
- Availability of PPE
DEVELOPING A BT PLAN

- Have a written BT preparedness plan
- Assess the feasibility and viability of the plan
- Disseminate the plan and ensure familiarity by all key stakeholders
- Use elements of daily practice as the backbone of the plan
- Incorporate internal mechanisms for intensified surveillance
- Ensure appropriate internal and external mechanisms of communication
- Test the plan periodically through drills
- Incorporate flexibility and build redundancy for key components
- Address logistics involving surge capacity
- Emphasize community preparedness

Shaikh Z. ID Clinics NA 2006;20:433-453
AN APPROACH TO BT PREPAREDNESS

- What is the external threat landscape? (Who/When)
  - State/non-state/lone wolves; covert vs overt; new biotech (gene editing)

- What is possible? What is feasible or likely? (What)
  - Bacteria, viruses, toxins
  - Combined attack - all hazards (chem/bio/rad/nuclear/cyber)

- What are routes of transmission & spread? (How/Where)
  - Respiratory, food/water, mail, bomb, what else?
  - Public places, transit hubs, restaurants, what else?

- What is the intended impact & gain? (Why)
  - Mass impact vs mass casualties
THE MISSION:
4 EYES FOR BIOTHREATS

● IDENTIFY
  ■ Clinicians & microbiologists

● ISOLATE
  ■ Clinicians, infection control, hospital admin

● INFORM
  ■ Clinicians/labs to public health authorities, government, media

● INVESTIGATE
  ■ Police, internal security, governments, international agencies
Gosden C, Gardner D. BMJ 2005;331:397
WE HAVE A DUTY TO BE PREPARED

2011, NYC, Attack by hijacked planes

1995, Tokyo, Attack subways with Sarin by Aum Shinriko cult
THANK YOU!!