Unit 6: Bioterrorism and Infectious Diseases

Instructor’s Background Text
Part 1 of 2

PKIDs’ Infectious Disease Workshop

Made possible by grants from the Northwest Health Foundation, the Children’s Vaccine Program at PATH and PKIDs.
PKIDs’ Infectious Disease Workshop

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Acknowledgements

Producing this workshop has been a dream of ours since PKIDs’ inception in 1996. It has been more than two years since we began work on this project, and many people helped us reach our goal. It’s not done, because it is by nature a living document that will evolve as science makes strides in the research of infectious diseases, but it’s a great beginning.

There are people who’ve helped us whose names are not on this printed list. That omission is not deliberate, but rather from our own clumsiness in losing important pieces of paper, and we apologize.

Without the funding and support of the Northwest Health Foundation and the Children’s Vaccine Program at PATH (Program for Appropriate Technology in Health), this would have been an impossible task. Dr. Katherine Vaughn, PKIDs’ Medical Director and Dr. Karen Steingart, scientific advisor to PKIDs, provided excellent guidance through their editorial oversight and knowledgeable contributions to the Infectious Disease Workshop.

On PKIDs’ staff are three individuals without whom this publication would never have been finished—Franji Mayes, Mylei Basich and Christine Kukka, all of whom gave their very best to ensure this workshop is accurate and user-friendly.

We are indebted to the following individuals who cheerfully gave us hours of their time and access to their resources: the American Society for Microbiology; Kathy A. Bobula, Ph.D., Coordinator, Early Childhood Education, Clark College, Vancouver, Wash.; Claudia Bratt, elementary school teacher, Truman Elementary, Vancouver, Wash.; Sue Campbell, Early Childhood Educator, Kindercare; many wonderful and helpful people at the Centers for Disease Control and Prevention, Atlanta, Georgia; Rachel Coyle, Case Aide and Residential Care Staff Lead, Jonathan’s Place; Tammy Dunn, Early Childhood Director, Portland Christian Schools, Portland, Oregon; Bruce Gellin, M.D., Director of the National Vaccine Program Office in the Office of the Assistant Secretary for Health, Department of Health and Human Services; Shannon Harrison, M.D., Internal Medicine and Infectious Diseases, Teton Hospital, Jackson, Wyoming; the Immunization Action Coalition; Brad Jensen, M.D., Southwest Washington Medical Center Pathology Department; Edgar Marcuse, M.D., Professor of Pediatrics, University of Washington and Director of Medical Services, Seattle Children’s Hospital and Regional Medical Center; Zack Mittge, law student, University of Oregon; the National Network for Immunization Information; Paul Offit, M.D., Chief, Section of Infectious Diseases and the Henle Professor of Immunologic and Infectious Diseases at The Children’s Hospital of Philadelphia; Carol Porter, Red Cross health room volunteer, Garland Independent School District, Garland, Texas; Sarah Theberge, Curriculum Instructor, Early Childhood Education, Clark College, Vancouver, Wash.; James Whorton, Ph.D., Professor, Department of Medical History and Ethics, University of Washington School of Medicine.

We thank the following for providing nonprofit rates for their microscopic images: Dennis Kunkel Microscopy, Inc., and Science Photo Library/Photo Researchers, Inc.
(Cover photo: Dennis Kunkel Microscopy, Inc./www.denniskunkel.com.)

Additional funding for this project provided by PKIDs (Parents of Kids with Infectious Diseases).

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and informative material on the subject matter covered. Any information obtained from this
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of any of the contents of this workshop.
Introduction

PKIDs (Parents of Kids with Infectious Diseases) is a national nonprofit agency whose mission is to educate the public about infectious diseases, the methods of prevention and transmission, and the latest advances in medicine; to eliminate the social stigma borne by the infected; and to assist the families of the children living with hepatitis, HIV/AIDS, or other chronic, viral infectious diseases with emotional, financial and informational support.

Remaining true to our mission, we have designed the **Infectious Disease Workshop (IDW)**, an educational tool for people of all ages and with all levels of understanding about infectious diseases. In this workshop, you will learn about bacteria and viruses, how to prevent infections, and how to eliminate the social stigma that too often accompanies diseases such as HIV or hepatitis C.

We hope that both instructors and participants come away from this workshop feeling comfortable with their new level of education on infectious diseases.

The IDW is designed to “train-the-trainer,” providing instructors not only with background materials but also with age-appropriate activities for the participants. Instructors do not need to be professional educators to use these materials. They were designed with both educators and laypersons in mind.

The IDW is comprised of a master Instructor’s Background Text, which is divided into six units: Introduction to Infectious Diseases, Disease Prevention, Sports and Infectious Disease, Stigma and Infectious Disease, Civil Rights and Infectious Disease, and Bioterrorism and Infectious Disease.

For each unit, instructors will find fun and helpful activities for participants in five age groups: 2 to 6 years of age, 6 to 9 years of age, 9 to 12 years of age, 13 to 18 years of age and adults.

We welcome any questions, comments, or feedback you may have about the IDW or any other issue relating to infectious diseases in children.

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PKIDs’ Infectious Disease Workshop

In February of 2002, Tara O’Toole, Michael Mair, and Thomas V. Inglesby from the Center for Civilian Biodefense Strategies, Johns Hopkins University, Baltimore, Maryland, published their findings on an exercise called “Dark Winter” in Clinical Infectious Diseases. Following is a synopsis of that exercise, and their conclusions:

On 22-23 June 2001, the Johns Hopkins Center for Civilian Biodefense Strategies, in collaboration with the Center for Strategic and International Studies, the Analytic Services Institute for Homeland Security, and the Oklahoma National Memorial Institute for the Prevention of Terrorism, held a senior-level exercise entitled “Dark Winter” that simulated a covert smallpox attack on the United States. The first such exercise of its kind, Dark Winter was constructed to examine the challenges that senior-level policy makers would face if confronted with a bioterrorist attack that initiated outbreaks of highly contagious disease.

The exercise was intended to increase awareness of the scope and character of the threat posed by biological weapons among senior national security experts and to catalyze actions that would improve prevention and response strategies.

Of all potential biological weapons, smallpox is historically the most ominous and feared. It is a disfiguring, communicable disease with a case-fatality rate of 30 percent. There is no effective medical treatment. The World Health Assembly officially declared smallpox eradicated worldwide in 1980. Since its eradication, smallpox vaccination programs and vaccine production have ceased around the world. The United States stopped its mandatory vaccination program in 1972. Thus, residents of the United States and indeed, the global population are now highly susceptible to an inadvertent or deliberate release of smallpox.

It has been argued that the smallpox virus is the organism least accessible to potential bioterrorists. Since its eradication, the only officially existing stocks of the smallpox virus have been stored in 2 World Health Organization reference laboratories located in the United States and Russia. Many experts believe, however, that the smallpox virus is not confined to these 2 official repositories and may be in the possession of states or subnational groups pursuing active biological weapons programs. Of particular importance and concern is the legacy of the former Soviet Union’s biological weapons program. It is widely known that the former Soviet Union maintained a stockpile of 20 tons of smallpox virus in its biological weapons arsenal throughout the 1970s, and that, by 1990, they had a plant capable of producing 80100 tons of smallpox per year.

The year is 2002. A suspected lieutenant of Osama bin Laden has recently been arrested in Rus-
sia in a sting operation while attempting to purchase 50 kg of plutonium and biological pathogens that had been weaponized by the former Soviet Union. The United Nation’s sanctions against Iraq are no longer in effect, and Iraq is suspected of reconstituting its biological weapons program. In the past 48 hours, Iraqi forces have moved into offensive positions along the Kuwaiti border. In response, the United States is moving an additional aircraft carrier battle group to the Persian Gulf.

The 12 members of the NSC (National Security Council) gather for what initially was to be a meeting to address the developing situation in southwest Asia but are given the news that a smallpox outbreak is occurring in the United States. In Oklahoma, 20 cases have been confirmed by the CDC, with 14 more suspected. There are also reports of suspect cases in Georgia and Pennsylvania. These cases are not yet confirmed. The initial exposure is presumed to have occurred on or about 1 December, given the 917-day incubation period for smallpox.

A total of 2000 smallpox cases have been reported in 15 states, with 300 deaths. The epidemic is now international, with isolated cases in Canada, Mexico, and the United Kingdom. Both Canada and Mexico request that the United States provide them with vaccine. All of the cases appear to be related to the 3 initial outbreaks in Oklahoma, Georgia, and Pennsylvania. The public health investigation points to 3 shopping malls as the initial sites of exposure. Only 1.25 million doses of vaccine remain, and public unrest grows as the vaccine supply dwindles. Vaccine distribution efforts vary from state to state, are often chaotic, and lead to violence in some areas. In affected states, the epidemic has overwhelmed the healthcare systems, and care suffers. The DoD (Department of Defense) expresses concern about diverting its critical supplies and personnel to the civilian health care system, given the evolving crisis in the Persian Gulf.

Several international borders are closed to US trade and travelers. Food shortages emerge in affected states as a result of travel problems and store closings. Sporadic violence has been reported against minorities who appear to be of Arab descent. There are no solid leads regarding who may have perpetrated this attack. The government response to the epidemic has been criticized. The media continues its 24 hour news coverage of the crisis. Misinformation regarding the smallpox outbreak begins to appear on the Internet and in the media, including false reports of cures for smallpox. Schools are closed nationwide. Public gatherings are limited in affected states. Some states limit travel and nonessential gatherings. The Department of Health and Human Services establishes a National Information Center. Three U.S. drug companies agree to produce new vaccine at the rate of 6 million doses per month, with first deliveries in 5 weeks. Russia offers to provide 4 million doses of vaccine.

NSC officials confront a growing set of challenges and decisions. Given the shortage of vaccine, how can the spread of smallpox be halted? Should patients with smallpox be confined to facilities dedicated to care for them? Should contacts of patients be forced to remain at home or in dedicated facilities until they are proven to be free of smallpox? Should national travel restrictions be imposed? How can disease containment best be balanced against economic disruption and the protection of civil liberties? To what extent can and should the government infringe upon civil liberties? Under what conditions can those powers be exercised? What federal ac-
tions can and should be taken to care for the sick? Should the National Guard be federalized (i.e., put under federal control)? What additional assistance can the federal government provide to the states? Should troops continue to deploy overseas to southwest Asia? What should the President tell the people of the United States? Who orchestrated this attack and why? Is the nation at war?

Information presented to NSC members, 22 December 2002 (13 days into the epidemic).
A total of 16,000 smallpox cases have been reported in 25 states (14,000 within the past 24 hours). One thousand people have died. Ten other countries report cases of smallpox believed to have been caused by international travelers from the United States. It is uncertain whether new smallpox cases have been transmitted by unidentified contacts of initial victims, by contacts who were not vaccinated in time, or by people who received ineffective vaccine, or are due to new smallpox attacks, or some combination of these. Vaccine supplies are depleted, and new vaccine will not be ready for at least 4 weeks. States have restricted nonessential travel. Food shortages are growing in some places, and the national economy is suffering. Residents have fled and are fleeing cities where new cases emerge. Canada and Mexico have closed their borders to the United States. The public demands mandatory isolation of smallpox victims and their contacts, but identifying contacts has become logistically impossible.

Although speculative, the predictions are extremely grim: an additional 17,000 cases of smallpox are expected to emerge during the next 12 days, bringing the total number of second-generation cases to 30,000. Of these infected persons, approximately one-third, or 10,000, are expected to die. NSC members are advised that administration of new vaccine combined with isolation measures are likely to stem the expansion of the epidemic. NSC members ask for worst-case projections. They are advised that in worst-case conditions, the third generation of cases could comprise 300,000 new cases of smallpox and lead to 100,000 deaths, and that the fourth generation of cases could conceivably comprise as many as 3,000,000 cases of smallpox and lead to as many as 1,000,000 deaths. It is again emphasized to participants that these numbers are worst-case projections and can be substantially diminished by large-scale and successful vaccination programs and disease-containment procedures.

With no vaccine remaining and new vaccine not expected for at least 4 weeks, how can the rapidly expanding epidemic be contained? What measures should the federal and state governments take to stop the epidemic, given the scope of the crisis, the lack of remaining vaccine, and rising stakes? Should the United States pull its forces out of the Gulf in response to the anonymous letters? With no conclusive evidence as to who orchestrated the attack, how and should the United States respond? If the United States discovers who is behind the attack, what is the proper response? Would the American people call for response with nuclear weapons?

LESSONS OF DARK WINTER
The authors of this article have drawn a series of lessons from the Dark Winter exercise. These lessons are based on an analysis of comments and decisions made by exercise participants during the exercise, subsequent Congressional testimony by exercise participants, and public interviews given by participants in the months after the exercise. The lessons learned reflect the
analysis and conclusions of the authors from the Johns Hopkins Center for Civilian Biodefense Strategies and do not necessarily reflect the views of the exercise participants or collaborating organizations.

In this section, these lessons are listed, each accompanied by a short explanatory note.

Leaders are unfamiliar with the character of bioterrorist attacks, available policy options, and their consequences. The senior decision makers in Dark Winter were largely unfamiliar with the sequence of events that would follow a bioterrorist attack. Important decisions and their implications were dependent on public health strategies and possible mechanisms to care for large numbers of sick people issues that the national security and defense communities have not typically analyzed in the past.

After a bioterrorist attack, leaders’ decisions would depend on data and expertise from the medical and public health sectors. In Dark Winter, even after the smallpox attack was recognized, decision makers were confronted with many uncertainties and wanted information that was not immediately available. (In fact, they were given more information on locations and numbers of infected people than would likely be available in reality.)

For example, it was difficult to quickly identify the locations of the original attacks; to immediately predict the likely size of the epidemic on the basis of initial cases; to know how many people were exposed; to find out how many were hospitalized and where; or to keep track of how many had been vaccinated. This lack of information, critical for leaders’ situational awareness in Dark Winter, reflects the fact that few systems exist that can provide a rapid flow of the medical and public health information needed in a public health emergency.

The lack of sufficient vaccine or drugs to prevent the spread of disease severely limited management options. In Dark Winter, smallpox vaccine shortages significantly affected the response available to contain the epidemic, as well as the ability of political leaders to offer reassurance to the American people. The increasing scarcity of smallpox vaccine led to great public anxiety and flight by people desperate to get vaccinated, and it had a significant effect on the decisions taken by political leaders.

The US healthcare system lacks the surge capacity to deal with mass casualties. In Dark Winter, hospital systems across the country were flooded with demands for patient care. The demand was highest in the cities and states directly attacked, but by the time many victims became symptomatic, they were geographically dispersed, with some having traveled far from the original site of attack. The numbers of people flooding into hospitals across the country included people with common illnesses who feared they had smallpox and people who were well but worried. The challenges of distinguishing the sick from the well and rationing scarce resources, combined with shortages of healthcare staff, who were themselves worried about becoming infected or bringing infection home to their families, imposed a huge burden on the health care system.
To end a disease outbreak after a bioterrorist attack, decision makers will require ongoing expert advice from senior public health and medical leaders. The leaders in Dark Winter were confronted with rapidly diminishing supply of smallpox vaccine and an expanding smallpox epidemic. Some members advised the imposition of geographic quarantines around affected areas, but the implications of these measures (e.g., interruption of the normal flow of medicines, food and energy supplies, and other critical needs) were not clearly understood at first. In the end, it is not clear whether such draconian measures would have led to a more effective interruption of disease spread.

Federal and state priorities may be unclear, differ, or conflict; authorities may be uncertain; and constitutional issues may arise. In Dark Winter, tensions rapidly developed between state and federal authorities in several contexts. State leaders wanted control of decisions regarding the imposition of disease-containment measures (e.g., mandatory vs. voluntary isolation and vaccination), the closure of state borders to all traffic and transportation, and when or whether to close airports. Federal officials argued that such issues were best decided on a national basis to ensure consistency and to give the President maximum control of military and public-safety assets. Leaders in states most affected by smallpox wanted immediate access to smallpox vaccine for all citizens of their states, but the federal government had to balance these requests against military and other national priorities. State leaders were opposed to federalizing the National Guard, which they were relying on to support logistical and public supply needs. A number of federal leaders argued that the National Guard should be federalized.

The individual actions of US citizens will be critical to ending the spread of contagious disease; leaders must gain the trust and sustained cooperation of the American people. Dark Winter participants worried that it would not be possible to forcibly impose vaccination or travel restrictions on large groups of the population without their general cooperation. To gain that cooperation, the President and other leaders in Dark Winter recognized the importance of persuading their constituents that there was fairness in the distribution of vaccine and other scarce resources, that the disease-containment measures were for the general good of society, that all possible measures were being taken to prevent the further spread of the disease, and that the government remained firmly in control despite the expanding epidemic.

CONCLUSION
In conducting the Dark Winter exercise, the intention was to inform the debate on the threat posed by biological weapons and to provoke a deeper understanding of the numerous challenges that a covert act of bioterrorism with a contagious agent would present to senior level policy makers and elected officials. Since the Dark Winter exercise, the country has endured the horrific events of 11 September, as well as anthrax attacks through the US postal system. Bioterrorism is no longer just the subject of war games and the source of “futuristic and disturbing topics for...[Congressional] committee meetings.” Many of the challenges and difficulties faced by the Dark Winter participants, unfortunately, have been paralleled in the response to the recent anthrax attacks. The Dark Winter exercise offers instructive insights and lessons for those with responsibility for bioterrorism preparedness in the medical, public health, policy, and national security communities and, accordingly, helps shine light on possible paths forward.
Almost a year has passed since these findings were published, and much has been done on the national, state and local levels to address the problem areas identified during the exercise.

For educational purposes, we have included on the following pages information about six biological agents that have the potential to be used as bioterrorist weapons. In part 2 of the Bioterrorism module, we present practical methods of preparing for both natural and man-made disasters.
ANTHRAX

As little as 100 kg of powdered *Bacillus anthracis* could cause 130,000 to 3 million deaths if released under the proper environmental circumstances into a densely populated region.

Although mainly a disease of grazing animals, an estimated 2,000 cases of cutaneous anthrax occur worldwide in humans each year. Gastrointestinal disease is seen infrequently. Prior to 11 September 2001, there had been no cases of inhalational anthrax in the United States in 20 years. There is currently no atmospheric warning system to detect an aerosol cloud of anthrax spores. The first sign would likely be patients with symptoms of inhalational anthrax, with a non-specific fever and cough.

Those ill with inhalational anthrax typically experience fever, dyspnea, headache, and chest pain. If caught early, inhalational anthrax can be treated successfully with antibiotics. If it isn’t caught early and more serious symptoms develop, inhalational anthrax usually results in death.

The United States has an anthrax vaccine that is not available to the civilian population and is not recommended for children under the age of 18. At this point, it is available only to the military because of the risk the military may encounter in their work. Vaccine supplies are limited and production capacity is limited.
Children and Anthrax: A Fact Sheet for Parents
(source: CDC)

Recent news reports of anthrax cases in several U.S. cities may have created fear among both children and adults. The CDC has prepared this fact sheet to provide parents with information and resources to 1) help their children cope with their fears about anthrax and 2) make decisions related to anthrax and their children.

How To Reduce Children’s Fears
Help your children feel safe. Let them talk about their fears and worries. Stick to family routines that help children feel comfortable and secure. Reassure them that parents, teachers, doctors, and government officials are doing everything possible to keep them safe and healthy.

Limit children’s viewing of television news. Children may be frightened, overwhelmed, or traumatized by news reports about bioterrorism. Supervise what they watch on television, and when they do watch, be sure to allow for family-discussion time during and after viewing to let them air their fears and concerns.

Arm yourself with the facts. Education is your best protection against unnecessary fear. Your children will be less fearful if they see that you are not afraid and if you spend time with them answering all of their questions.

What Every Parent Should Know
Anthrax is an illness caused by bacteria called *Bacillus anthracis*. These bacteria are found naturally in the soil. They can form a protective coat around themselves called spores, and they can release poisonous substances into the bodies of infected people.

You and your children cannot catch anthrax from each other or from any other person. Even if you were to become sick with anthrax, you could not pass on the illness to your children. Also, even if someone were to put the bacteria that causes anthrax in your workplace on purpose, it is highly unlikely that you would carry the bacteria home to your children on your clothes or hair.

People come into contact with (are “exposed” to) bacteria or become infected with bacteria that cause anthrax in three ways. They can be exposed and infected by breathing in (inhaling) the bacteria, by coming into contact with the bacteria through cuts or abrasions in the skin, or by eating something that contains the bacteria (usually undercooked meat from an infected animal). The chance of coming into contact with the bacteria in any of these ways is very low. Also, our bodies have defenses against bacteria, so not everyone who comes into contact with the bacteria will become ill with anthrax.

There are three kinds of anthrax, all of which are treatable with antibiotics:
1. Skin (cutaneous) anthrax is the least serious form of anthrax. The first symptom is a small, painless sore that develops into a blister. One or two days later, the blister develops a black scab in the center.
2. Gastrointestinal anthrax is more serious than skin anthrax. The initial symptoms are nausea, loss of appetite, and fever, followed by severe abdominal pain. This is the least common form of anthrax.

3. Inhalational anthrax is the most serious form of anthrax. This illness begins with symptoms similar to those for a cold or the flu. If caught early, inhalational anthrax can be treated successfully with antibiotics. If it isn’t caught early and more serious symptoms develop, inhalational anthrax usually results in death. Almost all cold and flu symptoms are not anthrax.

The signs and symptoms of anthrax infection in children older than 2 months of age are similar to those in adults. The illness affects children and adults in much the same way, though children may be more likely to suffer side effects from some of the antibiotics used to prevent or treat the disease.

Although you may be tempted to ask your doctor for a supply of antibiotics to keep on hand, neither the Centers for Disease Control and Prevention (CDC) nor the American Academy of Pediatrics recommends doing this. You should not obtain antibiotics for your children unless public health authorities have confirmed that it is likely that your children have come into contact with the bacteria that cause anthrax. Giving your children antibiotics when the antibiotics are not needed can do more harm than good. Many antibiotics have serious side effects in children, and using antibiotics when they are not needed can lead to the development of drug-resistant forms of bacteria in your children. If this happens, the antibiotics will not be able to kill the resistant bacteria the next time your child needs the same antibiotic to treat ear, sinus, or other infections that children frequently develop.

Currently, there is no anthrax vaccine for children. The anthrax vaccine used for adults has never been studied in children, and it is not recommended for people younger than 18 years old. It is currently available only for people in the military service, although public health officials are now considering its use for people in other high-risk professions.

The chances of your children coming into contact with bacteria that cause anthrax are extremely low. However, if public health officials confirm or suspect that you or your children have come into contact with the bacteria, your doctor or other health official will prescribe antibiotics to keep you and your children from developing anthrax. Early identification and treatment of anthrax in children is critical, so call your healthcare provider immediately with any questions or concerns. Remember: never give your child an antibiotic unless a doctor has examined your child and prescribed an antibiotic. Also, be sure to use any antibiotic exactly as directed by the doctor or pharmacy.

Facts About Anthrax

Anthrax is an acute infectious disease caused by the spore-forming bacterium Bacillus anthracis. Anthrax most commonly occurs in hoofed mammals and can also infect humans.

Symptoms of disease vary depending on how the disease was contracted, but usually occur
within 7 days after exposure. The serious forms of human anthrax are inhalational anthrax, cutaneous anthrax, and intestinal anthrax.

Initial symptoms of inhalational anthrax infection may resemble a common cold. After several days, the symptoms may progress to severe breathing problems and shock. Inhalational anthrax is often fatal.

The intestinal disease form of anthrax may follow the consumption of contaminated food and is characterized by an acute inflammation of the intestinal tract. Initial signs of nausea, loss of appetite, vomiting, and fever are followed by abdominal pain, vomiting of blood, and severe diarrhea.

Direct person-to-person spread of anthrax is extremely unlikely, if it occurs at all. Therefore, there is no need to immunize or treat contacts of persons ill with anthrax, such as household contacts, friends, or coworkers, unless they were exposed to the same source of infection.

In persons exposed to anthrax, infection can be prevented with antibiotic treatment.

Early antibiotic treatment of anthrax is essential—delay lessens chances for survival. Anthrax usually is susceptible to penicillin, doxycycline, and fluoroquinolones.

An anthrax vaccine also can prevent infection. Vaccination against anthrax is not recommended for the general public to prevent disease and is not available.

**Updated Information From the CDC About How to Recognize and Handle a Suspicious Package or Envelope**

This information supplements the CDC’s recommendations for recognizing and handling suspicious packages or envelopes that were published as a CDC Health Advisory on October 27, 2001, and replaces information about identifying suspicious packages that was published as a Health Advisory on October 12, 2001.

Letters containing *Bacillus anthracis* (anthrax) have been received by mail in several areas in the United States. In some instances, anthrax exposures have occurred, with several persons becoming infected. To prevent such exposures and subsequent infection, all persons should learn how to recognize a suspicious package or envelope and take appropriate steps to protect themselves and others.

**Identifying Suspicious Packages and Envelopes**

Some characteristics of suspicious packages and envelopes include the following:

- Inappropriate or unusual labeling.
- Excessive postage.
- Handwritten or poorly typed addresses.
- Misspellings of common words.
• Strange return address or no return address.
• Incorrect titles or title without a name.
• Not addressed to a specific person.
• Marked with restrictions, such as “Personal,” “Confidential,” or “Do not x-ray.”
• Marked with any threatening language.
• Postmarked from a city or state that does not match the return address.

Appearance:
• Powdery substance felt through or appearing on the package or envelope.
• Oily stains, discolorations, or odor.
• Lopsided or uneven envelope.
• Excessive packaging material such as masking tape, string, etc.

Other suspicious signs:
• Excessive weight.
• Ticking sound.
• Protruding wires or aluminum foil.

If a package or envelope appears suspicious, DO NOT OPEN IT.

Handling of Suspicious Packages or Envelopes
• Do not shake or empty the contents of any suspicious package or envelope.
• Do not carry the package or envelope, show it to others or allow others to examine it.
• Put the package or envelope down on a stable surface; do not sniff, touch, taste, or look closely at it or at any contents which may have spilled.
• Alert others in the area about the suspicious package or envelope. Leave the area, close any doors, and take actions to prevent others from entering the area. If possible, shut off the ventilation system.
• WASH hands with soap and water to prevent spreading potentially infectious material to face or skin. Seek additional instructions for exposed or potentially exposed persons.
• If at work, notify a supervisor, a security officer, or a law enforcement official. If at home, contact the local law enforcement agency.
• If possible, create a list of persons who were in the room or area when this suspicious letter or package was recognized and a list of persons who also may have handled this package or letter. Give this list to both the local public health authorities and law enforcement officials.
PLAGUE

There have been 390 cases of plague over the last 50 years in the United States, most of which have followed an infected flea bite. The vast majority (84 percent) of these cases have been of the bubonic variety. Septicemic plague without the formation of buboes occurred in 13 percent of cases. Pneumonic plague has been the least common, accounting for only 2 percent of cases, but this virulent variety would be the goal of a bioterrorist.

Direct aerosolization of plague bacilli would be necessary to initiate this process, and person-to-person contact would spread and perpetuate the disease.

Symptoms begin one to six days after exposure, with fever, cough, and bloody or purulent sputum. Mortality is substantial without treatment.

Because there is no vaccine, uninfected people who have contact with the agent should immediately begin taking antibiotics for seven days from last exposure.

Bubonic plague bacteria
Facts About Pneumonic Plague
(source: CDC)

Plague is an infectious disease that affects animals and humans. It is caused by the bacterium *Yersinia pestis*. This bacterium is found in rodents and their fleas and occurs in many areas of the world, including the United States.

*Y. pestis* is easily destroyed by sunlight and drying. Even so, when released into air, the bacterium will survive for up to one hour, although this could vary depending on conditions.

Pneumonic plague is one of several forms of plague. Depending on circumstances, these forms may occur separately or in combination:

- **Pneumonic plague** occurs when *Y. pestis* infects the lungs. This type of plague can spread from person to person through the air. Transmission can take place if someone breathes in aerosolized bacteria, which could happen in a bioterrorist attack. Pneumonic plague is also spread by breathing in *Y. pestis* suspended in respiratory droplets from a person (or animal) with pneumonic plague. Becoming infected in this way usually requires direct and close contact with the ill person or animal. Pneumonic plague may also occur if a person with bubonic or septicemic plague is untreated and the bacteria spread to the lungs.

- **Bubonic plague** is the most common form of plague. This occurs when an infected flea bites a person or when materials contaminated with *Y. pestis* enter through a break in a person’s skin. Patients develop swollen, tender lymph glands (called buboes) and fever, headache, chills, and weakness. Bubonic plague does not spread from person to person.

- **Septicemic plague** occurs when plague bacteria multiply in the blood. It can be a complication of pneumonic or bubonic plague or it can occur by itself. When it occurs alone, it is caused in the same ways as bubonic plague; however, buboes do not develop. Patients have fever, chills, prostration, abdominal pain, shock, and bleeding into skin and other organs. Septicemic plague does not spread from person to person.

**Symptoms and Treatment**

With pneumonic plague, the first signs of illness are fever, headache, weakness, and rapidly developing pneumonia with shortness of breath, chest pain, cough, and sometimes bloody or watery sputum. The pneumonia progresses for 2 to 4 days and may cause respiratory failure and shock. Without early treatment, patients may die.

**Early treatment of pneumonic plague is essential.**

To reduce the chance of death, antibiotics must be given within 24 hours of first symptoms. Streptomycin, gentamicin, the tetracyclines, and chloramphenicol are all effective against pneumonic plague.

Antibiotic treatment for 7 days will protect people who have had direct, close contact with infected patients. Wearing a close-fitting surgical mask also protects against infection.

A plague vaccine is not currently available for use in the United States.
Why are we concerned about pneumonic plague as a bioweapon?

_Yersinia pestis_ used in an aerosol attack could cause cases of the pneumonic form of plague. One to six days after becoming infected with the bacteria, people would develop pneumonic plague. Once people have the disease, the bacteria can spread to others who have close contact with them. Because of the delay between being exposed to the bacteria and becoming sick, people could travel over a large area before becoming contagious and possibly infecting others. Controlling the disease would then be more difficult. A bioweapon carrying _Y. pestis_ is possible, because the bacterium occurs in nature and could be isolated and grown in quantity in a laboratory. Even so, manufacturing an effective weapon using _Y. pestis_ would require advanced knowledge and technology.

Is pneumonic plague different from bubonic plague?

Yes. Both are caused by _Yersinia pestis_, but they are transmitted differently and their symptoms differ. Pneumonic plague can be transmitted from person to person; bubonic plague cannot. Pneumonic plague affects the lungs and is transmitted when a person breathes in _Y. pestis_ particles in the air. Bubonic plague is transmitted through the bite of an infected flea or exposure to infected material through a break in the skin. Symptoms include swollen, tender lymph glands called buboes. Buboes are not present in pneumonic plague. If bubonic plague is not treated, however, the bacteria can spread through the bloodstream and infect the lungs, causing a secondary case of pneumonic plague.

What are the signs and symptoms of pneumonic plague?

Patients usually have fever, weakness, and rapidly developing pneumonia with shortness of breath, chest pain, cough, and sometimes bloody or watery sputum. Nausea, vomiting, and abdominal pain may also occur. Without early treatment, pneumonic plague usually leads to respiratory failure, shock, and rapid death.

How do people become infected with pneumonic plague?

Pneumonic plague occurs when _Yersinia pestis_ infects the lungs. Transmission can take place if someone breathes in _Y. pestis_ particles, which could happen in an aerosol release during a bioterrorist attack. Pneumonic plague is also transmitted by breathing in _Y. pestis_ suspended in respiratory droplets from a person (or animal) with pneumonic plague. Respiratory droplets are spread most readily by coughing or sneezing. Becoming infected in this way usually requires direct and close (within 6 feet) contact with the ill person or animal. Pneumonic plague may also occur if a person with bubonic or septicemic plague is untreated and the bacteria spread to the lungs.

Does plague occur naturally?

Yes. The World Health Organization reports 1,000 to 3,000 cases of plague worldwide every year. An average of 5 to 15 cases occur each year in the western United States. These cases are usually scattered and occur in rural to semi-rural areas. Most cases are of the bubonic form of the disease. Naturally occurring pneumonic plague is uncommon, although small outbreaks do occur. Both types of plague are readily controlled by standard public health response measures.
Can a person exposed to pneumonic plague avoid becoming sick?
Yes. People who have had close contact with an infected person can greatly reduce the chance of becoming sick if they begin treatment within 7 days of their exposure. Treatment consists of taking antibiotics for at least 7 days.

How quickly would someone get sick if exposed to plague bacteria through the air?
Someone exposed to *Yersinia pestis* through the air—either from an intentional aerosol release or from close and direct exposure to someone with plague pneumonia—would become ill within 1 to 6 days.

Can pneumonic plague be treated?
Yes. To prevent a high risk of death, antibiotics should be given within 24 hours of the first symptoms. Several types of antibiotics are effective for curing the disease and for preventing it. Available oral medications are a tetracycline (such as doxycycline) or a fluoroquinolone (such as ciprofloxacin). For injection or intravenous use, streptomycin or gentamicin antibiotics are used. Early in the response to a bioterrorist attack, these drugs would be tested to determine which is most effective against the particular weapon that was used.

Would enough medication be available in the event of a bioterrorist attack involving pneumonic plague?
National and state public health officials have large supplies of drugs needed in the event of a bioterrorist attack. These supplies can be sent anywhere in the United States within 12 hours.

What should someone do if they suspect they or others have been exposed to plague?
Get immediate medical attention: To prevent illness, a person who has been exposed to pneumonic plague must receive antibiotic treatment without delay. If an exposed person becomes ill, antibiotics must be administered within 24 hours of their first symptoms to reduce the risk of death. Notify authorities: Immediately notify local or state health departments so they can begin to investigate and control the problem right away. If bioterrorism is suspected, the health departments will notify the CDC, FBI, and other appropriate authorities.

How can someone reduce the risk of getting pneumonic plague from another person or giving it to someone else?
People having direct and close contact with someone with pneumonic plague should wear tightly fitting disposable surgical masks. Patients with the disease should be isolated and medically supervised for at least the first 48 hours of antibiotic treatment. People who have been exposed to a contagious person can be protected from developing plague by receiving prompt antibiotic treatment.

How is plague diagnosed?
The first step is evaluation by a health worker. If the health worker suspects pneumonic plague, samples of the patient’s blood, sputum, or lymph node aspirate are sent to a laboratory for testing. Once the laboratory receives the sample, preliminary results can be ready in less than two hours. Confirmation will take longer, usually 24 to 48 hours.
How long can plague bacteria exist in the environment?
*Yersinia pestis* is easily destroyed by sunlight and drying. Even so, when released into air, the bacterium will survive for up to one hour, depending on conditions.

Is a vaccine available to prevent pneumonic plague?
Currently, no plague vaccine is available in the United States. Research is in progress, but we are not likely to have vaccines for several years or more.
SMALLPOX

The last naturally occurring case of smallpox on Earth occurred in Somalia, in 1977. In 1980 the World Health Assembly declared that smallpox had been eradicated from the planet. Currently, the only known remaining samples of smallpox virus are held in secure facilities at the Centers for Disease Control and Prevention in Atlanta, Georgia, and the Institute for Viral Preparations in Koltsovo, Russia.

As a result of the successful eradication program, the smallpox vaccine was removed from the commercial market in 1983.

Smallpox, a contagious and deadly blistering of the skin accompanied by pain and fever, has the potential to blow up into a worldwide plague. It is easily spread, has a 30 percent fatality rate, has no treatment, and no one in the United States has been vaccinated since 1972. Vaccination immunity acquired before that time has undoubtedly waned.

Smallpox is spread mainly by direct and fairly prolonged face-to-face contact, or from contact with contaminated clothing or bed linen.

It can take 12 to 14 days for symptoms, including high fever, malaise and prostration with headache and backache, to appear.

Smallpox virus
Facts About Smallpox

Smallpox is a serious, highly contagious, and sometimes fatal infectious disease. There is no specific treatment for smallpox disease, and the only prevention is vaccination. The name smallpox is derived from the Latin word for “spotted” and refers to the raised bumps that appear on the face and body of an infected person.

There are two clinical forms of smallpox. Variola major is the severe and most common form of smallpox, with a more extensive rash and higher fever. There are four types of variola major smallpox: ordinary (the most frequent type, accounting for 90 percent or more of cases); modified (mild and occurring in previously vaccinated persons); flat; and hemorrhagic (both rare and very severe). Historically, variola major has an overall fatality rate of about 30 percent; however, flat and hemorrhagic smallpox usually are fatal. Variola minor is a less common presentation of smallpox, and a much less severe disease, with death rates historically of 1 percent or less.

Smallpox outbreaks have occurred from time to time for thousands of years, but the disease is now extinct after a successful worldwide vaccination program. The last case of smallpox in the United States was in 1949. The last naturally occurring case in the world was in Somalia in 1977. After the disease was eliminated from the world, routine vaccination against smallpox among the general public was stopped because it was no longer necessary for prevention.

Where Smallpox Comes From
Smallpox is caused by the variola virus that emerged in human populations thousands of years ago. Humans are the only natural hosts of variola. Animals and insects do not carry or spread the variola virus. Except for laboratory stockpiles, the variola virus has been eliminated.

However, in the aftermath of the events of September and October, 2001, there is concern that the variola virus might be used as an agent of bioterrorism. For this reason, the U.S. government is taking careful precautions to be ready to deal with a smallpox outbreak.

Transmission
Generally, direct and fairly prolonged face-to-face contact is required to spread smallpox from one person to another. Smallpox also can be spread through direct contact with infected bodily fluids or infected objects such as bedding or clothing. Rarely, smallpox has been spread by virus carried in the air in enclosed settings such as buildings, buses, and trains. Smallpox is not known to be transmitted by insects.

A person with smallpox becomes infectious, or contagious, after a rash appears and is usually very sick and not able to move around in the community. After the appearance of a rash, the infected person is contagious until the last smallpox scab falls off.

Incubation Period
Not contagious
**Exposure to the virus** is followed by an incubation period during which people do not have any symptoms and may feel fine. This incubation period averages about 12 to 14 days, but can range from 7 to 17 days. During this time, people are not contagious.

**Initial Symptoms (Prodrome)**

*Not contagious*

The first symptoms of smallpox include fever, malaise, head and body aches, and sometimes vomiting. The fever is usually high, in the range of 101 to 104 degrees Fahrenheit. At this time, people are usually too sick to carry on their normal activities. This is called the prodrome phase and may last for 2 to 4 days.

**Days 1-4**

*Highly contagious*

A rash emerges first as small red spots on the tongue and in the mouth.

These spots develop into sores that break open and spread large amounts of the virus into the mouth and throat. At this time, the person becomes contagious.

Around the time the sores in the mouth break down, a rash appears on the skin, starting on the face and then spreading to the arms and legs and then to the hands and feet. Usually the rash spreads to all parts of the body within 24 hours. As the rash appears, the fever usually falls and the person may start to feel better.

By Day 3, the rash becomes raised bumps.

By Day 4, the bumps fill with a thick, opaque fluid and often have a depression in the center that looks like a belly-button. (This is a major distinguishing characteristic of smallpox.)

Fever often will rise again at this time and remain high until scabs form over the bumps.

**Days 5-10**

*Contagious*

Over the next 5 to 10 days, the bumps become pustules—sharply raised, usually round and firm to the touch. They feel like there’s a small round object under the skin. People often say it feels like there is a BB pellet embedded under the skin.

**Days 11-14**

*Contagious*

The pustules begin to form a crust and then scab. By Day 14, most of the sores have scabbed over.

**Days 15 - 21**

*Contagious*

The scabs begin to fall off, leaving marks on the skin that eventually become pitted scars. The
person is contagious to others until all of the scabs have fallen off. Most scabs will fall off after 3 weeks.

**After Day 21**

*Not contagious*

Scabs have fallen off. Person is no longer contagious.

**The Smallpox Vaccine**

The smallpox vaccine helps the body develop immunity to smallpox. The vaccine is made from a virus called vaccinia which is a “pox”-type virus related to smallpox. The smallpox vaccine contains the “live” vaccinia virus—not dead virus like many other vaccines. For that reason, the vaccination site must be cared for carefully to prevent the virus from spreading. Also, the vaccine can have side effects. The vaccine does not contain the smallpox virus and cannot give you smallpox.

Currently, the United States has a big enough stockpile of smallpox vaccine to vaccinate everyone who might need it in the event of an emergency. Production of new vaccine is underway.

**Length of Protection**

Smallpox vaccination provides full immunity for 3 to 5 years and decreasing immunity thereafter. If a person is vaccinated again later, immunity lasts even longer. Historically, the vaccine has been effective in preventing smallpox infection in 95 percent of those vaccinated. In addition, the vaccine was proven to prevent or substantially lessen infection when given within a few days of exposure. It is important to note, however, that at the time when the smallpox vaccine was used to eradicate the disease, testing was not as advanced or precise as it is today, so there may still be things to learn about the vaccine and its effectiveness and length of protection.

**Receiving the Vaccine**

The smallpox vaccine is not given with a hypodermic needle. It is not a shot as most people have experienced. The vaccine is given using a bifurcated (two-pronged) needle that is dipped into and holds a droplet of the vaccine. The needle is used to prick the skin 15 times in a few seconds. The poking is not deep, but it will cause a sore spot and one or two droplets of blood to form. The vaccine usually is given in the upper arm.

If the vaccination is successful, a red and itchy bump will develop at the vaccine site in three or four days. In a week, the bump becomes a large blister and fills with pus and begins to drain. During week two, the blister begins to dry up, and a scab forms. The scab falls off in the third week, leaving a small scar. People who are being vaccinated for the first time have a stronger reaction than those who are being revaccinated.

**Post-Vaccination Care**

After the vaccine is given, it is very important to follow instructions to care for the site of the vaccine. Because the virus is live, it can spread to other parts of your body, or even to other
people. The vaccinia virus (the live virus in the smallpox vaccine) may cause rash, fever, and head and body aches. In certain groups of people, complications from the vaccinia virus can be severe.

**Benefit of Vaccine Following Exposure**

Vaccination within 3 days of exposure will completely prevent or significantly modify smallpox in the vast majority of persons. Vaccination 4 to 7 days after exposure will also likely offer some protection from disease or modify the severity of disease.

**Smallpox Vaccine Safety**

The smallpox vaccine is the best protection you can get if you are exposed to the smallpox virus; however, the vaccine does have some risks. People most likely to have side effects are: people who now have, or have ever had, skin conditions, (especially eczema or atopic dermatitis); and people with weakened immune systems, such as those who have received a transplant, are HIV positive, or are receiving treatment for cancer or are currently taking medications like steroids that suppress the immune system. Also, women who are pregnant should not get the vaccine because of the risk it poses to the fetus. Individuals under 18 years of age and those allergic to the vaccine or any of its components should not receive the vaccine.

In the past, about 1,000 people for every 1 million people vaccinated for the first time experienced reactions that, while not life-threatening, were serious. These reactions included a toxic or allergic reaction at the site of the vaccination, spread of the vaccinia virus to other parts of the body (inadvertent inoculation) and spread of the vaccinia virus to other individuals (generalized vaccinia). These types of reactions typically do not require medical attention. In the past, between 14 and 52 people out of every 1 million people vaccinated for the first time experienced potentially life-threatening reactions to the vaccine. Based on past experience, it is estimated that 1 or 2 people in 1 million who receive the vaccine may die as a result. Careful screening of potential vaccine recipients is critical to ensure that those at increased risk do not receive the vaccine.

**Is there any way to treat bad reactions to the vaccine?**

Two treatments may help people who have certain serious reactions to the smallpox vaccine. These are vaccinia immune globulin (VIG) and cidofovir. Currently there are 700 doses of VIG on hand (enough for 6 million people vaccinated), and 3,500 doses of cidofovir (enough for 15 million people vaccinated). Additional doses of VIG are being produced, and measures are underway to increase supplies of cidofovir as well.

**Are diluted doses of smallpox vaccine as effective?**

Recent tests have indicated that a diluted (i.e., watered-down) smallpox vaccine is just as effective in providing immunity as the full-strength vaccine.

**Smallpox Vaccine Availability**

Routine vaccination of the American public against smallpox stopped in 1972 after the disease was eradicated in the United States. Until recently, the U.S. government provided the smallpox
vaccine only to a few hundred scientists and medical professionals who worked with smallpox and similar viruses in a research setting.

After the events of September and October, 2001, however, the U.S. government took further actions to improve its level of preparedness against terrorism. One of many such measures—designed specifically to prepare for an intentional release of the smallpox virus—included updating and releasing a smallpox response plan. In addition, the U.S. government ordered production of enough smallpox vaccine to immunize the American public in the event of a smallpox outbreak.

In the event of a smallpox outbreak, the U.S. government has prepared emergency guidelines to quickly vaccinate and contain a smallpox epidemic.

**Who Should NOT Receive the Smallpox Vaccine?**

*Unless they are Exposed to the Smallpox Virus*

- Expectant mothers?
- People with eczema or atopic dermatitis?
- People being treated for cancer?
- People who are HIV positive?
- People who have had an organ transplant?

*Answer: All of the Above*

Want to know why?

Some people are at greater risk of experiencing serious side effects from the smallpox vaccine.

Individuals who have any of the following conditions, or live with someone who does, should NOT receive the smallpox vaccine unless they have been exposed to the smallpox virus:

- Eczema or atopic dermatitis (even if the condition is mild or you only had it when you were a child);
- Other skin conditions such as burns, chickenpox, shingles, impetigo, herpes, severe acne, or psoriasis (you should not receive the vaccine until the condition has completely healed);
- Weakened immune system (for instance, from cancer treatment, an organ transplant, HIV, or medications such as steroids to treat autoimmune disorders and other illnesses); and
- Pregnancy or plans to become pregnant within one month of vaccination

In addition, individuals should not receive the smallpox vaccine if they:

- Are allergic to the vaccine or any of its ingredients,
- Have a moderate or severe short-term illness (these people should wait to receive the vaccine until they have recovered), or
- Are less than 18 years of age.

Smallpox vaccine is not recommended for routine use in infants and children.
If pregnant women are discouraged from getting the vaccine, is there a danger to them (and the unborn child) if broader vaccination occurs, i.e. contact with vaccinated people? Pregnant women should NOT be vaccinated in the absence of a smallpox outbreak, because of risk of fetal infection. Inadvertent transmission of the vaccinia virus to a pregnant woman could also put the fetus at risk. Vaccinated persons must be very cautious to prevent transmission of the vaccine virus to pregnant women or other contacts.

*Again, individuals who have been exposed to the smallpox virus, regardless of their health condition, should receive the vaccine.*

**Don’t Hesitate!**
If offered the smallpox vaccine, individuals should tell their immunization provider if they have any of the above conditions, or even if they suspect they might.

**In General**

**How serious is the smallpox threat?**
The deliberate release of smallpox as an epidemic disease is now regarded as a possibility and the United States is taking precautions to deal with such an eventuality.

**How dangerous is the smallpox threat?**
Smallpox is classified as a Category A agent by the Centers for Disease Control and Prevention. Category A agents are those that pose the greatest potential threat for adverse public health impact and have a moderate to high potential for large-scale dissemination. The public is generally more aware of category A agents and broad-based public health preparedness efforts are necessary. Other Category A agents are anthrax, plague, botulism, tularemia and viral hemorrhagic fevers.

**If smallpox is released in aerosol, how long does the virus survive?**
The smallpox virus is fragile and in the event of an aerosol release of smallpox, 90 percent of viruses will be inactivated or dissipated in about 24 hours.

**How many people would have to get smallpox before it is considered an outbreak?**
One suspected case of smallpox is considered a public health emergency.
BOTULINUM TOXIN

This toxin poses a major bioweapons threat because of its extreme potency and lethality; its ease of production, transport and misuse; and the potential need for prolonged intensive care in affected persons. Botulinum toxin is the single most poisonous substance known.

Human to human transmission has not been documented.

A number of states named by the U.S. State Department as “state sponsors of terrorism” have developed or are developing botulinum toxin as a biological weapon.

Naturally occurring botulism is the disease that results from the absorption of botulinum toxin into the circulation from a mucosal surface (gut, lung) or a wound. It does not penetrate intact skin. The toxin causes muscle paralysis, and in severe cases, can lead to a need for mechanical respiration.

The average incubation period is 12 to 72 hours after ingestion. Patients with botulism typically have difficulty speaking, seeing and/or swallowing. Patients may initially exhibit gastrointestinal distress, nausea, and vomiting preceding neurological symptoms.

Symptoms are similar for all toxin types, but the severity of illness can vary widely, in part depending on the amount of toxin absorbed. Recovery from paralysis can take weeks to months and requires the growth of new motor nerve endings.

There is an antitoxin available. In the event that there is a clinical suspicion of botulinum toxin, treatment with antitoxin should not be delayed for microbiological testing. In the U.S., licensed botulinum antitoxin is available from the CDC via state and local health departments.
Facts About Botulism

(source: CDC)

Botulism is a muscle-paralyzing disease caused by a toxin made by a bacterium called *Clostridium botulinum*. All forms of botulism can be fatal and are considered medical emergencies.

There are three main kinds of botulism:

- **Foodborne botulism** occurs when a person ingests pre-formed toxin that leads to illness within a few hours to days. Foodborne botulism is a public health emergency because the contaminated food may still be available to other persons besides the patient.
- **Infant botulism** occurs in a small number of susceptible infants each year who harbor *C. botulinum* in their intestinal tract.
- **Wound botulism** occurs when wounds are infected with *C. botulinum* that secretes the toxin.

With foodborne botulism, symptoms begin within 6 hours to 2 weeks (most commonly between 12 and 36 hours) after eating toxin-containing food. Symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and muscle weakness that always descends through the body: first shoulders are affected, then upper arms, lower arms, thighs, calves, etc. Paralysis of breathing muscles can cause a person to stop breathing and die, unless assistance with breathing (mechanical ventilation) is provided.

Botulism is not spread from one person to another. Foodborne botulism can occur in all age groups. Foodborne botulism can be especially dangerous, because many people can be poisoned by eating a contaminated food.

A supply of antitoxin against botulism is maintained by the CDC. The antitoxin is effective in reducing the severity of symptoms if administered early in the course of the disease. Most patients eventually recover after weeks to months of supportive care.

**What kind of germ is *Clostridium botulinum***?

*Clostridium botulinum* is the name of a group of bacteria commonly found in soil. These rod-shaped organisms grow best in low oxygen conditions. The bacteria form spores, which allow them to survive in a dormant state until exposed to conditions that can support their growth. There are seven types of botulism toxin designated by the letters A through G; only types A, B, E and F cause illness in humans.

**How common is botulism?**

In the United States an average of 110 cases of botulism are reported each year. Of these, approximately 25 percent are foodborne, 72 percent are infant botulism, and the rest are wound botulism. Outbreaks of foodborne botulism involving two or more persons occur most years and are usually caused by eating contaminated home-canned foods. The number of cases of foodborne and infant botulism has changed little in recent years, but wound botulism has increased because of the use of black-tar heroin, especially in California.
What are the symptoms of botulism?

The classic symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and muscle weakness. Infants with botulism appear lethargic, feed poorly, are constipated, and have a weak cry and poor muscle tone. These are all symptoms of the muscle paralysis caused by the bacterial toxin. If untreated, these symptoms may progress to cause paralysis of the arms, legs, trunk and respiratory muscles. In foodborne botulism, symptoms generally begin 18 to 36 hours after eating a contaminated food, but they can occur as early as 6 hours or as late as 10 days.

How is botulism diagnosed?

Physicians may consider the diagnosis if the patient’s history and physical examination suggest botulism. However, these clues are usually not enough to allow a diagnosis of botulism. Other diseases such as Guillain-Barré syndrome, stroke, and myasthenia gravis can appear similar to botulism, and special tests may be needed to exclude these other conditions. These tests may include a brain scan, spinal fluid examination, nerve conduction test (electromyography, or EMG), and a tensilon test for myasthenia gravis. The most direct way to confirm the diagnosis is to demonstrate the botulinum toxin in the patient’s serum or stool by injecting serum or stool into mice and looking for signs of botulism. The bacteria can also be isolated from the stool of persons with foodborne and infant botulism. These tests can be performed at some state health department laboratories and at the CDC.

How can botulism be treated?

The respiratory failure and paralysis that occur with severe botulism may require a patient to be on a breathing machine (ventilator) for weeks, plus intensive medical and nursing care. After several weeks, the paralysis slowly improves. If diagnosed early, foodborne and wound botulism can be treated with an antitoxin, which blocks the action of toxin circulating in the blood. This can prevent patients from worsening, but recovery still takes many weeks. Physicians may try to remove contaminated food still in the gut by inducing vomiting or by using enemas. Wounds should be treated, usually surgically, to remove the source of the toxin-producing bacteria. Good supportive care in a hospital is the mainstay of therapy for all forms of botulism. Currently, antitoxin is not routinely given for treatment of infant botulism.

Are there complications from botulism?

Botulism can result in death due to respiratory failure. However, in the past 50 years, the proportion of patients with botulism who die has fallen from about 50 percent to 8 percent. A patient with severe botulism may require a breathing machine as well as intensive medical and nursing care for several months. Patients who survive an episode of botulism poisoning may have fatigue and shortness of breath for years and long-term therapy may be needed to aid recovery.

How can botulism be prevented?

Botulism can be prevented. Foodborne botulism has often been from home-canned foods with low acid content, such as asparagus, green beans, beets and corn. However, outbreaks of botulism occur from more unusual sources such as chopped garlic in oil, chile peppers, tomatoes,
improperly handled baked potatoes wrapped in aluminum foil, and home-canned or fermented fish. Persons who do home canning should follow strict hygienic procedures to reduce the contamination of foods. Oils infused with garlic or herbs should be refrigerated. Potatoes that have been baked while wrapped in aluminum foil should be kept hot until served or refrigerated. Because the botulism toxin is destroyed by high temperatures, persons who eat home-canned foods should consider boiling the food for 10 minutes before eating it to ensure safety. Instructions on safe home canning can be obtained from county extension services or from the US Department of Agriculture. Because honey can contain spores of *Clostridium botulinum* and this has been a source of infection for infants, children less than 12 months old should not be fed honey. Honey is safe for persons 1 year of age and older. Wound botulism can be prevented by promptly seeking medical care for infected wounds and by not using injectable street drugs.

**What are public health agencies doing to prevent or control botulism?**

Public education about botulism prevention is an ongoing activity. Information about safe canning is widely available for consumers. State health departments and CDC have persons knowledgeable about botulism available to consult with physicians 24 hours a day. If antitoxin is needed to treat a patient, it can be quickly delivered to a physician anywhere in the country. Suspected outbreaks of botulism are quickly investigated, and if they involve a commercial product, the appropriate control measures are coordinated among public health and regulatory agencies. Physicians should report suspected cases of botulism to a state health department.
TULAREMIA

*Francisella tularensis*, the organism that causes tularemia, is one of the most infectious pathogenic bacteria known, requiring inoculation or inhalation of as few as 10 organisms to cause disease. It is considered to be a dangerous potential biological weapon because of its extreme infectivity, ease of dissemination, and substantial capacity to cause illness and death.

Human to human transmission has not been documented.

Aerosol dissemination of *F. tularensis* in a populated area would be expected to result in large numbers of cases of acute, non-specific febrile illness beginning three to five days later. Without antibiotic treatment, the clinical course could progress to respiratory failure, shock and death.

In the United States, a vaccine has been used to protect laboratory personnel routinely working with *F. tularensis*. Given the short incubation period of tularemia and incomplete protection of current vaccines against inhalational tularemia, vaccination is not recommended for post-exposure prophylaxis.

Given the lack of human-to-human transmission, isolation is not recommended for tularemia patients.
Facts About Tularemia  
*(source: CDC)*

**What is tularemia?**
Tularemia is an infectious disease caused by a hardy bacterium, *Francisella tularensis*, found in animals (especially rodents, rabbits, and hares).

**How do people become infected with the tularemia bacteria?**
Typically, persons become infected through the bites of arthropods (most commonly, ticks and deerflies) that have fed on an infected animal, by handling infected animal carcasses, by eating or drinking contaminated food or water, or by inhaling infected aerosols.

**Does tularemia occur naturally in the United States?**
Yes. It is a widespread disease of animals. Approximately 200 cases of tularemia in humans are reported annually in the United States, mostly in persons living in the south-central and western states. Nearly all cases occur in rural areas and are associated with the bites of infectious ticks and biting flies or with the handling of infected rodents, rabbits, or hares. Occasional cases result from inhaling infectious aerosols and from laboratory accidents.

**Why are we concerned about tularemia as a bioweapon?**
*Francisella tularensis* is highly infectious: a small number of bacteria (10-50 organisms) can cause disease. If *F. tularensis* were used as a bioweapon, the bacteria would likely be made airborne for exposure by inhalation. Persons who inhale an infectious aerosol would generally experience severe respiratory illness, including life-threatening pneumonia and systemic infection, if they were not treated. The bacteria that cause tularemia occur widely in nature and could be isolated and grown in quantity in a laboratory, although manufacturing an effective aerosol weapon would require considerable sophistication.

**Can someone become infected with the tularemia bacteria from another person?**
No. People have not been known to transmit the infection to others, so infected persons do not need to be isolated.

**How quickly would someone become sick if they were exposed to the tularemia bacteria?**
The incubation period for tularemia is typically 3 to 5 days, with a range of 1 to 14 days.

**What are the signs and symptoms of tularemia?**
Depending on the route of exposure, the tularemia bacteria may cause skin ulcers, swollen and painful lymph glands, inflamed eyes, sore throat, oral ulcers, or pneumonia. If the bacteria were inhaled, symptoms would include the abrupt onset of fever, chills, headache, muscle aches, joint pain, dry cough, and progressive weakness. Persons with pneumonia can develop chest pain, difficulty breathing, bloody sputum, and respiratory failure. Forty percent or more of persons with the lung and systemic forms of the disease may die if they are not treated with appropriate antibiotics.
What should someone do if they suspect they or others have been exposed to the tularemia bacteria?
Seek prompt medical attention. If a person has been exposed to *Francisella tularensis*, treatment with tetracycline antibiotics for 14 days after exposure may be recommended.

Local and state health departments should be immediately notified so an investigation and control activities can begin quickly. If the exposure is thought to be due to criminal activity (bioterrorism), local and state health departments will notify the CDC, the FBI, and other appropriate authorities.

How is tularemia diagnosed?
When tularemia is clinically suspected, the healthcare worker will collect specimens, such as blood or sputum, from the patient for testing in a diagnostic or reference laboratory. Laboratory test results for tularemia may be presumptive or confirmatory.

Presumptive (preliminary) identification may take less than 2 hours, but confirmatory testing will take longer, usually 24 to 48 hours.

Can tularemia be effectively treated with antibiotics?
Yes. After potential exposure or diagnosis, early treatment is recommended with an antibiotic from the tetracycline (such as doxycycline) or fluoroquinolone (such as ciprofloxacin) class, which are taken orally, or the antibiotics streptomycin or gentamicin, which are given intramuscularly or intravenously. Sensitivity testing of the tularemia bacterium can be done in the early stages of a response to determine which antibiotics would be most effective.

How long can *Francisella tularensis* exist in the environment?
*Francisella tularensis* can remain alive for weeks in water and soil.

Is there a vaccine available for tularemia?
In the past, a vaccine for tularemia has been used to protect laboratory workers, but it is currently under review by the Food and Drug Administration.
HEMORRHAGIC FEVER AGENTS

Viral hemorrhagic fever viruses may also be used as bioterrorist agents. These viruses induce fever, prostration and diffuse vascular damage, often leading to thrombocytopenic hemorrhage. Viral hemorrhagic fever patients require intensive medical care and substantial resources. Without proper isolation practices, the spread of these fever viruses is not uncommon.
Facts About Viral Hemorrhagic Fevers
(source: CDC)

What are viral hemorrhagic fevers?
Viral hemorrhagic fevers (VHFs) refer to a group of illnesses that are caused by several distinct families of viruses. In general, the term “viral hemorrhagic fever” is used to describe a severe multisystem syndrome (multisystem in that multiple organ systems in the body are affected). Characteristically, the overall vascular system is damaged, and the body’s ability to regulate itself is impaired. These symptoms are often accompanied by hemorrhage (bleeding); however, the bleeding is itself rarely life-threatening. While some types of hemorrhagic fever viruses can cause relatively mild illnesses, many of these viruses cause severe, life-threatening disease.

How are hemorrhagic fever viruses grouped?
VHFs are caused by viruses of four distinct families: arenaviruses, filoviruses, bunyaviruses, and flaviviruses. Each of these families share a number of features:
• They are all RNA viruses, and all are covered, or enveloped, in a fatty (lipid) coating.
• Their survival is dependent on an animal or insect host, called the natural reservoir.
• The viruses are geographically restricted to the areas where their host species live.

Humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another.

Human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. The occurrence of outbreaks cannot be easily predicted.

With a few noteworthy exceptions, there is no cure or established drug treatment for VHFs. In rare cases, other viral and bacterial infections can cause a hemorrhagic fever; scrub typhus is a good example.

What carries viruses that cause viral hemorrhagic fevers?
Viruses associated with most VHFs are zoonotic. This means that these viruses naturally reside in an animal reservoir host or arthropod vector. They are totally dependent on their hosts for replication and overall survival. For the most part, rodents and arthropods are the main reservoirs for viruses causing VHFs. The multimammate rat, cotton rat, deer mouse, house mouse, and other field rodents are examples of reservoir hosts. Arthropod ticks and mosquitoes serve as vectors for some of the illnesses. However, the hosts of some viruses remain unknown—Ebola and Marburg viruses are well-known examples.

Where are cases of viral hemorrhagic fever found?
Taken together, the viruses that cause VHFs are distributed over much of the globe. However, because each virus is associated with one or more particular host species, the virus and the disease it causes are usually seen only where the host species live(s). Some hosts, such as the ro-
dent species carrying several of the New World arenaviruses, live in geographically restricted areas. Therefore, the risk of getting VHF's caused by these viruses is restricted to those areas.

Other hosts range over continents, such as the rodents that carry viruses that cause various forms of hantavirus pulmonary syndrome (HPS) in North and South America, or the different set of rodents that carry viruses which cause hemorrhagic fever with renal syndrome (HFRS) in Europe and Asia. A few hosts are distributed nearly worldwide, such as the common rat. It can carry the Seoul virus, a cause of HFRS; therefore, humans can get HFRS anywhere the common rat is found.

While people usually become infected only in areas where the host lives, occasionally people become infected by a host that has been exported from its native habitat. For example, the first outbreaks of Marburg hemorrhagic fever, in Marburg and Frankfurt, Germany and in Yugoslavia, occurred when laboratory workers handled imported monkeys infected with the Marburg virus. Occasionally, a person becomes infected in an area where the virus occurs naturally and then travels elsewhere. If the virus is a type that can be transmitted further by person-to-person contact, the traveler could infect other people. For instance, in 1996, a medical professional treating patients with Ebola hemorrhagic fever (Ebola HF) in Gabon unknowingly became infected. When he later traveled to South Africa and was treated for Ebola HF in a hospital, the virus was transmitted to a nurse. She became ill and died. Because more and more people travel each year, outbreaks of these diseases are becoming an increasing threat in places where they rarely, if ever, have been seen before.

How are hemorrhagic fever viruses transmitted?
Viruses causing hemorrhagic fever are initially transmitted to humans when the activities of infected reservoir hosts or vectors and humans overlap. The viruses, carried in rodent reservoirs, are transmitted when humans have contact with urine, fecal matter, saliva, or other body excretions from infected rodents. The viruses associated with arthropod vectors are spread most often when the vector mosquito or tick bites a human, or when a human crushes a tick. However, some of these vectors may spread the virus to animals, livestock, for example. Humans then become infected when they care for or slaughter the animals.

Some viruses that cause hemorrhagic fever can spread from one person to another, once an initial person has become infected. Ebola, Marburg, Lassa and Crimean-Congo hemorrhagic fever viruses are examples. This type of secondary transmission of the virus can occur directly, through close contact with infected people or their body fluids. It can also occur indirectly, through contact with objects contaminated with infected body fluids. For example, contaminated syringes and needles have played an important role in spreading infection in outbreaks of Ebola hemorrhagic fever and Lassa fever.

What are the symptoms of viral hemorrhagic fever illnesses?
Specific signs and symptoms vary by the type of VHF, but initial signs and symptoms often include marked fever, fatigue, dizziness, muscle aches, loss of strength, and exhaustion. Patients with severe cases of VHF often show signs of bleeding under the skin, in internal organs, or
from body orifices like the mouth, eyes, or ears. However, although they may bleed from many sites around the body, patients rarely die because of blood loss. Severely ill patient cases may also show shock, nervous system malfunction, coma, delirium, and seizures. Some types of VHF are associated with renal (kidney) failure.

**How are patients with viral hemorrhagic fever treated?**
Patients receive supportive therapy, but generally speaking, there is no other treatment or established cure for VHF. Ribavirin, an anti-viral drug, has been effective in treating some individuals with Lassa fever or HFRS. Treatment with convalescent-phase plasma has been used with success in some patients with Argentine hemorrhagic fever.

**How can cases of viral hemorrhagic fever be prevented and controlled?**
With the exception of yellow fever and Argentine hemorrhagic fever, for which vaccines have been developed, no vaccines exist that can protect against these diseases. Therefore, prevention efforts must concentrate on avoiding contact with host species. If prevention methods fail and a case of VHF does occur, efforts should focus on preventing further transmission from person to person, if the virus can be transmitted in this way. Because many of the hosts that carry hemorrhagic fever viruses are rodents, disease prevention efforts include:
- controlling rodent populations.
- discouraging rodents from entering or living in homes or workplaces.
- encouraging safe cleanup of rodent nests and droppings.

For hemorrhagic fever viruses spread by arthropod vectors, prevention efforts often focus on community-wide insect and arthropod control. In addition, people are encouraged to use insect repellent, proper clothing, bednets, window screens, and other insect barriers to avoid being bitten.

For those hemorrhagic fever viruses that can be transmitted from one person to another, avoiding close physical contact with infected people and their body fluids is the most important way of controlling the spread of disease. Barrier nursing or infection control techniques include isolating infected individuals and wearing protective clothing. Other infection control recommendations include proper use, disinfection, and disposal of instruments and equipment used in treating or caring for patients with VHF, such as needles and thermometers.

In conjunction with the World Health Organization, the CDC has developed practical, hospital-based guidelines, titled *Infection Control for Viral Haemorrhagic Fevers In the African Health Care Setting*. The manual can help healthcare facilities recognize cases and prevent further hospital-based disease transmission using locally available materials and few financial resources.

**What needs to be done to address the threat of viral hemorrhagic fevers?**
Scientists and researchers are challenged with developing containment, treatment, and vaccine strategies for these diseases. Another goal is to develop immunologic and molecular tools for more rapid disease diagnosis and to study how the viruses are transmitted and exactly how the
disease affects the body (pathogenesis). A third goal is to understand the ecology of these viruses and their hosts in order to offer preventive public health advice for avoiding infection.

**Ebola Hemorrhagic Fever**

Ebola hemorrhagic fever is one example of a viral hemorrhagic fever.

**What is Ebola hemorrhagic fever?**

Ebola hemorrhagic fever (Ebola HF) is a severe, often-fatal disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees) that has appeared sporadically since its initial recognition in 1976.

The disease is caused by infection with the Ebola virus, named after a river in the Democratic Republic of the Congo (formerly Zaire) in Africa, where it was first recognized. The virus is one of two members of a family of RNA viruses called the Filoviridae. There are four identified subtypes of Ebola virus. Three of the four have caused disease in humans: Ebola-Zaire, Ebola-Sudan, and Ebola-Ivory Coast. The fourth, Ebola-Reston, has caused disease in nonhuman primates, but not in humans.

**Where is the Ebola virus found in nature?**

The exact origin, locations, and natural habitat (known as the “natural reservoir”) of the Ebola virus remain unknown. However, on the basis of available evidence and the nature of similar viruses, researchers believe that the virus is zoonotic (animal-borne) and is normally maintained in an animal host that is native to the African continent. A similar host is probably associated with Ebola-Reston which was isolated from infected cynomolgous monkeys that were imported to the United States and Italy from the Philippines. The virus is not known to be native to other continents, such as North America.

**Where do cases of Ebola hemorrhagic fever occur?**

Confirmed cases of Ebola HF have been reported in the Democratic Republic of the Congo, Gabon, Sudan, the Ivory Coast, Uganda, and the Republic of the Congo. An individual with serologic evidence of infection but showing no apparent illness has been reported in Liberia, and a laboratory worker in England became ill as a result of an accidental needle-stick. No case of the disease in humans has ever been reported in the United States. Ebola-Reston virus caused severe illness and death in monkeys imported to research facilities in the United States and Italy from the Philippines; during these outbreaks, several research workers became infected with the virus, but did not become ill.

Ebola HF typically appears in sporadic outbreaks, usually spread within a healthcare setting (a situation known as amplification). It is likely that sporadic, isolated cases occur as well, but go unrecognized. A table showing a chronological list of known cases and outbreaks is available.

**How is Ebola virus spread?**

Infections with Ebola virus are acute. There is no carrier state. Because the natural reservoir of
the virus is unknown, the manner in which the virus first appears in a human at the start of an outbreak has not been determined. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal.

After the first case-patient in an outbreak setting is infected, the virus can be transmitted in several ways. People can be exposed to Ebola virus from direct contact with the blood and/or secretions of an infected person. Thus, the virus is often spread through families and friends because they come in close contact with such secretions when caring for infected persons. People can also be exposed to Ebola virus through contact with objects, such as needles, that have been contaminated with infected secretions.

Nosocomial transmission refers to the spread of a disease within a healthcare setting, such as a clinic or hospital. It occurs frequently during Ebola HF outbreaks. It includes both types of transmission described above. In African healthcare facilities, patients are often cared for without the use of a mask, gown, or gloves. Exposure to the virus has occurred when healthcare workers treated individuals with Ebola HF without wearing these types of protective clothing. In addition, when needles or syringes are used, they may not be disposable or may not have been sterilized, but only rinsed before reinsertion into multi-use vials of medicine. If needles or syringes become contaminated with the virus and are then reused, numerous people can become infected.

Ebola-Reston appeared in a primate research facility in Virginia, where it may have been transmitted from monkey to monkey through the air. While all Ebola virus species have displayed the ability to be spread through airborne particles (aerosols) under research conditions, this type of spread has not been documented among humans in a real-world setting, such as a hospital or household.

**What are the symptoms of Ebola hemorrhagic fever?**
The incubation period for Ebola HF ranges from two to 21 days. The onset of illness is abrupt and is characterized by fever, headache, joint and muscle aches, sore throat, and weakness, followed by diarrhea, vomiting, and stomach pain. A rash, red eyes, hiccups and internal and external bleeding may be seen in some patients.

Researchers do not understand why some people are able to recover from Ebola HF and others are not. However, it is known that patients who die usually have not developed a significant immune response to the virus at the time of death.

**How is Ebola hemorrhagic fever clinically diagnosed?**
Diagnosing Ebola HF in an individual who has been infected only a few days is difficult because early symptoms, such as red eyes and a skin rash, are nonspecific to the virus and are seen in other patients with diseases that occur much more frequently. However, if a person has the constellation of symptoms described above and infection with the Ebola virus is suspected, isolate the patient and notify local and state health departments and the CDC.
**How is Ebola hemorrhagic fever treated?**
There is no standard treatment for Ebola HF. Patients receive supportive therapy. This consists of balancing the patient’s fluids and electrolytes, maintaining their oxygen status and blood pressure, and treating them for any complicating infections.

**How is Ebola hemorrhagic fever prevented?**
The prevention of Ebola HF in Africa presents many challenges. Because the identity and location of the natural reservoir of Ebola virus are unknown, there are few established primary prevention measures.

If cases of the disease do appear, current social and economic conditions often favor the spread of an epidemic within healthcare facilities. Therefore, healthcare providers must be able to recognize a case of Ebola HF should one appear. They must also have the capability to perform diagnostic tests and be ready to employ practical viral hemorrhagic fever isolation precautions, or barrier nursing techniques.

These techniques include the wearing of protective clothing, such as masks, gloves, gowns, and goggles; the use of infection-control measures, including complete equipment sterilization; and the isolation of Ebola HF patients from contact with unprotected persons. The aim of all of these techniques is to avoid any person’s contact with the blood or secretions of any patient. If a patient with Ebola HF dies, it is equally important that direct contact with the body of the deceased patient be prevented.

The CDC has developed a set of tools to meet healthcare facilities’ needs. In conjunction with the World Health Organization, the CDC has developed practical, hospital-based guidelines, entitled *Infection Control for Viral Haemorrhagic Fevers In the African Health Care Setting*. The manual describes how to recognize cases of viral hemorrhagic fever, such as Ebola HF and prevent further nosocomial transmission by using locally available materials and few financial resources. Similarly, a practical diagnostic test that uses tiny samples from patients’ skin has been developed to retrospectively diagnose Ebola HF in suspected case-patients who have died.

**What challenges remain for the control and prevention of Ebola hemorrhagic fever?**
Scientists and researchers are faced with the challenges of developing additional diagnostic tools to assist in early diagnosis of Ebola HF and conducting ecological investigations of the Ebola virus and its possible reservoir. In addition, one of the research goals is to monitor suspected areas to determine the incidence of the disease. More extensive knowledge of the natural reservoir of the Ebola virus and how the virus is spread must be acquired to prevent future outbreaks effectively.