General Information on Bioterrorism

The most likely agents are:
- Bacillus anthracis (anthrax).
- Yersinia pestis (plague); pulmonary syndrome.
- Francisella tularensis (tularemia); pulmonary syndrome.
- Variola (smallpox).
- Clostridium botulinum (botulism).
- Viral hemorrhagic fevers: Ebola, Marburg, Lassa, etc...

The most common syndromes are:
- Acute respiratory distress with fever.
- Influenza-like illness.
- Gastrointestinal illnesses.
- Skin lesions.
- Acute onset neuromuscular symptoms/signs.

Clues to unnatural occurrences of infections are:
- An unusual increase in numbers of patients presenting with a similar syndrome.
- A large number of fatal cases.
- Clusters of an illness from a single locale or temporally related.
- Any infection that is non-endemic in San Diego.
- Common infections occurring during unusual seasons (i.e. influenza in San Diego in summertime).
- Increase in sick or dead animals.
- Intelligence information.

Bioagents versus the Flu
- As several of the bioagents may produce febrile illnesses with respiratory symptoms/signs that could be confused with influenza, during the annual influenza season in San Bernardino (December - March) the clinician should consider performing specific, diagnostic tests for the presence of influenza virus or antigen.
- Several rapid diagnostic tests are commercially available and can be performed on sputum samples.
- Viral isolation is also available and may assist in the management of these patients and others in the community (i.e. use of specific anti-influenza medications and vaccine optimization).
- Negative rapid tests do not exclude influenza as a diagnosis, but a positive test will reassure you and the patient.
- Remember to give Flu vaccines, where indicated by the CDC guidelines.
Bioagent-Specific Infection Control Measures

- **Anthrax** Standard Precautions.
  - Pulmonary infection is **NOT** transmitted person to person.
  - Cutaneous infection can be transmitted by drainage.

- **Smallpox** Airborne Precautions (like tuberculosis).
- **Plague** Droplet Precautions (standard masks for 72 hours after Rx).
- **Botulism** Standard Precautions.
- **Tularemia** Standard Precautions.
- **Hemorrhagic Fever** Standard Precautions, Airborne Precautions, Droplet Precautions and Contact Precautions to avoid exposures due to excessive hemoptysis, or hematemesis.
  - Treat blood stained material as infectious.
Bioagent Infection Control Measures

Standard Precautions
- Standard precautions are employed in the care of ALL patients, under ALL circumstances.
- Wash hands after patient contact.
- Wear gloves when touching blood, body fluids, secretions, excretions and contaminated items.
- Wear a mask and eye protection, or a face shield during procedures likely to generate splashes or sprays of blood, body fluids, secretions or excretions.
- Handle used patient-care equipment and linen in a manner that prevents the transfer of microorganisms to people or equipment.
- Use care when handling sharps and use a mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation when practical.

Airborne Precautions
- Standard Precautions plus:
  - Place the patient in a private room that has monitored negative air pressure, a minimum of six air changes/hour, and appropriate filtration of air before it is discharged from the room.
  - Wear respiratory protection when entering the room.
  - Limit movement and transport of the patient. Place a mask on the patient if they need to be moved.
  - Conventional diseases requiring Airborne Precautions: measles, varicella, and pulmonary tuberculosis.
  - Biothreat diseases requiring Airborne Precautions: smallpox, viral hemorrhagic fevers.

Droplet Precautions
- Standard Precautions plus:
  - Place the patient in a private room or cohort them with someone with the same infection. If not feasible, maintain at least 3 feet between patients.
  - Wear a mask when working within 3 feet of the patient.
  - Limit movement and transport of the patient. Place a mask on the patient if they need to be moved.
  - Conventional diseases requiring Droplet Precautions: invasive haemophilus influenzae and meningococcal disease, drug-resistant pneumococcal disease, diphtheria, pertussis, mycoplasma, gabhs, influenza, mumps, rubella, parvovirus.
  - Biothreat diseases requiring Droplet Precautions: pneumonic plague, viral hemorrhagic fevers.
Bioagent Infection Control Measures (contd.)

Contact Precautions

- Standard Precautions plus:
- Place the patient in a private room or cohort them with someone with the same infection if possible.
- Wear gloves when entering the room. Change gloves after contact with infective material.
- Wear a 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 noncritical patient-care equipment (such as stethoscopes) to a single patient, or cohort of patients with the same pathogen. If not feasible, adequate disinfection between patients is necessary.
- Conventional diseases requiring Contact Precautions: MRSA, VRE, clostridium difficile, RSV, parainfluenza, enteroviruses, enteric infections in the incontinent host, skin infections (SSSS, HSV, impetigo, lice, scabies), hemorrhagic conjunctivitis.
- **Biothreat Diseases requiring Contact Precautions: viral hemorrhagic fevers and smallpox**
**Bacterial Agents of Bioterrorism**

**Anthrax**
- Description: a spore forming gram-positive rod, which can cause disease by inhalation, inoculation, or ingestion of spores, which, upon reversion to regular bacterial forms, produce potent “edema” and “lethal” toxins.
- The pneumonic, or inhalational, form starts 1-6 days after exposure with fever, myalgias cough and fatigue, which after a brief improvement, progress to an abrupt respiratory distress and shock. There are no specific physical findings, but the chest x-ray may show a widened mediastinum, with or without effusion, but mostly without, infiltrates, because the disease is primarily a mediastinitis. Fifty percent have associated meningitis.
- Diagnosis: widened mediastinum on CXR, Gram-positive rods may be found on gram stains of CSF or buffy coats, and positive blood cultures later in the illness.
- Treatment: IV doxycycline or quinolones (supernormal doses) for 4 weeks, plus vaccination.
- Prophylaxis: avoid inhalation of contaminated material, doxycycline or Ciprofloxacin x 8 weeks plus vaccination (3 doses).
- Pediatrics: doxycycline or penicillin.
- Inoculation (cutaneous) anthrax may appear in conjunction with inhalation cases. Local tissue destruction results in the formation of a black eschar or ulcer with (+/- severe) surrounding edema. Some develop septicemia.
- Gastrointestinal anthrax occurs when large numbers of spores are ingested. It may present with nausea and vomiting, abdominal pain, bloody diarrhea +/- ascites, which progresses to an acute abdomen. The toxins destroy the mesenteric lymph nodes and the circulation to the small bowel.

**Plague**
- Description: *Yersinia pestis* is a gram-negative rod, which causes disease in two forms.
- The pneumonic form begins 2-3 days after inhalation of an aerosol, either from an infected patient or from a bioterrorist aerosol source, with sudden onset of myalgias, high fevers, headache and cough with bloody sputum. Within one day it progresses to a fulminant pneumonia with dyspnea, stridor, cyanosis, septic shock with DIC and hepatocellular damage. The chest x-ray has consolidation /infiltrates. Six percent have associated meningitis.
- The bubonic form would probably not be used as a bioagent.
- Diagnosis: cultures and gram stains of blood, sputum, CSF and lymph node aspirates. Immunoassays available.
- Treatment: gentamicin, doxycycline or chloramphenicol (for meningitis).
- Prophylaxis: doxycycline.
- Isolation: mandatory for at least the first 48 hours of treatment.
- Pediatric: doxycycline or trimethoprim/sulfa for prophylaxis but gentamicin or chloramphenicol for treatment.
Tularemia

- Description: Tularemia is caused by *Francisella tularensis*, a small, fastidious Gram-negative bacillus. Human infections can occur via aerosols, contaminated food or water, from arthropod bites, or through skin exposure.

- The incubation period can be as short as 24 hours, but can be up to 14 days or longer. Sporadic cases of tularemia occur in most parts of the USA, and tularemia is endemic among small animals in California. Although the infectious dose of *F. tularensis* is very low, there is no evidence for person-to-person transmission of infection.

- Each route of infection produces a different clinical picture. Clinical or radiographic features cannot differentiate tularemia pneumonia from other serious bacterial pneumonias. The usual result of inhalation is pneumonia with hilar adenopathy and/or pleural effusions in about 1/3 of cases. High fever, chills, rigors, sore throat, myalgias (elevated CPK in some) and a non-productive cough are common. There may be pulse-temperature dissociation. Untreated, the mortality of tularemia pneumonia may reach 50%. Ingestion is more likely to cause exudative tonsillitis and suppurative cervical adenitis.

- Diagnosis is difficult because the bacteria are fastidious and grow slowly, they may not grow out of sputum on standard blood agar, or the laboratory may not recognize them. Rapid diagnostic tests are not available. Blood and pleural fluid cultures may be positive. Aspirates of enlarged lymph nodes will also yield the pathogen. Serology can be used for retrospective diagnosis. A four-fold titer increase or a titer above 1:160 is diagnostic, but this usually takes 10-14 days to develop.

- Treatment is with parenteral gentamicin 5mg/kg qd, or doxycycline 100 mg, or chloramphenicol 15mg/kg q 6h, or erythromycin 500 mg q 8h. Because this organism can be drug-resistant, in vitro susceptibility testing should guide subsequent treatment. Doxycycline or fluoroquinolones can be used for prophylaxis in people who were likely exposed but not yet ill. There is no available vaccine. Contaminated surfaces can be cleaned with 10% bleach and then wiped with 70% alcohol. Cloths and skin can be washed with soap and water.
Viral Agents of Bioterrorism

General Discussion

- Viral agents proposed for use as biologic weapons include Smallpox (variola virus), Venezuelan Equine Encephalitis Virus, and the multiple agents causing viral hemorrhagic fevers, typified by Ebola.
- General characteristics of these viruses include:
  - Initial presentation with non-specific flu-like symptoms.
  - Pathogenesis secondary to direct cytopathic effect, immune-complex deposition, or other processes often resulting in vascular injury and end-organ failure.
  - Vaccination most effective prophylaxis but few vaccines generally available for proposed agents.
  - Few antiviral agents have proven efficacy or are available.

Smallpox – Variola virus

- Declared eradicated 1980 by World Health Organization, known stockpiles of virus still remain at the CDC in Atlanta and at the Institute for Viral preparations in Moscow and possibly at other sites in the world. In the USA, civilian vaccination programs ended in the early 1980’s while the military stopped in 1989.
- Virus is spread by aerosol with incubation period averaging ~12 days (7-19 days).
- Clinical symptoms begin with abrupt onset of malaise, fevers, rigors, headache, emesis, backache, and delirium (15%) followed 2-3 days later by onset of rash on face, hands, forearms, and legs then spreading centrally with lesions progressing from macules to papules to pustular vesicles. Lesions typically are in the same stage of development.
- Patients are highly infectious during the initial respiratory phase and remain so until all eschars are off. Mortality is about 30% in unvaccinated population. Mortality is lower in vaccinated individuals, but no civilians have maximal protection because vaccination ceased 30 years ago.
- Characteristics differentiating the Rashes of Variola and Varicella:

<table>
<thead>
<tr>
<th></th>
<th>Variola</th>
<th>Varicella</th>
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<tr>
<td>Centrifugal</td>
<td>Centripetal</td>
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<td>Lesions all at the same stage</td>
<td>Lesions in various stages</td>
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<td>Slow evolution</td>
<td>Rapid evolution</td>
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<td>Deep lesions: circular and regular</td>
<td>Superficial lesions: oval or irregular</td>
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<td>Scarring: severe</td>
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Viral Agents of Bioterrorism (contd.)

- Clinical diagnosis of Varicella virus infection (i.e. chickenpox) is adequate if the clinical presentation is typical. Atypical or unusually severe cases of Varicella should prompt consideration of laboratory testing to confirm the diagnosis of Varicella; the exclusion of Varicella, either via rapid diagnostic testing for Varicella antigen or viral culture should suggest the possibility of a pox virus infection or another alternate diagnoses.
- Treatment: Cidofovir and other antivirals but none are proven effective. Isolation: Airborne.
- Vaccination within 3 days of exposure will prevent disease and within 5 days life-saving. CDC has 12 – 14 million doses of vaccine. Oral vaccine in development.

Equine Encephalitis Viruses

- Togaviridae, all can be infectious by aerosol, easily produced and stable. VEE studied as a weapon by USA. Susceptibility is high (90-100%) with ~ 100% of those infected develop acute disease.
- Incubation period of 1-6 days followed by acute febrile illness with malaise, myalgias, fevers, rigors, severe headache, and photophobia x 24-72 hours followed by nausea, emesis, cough, sore throat, and diarrhea. 0.5-4% will develop encephalitis with altered mental status.
- Diagnosis on clinical and epidemiological grounds. Exam is non-specific. Lab often with leukopenia and lymphopenia, increased AST, and lymphocytic pleocytosis in CSF. Confirmation provided by viral isolation (throat, serum, CSF), serology (IgM available) and PCR.
- Treatment is supportive, mortality < 1% (increased at extremes of life), vaccine is experimental. Isolation: Airborne.

Viral Hemorrhagic Fevers

- Caused by various RNA viruses, usually with an animal reservoir. All are potentially infectious by aerosol with high morbidity and mortality.
  - Arenaviridae: Lassa, Argentine, Bolivian, Venezuelan, and Brazilian
  - Bunyaridae: Rift Valley Fever, Congo-Crimean, Hantaviruses
  - Filoviridae: Ebola, Marburg
  - Flaviviridae: Yellow Fever
- All hemorrhagic fever viruses can cause capillary leak syndromes.
- Incubation period 5-10 days (Filoviridae) followed by malaise, fever, myalgias, prostration, conjunctival injection, petechiae, ecchymoses, shock, diffuse hemorrhage, neurologic dysfunction and pulmonary collapse. Increased LFT’s and renal dysfunction poor prognosis.
- Diagnosis based on clinical and epidemiologic parameters. Definitive diagnosis: serology, PCR, and viral isolation.
Viral Agents of Bioterrorism (contd.)

- Treatment is largely supportive, avoiding ASA/antiplatelet drugs, Ribavirin (Lassa, CCHF, HFRS, and RVF). Vaccine available for Yellow Fever, Argentine, Bolivian, and Rift Valley Fever. Isolation = Airborne.

Influenza Virus

- As several of the bioagents may produce febrile, respiratory symptoms/signs, during the annual influenza season, the clinician should consider performing specific, diagnostic tests for the presence of influenza virus or antigen. Several rapid diagnostic tests are commercially available and can be performed on sputum samples. Viral isolation is also available and may assist in the management of these patients and others in the community (i.e. use of specific anti-influenza medications and vaccine optimization).
Biological Toxins of Bioterrorism

General Discussion
Biological toxins are products of living organisms, which produce illness or death after aerosol inhalation or ingestion. Substances are non-volatile and not likely to produce secondary person-person exposure - use Standard Precautions.

Botulinum Toxin
- (Types A-G) Most poisonous substance known. Botulinum toxin prevents release of acetylcholine at presynaptic nerve terminal and blocks nerve transmission. Aerosolized or food borne, typically presents 12-72 hours after exposure
- Symptoms
  - 4D's - diplopia, dysarthria, dysphonia, dysphagia.
  - Ptosis, mydriasis, generalized weakness, dizziness, dry mouth and throat, blurred vision, respiratory failure.
  - Naturally occurring food-borne botulism more prone to preceding abdominal cramps, nausea, vomiting and diarrhea secondary to other bacterial metabolites in food.

- Clinical Diagnosis
  - Symmetrical descending flaccid paralysis with prominent bulbar palsies,
  - Afebrile
  - Clear sensorium.

- Differential Diagnosis
  - Guillain-Barre,
  - Myasthenia gravis,
  - Tick paralysis,
  - Conversion reaction

- Action
  - Call public health department,
  - Draw at least 30cc blood (red top),
  - Sample feces, gastric secretions or vomitus.
  - Refrigerate samples and submit any suspect food.
  - Send list of patient's medications with samples.
  - Mouse neutralization assay can confirm diagnosis.
### Biological Toxins of Bioterrorism (contd.)

**Decontamination**

- If suspected aerosol release, breathe through clothing.
- Intact skin is impermeable, but wash skin with 0.1% hypochlorite or soap/water.
- Persistence of aerosolized toxin is dependent on atmospheric conditions and is usually inactivated by 2 days.
- In food, the toxin is inactivated by heat.

**Treatment**

- Botulinum antitoxin (to be used at first signs of illness) will minimize severity, but not reverse existent paralysis. Paralysis can persist for weeks to months. Respiratory support, nutritional and fluid management, treatment of complications.
- Botulinum Toxoid Vaccine is an investigational agent for individuals at high risk and is not effective in post exposure prophylaxis.

**Staphylococcal Enterotoxin B (SEB)**

**Symptoms**

- 2-12 hours after exposure. Fever (for 2-5 days), chills, headache, myalgia, nonproductive cough (up to 4 weeks).
- May have SOB, retrosternal chest pain, nausea, vomiting, diarrhea, conjunctival injection, hypotension, CXR usually normal, but can have atelectasis, pulmonary edema.
- Incapacitation for up to 2 weeks is usual, but rarely can progress to sepsis/death.

**Diagnosis** - clinical; nonspecific labs, elevated WBC, ESR.
**Differential Diagnosis** - influenza, adenovirus, mycoplasma.
**Action** - Draw acute and convalescent sera, urine sample for public health lab.
**Decontamination** - hypochlorite 0.5% or 10-15 min soap/water.
**Treatment** - supportive, respiratory support, fluid management.

**Ricin**

- Derived from castor bean, inhibits protein synthesis which results in cell death.
- Symptoms - (in 4-8 hours) weakness, fever, cough, hypothermia.

- Inhalation - severe respiratory symptoms from necrosis and edema, hypoxia with respiratory failure in 36-72 hours.
- Ingestion - Nausea, vomiting, diarrhea, GI hemorrhage, vascular collapse, death. May cause DIC, multiple organ failure.
Biological Toxins of Bioterrorism (contd.)

- Diagnosis - Lab nonspecific, Serum ELISA available.
- Differential Diagnosis - SEB, Q Fever, tularemia, plague, phosgene. Collect serum samples.
- Decontamination - hypochlorite 0.5% solution, and/or soap/water.
- Treatment - supportive, O2, hydration. If ingestion, gastric lavage, superactivated charcoal followed by cathartics.

Trichothecene

- Mycotoxins, T2. Fungal toxin- stable to heat and UV. Inhibits protein and nucleic acid synthesis affecting rapidly proliferating tissues. If aerosolized, it appears as yellow droplets - "yellow rain" – which can adhere to and penetrate skin, be inhaled and swallowed.
- Symptoms - onset minutes-4 hours- skin pain, pruritis, redness, vesicles, epidermal slough, eye irritation, nose throat pain, sneezing, wheezing, cough, dyspnea, chest pain, hemoptysis, abdominal pain, vomiting, bloody diarrhea. Bone marrow suppression can lead to diffuse hemorrhage. If severe, prostration, ataxia, collapse, shock and death in hours to days.
- Diagnosis - urine, blood, tissue samples for liquid chromatography-mass spectrometry.
- Decontamination - remove and isolate clothing, irrigate eyes with saline; wash with soap/water.
- Treatment - symptomatic/ supportive. If ingested, superactivated charcoal. No antidote.
Chemical Agents of Terrorism

Nerve Agents

- Description
  - Organophosphates bind and inactivate acetylcholinesterase. Colorless, nearly odorless
  - Sarin (GB)
  - Tabun (GA)
  - Soman (GD)
  - VX - clear

- Diagnosis - acute onset cholinergic crisis. Sarin may cause death in 1-10 minutes

- Symptoms
  - Respiratory - irritation to mucous membranes, cough, airway constriction and increased secretions
  - Neuromuscular - twitch, weakness, paralysis, respiratory failure
  - Autonomic - blurred vision, pinpoint pupils, drooling, sweating, tearing, nausea, vomiting, abdominal pain, diarrhea
  - Central Nervous System - slurred speech, confusion, headache, convulsions, respiratory arrest
  - Cardiovascular - tachycardia, bradycardia, arrhythmia, heart block

- Decontamination - move victim to fresh air, remove and isolate clothing, wash skin/eyes with water/saline. 0.5% hypochlorite to skin if possible

- Treatment
  - Oxygen/respiratory support, suction secretions. Rush to healthcare facility
  - Atropine (antagonizes muscarinic effects) 2 mg deep IM injection, IV, or ET, Repeat q5-10min until secretions are drying and decreased airway resistance (to max 20 mg.) Infant (0.5mg IM or 0.02mg/kg), child 2-10 (1 mg IM), elderly (1mg) This will not have any effect on pupils or skeletal muscle.
  - Pralidoxime chloride (2 PAM chloride) - helps nicotinic neuromuscular sites. Separates nerve agent from AChE, (but once "aging" has occurred, nerve agent is permanently attached to AChE, 2PAM will no longer be effective) 1g IV over 20-30 min., may repeat in 1 hour (child< 20kg-15mg/kg, child >20kg - 600mg IM autoinjector, elderly 7.5mg/kg) Use Phentolamine for 2PAM induced hypertension (adult 5mg IV, child 1mg IV)
  - Diazepam - 10mg IM (2-5mg IV) Child 1mo-5yr- 0.2-0.5mg/kg; child >5y - 1 mg IV
  - Supportive care for weeks may be necessary
Chemical Agents of Terrorism (contd.)

Vesicants

- General Effects
  - Cell damage, tissue necrosis, toxic byproducts, metabolic acidosis, secondary infections, pulmonary insufficiency
- Mustard
  - HD H- latent period hours- erythema and blisters on skin, irritation, conjunctivitis, mild upper respiratory sx to marked airway damage. Also GI effects, nausea and vomiting, bone marrow suppression
  - Wash with water and dilute hypochlorite
  - Topical antibiotics, pulmonary support, analgesics
- Lewisite
  - L- immediate pain, skin and mucous membrane irritation, erythema, blisters skin, eye and airway
  - Wash water/hypochlorite. British Anti-Lewisite antidote (BAL)

Industrial Chemicals

- Phosgene - CG- odor of fresh cut grass, hay.
  - Damages alveolar-capillary membrane. Toxic to lungs by inhalation-immediate burning, eye and airway damage, SOB, cough; Pulmonary edema can develop in 2-12 hours
  - Treatment- Fresh air, wash with water, symptomatic management of lesions, pulmonary care, careful fluid replacement, absolute rest
- Cyanide
  - Inhibits the body’s ability to transfer oxygen and CO2 at the capillaries. Agent is volatile
  - Symptoms - seizures, respiratory, and cardiac arrest.
  - Decontamination - remove clothing; wash with water
  - Treatment- antidotes: intravenous sodium nitrite and sodium thiosulfate.
  - Supportive oxygen and correction of acidosis
- Riot Control Agents (Mace®, pepper spray)
  - Symptoms - burning pain skin, mucous membranes and eyes
  - Treatment - flush with water, soap and water or dilute sodium bicarbonate solution. (Hypochlorite should NOT be used)
  - Effects are self-limited, unless underlying asthma/emphysema or hysteria from fear of nerve agent exposure
Overview of Vaccines for Bioagents

Anthrax

- The anthrax vaccine was developed in the 1950s and is a strain producing a protective antibody response in 7 days. Doses are required at 0, 2, 4, 6, 12 and 18 months with annual boosters. The United States military first started mass vaccinating troops for the Gulf war in 1991. The military still routinely vaccinates personnel against anthrax. The anthrax vaccine is only recommended for people between 18 and 65.

- There is a great deal of debate about the safety and efficacy of the anthrax vaccine in the setting of intentional aerosol exposure. There is no solid data on anthrax vaccine safety, especially in large numbers of people, and the incidence of systemic adverse reactions appears to be about 0.006-.5%. There have been no randomized trials done in humans for intentional exposure.

- Although minor local reactions are common (about 30%), the best data suggest that systemic reactions are rare (0.06 - 0.5%). Unfortunately, the data from recent military vaccination programs has been incomplete. It's always possible that more adverse reactions will come to light when a vaccine like this is given to large numbers of people but, based on the existing data, it appears to be pretty safe (Moran, GJ. Biological Terrorism Part I and II. Emergency Medicine, 2000).

- Although no gold-standard double-blind, placebo controlled human efficacy trials have been conducted, a single-blind, placebo controlled trial using the less potent form of the vaccine was conducted in goat hair mill workers in New Hampshire from 1955-59. The vaccine conferred statistically significant reduction in the incidence of anthrax overall (cutaneous plus inhalational) and suggested a reduction in the incidence of inhalational anthrax, but the numbers of cases of inhalational disease were too small to attain statistical significance. In addition, trials on non-human primates and guinea pigs have shown that the vaccine is effective against fatal disease due to infection by the aerosol route. (Friedlander, A. M., P. R. Pittman, et al. (1999). "Anthrax Vaccine: Evidence for Safety and Efficacy Against Inhalational Anthrax." Journal of the American Medical Association 282:2104-6.)

- In the setting of a known or strongly suspected anthrax exposure, the potential benefit of the vaccine would likely exceed the risk. The risk/benefit balance for pre-exposure vaccination for large numbers of people is debatable, since the probability of exposure is very low for most (Moran, GJ. Biological Terrorism Part I and II. Emergency Medicine, 2000).

Smallpox

- The existing vaccine may prevent or ameliorate illness if given within 3-4 days of exposure. Passive immunization is capable through vaccinia immune globulin if given within the first 24 hours of exposure. There are approximately 5 to 10 million doses of the small pox vaccine in the United States, however no distribution program currently exists. (Gordon, S. M. (1999). "The Threat of Bioterrorism: A Reason to Learn More About Anthrax and Smallpox." Cleveland Clinic Journal of Medicine 66(10): 592-600.)
Overview of Vaccines for Bioagents (contd.)

- The United States has contracted with OraVax Inc (Cambridge, MA) who is subcontracting with Bio-Reliability (Washington, DC) to begin developing more vaccines. The initial production of 40 million doses is not expected to be complete until 2004 (www.LocalBusiness.com).

Viral Hemorrhagic Fevers
- An investigational new drug (IND) vaccine is available for yellow fever as well as for Argentine hemorrhagic fever (AHF) that may also protect for Bolivian hemorrhagic fever (BHF). There are also two vaccines for Rift Valley fever (RVF) designed by the military. The first vaccine requires 3 boosters and then is effective for 20 years. The second is a live attenuated strain that is still being tested. (Franz, D.R, e. a. (1997). "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents." Journal of the American Medical Association 278(5): 399-411.)

Plague
- A USA licensed formaldehyde-killed whole bacilli vaccine was discontinued in 1999 because it was only effective against bubonic plague. Research is currently underway for a vaccine to protect against pneumatic plague. (Inglesby, T. V. e. a. (2000). "Plague as a Biological Weapon." Journal of the American Medical Association 283(17): 228-90.)

Tularemia

Botulism

Viral Encephalitis
- Immunizations are available for Venezuelan equine encephalitis (VEE), western equine encephalitis (WEE), and eastern equine encephalitis (EEE) in the United States but may require multiple injections and are poorly immunogenic. Adequate immunization against encephalitis may require polyvalent vaccines. (Franz, D.R, e. a. (1997). "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents." Journal of the American Medical Association 278(5): 399-411.)