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Printed January 2000

Bio-Terrorism & Casualty Prevention

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Prepared by
Sandia National Laboratories
Albuquerque, New Mexico 87185 and Livermore, California 94550

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Bio-Terrorism & Casualty Prevention

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Abstract

The bio-terrorism threat has become the "poor man's" nuclear weapon. The ease of manufacture and dissemination has allowed an organization with only rudimentary skills and equipment to pose a significant threat with high consequences. This report will analyze some of the most likely agents that would be used, the ease of manufacture, the ease of dissemination and what characteristics of the public health response that are particularly important to the successful characterization of a high consequence event to prevent excessive casualties.

Forward

The basis for this report was to meet the class requirements for Health Education 492 at the University of New Mexico during fall 1999 which the author was enrolled. As Sandia National Laboratory moves to implement an initial plan for biotechnology capability and programs, the timely dissemination of the knowledge gathered for this report regarding biological threats seemed appropriate to share with the general laboratory community.

Acknowledgment

The author would like to thank Robert J. Koss of Department 2564, Neutron Tube Development, for his review and comments regarding this report.

Contents

FORWARD	1
ACKNOWLEDGMENT	2
CONTENTS	3
INTRODUCTION	5
WHAT IS BIO-TERRORISM?.....	5
WHO IS A BIO-TERRORIST?	5
HISTORY OF BIO-WARFARE	6
BIO-TERRORIST AGENTS.....	9
ANTHRAX – INHALATION	11
QUICK FACTS:	11
SIGNS AND SYMPTOMS:	11
DIAGNOSIS:	11
TREATMENT:	12
PROPHYLAXIS:.....	12
ISOLATION AND DECONTAMINATION:.....	13
SMALLPOX	14
QUICK FACTS:.....	14
SIGNS AND SYMPTOMS:	14
DIAGNOSIS:	15
TREATMENT:	15
PROPHYLAXIS:.....	15
ISOLATION AND DECONTAMINATION:.....	15
PLAGUE – PNEUMONIC.....	16
QUICK FACTS:	16
SIGNS AND SYMPTOMS:	16
DIAGNOSIS:	17
TREATMENT:	17
PROPHYLAXIS:.....	17
ISOLATION AND DECONTAMINATION:.....	17
BOTULINUM TOXIN	18
QUICK FACTS :	18
SIGNS AND SYMPTOMS:	18
DIAGNOSIS:	18
TREATMENT:	18
PROPHYLAXIS:.....	18
ISOLATION AND DECONTAMINATION:.....	18
OTHER POTENTIAL AGENTS	19
BACTERIAL AGENTS:.....	19
VIRAL AGENTS:.....	19

BIOLOGICAL TOXINS:	20
DELIVERY SYSTEMS / LOCATION	22
DELIVERY LOCATION	22
AERIAL.....	22
FOOD / WATER.....	24
MAIL	24
EXPLOSIVE DEVICES	24
VECTORS	24
EPIDEMIOLOGICAL CLUES OF A TERRORIST ACT	24
PUBLIC HEALTH RESPONSE	25
FIRST RESPONDERS	25
STATE RESPONSE	25
FEDERAL RESPONSE	26
CASUALTY PREVENTION STRATEGIES	26
THE PUBLIC HEALTH MODEL.....	26
THE HADDON MATRIX	27
EVALUATION OF RESPONSE.....	29
CONCLUSIONS	29
APPENDIX A – NOMENCLATURE	31
APPENDIX B – CDC RESTRICTED AGENTS LIST	43
VIRUSES	43
BACTERIA.....	43
RICKETTSIAE.....	43
FUNGI.....	44
TOXINS	44
RECOMBINANT ORGANISMS/MOLECULES.....	44
APPENDIX C – PRECAUTIONS FOR HEALTH CARE WORKERS	45
APPENDIX D – FIGURES	46
APPENDIX E – BIBLIOGRAPHY	47

Introduction

This report is an overview of the biological threat as it is defined today and assesses the readiness of the civilian sector, state government, and the federal response that can be anticipated should an incident occur.

We will take a brief look at the following topics:

- Short History of Bio-Warfare
- Agents of the Bio-Terrorist
- Delivery Systems
- Public Health Detection
- Public Health Response
- Could it happen?

What is Bio-Terrorism?

Bio-Terrorism is defined as the use of any biological agent or toxin to cause wide spread morbidity and mortality of a civilian population, animals and plants in an effort to further one's ideological cause.

These biological agents can be living organisms, viruses or rickettsia or the compounds produced by living organisms that are toxic to other living organisms. The distinguishing factor between toxins and chemical agents is; chemical agents are manufactured, while toxins are produced by a living organism.

It is also important to make the distinction between bio-terrorism and bio-warfare. A bio-terrorist act would be primarily aimed at a civilian population while a bio-warfare attack would be aimed at a military target. This is not to say that the military can not be a victim of a terrorist attack, as evidenced in the bombing of the compound in Beirut nor that civilians can be victims of a war, as evidenced by the gassing of the Kurds in northern Iraq. However, a bio-warfare attack could have a much more diverse selection of agents and delivery mechanisms than that of a terrorist action.

Who is a Bio-Terrorist?

There are likely three principle categories of terrorist organizations. First, the state sponsored organization. This would be a highly funded, highly technical, well-organized group with a specific goals. This could be associated with what could be called a "rogue" political state. This type of organization would have the financial resources to develop not only bacterial agents but viral as well.

Secondly, the political/religious organization that stands alone. These groups could be slightly less organized with funding ranging the gamut from very good to very poor. This type of organization could act out for any number of reasons. In September 1984, the Rajneeshees a religious cult in Oregon contaminated restaurant salad bars in an attempt to sway a local political vote. The Tokyo Subway attack in March 1995 and the Matsumoto attack in June 1994 by the apocalyptic sect AUM Shinrikyo are all examples of a sect or cult utilizing biological agents to further their cause.

Third, there is the extremist individual or group that advances their cause by terrorist activities. This "amateur terrorist" would be an individual (or small group) that is not funded by any "organization". This could be a high school or college student or an individual with a poorly defined grudge against someone or something. This individual could be acting to retaliate against a perceived injustice of life, for example; loss of a job, being a disgruntled employee or customer, the breakup with a girlfriend, an arrest, or the way an organization handles a particular issue.

History of Bio-Warfare

Bio-warfare has been used for hundreds of years. The first known use of a biological agent was in the 6th century BC, when the Assyrians poisoned water wells of their enemy with corpses of humans and animals that had died in epidemics.

During the Siege of Kaffa in 1346 the Tartars catapulted plague-infected corpses over the walls of Kaffa. This resulted in the fall of Kaffa. The defeated forces then boarded ships and sailed to Constantinople, Genoa, Venice and other Mediterranean ports. This contributed to the second plague pandemic in Europe.

During the French and Indian war (1754 - 1767), the British forces gave Native American Indians loyal to the French smallpox-laden blankets. This decimated the indigenous Indian population since they had never been exposed to smallpox.

In more recent times, the first presumed use of a biological agent was by the Germans in World War I to infect livestock of neutral trading partners of the Allied forces. The only known tactical use by the Germans in WWI was the contamination of a large water reservoir in northwestern Bohemia with sewage.

During World War II (WWII), Germany, Russia, Japan, Great Britain, and The United States all developed offensive biological programs. Great Britain started research in 1940 at Porton Down attempting to weaponize anthrax while the United States formally started research in 1942 at Camp Detrick (now home of United States Army Medical Research Institute Infectious Diseases - USAMRIID). Production, storage and dispersion methods were carried out here. Between 1949 and 1968 the cities of New York City and San Francisco were covertly used as laboratories to study dispersal methods using bio-weapon agent simulants.

Japan's Unit 731 located in occupied Manchuria during WWII, experimented with biological agents by exposing prisoners of war to agents such as anthrax, shigella, cholera, and plague. Over 10,000 prisoners of war were killed either as direct result of infection or were executed afterward.

The Soviet Union's biological research organization, Biopreparat, under the Ministry of Defense developed their offensive program, 6 research laboratories and 5 production facilities. This program continued well into 1992 after the Biological Weapons Convention treaty had been drafted in 1972 and portions of the program most likely are still in existence today. A 1995 US Naval Institute report estimated the Russian program still employs 25,000 to 30,000 people.

In 1978 Georgi Markov, a Bulgarian defector, was injected with pellet of ricin toxin (derived from castor beans) from the tip of an umbrella in a successful assassination attempt. This utilized technology of The Former Soviet Union with the assassination carried out by Bulgarian Government

In 1979 at Sverdlovsk (now Yekaterinberg), USSR an anthrax epidemic occurred. This incident killed between 200 and 800 people. The Soviet government contended that the epidemic was from the ingestion of contaminated meat from the black market. Located in Sverdlovsk, was a Biopreparat facility actively doing research on the weaponization of anthrax bacteria. In 1992, Boris Yeltsin reluctantly confirmed that the epidemic was in fact an unintentional release of anthrax from the Biopreparat facility.

After the Tokyo subway attack by the terrorist organization Aum Shinrikyo in March 1995, police raids revealed the cult's experimentation on biological weapons and drone aircraft equipped with spray tanks. The cult allegedly attempted other unsuccessful biological attacks in Japan. One in the city of Matsumoto killing over 140 people.

There have been several nations that have signed the 1972 Biological Weapons Convention Treaty and have pursued activities specifically outlawed by the treaty, most notably Iraq and the former Soviet Union.

In Dalles, Oregon (pop. 10,500) in September 1984, 751 persons were infected with Salmonellosis by the intentional contamination of salad bars by the Religious group – Rajneeshees. Their motivation - an attempt to sway a local political vote.

A medical center in Texas - October/November 1996, 45 persons were infected with Shigella Dysenteriae by the intentional contamination of pastries by a disgruntled employee.

When terrorist activities on the scale of the World Trade Center bombing (an attempt to topple the tower) and the Aum Shinrikyo Tokyo subway poisoning attempt such daring and massive attacks on civilians, it doesn't take much of an imagination to envision a biological attack on a major city somewhere in the world.

These activities underscore the difficulty in preventing the dissemination of biological agents. The threat of bio-terrorism is real and growing. Most authorities believe that it is only a matter of when, not if, a large scale biological attack will occur.

Bio-Terrorist Agents

There are many agents that a terrorist organization can choose from. Some of the desirable qualities for an agent that are particularly of concern to a terrorist are:

- Inexpensive
- Easy to get / grow
- Easy to disperse
- High morbidity / mortality rates with low dose
- Highly contagious (person-to-person)
- Non-descript prodrome / Ineffective treatment options

An effective biological weapon system could be built by a small group of individuals with skills in under-graduate microbiology and mechanical engineering to develop a dispersion system. This manufacturing facility would require approximately 800-1000 square feet, the size of a large apartment. There is a vast wealth of information on the advantages of one organism over another, production techniques, and human lethality in the open literature. It is a trivial task to search the World-Wide-Web (WWW) and find information on biological agents, manufacture, dissemination and to order the necessary equipment from vendors anonymously.

Funding for a “high-end” terrorist manufacturing facility could be on the order of a few hundred thousand dollars. Enough to purchase the required equipment, seed stock, and supplies. This is well within the reach of a non-state sponsored organization and certainly a state sponsored organization. However, a well-versed college or high school student could grow an agent with little worry about being detected either at home or school by using equipment and supplies from a well stocked biology department.

First, the basic technique of producing a biological weapon requires acquiring the seed stock. This could be done covertly through deception (formation of a paper research facility), theft or one may choose to “harvest” an organism that is endemic to a specific area of the world or from a naturally occurring outbreak.

Second, production of the organism in large quantities. Equipment for the manufacture of a biological agent is of a “dual use” nature. There are legitimate uses for the equipment in the food industry, medicine, bio-technology and for the hobbyist. Many agents can be grown in equipment designed for the home brewery hobbyist and purchased in just about any reasonably sized city in America. Certainly, the WWW has made the purchase of equipment far easier than just a few years ago.

Third, develop a system for the dispersion of the agent. This can be done using off-the-shelf items intended for agricultural purposes or this equipment could be designed from scratch. To achieve maximum effect of an agent, it must be delivered in an aerosol that

produces a particle size in the 1 to 5 microns range. This size is easily inhaled deep into the lungs and will remain airborne for large periods of time.

The use of endemic organisms and the dual use nature of much of the manufacturing and distribution equipment make the detection of a covert biological laboratory difficult. Water, electrical consumption and odors would be similar to that of a home photo darkroom – not noticeable to the general public if a minimal amount of caution is exercised by the terrorist.

It should be noted that an “amateur terrorist” and most likely the non-state sponsored organizations would limit themselves to bacterial agents and toxins, due to the ease of manufacture, while the highly funded state terrorist organization would most likely attempt to manufacture the much more technically challenging viral agents.

With these factors and others in mind the CDC has established a Restricted Agent List. These are agents that have the highest probability to be used in a terrorist incident. (See appendix A).

While the CDC Critical Agents list is long, there are several agents that are more plausible than others. Those agents are inhalation anthrax, smallpox, pneumonic plague and botulinum toxin. We will now look at each of these agents in detail.

Anthrax – Inhalation

Bacillus anthracis is the causative agent of Anthrax. It is a rod-shaped, gram-positive, sporulating bacteria. It is these spores that constitute the usual infective form. Found in nature, anthrax is primarily a zoonotic disease of herbivores, with cattle, sheep and horses being the usual domesticated animal hosts, but other animals may be infected including humans.

In humans, the disease may be contracted by handling contaminated hair, wool, hides, flesh, blood and excreta of infected animals and from manufactured products such as bone meal, as well as by purposeful dissemination of spores. Historically, persons in the wool processing industry were at high risk for contraction of anthrax.

Typically, the infection is introduced through scratches or abrasions of the skin, wounds, eating insufficiently cooked infected meat, or by flies. Rarely does inhalation of spores occur. This would be indicative of possibly a “non-natural” transmission modality such as a deliberate release.

All human populations are susceptible. Recovery from an attack of the disease may be followed by immunity. The spores are very stable and may remain viable for 40 years or more in soil and water.

Quick Facts:

- Infective Dose - 8,000 - 50,000 spores
- Incubation period - 1 to 6 days
- Lethality - High (fatal if untreated)
- Communicable - No
- Persistence - very stable > 40 years
- Prodrome - non-specific findings (flu-like)
- Treatment - limited after symptoms appear / high dose antibiotic / supportive care

Signs and Symptoms:

Incubation period is 1-6 days. Fever, malaise, fatigue, cough and mild chest discomfort is followed by severe respiratory distress with dyspnea, diaphoresis, stridor, and cyanosis. Shock and death occurs within 24-36 hours after onset of severe symptoms.

Diagnosis:

Physical findings are non-specific. A widened mediastinum may be seen on chest x-ray in advanced cases. Detectable by gram stain of the blood and by blood culture late in the course of illness.

**Fig.1 Chest radiograph showing widened mediastinum due to inhalation anthrax.
Radiograph taken 22 hours before death.**

Treatment:

Although effectiveness may be limited after symptoms are present, high dose antibiotic treatment with penicillin, ciprofloxacin, or doxycycline should be undertaken. Supportive therapy may be necessary.

Prophylaxis:

There is a FDA licensed vaccine available with a vaccination schedule of 0, 2, 4 weeks, then 6, 12, and 18 months for the primary series, followed by annual boosters. Use of oral ciprofloxacin or doxycycline for known or imminent exposure is recommended.

Isolation and Decontamination:

Standard precautions for healthcare workers should be used (Appendix C). After an invasive procedure or autopsy is performed, the instruments and area used should be thoroughly disinfected with a sporicidal agent (chlorine).

Smallpox

The variola virus causes smallpox. It is an Orthopox virus occurring in two strains, variola major and the milder disease, variola minor.

The World Health Organization's (WHO) global eradication of smallpox and continued availability of a vaccine, has made the potential weaponization of variola pose a significant civilian/military threat. The widespread susceptibility of the general population and the age of most smallpox vaccinations in the population make this a particularly powerful agent.

This threat can be attributed to the aerosol infectivity of the virus and the relative ease of large-scale production. The fully developed cutaneous eruption of smallpox is unique but, earlier stages of the rash could be easily mistaken for varicella (chickenpox).

The secondary spread of infection constitutes a nosocomial hazard from the time of onset of a smallpox patient's exanthem until scabs have separated. Patient quarantine with respiratory isolation should be applied to secondary contacts for 17 days post-exposure.

A vaccinia vaccination and vaccinia immune globulin each possess some efficacy in post-exposure prophylaxis.

Quick facts:

- Infective Dose - 10 to 100 virions
- Incubation period - 7 to 17 days (average 12)
- Lethality - high to moderate
- Communicable - High
- Persistence - stable
- Prodrome - non-specific findings, then synchronously developing lesions in 2-3 days
- Treatment - supportive care

Signs and Symptoms:

Clinical manifestations begin acutely with malaise, fever, rigors, vomiting, headache, and backache. 2-3 days later lesions appear which quickly progress from macules to papules, and eventually to pustular vesicles. They are more abundant on the extremities and face, and develop synchronously.

Fig. 2 Smallpox lesions on skin of trunk
Bangladesh

Diagnosis:

Electron and light microscopy are not capable of discriminating variola from vaccinia, monkeypox or cowpox.

Treatment:

At present there is no effective chemotherapy, and treatment of a clinical case remains supportive.

Prophylaxis:

Immediate vaccination or revaccination should be undertaken for all personnel exposed. Vaccinia immune globulin (VIG) is of value in post-exposure prophylaxis of smallpox when given within the first week following exposure.

Isolation and Decontamination:

Droplet and Airborne Precautions (Appendix C) for a minimum of 16-17 days following exposure for all contacts should be implemented. Patients should be considered infectious until all scabs separate.

Plague – Pneumonic

Plague caused by *Yersinia pestis*, is a rod-shaped, non-motile, non-sporulating, gram-negative, bipolar staining, facultative anaerobic bacterium.

Naturally, Plague is a zoonotic disease of rodents (e.g., rats, mice, ground squirrels). Fleas, which live on the rodents, then pass the bacteria to human beings via a bite, whom then suffer from the bubonic form of plague.

The pneumonic form of the disease would be seen as the primary form after purposeful aerosol dissemination of the organisms. The bubonic form would be seen after purposeful dissemination through the release of infected fleas.

**Fig.3 Prairie Dog
(genus *Cynomys*)**

Generally, all human populations are susceptible.

Recovery from the disease may be followed by temporary immunity. The organism will remain viable in water and moist meals and grains for several weeks. At near freezing temperatures, it will remain alive from months to years but is killed by 15 minutes exposure to 72 °C. It also remains viable for some time in dry sputum, flea feces, and buried bodies but is killed within several hours of exposure to sunlight.

Quick Facts:

- Infective Dose - 100 to 500 organisms
- Incubation period - 2 to 3 days
- Lethality - High (fatal if untreated)
- Communicable - Yes
- Persistence - very stable > 1 year
- Prodrome - non-specific findings (flu like), rapid progression to dyspnea, stridor, cyanosis, death
- Treatment - early high dose antibiotics / supportive care

Signs and Symptoms:

Pneumonic plague incubates in 2-3 days. High fever, chills, headache, hemoptysis, and toxemia, progressing rapidly to dyspnea, stridor, and cyanosis.

Death results from respiratory failure, circulatory collapse, and a bleeding diathesis.

Bubonic plague incubates in 2-10 days. Malaise, high fever, and tender lymph nodes (buboes); may progress spontaneously to the septicemic form, with spread to the Central nervous system and lungs.

Diagnosis:

Gram or Wayson stain of lymph node aspirates, sputum or cerebral spinal fluid can make presumptive diagnosis. Plague bacilli may also be cultured on standard media.

Treatment:

Early administration of antibiotics is very effective. Supportive therapy is required.

Prophylaxis:

A licensed, killed vaccine is available. Primary series of an initial dose followed by a second smaller dose 1-3 months later, and a third dose 5-6 months after the second dose. Give 3 booster doses at 6 month intervals following dose 3 of the primary series then every 1-2 years. This vaccine is effective against bubonic plague, but probably not against aerosol exposure.

Isolation and Decontamination:

Standard Precautions for healthcare workers exposed to bubonic plague (Appendix C). Droplet Precautions for healthcare workers exposed to pneumonic plague. Heat, disinfectants (2-5% hypochlorite) and exposure to sunlight renders bacteria harmless.

Botulinum Toxin

The botulinum toxins are a group of seven related neurotoxins produced by the bacillus *Clostridium botulinum*. These toxins, types A through G, could be delivered by aerosol. When inhaled, these toxins present clinically very similar to foodborne intoxication, although the time to onset of paralytic symptoms may actually be longer than for foodborne case. The clinical syndrome produced by one or more of these toxins is known as "botulism".

Quick Facts :

- Infective Dose - .001ug/kg (LD50)
- Incubation period - 1 to 2 days
- Lethality - High (24-72 hrs.)
- Communicable - No
- Persistence - weeks
- Prodrome - weakness, flaccid paralysis, respiratory failure
- Treatment - ventilatory support / botulinum antitoxin / supportive care

Signs and Symptoms:

Ptosis, generalized weakness, dizziness, dry mouth and throat, blurred vision and diplopia, dysarthria, dysphonia, and dysphagia followed by symmetrical descending flaccid paralysis and development of respiratory failure. Symptoms begin as early as 24-36 hours but may take several days after inhalation of toxin.

Diagnosis:

Clinical diagnosis. No routine laboratory findings. Bioterrorist attack should be suspected if multiple casualties simultaneously present with progressive descending bulbar, muscular, and respiratory weakness.

Treatment:

Intubation and ventilatory assistance for respiratory failure. Administration of heptavalent botulinum antitoxin (IND product) may prevent or decrease progression to respiratory failure and hasten recovery.

Prophylaxis:

Pentavalent toxoid vaccine (types A, B, C, D, and E) is available as an IND product for those at high risk of exposure.

Isolation and Decontamination:

Standard Precautions for healthcare workers should be implemented (Appendix C). Toxin is not dermally active and secondary aerosols are not a hazard from patients. Hypochlorite (0.5% for 10-15 minutes) and/or soap and water.

Other Potential Agents

Bacterial Agents:

Bacteria are unicellular organisms that vary in shape and size from spherical cells - cocci - with a diameter of 0.5-1.0 μm (micrometer), to long rod-shaped organisms - bacilli - which may be from 1-5 μm in size. Chains of bacilli may exceed 50 μm . The shape of the bacterial cell is determined by the rigid cell wall.

Interior to the cell wall contains the nuclear material (DNA/RNA), cytoplasm, and cell organelles that are necessary for the life and reproduction of the bacterium. Many bacteria also have glycoproteins on their outer surfaces which aid in bacterial attachment to surface receptors on cells of the host.

Some types of bacteria can transform into spores (a vegetative state), as in the case of Anthrax when the environmental conditions are not advantageous for life. The spore of the bacterial cell is more resistant to cold, heat, drying, chemicals and radiation than the bacterium itself. Spores are a dormant form of the bacterium and, like the seeds of plants, they can germinate when conditions such as moisture and temperature are more favorable.

Bacteria can cause diseases in human beings and animals by means of two mechanisms, which differ in principle: first by invading the tissues or second by producing toxins as in *Clostridium botulinum*. In many cases pathogenic bacteria possess both properties. The diseases they produce often respond to specific therapy with antibiotics.

Some of the additional Bacterial agents that have a bio-terrorist / bio-warfare are the following:

- Brucellosis
- Cholera
- Glanders
- Tularemia
- Q Fever

Viral Agents:

Viruses are the simplest type of microorganism bordering on the inanimate. Viruses are much smaller than bacteria and vary in size from 0.02 μm to 0.2 μm (1 μm = 1.0×10^{-6} mm). The fundamental structure of a virus consists of a nucleocapsid protein coat containing genetic material, either RNA or DNA and enzymes for the transcription of the RNA into DNA.

Viruses lack a system for their own metabolism and are dependent on the synthetic machinery of their host cells: viruses are intracellular parasites. This also means that the

virus, unlike the bacterium, cannot be cultivated in synthetic nutritive solutions but requires living cells in order to multiply. The host cells can be from human beings, animals, plants, or bacteria. Every virus needs its own special type of host cell because a complicated interaction is required between the cell and virus if the virus is to be able to multiply. A virus normally brings about changes in the host cell such that the cell dies. Many virus specific host cells can be cultivated in synthetic nutrient solutions and afterwards can be infected with the virus in question. The cultivation of viruses is costly, demanding, and time-consuming and would thus only be attempted by a well-funded, technically robust organization.

Some of the additional viral agents that have a bio-terrorist / bio-warfare are the following:

- Venezuelan Equine Encephalomyelitis (VEE)
- Viral Hemorrhagic Fevers
- Ebola
- Marburg
- Congo-Crimean
- Hantavirus
- Dengue Fever
- Argentine Hemorrhagic Fever

Biological Toxins:

Biological Toxins are any toxic substance of natural origin produced by an animal, plant, or microbe. They are non-volatile, are usually not dermally active (mycotoxins are an exception), and tend to be more toxic per weight than many chemical agents.

The bacterial toxins, such as botulinum toxins or shiga toxin, tend to be the most toxic of the toxins in terms of dose required for lethality, whereas the mycotoxins tend to be among the least toxic compounds, thousands of times less toxic than the botulinum toxins. Some toxins are more toxic by the aerosol route than when delivered orally or parenterally (ricin, saxitoxin, and T2 mycotoxins are examples), whereas botulinum toxins have lower toxicity when delivered by the aerosol route than when ingested. However, botulinum is so inherently toxic that this characteristic does not limit its potential as a biological agent.

With toxins incapacitation as well as lethality must be considered. Several toxins cause significant illness at levels much lower than the level required for lethality, and are thus significant in their ability to incapacitate.

Some of the additional Bacterial agents that have a bio-terrorist / bio-warfare are the following:

- Ricin
- Staphylococcal Enterotoxin B
- T-2 Mycotoxins

Delivery Systems / Location

Delivery Location

For the Terrorist to achieve maximum gain from the dispersal of a biological agent a basic requirement is high exposure to the civilian population being targeted. A large gathering of people represents the ideal setting, achieving both maximum population exposure but also achieving maximum panic in that population post exposure.

Consider the International Albuquerque Balloon Fiesta. The Fiesta boasts a large international gathering of people (approx. 1×10^6 individuals over the course of the 9-day run) in a relatively small outdoor area. Should an agent be dispersed upwind on the last day of the fiesta, the prodrome would not make itself known for several days. By this time many of the visitors would have gone back home both nationally and internationally complicating the detection of an attack. A highly contagious agent like smallpox could start a worldwide pandemic with a single release.

Consider a large building such as the World Trade Center with an approximate residency of 100,000 individuals (or any of the thousands of lesser know buildings in any large city). An agent dispersed by aerosol into the HVAC system could expose many of the occupants and visitors with quite efficiency.

The terrorist is attempting to achieve three goals. First, incapacitate or kill as many people as possible, second to achieve maximum secondary panic and third a nosocomial spread in the general population.

Aerial

An aircraft – upwind, perpendicular to the intended target area at early morning or late night would have the optimum meteorological conditions for maximum plume dispersion. The World Health Organization (WHO) estimates (see table below) for a hypothetical release of 50kg of a biological agent by an aircraft along a 2km line upwind from a population center of 500,000 people. Using the World Health Organization estimates on the dispersion and downwind reach of an agent such as anthrax, it becomes evident that an attack on a city similar in size to Albuquerque would lead to catastrophic consequences exposing a vast majority of the cities civilian, business and health infrastructure.

Agent	Downwind Reach, km	Number Dead	Number Incapacitated
Anthrax	>20	95,000	125,000
Tularemia	>20	30,000	125,000
Q Fever	>20	150	125,000
Typhus	5	19,000	85,000
Rift Valley Fever	1	400	35,000

Albuquerque, New Mexico with a population of approximately 442,300 and an estimated post agent release of 125,000 injuries, the local health system would be overwhelmed quickly.

Fig. 4
Dispersion plume over a metropolitan area

Other locations for agent dispersion within a metropolitan center are in a closed area, e.g. subway, shopping center, office building, enclosed stadium or arena. Aerosol dispersion is possible from a high position such as from a tall building. The dispersion plume is less predictable and covers a smaller area however, the potential for large population exposure with maximum panic is ever present.

Food / Water

Contamination of a water reservoir is more difficult due to the large amounts of agent required and the chlorination procedures most cities' employ. However, there have been accidental contaminations of city drinking water systems in several cities with coliform bacterium and feces. This indicates that an intentional contamination is possible

Intentional contamination of a food distribution system is entirely possible. There have been several accidental contaminations of fresh fruit (strawberries) over the past several years. This method of a terrorist attack would not be as specific as an attack on a city or facility

Mail

Postal letters pose an interesting threat. A simple envelope with a piece of non-descript paper inside could lead to a biological threat. Anthrax spores could easily be mailed and would stay virulent during the postal process. With the ease of access to mailing lists from mailing list providers a mass mailing could target a large specialized portion of the population.

Packages have always been an easy method of sending explosive devices as evidenced by the Unabomber. An explosive device with a biological agent would disperse the agent through the building (possibly the surrounding city) with ease. First responders would not have any idea that a biological threat existed and would be exposed.

Explosive Devices

Small explosive devices positioned at a location of a large gathering could be in addition to being "anti-personnel" in nature with the nails (used as shrapnel) having the addition of a biological agent.

Vectors

Flies /Mosquitoes have been used in the past for bio-warfare and the release of a natural vector would work well in a terrorist attack. Fleas or mosquitoes would have the added benefit of being difficult to eradicate. Several biological agents lend themselves to use by a vector, Venezuelan Equine Encephalomyelitis virus (VEE), Plague, and Rift Valley Fever are all transmitted in nature by fleas or mosquitoes.

Epidemiological Clues of a Terrorist Act

After a terrorist attack (which may be announced or not) the determination that an actual incident has taken place is critical in dealing with the attack effectively. In the case of an announced attack preventive measures could be initiated immediately, should the threat be taken seriously. The problem is much harder to deal with an unannounced attack as casualties are presenting to the local medical system.

An additional source of confusion could be those claims of responsibility by a non-participant organizations attempting to “take credit” for the attack.

As casualties present to the local medical system there are clues that something of an intentional release has occurred which are:

- Large number of persons with similar syndrome
- Unusual illness for population (Flaccid paralysis - Bot. toxin)
- Single case of uncommon agent (Smallpox)
- Unusual geographic or seasonal distributions (Plague in winter)
- Atypical illness for a population (Measles in adults)
- Unexplained increase in incidence (Stable endemic - Hantavirus)
- Atypical mode of transmission (Aerosol -Inhalation anthrax)
- Numerous ill persons seek treatment at same time (Point source)
- No persons ill who where not exposed (Outside point source no illness)
- Unusual pattern of death in animals (frequently accompanies illness/death in humans)

Public Health Response

First Responders

In the case of a covert release of a biological agent, EMT's, the Fire Department and Local Law Enforcement would not be initially involved. The local health care providers will carry the brunt of the load. A rapid ability to detect and make a presumptive diagnosis of the agent would be critical in the effective treatment of those people that are asymptomatic and symptomatic.

Primary Care Physicians, hospitals and clinics would be responsible for initiating a disaster plan at their respective facility and the prompt notification of the State Health Department.

State Response

In the event of a terrorist act the local health department would notify the State Emergency Management Agency. This agency would start support activities for the location that the incident has occurred. The Governor may elect to mobilize the National Guard to provide medical, decontamination, transportation and other support activities. However, the National Guard will require 12 to 24 hours to mobilize, a long period of time in a fast moving situation.

The Governor could then request federal assistance to provide emergency support and specialized equipment and expertise. This federal response would be delayed by several more hours.

In the event of an attack, the local health system is going to have to deal with the crisis alone for the first 24 to 36 hours.

Federal Response

Presidential Directive 39 signed by President Clinton on June 21, 1995 outlines the federal response to domestic terrorism. For all cases the FBI is assigned the lead responsibility for crisis management, and the measures to prepare a criminal case against the perpetrators of the act.

The Federal Emergency Management Agency (FEMA) is assigned the lead role in coordination of the federal response to the state local governments including measures to protect the public health and safety.

Other agencies, Departments of Defense, Energy, Transportation, Agriculture, Health and Human Services and the EPA all provide functional support to FEMA during the incident as required.

Casualty Prevention Strategies

Injury prevention is based on the predicate that injuries can be prevented. With proper planning and implementation of countermeasures the bio-terrorist attack consequences could be prevented or greatly mitigated. Unfortunately, prevention is far more difficult than first meets the eye and one must be prepared to deal with the high consequences should an attack occur. To fully understand the prevention model we must look at some basics of injury prevention from a public health perspective.

The Public Health Model

The Public Health Model of disease control can be used to understand the epidemiological mechanisms of disease and to better control those mechanisms. Careful examination of the conditions that leads to a disease outbreak can lead to strategies that can prevent a similar outbreak in the future, whether the outbreak is intentional or not.

The Public Health Model identifies three factors that interact in the outbreak of a disease. These are the host – typically the one who falls ill, the agent – typically the vector or disease producing organism and the environment – the physical situation that brings the agent and the host together to interact, in our case the terrorist act. With the Public Health

Model it is easy to see that by breaking any one side (e.g. modifying behavior) of the triangle the interaction that leads to the disease state is interrupted and the consequences are mitigated.

The Haddon Matrix

The Haddon Matrix developed by Dr. William Haddon, Jr. in 1970 can be used to illustrate various aspects of a biological attack and will assist in planning effective countermeasures to minimize casualties. The Haddon Matrix allows for a more thorough analysis than the Public Health Model. The Haddon Matrix looks at pre-event, event, and post-event. Recognizing that the best prevention is preventing the outbreak (or attack) from occurring in the first place, and that should an outbreak occur, strategies for preventing long lasting disability are addressed.

- The pre-event phase includes everything that determines whether the event takes place.
- The event phase encompasses the event itself, and all that determines the nature and severity of the event.
- The post-event phase occurs after the event, including anything that determines whether the injury is limited, exacerbated or repaired.

	Pre-event	Event	Post-event
Host			
Agent			
Physical Environment			
Social/Cultural Environment			

In addition to the Haddon Matrix, Dr. Haddon has developed ten strategies for the prevention of injury. Taking these injury prevention strategies and adapting them to the prevention/mitigation of consequences from a biological attack, they become the following:

1. Prevent the initial marshaling of the agent.
2. Reduce the amount of agent marshaled.
3. Prevent the release of the agent.
4. Modify the rate or spatial distribution of the agent from its source.
5. Separate in time and space, the agent from susceptible persons.
6. Separate the susceptible person with a material barrier.
7. Modify the contact surface, subsurface, or the basic characteristics of the agent.
8. Strengthen the resistance of the people who might otherwise be damaged.
9. Counter the continuation and extension of the damage.

10. Repair and rehabilitate.

Within the context of a covert terrorist biological attack, the Haddon Matrix could be developed with the following data:

Haddon Matrix for a Biological Attack

	Pre-event	Event	Post-event
Host	<ul style="list-style-type: none"> • Civilians 	<ul style="list-style-type: none"> • Civilians • First Responders • Health Care Providers 	<ul style="list-style-type: none"> • Civilians • First Responders • Health Care Providers
Agent	Biological Agent : <ul style="list-style-type: none"> • Bacteria • Virus • Toxin 	Biological Agent : <ul style="list-style-type: none"> • Bacteria • Virus • Toxin 	Biological Agent : <ul style="list-style-type: none"> • Bacteria • Virus • Toxin
Physical Environment	<ul style="list-style-type: none"> • Agent Controls • National stockpile of antibiotics / vaccines • Physical Security • Bio-detection systems 	Protection <ul style="list-style-type: none"> • Dermal • Respiratory • Food & Water Medical management: <ul style="list-style-type: none"> • Rapid Diagnoses • Cohort Definition • Quarantine • Prophylaxis admin. 	<ul style="list-style-type: none"> • Quarantine • Post – mortem management
Social/Cultural Environment	<ul style="list-style-type: none"> • Intelligence • Laws Information Management: <ul style="list-style-type: none"> • Panic Control • Decision to Warn 	Information Management: <ul style="list-style-type: none"> • Panic Control 	Information Management: <ul style="list-style-type: none"> • Panic Control

Looking at the pre-event column in the Haddon Matrix and incorporating the ten strategies for injury prevention we see that the countermeasures that provide the maximum event mitigation are control of the biological agent, intelligence of subversive groups activities, early warning and the physical security of the civilian population. While there are many laws controlling the dissemination of biological agents it is still possible to circumvent them. The physical security of a civilian population must be weighted against any perceived infringement of basic rights.

Should a biological attack occur, the Haddon Matrix column –“Event” addresses what areas that could be looked at for effective management of the event and to prevent a bad situation from getting worse. For instance, not only is the civilian population at risk, but First Responders and Health Care Workers could be at risk. The nature of the organism will have a profound effect on the nature of the ease of care, depending on the precautions that the health care workers will have to employ. In a covert attack, it will be the Health Care Workers that sound the first alarm and it will be the Health Care Workers that will play a critical part in the early presumptive diagnoses of the causative agent. Once a “warning flag” has been raised, additional resources from the state and the federal levels will be available for assistance.

Decisions about prophylaxis administration – Who and when? Should the National stockpile of antibiotics and vaccines be called upon? Quarantine – When and for how many individuals. Information management – Who will keep the public informed and prevent panic? The decision to warn – involving the detection and assessment of the hazard as well as notification of the public. Who will make that decision, how will the word be spread? A warning has within it two critical processes. First, the alert – informing the public of impending danger and second, notification and how will the public interpret the information. Wrong interpretation of the information could make the situation far worse and spread panic. These and many other issues will all have to be addressed within the confines of the local resources.

The post-event time period could be critical in the containment of the biological agent. Mortuary services, patient decontamination and facility decontamination will all play important roles here. In addition, the continuing medical management of the injured will place a burden on the health care system.

The public health response to an actual biological event will transcend all levels of government starting with the First Responders and ending with the mobilization of federal agencies. The successful communication between this widely diverse group of organizations will dictate the success of dealing with the event. The local, state and federal agents must plan, organize and put in place the procedures and open the channels of communication now. After a biological event has taken place there will be no time.

Evaluation of Response

Evaluation of a complex interaction between Federal, State and Local organizations is difficult at best. Ultimately, deterring a biological attack either through the implementation of laws, controls on agents or by the use of intelligence sources is the goal to be strived for. However, since ideology can not be legislated there will always be the threat of a biological attack.

Crisis management by keeping the number of casualties to a minimum and providing adequate medical care is of the utmost importance. Providing accurate information to the public about symptoms and what they should do, will help to relieve panic.

Conclusions

The threat of a covert biological release by a rogue political state or an amateur terrorist is a real threat. The ease of availability of biological agent information, production equipment, seed biological stock and the ease at which a production facility could be covertly setup are within the grasp of a determined person or organization.

To mitigate the biological threat the following is a list of recommendations that could help to hinder a terrorist organization and to help to minimize casualties should an attack occur.

1. Strengthen and/or enact laws pertaining to the unauthorized possession or use of a biological agent. This should also include possession of the necessary equipment to manufacture or disperse an agent.
2. Develop a Rapid Biological (Early warning) Detection system for use at high consequence events such as the Olympics, the Albuquerque Balloon Fiesta, the Super Bowl etc. with a detection capability of several kilometers. This would most likely be a joint development with the military.
3. Develop a laboratory procedure for the rapid (<1 hr) definitive identification of agents.
4. Establish a Biological Emergency Search Team (BEST) team similar to the DOE's Nuclear Emergency Search Team (NEST). This team would have advanced training for the detection and definitive identification of a proposed biological agent as well as equipment and training for the effective management of a terrorist act.
5. Improve epidemiological surveillance of known disease states. Having good baseline information will help in the determination of an outbreak.
6. Information management via the WWW. During a biological event information management will be critical to successful outcome. Information such as cohort definitions, epidemiological data, treatment options as well as logistical information will be needed by those at the scene of the release.
7. Integrated response of The Public Health system (Local and federal). Have disaster drills with federal and local response to evaluate logistical interaction between agencies.
8. Local training for first responders / medical personnel on the detection and crisis intervention for a biological attack.

Appendix A – Nomenclature

Adapted from Stedman's Electronic Medical Dictionary,
Williams & Wilkins, Baltimore, MD, 1996 and
Principles and Practice of Infectious Diseases,
Mandell et al, Third Edition.

Acetylcholine (ACH, Ach) - The neurotransmitter substance at cholinergic synapses, which causes cardiac inhibition, vasodilation, gastrointestinal peristalsis, and other parasympathetic effects. It is liberated from preganglionic and postganglionic endings of parasympathetic fibers and from preganglionic fibers of the sympathetic as a result of nerve injuries, whereupon it acts as a transmitter on the effector organ; it is hydrolyzed into choline and acetic acid by acetylcholinesterase before a second impulse may be transmitted.

Active immunization - The act of artificially stimulating the body to develop antibodies against infectious disease by the administration of vaccines or toxoids.

Adenopathy - Swelling or morbid enlargement of the lymph nodes.

Aleukia - Absence or extremely decreased number of leukocytes in the circulating blood.

Analgesic - 1. A compound capable of producing analgesia, i.e., one that relieves pain by altering perception of nociceptive stimuli without producing anesthesia or loss of consciousness. 2. Characterized by reduced response to painful stimuli.

Anaphylaxis - The term is commonly used to denote the immediate, transient kind of immunologic (allergic) reaction characterized by contraction of smooth muscle and dilation of capillaries due to release of pharmacologically active substances (histamine, bradykinin, serotonin, and slow-reacting substance), classically initiated by the combination of antigen (allergen) with mast cell-fixed, cytophilic antibody (chiefly IgE).

Anticonvulsant - An agent which prevents or arrests seizures.

Antitoxin - An antibody formed in response to and capable of neutralizing a biological poison an animal serum containing antitoxins.

Arthralgia - Severe pain in a joint, especially one not inflammatory in character.

AST - Abbreviation for aspartate aminotransferase, a liver enzyme.

Asthenia - Weakness or debility.

Ataxia - An inability to coordinate muscle activity during voluntary movement, so that smooth movements occur. Most often due to disorders of the cerebellum or the posterior columns of the spinal cord; may involve the limbs, head, or trunk.

Atelectasis - Absence of gas from a part or the whole of the lungs, due to failure of expansion or resorption of gas from the alveoli.

Atropine - An anticholinergic, with diverse effects (tachycardia, mydriasis, cycloplegia, constipation, urinary retention) attributable to reversible competitive blockade of acetylcholine at muscarinic type cholinergic receptors; used in the treatment of poisoning with organophosphate insecticides or nerve gases.

Bilirubin - A red bile pigment formed from hemoglobin during normal and abnormal destruction of erythrocytes. Excess bilirubin is associated with jaundice.

Blood agar - A mixture of blood and nutrient agar, used for the cultivation of many medically important microorganisms.

Bronchiolitis - Inflammation of the bronchioles, often associated with bronchopneumonia.

Bronchitis - Inflammation of the mucous membrane of the bronchial tubes.

Brucella - A genus of encapsulated, nonmotile bacteria (family Brucellaceae) containing short, rod-shaped to coccoid, Gram-negative cells. These organisms are parasitic, invading all animal tissues and causing infection of the genital organs, the mammary gland, and the respiratory and intestinal tracts, and are pathogenic for man and various species of domestic animals. They do not produce gas from carbohydrates.

Bubo - Inflammatory swelling of one or more lymph nodes, usually in the groin; the confluent mass of nodes usually suppurates and drains pus.

Bulla, gen. and pl. bullae - A large blister appearing as a circumscribed area of separation of the epidermis from the subepidermal structure (subepidermal bulla) or as a circumscribed area of separation of epidermal cells (intraepidermal bulla) caused by the presence of serum, or occasionally by an injected substance.

Carbuncle - Deep-seated pyogenic infection of the skin and subcutaneous tissues, usually arising in several contiguous hair follicles, with formation of connecting sinuses; often preceded or accompanied by fever, malaise, and prostration.

Cerebrospinal - Relating to the brain and the spinal cord.

Chemoprophylaxis - Prevention of disease by the use of chemicals or drugs.

Cholinergic - Relating to nerve cells or fibers that employ acetylcholine as their neurotransmitter.

CNS - Abbreviation for central nervous system.

Coagulopathy - A disease affecting the coagulability of the blood.

Coccobacillus - A short, thick bacterial rod of the shape of an oval or slightly elongated coccus.

Conjunctiva, pl. conjunctivae - The mucous membrane investing the anterior surface of the eye-ball and the posterior surface of the lids.

CSF - Abbreviation for cerebrospinal fluid.

Cutaneous - Relating to the skin.

Cyanosis - A dark bluish or purplish coloration of the skin and mucous membrane due to deficient oxygenation of the blood, evident when reduced hemoglobin in the blood exceeds 5 g per 100 ml.

Diathesis -The constitutional or inborn state disposing to a disease, group of diseases, or metabolic or structural anomaly.

Diplopia -The condition in which a single object is perceived as two objects.

Distal - Situated away from the center of the body, or from the point of origin; specifically applied to the extremity or distant part of a limb or organ.

Dysarthria - A disturbance of speech and language due to emotional stress, to brain injury, or to paralysis, incoordination, or spasticity of the muscles used for speaking.

Dysphagia, dysphagy - Difficulty in swallowing.

Dysphonia - Altered voice production.

Dyspnea - Shortness of breath, a subjective difficulty or distress in breathing, usually associated with disease of the heart or lungs; occurs normally during intense physical exertion or at high altitude.

Ecchymosis - A purplish patch caused by extravasation of blood into the skin, differing from petechiae only in size (larger than 3 mm diameter).

Eczema - Generic term for inflammatory conditions of the skin, particularly with vesiculation in the acute stage, typically erythematous, edematous, papular, and crusting;

followed often by lichenification and scaling and occasionally by duskininess of the erythema and, infrequently, hyperpigmentation; often accompanied by sensations of itching and burning.

Edema - An accumulation of an excessive amount of watery fluid in cells, tissues, or serous cavities.

Enanthem, enanthema - A mucous membrane eruption, especially one occurring in connection with one of the exanthemas.

Encephalitis, pl. encephalitides - Inflammation of the brain.

Endotoxemia - Presence in the blood of endotoxins.

Endotracheal intubation - Passage of a tube through the nose or mouth into the trachea for maintenance of the airway during anesthesia or for maintenance of an imperiled airway.

Enterotoxin - A cytotoxin specific for the cells of the intestinal mucosa.

Epistaxis - Profuse bleeding from the nose.

Epizootic - 1. Denoting a temporal pattern of disease occurrence in an animal population in which the disease occurs with a frequency clearly in excess of the expected frequency in that population during a given time interval. 2. An outbreak (epidemic) of disease in an animal population; often with the implication that it may also affect human populations.

Erythema - Redness of the skin due to capillary dilatation.

Erythema multiforme - An acute eruption of macules, papules, or subdermal vesicles presenting a multiform appearance, the characteristic lesion being the target or iris lesion over the dorsal aspect of the hands and forearms; its origin may be allergic, seasonal, or from drug sensitivity, and the eruption, although usually self-limited (e.g., multiforme minor), may be recurrent or may run a severe course, sometimes with fatal termination (e.g., multiforme major or Stevens-Johnson syndrome).

Erythrocyte - A mature red blood cell.

Erythropoiesis - The formation of red blood cells.

Exanthema - A skin eruption occurring as a symptom of an acute viral or coccal disease, as in scarlet fever or measles.

Extracellular - Outside the cells.

Extraocular - Adjacent to but outside the eyeball.

Fasciculation - Involuntary contractions, or twitchings, of groups (fasciculi) of muscle fibers, a coarser form of muscular contraction than fibrillation.

Febrile - Denoting or relating to fever.

Fomite - Objects, such as clothing, towels, and utensils that possibly harbor a disease agent and are capable of transmitting it.

Formalin - A 37% aqueous solution of formaldehyde.

Fulminant hepatitis - Severe, rapidly progressive loss of hepatic function due to viral infection or other cause of inflammatory destruction of liver tissue

Generalized vaccinia - Secondary lesions of the skin following vaccination which may occur in subjects with previously healthy skin but are more common in the case of traumatized skin, especially in the case of eczema (eczema vaccinatum). In the latter instance, generalized vaccinia may result from mere contact with a vaccinated person. Secondary vaccinal lesions may also occur following transfer of virus from the vaccination to another site by means of the fingers (autoinnoculation).

Glanders - A chronic debilitating disease of horses and other equids, as well as some members of the cat family, caused by *Pseudomonas mallei*; it is transmissible to humans. It attacks the mucous membranes of the nostrils of the horse, producing an increased and vitiated secretion and discharge of mucus, and enlargement and induration of the glands of the lower jaw.

Granulocytopenia - Less than the normal number of granular leukocytes in the blood.

Guarnieri bodies - Intracytoplasmic acidophilic inclusion body's observed in epithelial cells in variola (smallpox) and vaccinia infections, and which include aggregations of Paschen body's or virus particles.

Hemagglutination - The agglutination of red blood cells; may be immune as a result of specific antibody either for red blood cell antigens per se or other antigens which coat the red blood cells, or may be nonimmune as in hemagglutination caused by viruses or other microbes.

Hemagglutinin - A substance, antibody or other, that causes hemagglutination.

Hematemesis - Vomiting of blood.

Hemopoietic - Pertaining to or related to the formation of blood cells.

Hematuria - Any condition in which the urine contains blood or red blood cells.

Hemodynamic - Relating to the physical aspects of the blood circulation.

Hemolysis - Alteration, dissolution, or destruction of red blood cells in such a manner that hemoglobin is liberated into the medium in which the cells are suspended, e.g., by specific complement-fixing antibodies, toxins, various chemical agents, tonicity, alteration of temperature.

Hemolytic Uremic Syndrome - Hemolytic anemia and thrombocytopenia occurring with acute renal failure.

Hemoptysis - The spitting of blood derived from the lungs or bronchial tubes as a result of pulmonary or bronchial hemorrhage.

Hepatic - Relating to the liver.

Heterologous - 1. Pertaining to cytologic or histologic elements occurring where they are not normally found. 2. Derived from an animal of a different species, as the serum of a horse is heterologous for a rabbit.

Hyperemia - The presence of an increased amount of blood in a part or organ.

Hyperesthesia - Abnormal acuteness of sensitivity to touch, pain, or other sensory stimuli.

Hypotension - Subnormal arterial blood pressure.

Hypovolemia - A decreased amount of blood in the body.

Hypoxemia - Subnormal oxygenation of arterial blood, short of anoxia.

Idiopathic - Denoting a disease of unknown cause.

Immunoassay - Detection and assay of substances by serological (immunological) methods; in most applications the substance in question serves as antigen, both in antibody production and in measurement of antibody by the test substance.

In vitro - In an artificial environment, referring to a process or reaction occurring therein, as in a test tube or culture media.

In vivo - In the living body, referring to a process or reaction occurring therein.

Induration - 1. The process of becoming extremely firm or hard, or having such physical features. 2. A focus or region of indurated tissue.

Inguinal - Relating to the groin.

Inoculation - Introduction into the body of the causative organism of a disease.

Leukopenia - The antithesis of leukocytosis; any situation in which the total number of leukocytes in the circulating blood is less than normal, the lower limit of which is generally regarded as 4000-5000 per cu mm.

Lumbosacral - Relating to the lumbar vertebrae and the sacrum.

Lumen, pl. lumina - The space in the interior of a tubular structure, such as an artery or the intestine.

Lymphadenopathy - Any disease process affecting a lymph node or lymph nodes.

Lymphopenia - A reduction, relative or absolute, in the number of lymphocytes in the circulating blood.

Macula, pl. maculae - 1. A small spot, perceptibly different in color from the surrounding tissue. 2. A small, discolored patch or spot on the skin, neither elevated above nor depressed below the skin's surface.

Mediastinitis - Inflammation of the cellular tissue of the mediastinum.

Mediastinum - The median partition of the thoracic cavity, covered by the mediastinal pleura and containing all the thoracic viscera and structures except the lungs.

Megakaryocyte - A large cell with a polyploid nucleus that is usually multilobed; megakaryocytes are normally present in bone marrow, not in the circulating blood, and give rise to blood platelets.

Melena - Passage of dark-colored, tarry stools, due to the presence of blood altered by the intestinal juices.

Meningism - A condition in which the symptoms simulate a meningitis, but in which no actual inflammation of these membranes is present.

Meningococcemia - Presence of meningococci (*N. meningitidis*) in the circulating blood.

Meninges - Any membrane; specifically, one of the membranous coverings of the brain and spinal cord.

Microcyst - A tiny cyst, frequently of such dimensions that a magnifying lens or microscope is required for observation.

Microscopy - Investigation of minute objects by means of a microscope.

Moribund - Dying; at the point of death.

Mucocutaneous - Relating to mucous membrane and skin; denoting the line of junction of the two at the nasal, oral, vaginal, and anal orifices.

Myalgia - Muscular pain.

Mydriasis - Dilation of the pupil.

Narcosis - General and nonspecific reversible depression of neuronal excitability, produced by a number of physical and chemical agents, usually resulting in stupor rather than in anesthesia.

Necrosis - Pathologic death of one or more cells, or of a portion of tissue or organ, resulting from irreversible damage.

Nephropathia epidemica - A generally benign form of epidemic hemorrhagic fever reported in Scandinavia.

Neutrophilia - An increase of neutrophilic leukocytes in blood or tissues; also frequently used synonymously with leukocytosis, inasmuch as the latter is generally the result of an increased number of neutrophilic granulocytes in the circulating blood (or in the tissues, or both).

Nosocomial - Denoting a new disorder (not the patient's original condition) associated with being treated in a hospital, such as a hospital-acquired infection.

Oliguria - Scanty urine production.

Oropharynx - The portion of the pharynx that lies posterior to the mouth; it is continuous above with the nasopharynx via the pharyngeal isthmus and below with the laryngopharynx.

Osteomyelitis - Inflammation of the bone marrow and adjacent bone.

Pancytopenia - Pronounced reduction in the number of erythrocytes, all types of white blood cells, and the blood platelets in the circulating blood.

Pandemic - Denoting a disease affecting or attacking the population of an extensive region, country, continent; extensively epidemic.

Papule - A small, circumscribed, solid elevation on the skin.

Parasitemia - The presence of parasites in the circulating blood; used especially with reference to malarial and other protozoan forms, and microfilariae.

Passive immunity - Providing temporary protection from disease through the administration of exogenously produced antibody (i.e., transplacental transmission of antibodies to the fetus or the injection of immune globulin for specific preventive purposes).

PCR - see below for polymerase chain reaction.

Percutaneous - Denoting the passage of substances through unbroken skin, for example, by needle puncture, including introduction of wires and catheters.

Perivascular - Surrounding a blood or lymph vessel.

Petechia, pl. petechiae - Minute hemorrhagic spots, of pinpoint to pinhead size, in the skin, which are not blanched by pressure.

Pharyngeal - Relating to the pharynx.

Pharyngitis - Inflammation of the mucous membrane and underlying parts of the pharynx.

Phosgene - Carbonyl chloride; a colorless liquid below 8.2°C, but an extremely poisonous gas at ordinary temperatures; it is an insidious gas, since it is not immediately irritating, even when fatal concentrations are inhaled.

Photophobia - Morbid dread and avoidance of light. Photosensitivity, or pain in the eyes with exposure to light, can be a cause.

Pleurisy - Inflammation of the pleura.

Polymerase chain reaction - An in vitro method for enzymatically synthesizing and amplifying defined sequences of DNA in molecular biology. Can be used for improving DNA-based diagnostic procedures for identifying unknown BW agents.

Polymorphonuclear - Having nuclei of varied forms; denoting a variety of leukocyte.

Polyuria - Excessive excretion of urine.

Presynaptic - Pertaining to the area on the proximal side of a synaptic cleft.

Prophylaxis, pl. prophylaxes - Prevention of disease or of a process that can lead to disease.

Prostration - A marked loss of strength, as in exhaustion.

Proteinuria - Presence of urinary protein in concentrations greater than 0.3 g in a 24-hour urine collection or in concentrations greater than 1 g/l in a random urine collection on two or more occasions at least 6 hours apart; specimens must be clean, voided midstream, or obtained by catheterization.

Pruritus - Syn: itching.

Ptosis, pl. ptoses - In reference to the eyes, drooping of the eyelids.

Pulmonary edema -Edema of the lungs.

Pyrogenic - Causing fever.

Retinitis - Inflammation of the retina.

Retrosternal - Posterior to the sternum.

Rhinorrhea - A discharge from the nasal mucous membrane.

Sarin - A nerve poison which is a very potent irreversible cholinesterase inhibitor and a more toxic nerve gas than tabun or soman.

Scarification -The making of a number of superficial incisions in the skin. It is the technique used to administer tularemia and smallpox vaccines.

Septic shock - 1. shock associated with sepsis, usually associated with abdominal and pelvicinfection complicating trauma or operations; 2. Shock associated with septicemia caused by Gram-negative bacteria.

Sequela, pl. sequelae - A condition following as a consequence of a disease.

Shigellosis - Bacillary dysentery caused by bacteria of the genus *Shigella*, often occurring in epidemic patterns.

Soman - An extremely potent cholinesterase inhibitor, similar to sarin and tabun.

Sterile abscess - An abscess whose contents are not caused by pyogenic bacteria.

Stridor - A high-pitched, noisy respiration, like the blowing of the wind; a sign of respiratory obstruction, especially in the trachea or larynx.

Superantigen - An antigen that interacts with the T cell receptor in a domain outside of the antigen recognition site. This type of interaction induces the activation of larger numbers of T cells compared to antigens that are presented in the antigen recognition site.

Superinfection - A new infection in addition to one already present.

Tachycardia - Rapid beating of the heart, conventionally applied to rates over 100 per minute.

Teratogenicity - The property or capability of producing fetal malformation.

Thrombocytopenia - A condition in which there is an abnormally small number of platelets in the circulating blood.

Toxoid - A modified bacterial toxin that has been rendered nontoxic (commonly with formaldehyde) but retains the ability to stimulate the formation of antitoxins (antibodies) and thus producing an active immunity. Examples include Botulinum, tetanus, and diphtheria toxoids.

Tracheitis - Inflammation of the lining membrane of the trachea.

Urticaria - An eruption of itching wheals, usually of systemic origin; it may be due to a state of hypersensitivity to foods or drugs, foci of infection, physical agents (heat, cold, light, friction), or psychic stimuli.

Vaccine - A suspension of attenuated live or killed microorganisms (bacteria, viruses, or rickettsiae), or fractions thereof, administered to induce immunity and thereby prevent infectious disease.

Vaccinia - An infection, primarily local and limited to the site of inoculation, induced in man by inoculation with the vaccinia (cowpox) virus in order to confer resistance to smallpox (variola). On about the third day after vaccination, papules form at the site of inoculation which become transformed into umbilicated vesicles and later pustules; they then dry up, and the scab falls off on about the 21st day, leaving a pitted scar; in some cases there are more or less marked constitutional disturbances.

Varicella - An acute contagious disease, usually occurring in children, caused by the varicella-zoster virus, a member of the family Herpesviridae, and marked by a sparse eruption of papules, which become vesicles and then pustules, like that of smallpox although less severe and varying in stages, usually with mild constitutional symptoms; incubation period is about 14 to 17 days. Syn: chickenpox

Variola - Syn: smallpox.

Variolation - The historical practice of inducing immunity against smallpox by “scratching” the skin with the purulency from smallpox skin pustules. The first inoculation for smallpox is said to have been done in China about 1022 B.C.

Viremia - The presence of virus in the bloodstream.

Virion - The complete virus particle that is structurally intact and infectious.

Zoonosis - An infection or infestation shared in nature by humans and other animals that are the normal or usual host; a disease of humans acquired from an animal source.

Appendix B – CDC Restricted Agents List

Viruses

- Crimean-Congo haemorrhagic fever virus
- Eastern Equine Encephalitis virus
- Ebola viruses
- Equine Morbillivirus
- Lassa fever virus
- Marburg virus
- Rift Valley fever virus
- South American Haemorrhagic fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)
- Tick-borne encephalitis complex viruses
- Variola major virus (Smallpox virus)
- Venezuelan Equine Encephalitis virus
- Viruses causing hantavirus pulmonary syndrome
- Yellow fever virus

Exemptions: Vaccine strains of viral agents (Junin Virus strain candid #1, Rift Valley fever virus strain MP-12, Venezuelan Equine encephalitis virus strain TC-83, Yellow fever virus strain 17-D) are exempt.

Bacteria

- *Bacillus anthracis*
- *Brucella abortus*, *B. melitensis*, *B. suis*
- *Burkholderia (Pseudomonas) mallei*
- *Burkholderia (Pseudomonas) pseudomallei*
- *Clostridium botulinum*
- *Francisella tularensis*
- *Yersinia pestis*

Exemptions: vaccine strains as described in Title 9 CFR, Part 78.1 are exempt.

Rickettsiae

- *Coxiella burnetii*
- *Rickettsia prowazekii*
- *Rickettsia rickettsii*

Fungi

- *Coccidioides immitis*

Toxins

- Abrin
- Aflatoxins
- Botulinum toxins
- *Clostridium perfringens* epsilon toxin
- Conotoxins
- Diacetoxyscirpenol
- Ricin
- Saxitoxin
- Shigatoxin
- Staphylococcal enterotoxins
- Tetrodotoxin
- T-2 toxin

Exemptions: Toxins for medical use, inactivated for use as vaccines, or toxin preparations for biomedical research use at an LD50 for vertebrates of more than 100 nanograms per kilogram body weight are exempt. National standard toxins required for biologic potency testing as described in 9 CFR Part 113 are exempt.

Recombinant organisms/molecules

1. Genetically modified microorganisms or genetic elements from organisms from this Appendix, shown to produce or encode for a factor associated with a disease.
2. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins listed in this Appendix, or their toxic subunits.

Appendix C – Precautions for Health Care Workers

Standard Precautions

- Hand washing after patient contact.
- Use of gloves when touching blood, body fluids, secretions, excretions and contaminated items.
- Use of mask, eye protection, and gown during procedures likely to generate splashes or sprays of blood, body fluids, secretions or excretions
- Handle contaminated patient-care equipment and linen in a manner that prevents the transfer of microorganisms to people or equipment.
- Practice care when handling sharps and use a mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation when practical.
- Place the patient in a private room when feasible if they may contaminate the environment.

Airborne Precautions (Standard Precautions plus):

- Place the patient in a private room that has negative air pressure, at least six air changes/hour, and appropriate filtration of air before it is discharged from the room.
- Use of respiratory protection when entering the room.
- Limit movement and transport of the patient. Use a mask on the patient if they need to be moved.

Droplet Precautions (Standard Precaution plus):

- Place the patient in a private room or with someone with the same infection. If not feasible, maintain at least 3 feet between patients.
- Use of a mask when working within 3 feet of the patient.
- Limit movement and transport of the patient. Use a mask on the patient if they need to be moved.

Contact Precautions (Standard Precautions plus):

- Place the patient in a private room or with someone with the same infection if possible.
- Use of gloves when entering the room. Change gloves after contact with infective material.
- Use of gown when entering the room if contact with patient is anticipated or if the patient has diarrhea, a colostomy or wound drainage not covered by a dressing.
- Limit the movement or transport of the patient from the room.
- Ensure that patient-care items, bedside equipment, and frequently touched surfaces receive daily cleaning.
- Dedicate use of non-critical patient-care equipment to a single patient, or cohort of patients with the same pathogen. If not feasible, adequate disinfecting between patients is necessary.

Appendix D – Figures

Fig. 1. CDC/Dr. P.S. Brachman, Chest radiograph showing widened mediastinum due to inhalation anthrax. Public Health Image Library

<http://phil.cdc.gov/Phil/default.asp> 1961

Fig. 2. CDC/James Hicks, Smallpox lesions on skin of trunk. Public Health Image Library, <http://phil.cdc.gov/Phil/default.asp> 1973

Fig. 3. CDC, Prairie Dog. Public Health Image Library, <http://phil.cdc.gov/Phil/default.asp>

Fig. 4. US Census Bureau, U.S. Gazetteer.

<http://www.census.gov/cgi-bin/gazetteer?city=albuquerque&state=&zip=Appendix E> –
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