Biological Agents
Advantages / Disadvantages of Biological Agents

**Advantages**
- Available
- Hard to detect
- Used covertly
- Easily spread
- Tie up resources
- Psychological impact
- Difficult to prepare for

**Disadvantages**
- Delayed effects may be counterproductive
- Production and deployment hazardous to terrorist
History

Use of biological agents as weapons of war has occurred throughout history. Notable examples include:

- In 184 BC, Hannibal ordered that pots filled with serpents be thrown onto the decks of enemy ships.

- In 1346, the Tartar army catapulted bodies of plague victims into the city of Caffa.

- In 1763, the British army provided the Delaware Indians with blankets that had been used by smallpox patients.

- During World War I, the Germans used various human and animal pathogens as agents of germ warfare in Europe.

- During World War II, the Japanese used germ warfare against the Chinese and the Soviets.
History

Following World War II, several countries maintained biological weapons programs, including the United States, the Soviet Union, Canada, and the United Kingdom.

However, the United States, Canada, and the United Kingdom all ended their programs by the early 1970s.

In 1972, more than 140 countries signed the Biological and Toxin Weapons Convention, which called for termination of all offensive biological weapons research and development and destruction of existing biological weapons stocks.
History

Despite these positive events aimed at curtailing the availability of biological weapons, the Soviet Union continued to expand its biological weapons program throughout the 1980s and early 1990s.

Key aspects of the program included the production of large amounts of smallpox virus and the development of mechanisms to weaponize it.

Eradication of naturally occurring smallpox and the cessation of routine vaccination against the disease in 1980 was seen by the Soviet Union as an opportunity to use smallpox virus as a biological weapon.

Anthrax was another disease actively studied by the Soviet Union, as evidenced by the outbreak of inhalational anthrax that followed release of aerosolized anthrax from the Sverdlosk bioweapons production facility in 1979. Seventy-seven cases of anthrax were identified and 66 of the patients died.
Recent History

In 1992, 20 people were administered chemoprophylaxis after a Virginia man sprayed his roommates with a substance that he claimed was anthrax.

In 1994, a Japanese sect of the Aum Shinrikyo cult attempted an aerosolized release of anthrax from the tops of buildings in Tokyo.

In 1995, 2 members of a Minnesota militia group were convicted of possession of ricin, which they had produced themselves for use in retaliation against local government officials.

In 1996, an Ohio man was able to obtain bubonic plague cultures through the mail.

2001 Anthrax Letters
2003 Ricin Letters
Present

Because weaponized forms of certain biological agents have been developed, the threat of using such agents against civilian populations through bioterrorism attacks has emerged over the past few years.

17 countries are suspected of having an offensive BW program.

Bioterrorism, which had been largely a topic of speculation, became a serious reality for the United States in October 2001, when anthrax cases following exposure to contaminated mail occurred in New York, New Jersey, and Washington, DC.
The Most Likely Biological Agents (CDC)

Category A agents:

• Can be easily disseminated or transmitted person-to-person
• Cause high mortality with potential for major public health impact
• Might cause public panic and social disruption
• Require special action for public health preparedness

Include:
  Bacillus anthracis (anthrax)
  Clostridium botulinum toxin (botulism)
  Yersinia pestis (plague)
  Francisella tularensis (tularemia)
  Variola major virus (smallpox)
  Ebola, Marburg, Lassa, and South American hemorrhagic fever viruses (viral hemorrhagic fever)
The Most Likely Biological Agents (CDC)

Category B agents:

- Are moderately easy to disseminate
- Cause moderate morbidity and low mortality
- Require specific enhancements of diagnostic capacity and disease surveillance

Include:
- Coxiella burnetti (Q fever)
- Brucella species (brucellosis)
- Burkholderia mallei (glanders)
- Alphaviruses (Venezuelan encephalomyelitis and eastern and western equine encephalomyelitis)
- Ricin toxin from Ricinus communis (castor beans)
- Epsilon toxin of Clostridium perfringens
- Staphylococcus enterotoxin B
- Salmonella species
The Most Likely Biological Agents (CDC)

Category C agents:
Include emerging pathogens that could be engineered for mass dissemination in the future because of:
• Availability
• Ease of production and dissemination
• Potential for high morbidity and mortality and major health impact

Include:
Nipah virus
Hantaviruses
Tickborne hemorrhagic fever viruses
Tickborne encephalitis viruses
Yellow fever virus
Multidrug-resistant Mycobacterium tuberculosis
Means of Dissemination

Biological agents used in a bioterrorism attack would likely enter the human body through one of several routes:

• **Inhalation** of small particles into the lungs

• **Ingestion** of contaminated food or water

• **Injection** or contamination of the skin or absorption of toxins through the skin
Means of Dissemination

Inhalation

The inhalational route is of greatest concern, since all of the Category A agents listed above can be effectively disseminated through aerosolization.

Use of aerosols is an efficient way to affect the maximum number of people with a single attack.

Aerosolized particles of 1 to 5 microns in size can easily be inhaled deeply into the lungs of intended victims.
Means of Dissemination
Aerosols

Aerosols can be delivered in either wet or dry form. 2001 outbreak of anthrax on the East Coast of the United States involved use of a fine, dry, anthrax-containing powder.

Mechanisms to disseminate aerosols include:

• Wide-scale dissemination out-of-doors through use of crop-dusting planes and equipment

• Use of small aerosol-generating devices in closed spaces (eg, subway systems, shopping malls, theaters)

• Installation of aerosols into the ventilation systems of buildings

• Contamination of items in the environment with fine powders that are easily aerosolized when disrupted (as with the recent anthrax cases in the United States, which have been caused by contaminated mail)
Means of Dissemination
Ingestion

Although not as efficient as aerosol transmission, ingestion of contaminated food or water remains a concern.

Two disease outbreaks in the United States have been caused by deliberate contamination of food.

The first occurred in The Dalles, Oregon, where members of the Rajneashee religious cult contaminated salad bars with Salmonella; over 700 people became ill.

A second outbreak occurred in a laboratory in Texas where an employee contaminated bakery goods with Shigella dysenteriae; 12 people became ill.
Means of Dissemination
Injection/Absorption

• Transmission of infection via the skin was demonstrated with the 2001 cases of cutaneous anthrax that resulted from direct contact with contaminated mail.

• 1968 Georgi Markov injected with .01 grams of ricin. His health quickly deteriorated, and he died three days later.
Means of Dissemination

A large-scale bioterrorist attack involving ingestion of food and water is less likely than an attack involving the airborne route for the following reasons:

• Most of the Category A agents are not transmitted via food and water.

• Most of the illnesses transmitted through food and water involve short-term vomiting and diarrhea with relatively quick recovery, so these agents are of less interest to terrorists.

• Current water treatment procedures effectively kill biological agents and rapidly inactivate botulism toxin.

• Chemical contamination of water is unlikely because very large amounts of toxin would be needed to effectively contaminate a water supply because of the dilution factor.

• Thorough heating and cooking of food destroys biological agents and botulism toxin, and widespread contamination of an uncooked food item is relatively unlikely.
Introduction to Biological Agents
“Living” Biological Agents

**Bacteria** – Single-celled organisms, capable of causing a variety of diseases in animals, plants, and humans. They may also produce extremely potent toxins inside the human body. These single-celled organisms may also be cultured in nutrient media.

**Rickettsia** - A class of cellular life smaller than bacteria but larger than viruses, rickettsia can only multiply inside living cells. They cause diseases such as Q fever and typhus.
BACTERIA AND RICKETTSIA
“Living” Biological Agents

• Anthrax
• Plague
• Tularemia
• Brucellosis
• Q-Fever
Introduction to Biological Agents

“Living” Biological Agents

Viruses – They are smaller than bacteria, and unlike bacteria and rickettsia, they are totally dependent on the host’s living cells for reproduction.

- Smallpox
- Venezuelan Equine Encephalitis (VEE)
- Viral Hemorrhagic Fevers (VHF)
“Living” Biological Agents Characteristics

• Incubation
  • Days to weeks
• Generally non-contagious except plague & smallpox
• Most cause flu-like symptoms
• Routes of exposure
  • Inhalation – most severe
  • Ingestion, injection (varies by agent)
Introduction to Biological Agents

Toxins – Potent poisons are produced by a variety of living organisms—including bacteria, plants, and animals; some biological toxins are the most toxic substances known. Some of the botulinum toxins are 10,000 times more toxic than the nerve agent sarin. (Ricin is 20 to 50 times more toxic than sarin depending on route of entry.)
Toxins

• Botulinum

• Staphylococcal Enterotoxins (SEB)

• Ricin

• Mycotoxins
Toxins Characteristics

• Rate of action
  • Minutes to hours
• Not contagious
• Symptoms vary widely
• Routes of exposure (all four routes)
  • Inhalation
  • Ingestion
  • Injection
  • Absorption
General Characteristics
Common to the broad spectrum of biological agents

• Range of effects: Biological agents have a variety of effects depending on the organism, how it affects humans, the dose received, and the route of entry. This range can vary from mild effects to death.

• Obtained from nature: Most biological agents have a natural host. Some biological agents (toxins) are the by-products or waste products of other biological agents.
General Characteristics

Common to the broad spectrum of biological agents

• Relatively easy to produce: This ties to the last characteristic. The key term here is relatively. If one can obtain a culture of an organism and know how to culture it (provide a suitable environment, provide nutrients, allow it to reproduce), one can increase the quantity using basic procedures and easily obtainable equipment.

• Invisible to the senses: The initial exposure to biological agents may not be detectable to the senses, especially when the agent is disseminated in an aerosol form.

• Have delayed effects: Most biological agents require days to weeks before the effects are felt. Once the incubation period is completed, victims will begin to exhibit effects of the exposure that occurred days or weeks before.
## Bio-Agent Information

<table>
<thead>
<tr>
<th>Agent</th>
<th>Contagious</th>
<th>Lethality</th>
<th>Incubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>No (skin slight)</td>
<td>High</td>
<td>1-7 days</td>
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<tr>
<td>Plague</td>
<td>Yes</td>
<td>High</td>
<td>1-6 days</td>
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<tr>
<td>Tularemia</td>
<td>No</td>
<td>Moderate</td>
<td>1-10 days</td>
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<td>Brucellosis</td>
<td>No</td>
<td>Low</td>
<td>1-3 weeks</td>
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<tr>
<td>Q-fever</td>
<td>Rarely</td>
<td>Low</td>
<td>10-21 days</td>
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<tr>
<td>Smallpox</td>
<td>Yes</td>
<td>Moderate</td>
<td>7-17 days</td>
</tr>
<tr>
<td>VEE</td>
<td>Mildly</td>
<td>Low</td>
<td>1-6 days</td>
</tr>
<tr>
<td>VHF</td>
<td>Moderate</td>
<td>Moderate to high</td>
<td>Varies</td>
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</tbody>
</table>
BIOLOGICAL AGENTS SIMILARITIES WITH CHEMICAL AGENTS

- Can cover large areas (aerosols)
- Produce mass casualties
- Relatively inexpensive to produce
BIOLOGICAL AGENTS DIFFERENCES FROM CHEMICAL AGENTS

- Delayed effects
- Non-volatile
- Generally more toxic by weight
- Less skin hazard
- Possibly contagious
DETECTION OF BIOLOGICAL ATTACKS

• Recognizing a biological attack is difficult
• Symptoms unlikely at scene
• Calls to 9-1-1 and EMS responses
• Medical community response
• Epidemiology
WARNING SIGNS AND CLUES (con’t)

- Abandoned spray devices
- Chemical containers or lab equipment
- Biohazard labels
WARNING SIGNS AND CLUES

• Verbal or written threats

• Suspicious incidents, such as bombings with little fire or physical damage
BIOLOGICAL FIELD DETECTION AND IDENTIFICATION SYSTEM

- “SMART” tickets
- Biological laboratory
- Biological integrated detection system (BIDS)
PROPER SELF-PROTECTION

• Respiratory protection
• Clothing
• Sanitation measures
• Decontamination
DECONTAMINATION

Wet → Strip → Flush → Cover
PROPER SELF-PROTECTION

Most aerosolized biological agents do not penetrate unbroken skin, and few organisms adhere to skin or clothing.

After an aerosol attack, simple removal of clothing eliminates a great majority of surface contamination.

Thorough showering with soap and water removes 99.99% of the few organisms left on the victim's skin after disrobing.
DECONTAMINATION (con’t)

• Emergency Decon:
  – Self
  – Small/large group
  – Mass casualty

• Technical Decon:
  – Tools
  – Suits
  – Other equipment
Treatment

Broad-spectrum intravenous antibiotic coverage is recommended initially for victims when a BW agent is suspected. Institute this even prior to the identification of the specific BW agent.

Vaccinations currently are available for anthrax, botulinum toxin, tularemia, plague, Q fever, and smallpox.

The widespread immunization of nonmilitary personnel has not been recommended by any governmental agency.

Immune protection against ricin and staphylococcal toxins may be feasible in the near future.
KEY POINTS

• First indication may be 9-1-1 calls or patient “surge” on medical facilities
  – Good sanitary procedures/universal precautions on site
  – Protective mask/HEPA mask, properly fitted
  – Seek medical attention immediately
  – Treatments are available
PART 2
SOME POTENTIAL BIOLOGICAL AGENTS

- Anthrax
- Plague (yersinia pestis)
- Q fever (coxiella burnetii)
- Smallpox
- Viral hemorrhagic fevers (ebola, marburg, lassa, rift valley, dengue, etc.)
- Venezuelan equine encephalitis (VEE)
- Seb
- Botulinum neurotoxins
- Ricin
VIRUSES

- Smaller than bacteria
- Use living cells to reproduce

Ebola Virus
TOXINS

• Castorbean plant: *ricinus communis*
ROUTES OF ENTRY

- Inhalation
- Ingestion
- Skin
AEROSOL DISTRIBUTION
INGESTION

- In Oregon, a religious sect strayed solutions containing salmonella on salad bars.
DERMAL EXPOSURE
BIOLOGICAL AGENTS
CHARACTERISTICS

• Range of effects
• Obtained from nature
• Relatively easy to produce
• Invisible to the senses
• Have delayed effects
ANTHRAX

• Skin, digestive, respiratory

• Symptoms: itching, lesions, fever, fatigue, non-productive cough, and chest discomfort

• Mortality
  – 5 to 20 % (percutaneous)
  – 90 to 95% (inhalation)

• Incubation: 1 to 7 days
Vegetative cells form spores when nutrients in the environment are exhausted. Spores have been shown to survive in the environment for more than 40 years.

Spores germinate and form vegetative cells in environments rich in nutrients (e.g., glucose, amino acids, nucleosides).
ANTHRAX
(Bacteria)

Naturally Occurring Anthrax

*B. anthracis* exists in the endospore form in soil in many areas of the world.

Endospores are resistant to drying, heat, ultraviolet light, gamma radiation, and some disinfectants. Spores can persist in soil for decades, as illustrated by biological warfare experiments during World War II on the Scottish island of Gruinard.
ANTHRAX
(Bacteria)

Anthrax in Animals

Anthrax is predominantly a disease of animals.

Livestock or other herbivores (eg, cattle, sheep, goats, pigs, bison, water buffalo) acquire infection from consuming contaminated soil or feed.

Found in:
- Most areas of the Middle East
- Most areas of equatorial Africa
- Mexico and Central America
- Chile, Argentina, Peru, and Bolivia
- Certain Southeast Asian countries (eg, Myanmar, Vietnam, Cambodia, Thailand)
- Papua New Guinea
- China
- Some Mediterranean countries

In the United States, outbreaks in animals have occurred since 1990 in the Midwest (Kansas, Nebraska, North Dakota, South Dakota, Missouri); in the West (California, Nevada); and in Texas and Oklahoma.
ANTHRAX (Bacteria)

Inhalational Anthrax
• Incubation period 2-43 days (may be longer)*

Cutaneous anthrax
• Incubation period 1-7 days (may be as long as 12 days)

Gastrointestinal anthrax
• Incubation period 1-7 days (usually 2-5 days)
ANTHRAX (Bacteria)

Modes of Transmission

Illness in humans most commonly occurs following exposure to infected animals or contaminated animal products; such exposures include:

- Contact with infected tissues of dead animals (eg, butchering, preparing contaminated meat), which generally leads to cutaneous anthrax

- Consumption of contaminated undercooked meat, which can lead to gastrointestinal or oropharyngeal anthrax

- Contact with contaminated hair, wool, or hides (particularly during processing) or contact with products made from them, which can lead to either inhalational or cutaneous anthrax
ANTHRAX
(Bacteria)

Anthrax in Humans—United States

Approximately 130 cases occurred annually in the United States in the early 1900s. The incidence has gradually declined over time, with less than 10 cases reported each year since the early 1960s.

About 95% of naturally occurring cases in the United States are cutaneous and 5% are inhalational. Gastrointestinal infection has not been recognized in this country.
ANTHRAX (Bacteria)

Anthrax in Humans—Global Perspective

- An estimated 2,000 to 20,000 human cases of anthrax occur globally each year.

- Most cases are cutaneous, with inhalational and gastrointestinal cases occurring less frequently.

- Human cases generally follow disease occurrence in hoofed animals and are most prevalent in Africa, the Middle East, and parts of Southeast Asia.
Outbreaks of Naturally Occurring Disease

Outbreaks have been reported in industrial settings where animal products are processed and in agricultural settings following consumption of or exposure to ill animals.

Notable examples of outbreaks include the following:

• A major outbreak involving nearly 10,000 cases (most of them cutaneous infection) occurred in Zimbabwe during the late 1970s and early 1980s

• An outbreak involving nine cases (five inhalational and four cutaneous) occurred in 1957 in the United States in a New Hampshire goat-hair processing plant. This was the last recognized outbreak of naturally occurring infection in this country.
ANTHRAX (Bacteria)

Anthrax as a Bioterrorist Weapon

Aerosol release of weaponized spores is the most likely mechanism for use of anthrax as a biological weapon.

However, deliberate contamination of food also potentially could occur.

During World War II, the Japanese reportedly impregnated chocolate with anthrax to kill Chinese children.

The apartheid government of South Africa also experimented with anthrax in chocolate.
Anthrax as a Bioterrorist Weapon

The impact of a large aerosol release of weaponized anthrax remains unknown; however, scenarios have been hypothesized, including:

• A 1970 WHO report estimated that an aerosol release of 50 kg of dried powder containing $6 \times 10^{15}$ anthrax spores over a city of 5 million people in an economically developed country (such as the United States) would produce 250,000 incapacitating illnesses and up to 100,000 deaths

• A 1993 Office of Technology Assessment (OTA) study estimated that up to 3 million deaths could occur following the release of 100 kg of B anthracis
**ANTHRAX**  
(Bacteria)

**Anthrax as a Bioterrorist Weapon**

Deliberate contamination of food or water with anthrax spores also is a possibility.

Even though contamination of a water supply is unlikely owing to the large volume of water involved and the chlorination process, contamination of smaller water sources is theoretically feasible since spore counts remain stable in water for at least several days following inoculation.

Since *B. anthracis* spores are not destroyed by pasteurization, contamination of milk is another theoretical possibility.
ANTHRAX (Bacteria)

Weaponized anthrax has caused two outbreaks of disease:

The Sverdlovsk Outbreak—1979

United States—2001
ANTHRAX
(Bacteria)

The Sverdlovsk Outbreak—1979

• This outbreak in the USSR resulted from accidental release of anthrax spores from a military microbiologic facility where weaponized anthrax was being produced

• A recent statistical analysis of available data suggests that 250 cases with 100 fatalities may actually have occurred

• The mean incubation period was 9 to 10 days (range, 2 to 43 days), and the mean time between illness onset and death was 3 days.

• Investigators postulated that the weight of spores released as aerosol "could have been as little as a few milligrams or as much as nearly a gram."
ANTHRAX
(Bacteria)

United States—2001

• The outbreak predominantly involved direct exposure to mail that was deliberately contaminated with anthrax spores.

• Several contaminated letters were sent and one was reported to contain 2 g of powder, with 100 billion to 1 trillion anthrax spores per gram.

• Twenty-two cases (11 inhalational and 11 cutaneous) were identified. Five of the patients with inhalational anthrax died, for a case-fatality rate of 45% among that group.
ANTHRAX
(Bacteria)

United States—2001

• Cases occurred in residents of seven states along the East Coast of the United States (Connecticut, Florida, Maryland, New Jersey, New York, Pennsylvania, and Virginia), with illness onsets between September 22 and November 16, 2001.

• Four contaminated letters were recovered; all four were mailed in or around Trenton, New Jersey. Two were postmarked September 18, 2002, and two were postmarked October 9, 2002.
ANTHRAX (Bacteria)

United States—2001

The outbreak demonstrated several important points about weaponized anthrax:

- Mail can be an effective vehicle for disseminating anthrax spores.
- Cross-contamination of mail likely can occur within postal facilities.
- Persons who handle or process unopened contaminated mail are at risk of acquiring anthrax.
- Substantial environmental contamination can occur in facilities handling contaminated mail or in offices where contaminated mail is opened.
SMALLPOX

- Respiratory
- Contagious
- Symptoms: rash, maybe fever, muscular rigidity, headaches, and vomiting
- Mortality: 3 to 30%
- Incubation: 10 to 12 days
SMALLPOX
(Virus)

The case-fatality rate was usually about 30% in unvaccinated persons (range, 15% to 45%)

Incubation period* — 10-13 days (usually about 12 days)
— May be as short as 7 days and as long as 19 days

Rash
- First few skin lesions often appear on face ("herald spots")
- Lesions spread to trunk and proximal extremities and then to distal extremities
SMALLPOX
(Virus)

Occurrence of Smallpox in the Pre-eradication Era

- Smallpox likely originated in Egypt or India over 3,000 years ago

- Egyptian mummies dating from as early as 1500 BC showed characteristic pox-like skin lesions suggestive of smallpox.

- By the mid-1700s, smallpox was a major endemic disease throughout the world, except in Australia, where it was first introduced in 1789 and again in 1829.
SMALLPOX
(Virus)

Global Eradication of Smallpox

- By the early 1950s, endemic smallpox had been eradicated from Europe, the USSR, and North and Central America

- However, the disease remained endemic throughout most of the developing world, with an estimated 50 million cases occurring each year
Global Eradication of Smallpox

- In 1959, the 12th World Health Assembly of the World Health Organization (WHO) passed the first resolution for global eradication of smallpox; however, it was not until 1967 that substantial resources were dedicated to the project.

- The basic strategy of smallpox eradication included: (1) mass smallpox vaccination campaigns and (2) surveillance and containment of outbreaks.

- After an extensive, sustained, international collaboration over a 12-year period, the International Commission for the Global Certification of Smallpox Eradication declared in December 1979 that smallpox had been globally eradicated.
SMALLPOX
(Virus)

The following epidemiologic features of smallpox facilitated global eradication:

• Humans are the only natural reservoir for variola virus.
• Vectorborne transmission of the virus does not occur.
• The virus does not survive in nature for prolonged periods of time.
• The full-blown clinical illness is easily recognizable, allowing for accurate clinical surveillance of the disease.
• The infectivity of variola virus is relatively low (ie, transmission generally requires relatively close face-to-face contact except in uncommon circumstances), making it possible to effectively interrupt chains of transmission.
• An effective vaccine exists.
• The incubation period (ie, 10 to 12 days) is long enough for a vaccination/containment strategy to be effective.
SMALLPOX
(Virus)

• Before global eradication, the only reservoir for variola virus was humans. No natural reservoir for the virus currently exists.

• Stocks of variola virus have been retained in two WHO-approved collaborating centers: the Centers for Disease Control and Prevention (CDC) in Atlanta and the Russian State Centre for Research on Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation)

• There are concerns that not all the smallpox preparations developed in the Russian bioweapons program can be accounted for and that unknown caches of variola virus may exist.
SMALLPOX
(Virus)

Modes of Transmission

• Variola virus is predominantly transmitted person-to-person via inhalation of droplet nuclei. Transmission occurs most commonly among those with close face-to-face contact with an infected patient.

• Airborne transmission has been documented in two outbreaks that occurred in hospitals in the Federal Republic of Germany (one in 1961 and one in 1970)

• Fomite transmission (eg, from laundry and bedding) has been reported. Contaminated fomites (ie, blankets) were used for intentional transmission of smallpox during the French-Indian wars in the United States in the 1700s

• Transmission via direct contact with skin lesions and infected body fluids also has been recognized
SMALLPOX
(Virus)

Communicability

- The infectious dose is presumed to be low (10 to 100 organisms).

- Most epidemiologic data suggested that infectiousness in smallpox correlated with rash onset.

- However, patients with smallpox should be considered infectious from the time of onset of fever, because virus is present in, and shed from, the oral lesions as they ulcerate during the 1 to 2 days of fever preceding rash onset.

- Infectiousness is considered to be highest during the first week after rash onset when lesions in the mouth ulcerate and release large amounts of virus into the saliva.

- The period of communicability lasts until all the lesions have scabbed over and the scabs have fallen off.
SMALLPOX
(Virus)

Use of Smallpox as a Biological Weapon

• Smallpox was used as a biological weapon during the French-Indian wars in the United States (1754-1767), when British soldiers gave the Indians blankets that had been used by smallpox patients

• In 1972, more than 140 countries signed the Biological and Toxin Weapons Convention, which called for termination of all offensive biological weapons research and development and destruction of existing biological weapons stocks.

• Despite participating in the 1972 convention, the former Soviet Union continued to expand its biological-weapons program throughout the 1980s and early 1990s. During that time, the Soviet Union reportedly developed weaponized variola virus that could be mounted in intercontinental ballistic missiles and bombs for strategic use
SMALLPOX
(Virus)

Use of Smallpox as a Biological Weapon

• Currently, variola virus is known to be stored in two facilities (at the CDC in Atlanta and at the Russian State Centre for Research on Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation).

• In the early 1980s, WHO recommended that all existing stocks of variola virus held in other countries be either destroyed or shipped to one of the two WHO-approved collaborating centers.

• All countries reported compliance; however, there has been no systematic way to assure that all countries actually did comply with the WHO recommendations.

• Also, there is no way to be certain that the virus has not fallen into the hands of rogue nations or potential terrorists.
SMALLPOX
(Virus)

Use of Smallpox as a Biological Weapon

Smallpox is of concern as a biological weapon for several reasons:

- Much of the population is susceptible to infection
- Virus carries a high rate of morbidity and mortality
- Vaccine is not yet available for general use
- Past experience has demonstrated that introduction of the virus creates a great deal of havoc and panic
Use of Smallpox as a Biological Weapon

- Aerosol release of virus (such as into an airport or subway system) would be the most efficient form of release and would likely result in the highest number of cases.

- Other possibilities include use of "human vectors" (i.e., persons who have been deliberately infected with smallpox) and use of fomites (e.g., contamination of letters sent through the mail)
Use of Smallpox as a Biological Weapon

Several studies have used modeling to examine the impact of a deliberate release of smallpox virus.

- In a recent model, investigators estimated that 100 index smallpox cases in a city of 2 million would result in 730 additional cases, assuming that control measures begin at 25 days after release and that the outbreak is controlled with ring vaccination and case isolation.

- Another model also demonstrated that ring vaccination can be successful if infectious cases are rapidly diagnosed; however, the size and duration of contained outbreaks was highly variable.
SMALLPOX (Virus)

Use of Smallpox as a Biological Weapon

- Given the recent attention to smallpox, ongoing global vigilance to rapidly detect any recurrence through accidental or intentional release is necessary.

- Furthermore, even if all stocks of naturally occurring smallpox virus are destroyed, it is now possible to genetically engineer a similar viral agent in the laboratory setting.

- This capability requires that the medical and public health communities maintain smallpox preparedness into the foreseeable future.
SMALLPOX
(Virus)

Smallpox Vaccination
Routine smallpox vaccination in the United States stopped in 1972 for children and in 1976 for healthcare workers. Prior to 1972, smallpox vaccine was recommended for all children in the United States at 1 year of age.
SMALLPOX
(Virus)

Smallpox Vaccination

On December 13, 2002, President Bush announced the following US policy:

- Smallpox vaccinations are required for military personnel. According to the Department of Health and Human Services (DHHS), approximately 500,000 military personnel will be vaccinated.

- Smallpox vaccinations are recommended for smallpox response teams comprised of public health staff and healthcare workers likely to be involved in the initial care of any patients with smallpox.

- Smallpox vaccinations also are being offered to other healthcare workers and to first-responders (including police officers, firefighters, and emergency medical technicians).

- Smallpox vaccinations may be made available to the general public on a voluntary basis once large stockpiles of the vaccine are licensed.
SMALLPOX
(Virus)

Smallpox Vaccination
Smallpox response teams and healthcare worker teams
• Smallpox vaccination is recommended for persons designated by the appropriate bioterrorism and public health authorities to conduct investigation and follow-up of initial smallpox cases (ie, smallpox response teams).

• These teams might include medical team leaders, public health advisors, medical epidemiologists, disease investigators, diagnostic laboratory scientists, nurses, personnel who would administer smallpox vaccines, and security/law enforcement personnel.
Liability Issues Following Smallpox Vaccine Administration

The Homeland Security Act of 2002 (Section 304) addresses issues regarding liability following smallpox vaccination

Smallpox Emergency Personnel Protection Act of 2003. The law establishes a no-fault program to provide benefits and compensation to certain individuals (ie, healthcare workers and emergency responders) who are injured as a result of administration of smallpox vaccination or other smallpox countermeasures
Use of Vaccine During a Smallpox Emergency

“Ring vaccination” strategy - involves creating a circle of vaccinated persons around each case to interrupt the chain of transmission.

- Rapid identification and isolation of all smallpox cases
- Identification and vaccination of contacts of smallpox cases
- Monitoring contacts for development of fever and isolating them if fever occurs
- Vaccination of household members of contacts if no contraindications to vaccination exist
Use of Vaccine During a Smallpox Emergency

In addition to ring vaccination, rapid voluntary vaccination of a large population may be required to:

- Supplement priority surveillance and containment control strategies in areas with smallpox cases
- Reduce the "at-risk" population for additional intentional releases of smallpox virus if the probability of such occurrences is considered significant
- Address heightened public or political concerns regarding access to voluntary vaccination
- Large-scale voluntary smallpox vaccination would only be initiated in certain situations under recommendations from the Secretary of Health and Human Services. Wide-scale quarantine of communities likely would not be effective and, therefore, would not be recommended
PLAGUE

- Vector and respiratory
- Mortality: 90 to 100% (untreated)
- Incubation: 2 to 3 days
- Symptoms: cough with bloody sputum, fever, chills, shortness of breath
VENEZUELAN EQUINE ENCEPHALOMYELITIS (VEE)

• Vectors

• Mildly contagious

• Symptoms: fever, headaches, myalgia, vomiting, chills, sore throat, and diarrhea

• Mortality: 1 to 20%

• Incubation: 1 to 5 days
BOTULINUM

• Digestive and respiratory

• Symptoms: weakness in extremities and respiratory paralysis

• Onset of symptoms: 24 to 72 hours

• LD$_{50}$ 0.001 μg/kg
STAPHYLOCOCCAL ENTEROTOXINS

• Routes of entry
  – Digestive
  – Respiratory

• Symptoms: food poisoning (ingested), high fever, prostration (inhaled)

• LD$_{50}$ 27.0 $\mu$g/kg

• Intoxication: 4-6 hours (ingested), 1 to 2 weeks (inhaled)
Tularemia
RICIN

- Symptoms include
  - Pneumonia
  - Fluid in lungs
  - Gastric bleeding
  - Inflammation of spleen
  - Pulmonary congestion
  - Necrosis of liver and lymph nodes
  - Tissue killing lesions

- $LD_{50}$ 3.0 $\mu$g/kg

Castorbean Plant (Ricinus communis)
Caster Bean Photos
Ricinus Communis
Castor Beans
Ricin Characteristics

• Ricin is a potent biological toxin that is derived from castor beans

• Ricin can be prepared in a liquid, crystalline, or dry powder form

• Ricin is water soluble, odorless, tasteless, and stable under ambient conditions

• Its mechanism of action in the body is inhibition of protein synthesis.
RICIN
(Toxin)

What ricin is
• Ricin is a poison that can be made from the waste left over from processing castor beans.
• It can be in the form of a powder, a mist, or a pellet, or it can be dissolved in water or weak acid.
• It is a stable substance. For example, it is not affected much by extreme conditions such as very hot or very cold temperatures.
**RICIN**  
*(Toxin)*

*Where ricin is found and how it is used*

- Castor beans are processed throughout the world to make castor oil. Ricin is part of the waste “mash” produced when castor oil is made.

- Ricin has some potential medical uses, such as bone marrow transplants and cancer treatment (to kill cancer cells).
RICIN
(Toxin)

How you could be exposed to ricin

• It would take a deliberate act to make ricin and use it to poison people. Accidental exposure to ricin is highly unlikely.

• People can breathe in ricin mist or powder and be poisoned.

• Ricin can also get into water or food and then be swallowed.

• Pellets of ricin, or ricin dissolved in a liquid, can be injected into people’s bodies.

• Depending on the route of exposure (such as injection or inhalation), as little as 500 micrograms of ricin could be enough to kill an adult.

• A 500-microgram dose of ricin would be about the size of the head of a pin. A greater amount would likely be needed to kill people if the ricin were swallowed.

• Ricin poisoning is not contagious. It cannot be spread from person to person through casual contact.
RICIN
(Toxin)

How ricin works
• Ricin works by getting inside the cells of a person’s body and preventing the cells from making the proteins they need. Without the proteins, cells die. Eventually this is harmful to the whole body, and death may occur.

• Effects of ricin poisoning depend on whether ricin was inhaled, ingested, or injected.
• Ricin is a potent biological toxin that is derived from castor beans.

• Its mechanism of action in the body is inhibition of protein synthesis.

Clinical manifestations are dependent on the route of exposure.

• Ingestion of ricin typically leads to profuse vomiting and diarrhea followed by multisystem organ failure and possibly death within 36 to 72 hours of exposure.

• Inhalation of ricin typically leads to respiratory distress, fever, and cough followed by the development of pulmonary edema, hypotension, respiratory failure, and possibly death within 36 to 72 hours.
RICIN
(Toxin)

Signs and symptoms of ricin exposure

• Initial symptoms of ricin poisoning by inhalation may occur within 8 hours of exposure. Following ingestion of ricin, initial symptoms typically occur in less than 6 hours.

• **Inhalation:** Within a few hours of inhaling significant amounts of ricin, the likely symptoms would be respiratory distress (difficulty breathing), fever, cough, nausea, and tightness in the chest. Heavy sweating may follow as well as fluid building up in the lungs (pulmonary edema). This would make breathing even more difficult, and the skin might turn blue. Finally, low blood pressure and respiratory failure may occur, leading to death. In cases of known exposure to ricin, people having respiratory symptoms that started within 12 hours of inhaling ricin should seek medical care.

• **Ingestion:** If someone swallows a significant amount of ricin, he or she would develop vomiting and diarrhea that may become bloody. Severe dehydration may be the result, followed by low blood pressure. Other signs or symptoms may include hallucinations, seizures, and blood in the urine. Within several days, the person's liver, spleen, and kidneys might stop working, and the person could die.

• **Skin and eye exposure:** Ricin in the powder or mist form can cause redness and pain of the skin and the eyes.

• Death from ricin poisoning could take place within 36 to 72 hours of exposure, depending on the route of exposure (inhalation, ingestion, or injection) and the dose received. If death has not occurred in 3 to 5 days, the victim usually recovers.
### RICIN (Toxin)

#### How ricin poisoning is treated

Ricin poisoning is treated by giving victims supportive medical care to minimize the effects of the poisoning.

The types of supportive medical care would depend on several factors, such as the route by which victims were poisoned (that is, whether poisoning was by inhalation, ingestion, or skin or eye exposure).

Care could include such measures as helping victims breathe, giving them intravenous fluids (fluids given through a needle inserted into a vein), giving them medications to treat conditions such as seizure and low blood pressure, flushing their stomachs with activated charcoal (if the ricin has been very recently ingested), or washing out their eyes with water if their eyes are irritated.
RICIN
(Toxin)
Mechanism of Action and Toxicity of Ricin
Category B Diseases/Agents

• are moderately easy to disseminate;
• result in moderate morbidity rates and low mortality rates; and
• require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance.
Other Category B Bioterrorism Agents

• Brucellosis
• Glanders
• Q Fever
• Typhus Fever
• Psittacosis
• Staphylococcal Enterotoxin B
Ricin Exposure

- Inhalation and intravenous injection are the most lethal routes
- Ricin is not well absorbed orally or dermally
Oral Administration

• The absorption of orally administered ricin is poor, but if enough ricin is ingested, the potential for significant morbidity and mortality exists.
Ricin Absorption

• Not likely to be absorbed through unabraded skin; however, there are no reported studies on the dermal toxicity of ricin
• The effect of adding a carrier solvent to ricin to increase dermal absorption is unknown
Nonterroism Ricin Poisoning

- Over 400 cases of poisoning by ingestion
- 14 deaths (12 prior to 1930)
Ricin: Aerosol Exposure
Ricin and Terrorism

- Properties make it a potential terrorist agent
- Would need to be aerosolized, added to food, beverage or consumer products
Ricin and Terrorism

In 1978, Georgi Markov, a Bulgarian writer and journalist who was living in London, died after he was attacked by a man with an umbrella. The umbrella had been rigged to inject a poison ricin pellet under Markov’s skin.
Ricin and Terrorism

- 1991 - Unsuccessful dermal attack plan to kill 100 people
- 1995 - Agents find 130 grams of ricin at Canadian border, enough to kill 10,000 people.
Ricin and Terrorism
Ricin and Terrorism

- December 2002, six terrorist suspects were arrested in Manchester, England
- January 2003, subtoxic quantities of ricin were found in the Paris Metro, leading to an investigation of a plan to attack the Russian embassy
Osama bin Ladin
Clinical Manifestation
Route of Exposure

- Inhalation
- Ingestion
- Parenteral
Aerosol Dispersion

- Not considered persistent in the environment
- Particles under 5 microns may stay suspended for many hours
- Re-suspension of settled ricin may occur
- Technologically difficult to produce particles of this small size
Systemic Toxicity

• Severe systemic toxicity has been described in humans only following ingestion or injection of ricin into the body
Ricin Ingestion

- Ricin release from beans requires mastication
- Swallowing whole beans not likely to poison
- Beans have bitter taste
- No reports of people who have ingested purified ricin
Ricin Fatal Dose

- Ingestion and mastication of 3-6 beans is the estimated fatal dose in adults (presumed less in children)
Ricin: Mild Toxicity Symptoms

- Nausea
- Vomiting
- Diarrhea
- Abdominal cramping
- Oropharyngeal irritation
Onset of Gastrointestinal Symptoms

• Typically occurs in less than 10 hours.
• Delayed presentation of gastrointestinal symptoms, beyond ten hours of ingestion, is unlikely to occur.
Moderate to Severe Toxicity

- Gastrointestinal symptoms persistent vomiting, voluminous diarrhea-bloody or non-bloody (which typically leads to significant fluid losses)

- Dehydration, hypovolemic shock, tachycardia, hypotension, decreased urine output, altered mental status (e.g., confusion, disorientation).
Severe Poisoning

• Hepatic and renal failure and death are possible within 36 – 72 hours of exposure
Ricin Inhalation

- Very limited data in humans
- Animal studies suggest it is the most lethal form of exposure.
Ricin Allergic Syndrome

- Nasal and throat congestion
- Eye irritation
- Hives and other skin irritation
- Chest tightness
- Wheezing (severe cases)
1940’s: An Unintentional and Sublethal Aerosol Exposure

- Fever
- Chest tightness
- Cough
- Dyspnea
- Nausea
- Arthralgias
- Diaphoresis
- No reported progression
Progression

- Pulmonary edema and hemorrhage
- Hypotension
- Respiratory failure
- Death within 36-72 hours
Clinical Trial

- Flu-like symptoms
- Fatigue
- Myalgias
- Symptoms lasting 1-2 days
Lethal Injection
(Markov-1978)

- Immediate pain
- Weakness within 5 hours
- Fever
- Vomiting
- Shock
- Multi-organ failure
- Death in 3 days
Lethal Injection Example 2

- Nausea
- Weakness
- Dizziness
- Myalgias
- Anuria
- Hypotension
- Hepatorenal and cardiorespiratory failure
- Death
Ricin: Clinical Course
Significant ricin poisoning through inhalation, ingestion and parenteral exposure would consist of progressive worsening of symptoms over approximately 4-36 hours.
Early Ricin poisoning through ingestion may resemble typical gastroenteritis-type or a respiratory illness through inhalation.
May be difficult to discern early poisoning from other common and less virulent illnesses such as an upper respiratory infection or gastroenteritis.
Cases should be deemed suspicious in conjunction with

• A highly suspected or known exposure
• A credible threat
• An epidemiologic clue suggestive of a chemical release.
Differential Diagnosis
Inhalation:

- Staphylococcal enterotoxin B
- Exposure to pyrolysis by-products of organofluorines (Teflon, Kevlar)
- Oxides of nitrogen
- Phosgene
- Influenza
- Anthrax
- Q-fever
- Pneumonic plague
Ingestion:

- Enteric pathogens (e.g., salmonella, shigella)
- Mushrooms
- Caustics
- Iron
- Arsenic
- Colchicine
Clinical Diagnosis
Overt Event

• Letter identifying ricin in contents of package

Covert Event

• Restaurant patrons unknowingly consume food contaminated with ricin
Illness Resulting from Covert Event

- Symptoms similar to flu or gastroenteritis
- Early symptoms may be nonexistent or mild
- Reports of illness may occur over a long period and in multiple locations
Illness Resulting from Covert Event

• Symptoms may not suggest a single chemical
• Healthcare providers may be less familiar with clinical presentations of chemical or biological-induced poisonings
Epidemiologic Clues Suggesting Covert Release of a Chemical or Biological toxin

- Unusual increase in patients with possible chemical or biological toxin related illness
- Unexplained deaths among healthy or young people
- Unexplained odors on patients
- Clusters of illness in people with common characteristics
Epidemiologic Clues Suggesting Covert Release of a chemical or biological toxin

- Rapid onset of symptoms
- Unexplained death of plants, fish, or animals
- Presence of a particular syndrome associated with a chemical agent or biological toxin
• Clinical diagnosis largely depends on route of exposure
• Clinical findings associated with ricin poisoning may be nonspecific and may mimic signs and symptoms of less virulent diseases
Confirmation of Ricin Poisoning

• Clinical manifestations of illness
• Laboratory detection of ricin in biological fluids or environmental samples
Laboratory Testing

- No validated assays for detection of ricin in biologic fluids
- Testing of environmental samples may not be immediately available to assist in clinical decision making
Suspicion and clinical diagnosis of ricin poisoning should occur when clinically compatible illness is present in conjunction with:

- A highly suspected or known exposure,
- A credible threat, OR
- An applicable epidemiologic clue
Decontamination and Personal Protective Equipment
Patient Contaminated with Ricin

- Provide gross decontamination at the scene unless medical condition dictates immediate transport to hospital
**Gross Decontamination**

- Cut away/remove all suspected contaminated clothing
- Remove jewelry and watches
- Wash off obvious contamination with soap and copious amount of water
- Shower with liquid soap and warm water
Gross Decontamination

- Provide privacy
- Secure personal belongings
- Explain procedure to victims
Decontamination

- Clean environmental surfaces or equipment with soap and water or 0.1% sodium hypochlorite solution
- Double bag, label and secure victims’ clothing
Decontamination of Nondisposable PPE

- Thoroughly rinse with soap and water
- Soak in 0.1% sodium hypochlorite solution for 15 minutes
- Rinse with water and air dry
PPE for First Responders

- Determined by incident commander
- Based on hazard assessment and site conditions
- PPE should prevent droplets from contacting broken skin or mucosal membranes
PPE if Victims Inadequately Decontaminated at Scene

• Chemical-resistant suit with gloves
• Surgical mask
• Eye/face protection
Decontamination

• Should be done at scene or hospital but prior to entering emergency department
• Removing contaminated clothing reduces contaminant 75%-90%
Standard Precautions

- Scrubs or disposable gown
- Lab coat
- Disposable nitrile gloves
- Surgical mask
- Safety glasses, goggles, or face shield
- Good hand hygiene
CDC Ricin Website

www.bt.cdc.gov/agent/ricin