
UNIVERSITY OF NORTH TEXAS
HEALTH SCIENCE CENTER AT FORT WORTH
1970

Perkins, Christopher J., Epidemiological Modeling of a Bioterrorism Event In A Noncombat Environment. Master of Public Health (Biomedical Sciences), July, 1999, 60 pp., 8 tables, 4 illustrations, references, 31 titles.

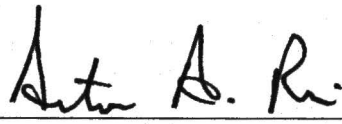
The challenge to government, medical and public health officials is to advocate for American citizens the safest environment possible to live and work. A threat to the safety of all Americans has initiated preparations from national, state, and local jurisdictions in an attempt to counter the probability of biological terrorism.

Bioterrorism is not only a threat to humans but also a threat to the nation's water and food supplies. Epidemiological Modeling of a Bioterrorism Event demonstrates the importance in preparations to reduce the numbers of casualties and fatalities. Using Epidemiological Modeling of bioterrorism events will aid public health and medical personnel in the planning and initiation of appropriate public health actions and medical therapies should such events occur.

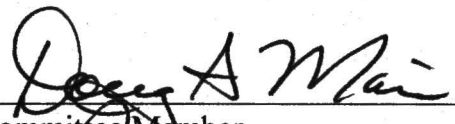
EPIDEMIOLOGICAL MODELING OF
A BIOTERRORISM EVENT
IN A NONCOMBAT ENVIRONMENT

Christopher J. Perkins, D.O.

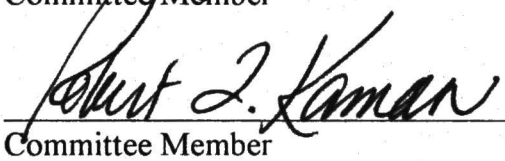
APPROVED:



Major Professor

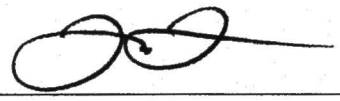


Committee Member

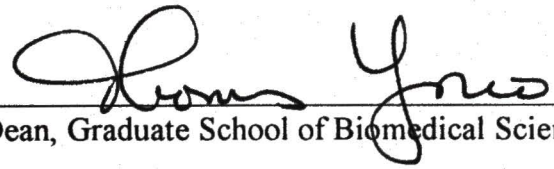


Committee Member

Committee Member



Chair, Public Health Program



Dean, Graduate School of Biomedical Sciences

EPIDEMIOLOGICAL MODELING OF A BIOTERRORISM EVENT IN A NONCOMBAT ENVIRONMENT

THESIS

Presented to the Graduate Council of the

Graduate School of Biomedical Sciences

University of North Texas
Health Science Center at Fort Worth

In Partial Fulfillment of the Requirements

For the Degree of

MASTER OF PUBLIC HEALTH

By

Christopher J. Perkins, D.O.

Fort Worth, Texas

July 1999

ACKNOWLEDGMENTS

I am indebted to Lieutenant-Commander Shirley Bowens, United States Navy, for her support of my thesis and for providing me the guidance necessary to complete it. A special thanks to my committee members Drs. Rene, Mains, Ramirez, and Kaman. Your dedication, suggestions, and critiques during the writing of this paper are greatly appreciated.

Special thanks to my family for the love and support during my efforts to attain my M.P.H. during the academic year of my aerospace medicine residency. Now I am on my way to Pensacola, Florida, to complete my residency and start a career as a Navy Flight Surgeon.

TABLE OF CONTENTS

LIST OF TABLES

INTRODUCTION

Statement of the Problem

A significant bioterroristic event is highly probable on the North American Continent within the next decade. With existing technologies, crude bioweapons can be manufactured and delivered upon vulnerable populations. The resultant exposure and disease can remit massive illness and death.

Biological weapons are tickets to power, stature, and confidence for rogue nations in a regional war. As for terroristic groups, the threat of their use can be a lethal form of intimidation to civilian populations that can result in mass panic and chaos.

Leaders of nations that deliberately violate the international laws of warfare (Geneva Conventions) can be persecuted for war crimes. Similar laws exist concerning civilian populations. Therefore, it might be thought that with the Geneva Protocol of 1925 which prohibits the use in war of biological (bacteriological) weapons, and the Biological and Toxin Weapons Convention (BWC) of 1972 prohibiting the development, production, acquisition, and stockpiling of biological weapons, this subject would not be an issue. Today, however, there are security concerns about deliberate spread of disease or biological warfare.(1)

Significance of Epidemic Modeling of Bioterroristic Agents

In the event of bioterrorism, the most probable pathogens must be rapidly identified. Medical and public health officials must have an understanding of the agent's disease causing mechanisms in order to initiate public health measures and medical therapies. Vague signs and symptoms of flu-like illnesses and dematologic conditions are well documented in persons that acquired infections naturally from the most probable agents of bioterrorism. There is a lengthy history of disease and death in societies worldwide after exposure to smallpox, anthrax, plague, and other bioweapon pathogens.

Using Epidemiological Models of bioterrorism events will aid public health and medical personnel in the planning and initiation of appropriate public health actions and medical therapies should such events occur. Epidemiologic modeling utilizing the attack rates, lethality rates, natural cure rates, and environmental conditions at the time of the pathogens release can predict the severity of a bioterrorism event in a vulnerable and untreated population. The purpose of this project is to review different epidemiological models for predictions of the outcome of different bioterrorism events.

LITERATURE REVIEW

Classes of Biological Pathogens

Organisms initiated natural biological warfare: poisons, mechanical barriers and camouflage. These mechanisms developed through the evolution of living species and in the pursuit for survival. Consequently, plants, animals, and other kingdoms of living creatures occupied virtually all of Earth's ambience.

Humans, while competing for dominance of the environment, developed a convoluted immune system that evolved as a direct result of the onslaught of microorganisms; nevertheless, this natural biological warfare (infectious disease) is a constant threat to humans everywhere. In addition to the body's immune system and antimicrobial therapies, there has been a decrease in infectious diseases in western nations in this century which is mostly the result of public health measures.

The body has several mechanisms to defend itself against infectious microorganisms. Some are as simple as physical barriers, such as like the skin's tough outer keratin layer, which shields the living cells beneath it from the hostile environment of earth. Other mechanisms include biochemical substances that offer relatively nonspecific protection against an extensive range of microorganisms (i.e., enzyme lysozyme in tears and other bodily secretions).

There are blood proteins, which are more complex chemical barriers that are triggered by molecular features of some microorganisms. The presence of these proteins promotes lysis or enhanced phagocytosis of the foreign invader by leukocytes. During

serious infections, these acute phase proteins come into action to promote destruction of microorganisms through a complement cascade.

The leukocytes perform the most complex, dynamic, and effective defense strategies. These are the "stealth fighters" of the body that travel throughout to search and destroy microorganisms and other foreign substances.(2)

Those microorganisms that are pathogenic are indigenous to different areas of the earth. For thousands of years, human migration has introduced pathogens from one region to another region. Consequently, epidemics and pandemics occurred resulting in population reduction through disease and death. As human tribes maintained vast distances between each other, the threat of epidemics were at minimal. However, as populations grew due to technological advances, the risks of encountering an unknown or different pathogen grew.

To many non-medical professionals in the western world, an infection means bacteria. The bacteria are often seen as being negative, a source of being unclean. The obsession of westerners regarding bacteria exceeds a reasonable concern. This has led to an increased demand for antibiotics by patients resulting in increased microbial resistance to many classes of antibiotics. Unfortunately, this could be due to the lack of patients' understanding that many infections are viral in origin. Conversely, some bacteria are beneficial to humans' survival. For example, intestinal bacteria aid in digestion and in the production of Vitamin K. The indigenous bacteria (normal flora) aid in defense against pathogenic bacteria.

Those bacteria that are pathogenic generally cause disease by two major mechanisms: (1) toxin production and (2) invasiveness. Toxins fall into two general categories: exotoxins and endotoxins. Each type of toxin can cause symptoms; the presence of the bacteria in the host is not required. On the other hand, invasive bacteria grow to large numbers locally and cause symptoms in that area by producing a variety of enzymes that damage adjacent host cells.

Other infectious organisms that are known to cause disease among humans and animals can and have been as devastating as bacteria in causing illness. The viruses, causative agents of many cancers and a suspected cause of Type I Diabetes, consist of two representative types: RNA and DNA, which can be either single stranded or double stranded and arranged into either a linear or circular configuration. Resultant viral infections are either localized to the portal of entry (i.e., common cold) or spread systemically (i.e., poliomyelitis, and human immunodificiency virus) throughout the body.

The remaining infectious agents are less of a threat in the western world today but have the potential to result in catastrophic diseases. The systemic fungi infections tend to occur in humans as granulomas because of the cell-mediated response of neutrophilic white blood cells. Other fungal diseases can occur in patients after ingestion (mycotoxicoses) and through the development of allergies to fungal spores.

Parasites occur in two distinct forms: single-celled protozoa and multicellular metazoa known as helminths or worms. These organisms can cause infections after

ingestion of some uncooked food products, transmission through a vector (insect or animal bite), or inhalation or penetration of the organism through the skin.

It is important for health practitioners to understand the mechanisms of how microorganisms cause diseases in humans. With this understanding, treatments can be geared toward classes of microorganisms that have similar disease producing capabilities. Research continues to develop strategies that would serve as barriers between exposure to pathogens and infection.(27)

Biological weapons are produced with microorganisms or toxins derived from living organisms to intentionally cause disease or death in humans, animals, or plants. Biological and chemical agents are often considered together since both are weapons of mass destruction. Delivery systems are frequently similar: movement of agents to targets is generally aerosol or vapor form and which can be carried or controlled by wind and weather. Chemical and potential biological agents have become the "nuclear weapons" of third world rogue nations and terrorist groups. They are easy to use by being cheap and easy to conceal.

Diseases resulting from biological agents have incubation period of days or weeks, whereby chemical weapons usually result in violent disease syndromes within minutes at the site of exposure. The resultant diseases that may occur after a bioterroristic attack requires public health officials to use accepted diagnostic and epidemiological principles to quickly identify and prevent the spread of disease. With appropriate therapy, the impact of a terrorist attack will be greatly reduced.(3)

Consequently, those in public health should utilize epidemiological modeling of different bioterrorism pathogens in preparation to minimize the severity of an event across the nation or globe. If an incidence of a previously controlled or exotic disease is due to natural or man-made interaction, epidemiologists should lead the way in the investigation and notify the appropriate law enforcement agencies if necessary. Physicians and other health providers, accordingly, should remember that possibly every person could be in one of the stages of an acute infectious disease: incubation period, prodrome period, specific-illness period, and recovery period.(24) Medical practitioners must become knowledgeable about the signs and symptoms of probable bioterrorism agents. The vague and unusual symptoms of a patient should cause the health provider to consider one of these agents in the differential list of clinical diagnoses.

In 1994, the pneumonic version of the plague resurfaced in Western India in the city of Surat near Bombay. Some 6,000 persons were hospitalized and at least 55 died. Many people fled from the area in a panic and some infected persons spread the disease to other localities. The disease is curable if treated early by antibiotics. This modern-day outbreak of a supposedly vanished disease was a sharp reminder of the relationship between health and social conditions. It also showed what could possibly result if a bioterrorism assault occurred against a vulnerable population. This outbreak in India was the consequence of a migrant worker from Central India moving into a densely packed shantytown in the city of Surat.

In conclusion, as long as human beings lived as nomads or in widely scattered and isolated communities, the danger from epidemics and infectious disease was relatively

slight. Today, with mega-cities and the ease of travel from one region to another, the threat of a biological incidence against civilians in a non-combat environment is a very probable event in the near future. When diseases that were seen by the scientific community as being no longer a threat reappear, public health officials must become suspicious of possible bioterrorism.

History of Biological Warfare

The earliest evidence of biological warfare in secular history was 2,600 years ago. Persian, Greek, and Roman literature from 600 B.C. onward site examples of the use of animal cadavers to contaminate wells and other sources of water. The Athenian army poisoned the water supply to the city of Kirrha in 600 B.C. using toxin derived from the hellebore plant.(1) The Scythian's archers during 400 B.C. infected arrows by dipping them in decomposing cadavers or in blood mixed with manure.(4)

In A.D. 1155, at a battle in Tortona, Italy, the army leader, Barbarossa, broadened the scope of biological warfare using the bodies of dead soldiers as well as diseased animals to pollute wells.(5) In 1171, a Venetian Military Fleet contracted a contagious disease allegedly from contaminated wells and was forced to return to Venice.

During medieval times, human corpses and diseased animals were catapulted into walled cities and fortifications.(6) In 1495, Cesalpino, an Italian physician recounted an attempt by Spanish soldiers to contaminate the food of French forces with wine infected with blood from leprosy patients.(4)

In the 1700's, the corpses of individuals who were known to have a specific disease were used in warfare. In 1710, the Russians besieging the Swedish forces at Reval in Estonia returned to the well-tested practice of casting plague cadavers over walls. Also, bacterial agents were used in the U.S.-Indian Wars, unfortunately, to conquer the Native Americans with exposure and disease.

The British, prior to the Americans, used specific disease application of smallpox in an attempt to hold on to the American frontier in the 1760's. In the spring of 1763, Sir Jeffrey Armherst, Commander-in-Chief of British forces in North America, believed that British control of the western frontier was deteriorating rapidly. Western Pennsylvania being virtually deserted and the Fort Pitt isolated due to a lack of support from England and transportation problems, assigning additional troops was not an option. Amherst wrote Captain Ecuyer to suggest that "could it not be contrived to send the smallpox among those disaffected tribes of Indians? We must, on this occasion, use every strategy in our power to reduce them." [Signed] J.A. Sir Armherst's plan for his field generals was that "you will try to inoculate the Indians, by means of blankets, as well as try every other method, that can serve to extirpate this execrable race."(5)

Biological warfare was entrenched in the U.S. war machine by the time of the American Civil War. The United States and Confederate States of America Armed Forces used it. 'The manpower that was lost in internecine warfare by microorganisms within an army was far greater than the loss in battle between enemy armies; nevertheless, the casualties produced in battle often determined the outcome of that clash of arms because they all came within a brief period of time. The losses from disease

consequently were usually more scattered and hence less important, but a number of sharp epidemics occurred that had the military effectiveness of a battle.' In July 1863, General Joseph E. Johnston of the Confederacy ordered his forces to shoot farm animals after herding them into ponds to contaminate the water.(4)

However, in the 20th century after the formation of Koch's postulates and the development of modern microbiology in the 19th century, scientists have had the capability to isolate and produce stocks of specific pathogens; accordingly, nations escalated their use of biological agents.

Germany was accused of using cholera in Italy and the plague in St. Petersburg in 1915. There is evidence that Germany used anthrax to infect horses and cattle in Bucharest in 1916. Substantial evidence exists that Germany also used covert operations on neutral trading partners of the Allies to infect livestock and contaminate animal feed to be exported to Allied forces.

The Germans considered *Bacillus anthracis and Pseudomonas mallei*, the etiologic agents of anthrax and glanders, as agents to infect Romanian sheep planned for export to Russia. German saboteurs operating in Mesopotamia allegedly used *Pseudomonas mallei* to inoculate 4,500 mules. The Germans were able to infect horses in France of the French Calvary. These two biological agents were confiscated from German Legation in Romania in 1916. However, Germany issued official denials of these accusations.

Argentinean livestock intended for export to Allies forces were infected with *B. anthracis and P. mallei*, resulting in the deaths of more than 200 mules from 1917 to

1918. Operations in the United States included attempts to contaminate animal feed and to infect horses intended for export during World War I.

In 1925, the Geneva Convention issued a protocol for the Prohibition of the Use in War of Asphyxiating Poisonous or Other Gases, and of Bacteriological Methods of Warfare. Although most nations ratified and signed the treaty, it was withdrawn from the United States Senate by President Truman in 1947 and was not ratified by Congress until 1975.

The Geneva Protocol of 1925 did not ban laboratory and field research. By 1940, all major powers of the time had their own biological weapon research programs. Most of the research concluded that anthrax, brucellosis, tularemia, psittacosis, Q fever and Venezuelan equine encephalitis (VEE) were best suited as weapons. Subsequently, in 1969, President Nixon renounced biological warfare and announced that the U.S. would eliminate its stockpiles of biological weapons after the U.S. military concluded that biological warfare had little strategic value and insignificant impact on the battlefield.

Japan was a major player in the use of biological weapons research in the World War II Theater. The Japanese biological weapons program had six campuses and a staff of more than 3,000 scientists and technicians. There, prisoners were infected with pathogens including *B. anthracis, Neisseria meningtitidis*, *Shigella* spp., *Vibrio cholerae, and Yersinia pestis*. As a result of experimental infection or execution following experimentation during the program, at least 10,000 prisoners died between 1932 and 1945.

Participants in the Japanese program who had been captured by the Soviet Union during World War II admitted to 12 large-scale field trials of biological weapons in testimony obtained during war crimes prosecution. At least 11 Chinese cities were attacked with biological agents. Attacks featured contaminating water supplies and food items with pure cultures of *B. anthracis, V. Cholerae, Shigella* spp. and *Y. pestis.* Cultures were tossed directly into homes and sprayed from aircraft. Also, plague was allegedly developed as a biological weapon by allowing laboratory-bred fleas to feed on plague-infected rats. Those potentially infected fleas were then harvested and released from aircraft over Chinese cities. As many as 15 million fleas were released per attack to initiate epidemics of plague.

In spite of the Japanese biological weapons research, they had not adequately prepared, trained, or equipped their own troops for the hazards of biological weapons. An attack on Changteh in 1941 reportedly led to approximately 10,000 biological casualties and 1,700 deaths among Japanese troops, with most cases due to cholera.

The Allies developed biological weapons for potential retaliatory use in response to German biological attacks during World War II. Bomb experiments of weaponized spores of *B. anthracis* were conducted on Gruinard Island near the coast of Scotland. This resulted in heavy contamination of the local environment. Viable anthrax spores persisted until the island was decontaminated with formaldehyde and seawater during 1986.(6)

U.S. Biological Warfare Industry

In the United States, an offensive biological program begun in 1942 under the direction of a civilian agency, the War Reserve Service. The program had a research and development facility at Fort Detrick, Maryland. Testing sites were in Mississippi and Utah. A production facility was located in Terre Haute, Indiana. Experiments were conducted using pathogens including *B. anthracis* and *Brucella suis*. Approximately 5,000 anthrax bombs were produced at Fort Detrick. After the war, the facility was leased and converted to commercial pharmaceutical production. However, basic research and development activities continued there.

The U.S. program expanded during the Korean War (1950-1953). A new production facility was constructed at Pine Bluff, Arkansas. Production and

[illegible] countermeasures including vaccines, antisera, and therapeutics agents to protect U.S. armed forces against a biological attack were begun.

Furthermore, human experimentation using military and civilian volunteers was initiated in 1955. They were exposed to various microorganisms in aerosolized chambers. These and other studies were done to determine vulnerability to aerosolized pathogens and the efficacy of vaccines, prophylaxis, and therapies under development at the time. Nonpathogenic microorganisms were used to study the behavior of aerosols over large geography areas. New York City, San Francisco and other sites were used as laboratories during covert experiments between 1949 and 1968 so that the effects of solar and climatic conditions on the viability of aerosolized organisms could be tested.

The U.S. military developed a biological arsenal that included many pathogens, toxins, and fungal plant pathogens that could be directed against crops to induce crop failure and famine by the late 1960's. In addition, the Central Intelligence Agency developed weapons for covert use using cobra venom, saxitoxin, and other toxins for use. The records regarding biological weapons development and usage were destroyed during 1972.

The United States was accused by other countries of using biological warfare against North Korea and China during the Korean War. These accusations were supported by a series of investigations conducted by the International Scientific Commission, a group of scientists, and other organizations not part of the commission. The U.S. admitted to having biological warfare capabilities, but denied using biological weapons.

The credibility of the United States was undermined by its failure to ratify the 1925 Geneva Protocol, by knowledge of its offensive biological warfare program, and its suspected covert collaboration with Unit 731 scientists. This Unit 731 consisted of Japanese scientists that were in American custody for war crimes prosecution. These scientists were granted immunity for disclosure of information concerning the Japanese biological warfare program. (16)

Although unsubstantiated, allegations were made against the United States during the cold war era. Similar, the U.S. alleged that Soviet armed forces and their proxies had used aerosolized trichothecene mycotoxins ("yellow rain"), potent inhibitors of DNA and protein synthesis derived from fungi of the genus Fusarium in Laos (1975-81),

Kampuchea (1979-81) and Afghanistan (1979-81). However, these allegations are widely regarded as erroneous.(6)

Biological Warfare Incidences in a Noncombat Environment

The terrorist attack on March 20, 1995 in Tokyo, Japan, in which sarin gas (chemical weapon) was released by the Aum Shinrikyo cult onto five subway cars operating on three rail lines sent an alarm throughout the world. The attack resulted in 12 deaths and over 5,000 casualties. This incidence brought to the forefront the vulnerability of western societies to biochemical terrorists. This cult had intentions of bring total anarchy to the city of Tokyo. There is evidence that a Russian helicopter was purchased by the cult with the intentions of an aerial assault of the city.

In 1992, Aum Shinrikyo cult had a team residing in Zaire, Africa, assisting in the treatment of individuals infected with the Ebola virus. It is claimed that the cults aim was to obtain samples of the virus for culturing purposes back in Japan for the production of biological weapons.(1)

In addition to "the end of the Cold War" the threat of global nuclear war has been reduced. However, today the new threat is the rising global spread of nuclear, biological, and chemical weapons. The technology and the homegrown ability to make them using ballistic missiles as the means of delivery can remit massive annihilation, poison, and death hundred of miles away. For rogue nations, these weapons are tickets to power, stature, and confidence in a regional war.(7)

The threat of bioterrorism is highly probable; therefore, escalating concerns in the United States about this threat has marked the past four years. At first, discussions about the implications of this threat and its possible scenarios were confirmed primarily to those in the military, diplomatic, law enforcement and intelligence communities and to those concerned with arms reduction issues. Only recently have the civilian medical and public health communities begun to engage in examining the practical challenges posed by this threat.(8)

Several noncombat biological incidences have occurred in North America. In Dalles, Oregon, during September 1984, 750 people became sick after eating in several restaurants because a religious group member of a sect founded by Bhagwan Shree Rajneesh had contaminated salad bars with salmonella. This was done in local taverns by the sect in an attempt to disrupt elections.

Canadian customs officials apprehended an U.S. citizen in 1993 who was in possession of four guns, 20,000 rounds of ammunition and probably enough ricin (castor bean toxin) to kill up to 30 million people.

Yersinia pestis, the etiologic agent of bubonic plague was obtainable via mail order from biomedical supply houses. Federal authorities detained a laboratory worker in Ohio, in May 1995, after being alerted by his persistence and impatience with the mail delivery schedule.(1)

The CDC received reports of a series of bioterroristic threats of anthrax exposure from October 30 through December 23,1998. Letters alleged to contain anthrax were sent to health clinics on October 30, 1998, in Indiana, Kentucky, and Tennessee. During

December 17-23 in California, a letter alleged to contain anthrax was sent to a private business, and three telephone threats of anthrax contamination of ventilation systems were made to private and public buildings. All threats were hoaxes and were investigated by the FBI and local law enforcement officials. The investigations and findings will be used to assist in developing national public health guidelines for responding to bioterrorism.(9)

Probably the most documented biological incidence in the world was in Sverdlovsk, Russia (now Ekatorinburg). An outbreak of anthrax occurred there in April 1979. Anthrax spores were released from a biological plant due to a displaced filter and carried downwind toward the city. Approximately 100 were infected; of these, 64 died. Four and one-half weeks after the incidence, the then Soviet government initiated vaccinations for the population. The official explanation for the anthrax outbreak was explained as cutaneous and gastrointestinal exposure due to handling and ingesting meat from infected animals.(10)

Epidemiological Modeling of Hypothetical Scenarios of Bioterrorism

Dispersal experiments with species *Bacillus globii* in the New York subway system in the 1960s suggested that release of a similar amount of *B. anthracis* during the rush hour would result in 10,000 deaths. Today, those numbers would be significantly higher. The World Health Organization (WHO) in 1970 estimated using epidemiological modeling the potential impact of biological assaults upon a developed nation. The hypothetical agent was *B. anthracis*.

The WHO model estimated that 220,000 (95,000 dead) casualties would result from the release of 50 kilograms of anthrax spores by an airplane two kilometers upwind from a population center of 500,000 unprotected people in ideal meteorological conditions. An analysis by the Office of Technology Assessment of the U.S. Congress estimated that 130,000 to 3 million deaths could occur following the release of 100 kilograms of aerosolized anthrax over Washington D.C., making such an attack as lethal as a hydrogen bomb. (29)

If *Francisella tularensis* were dispensed, the number of casualties would be approximately 155,000 (30,000 dead).(5) Typhus released over the same population could result in 100,000 (19,000 dead) casualties. Q fever upwards of 125,000 (150 dead) casualties. Rift Valley fever exposure could result in 35,000 (400 dead) casualties (see Table 1).(6)

The mostly likely agents considered as possible biological weapons now includes Ebola/Marburg viruses (see Table 2). These biological agents vary in how they are transmitted to humans and how they enter the body. They also vary with regard to infectious dose and in time of onset of disease (see Table 3).(11)

A terrorist group announced 24 hours after releasing anthrax spores via aerosol into a ventilation system of a metropolitan shopping mall that everyone there was exposed and would die. Terror soon spreads throughout the region. At the time of the attack, public health and mall officials estimated that approximately 10,000 persons were present within the mall. It was estimated that 90 percent of the mall patrons were exposed. Ninety percent of the exposed was started on antibiotics by the end of day two,

while 10 percent could not be initially found. Four thousand nine hundred and fifty exposed persons had to be hospitalized. Of the hospitalized, approximately 3,000 required intensive care. Two thousand and six hundred patients requiring intensive care needed intubation and placement on ventilators.

The greater metropolitan region had only 300 ICU beds. During this acute inhalation epidemic, only 150 ICU beds were available. By comparison, the U.S. military deployed 1,300 ICU beds (there were 13,000 total medical beds) to the Persian Gulf Region for Operation Desert Storm in the early 1990's. The number of ICU beds there could not provide enough ICU beds for this hypothetical anthrax attack at a regional shopping mall.(28)

Table 1. Casualties Estimates by the World Health Organization's Epidemiological Model in a Hypothetical Biological Attack

Agent	Downwind Reach, Km	No. Dead	No. Incapacitated
Rift Valley fever	1	400	35,000
Tick-borne encephalitis	1	9,500	35,000
Typhus	5	19,000	85,000
Brucellosis	10	500	125,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>20	95,000	125,000

Estimates based on the release of 50 kilograms of the biological agent 2 kilometers upwind from a population center of 500,000 unprotected people in ideal meterological conditions.

Table 2. Potential Biological Weapons

Organism	Disease	Transmission	%Lethal	Stability
Bacillus anthracis	Anthrax	Air--respiratory tract, Direct contact--skin	85	4+
Yersinia pestis	Plague	Air--respiratory tract, direct contact--skin	80	2+
Clostridium botulinum	Botulism	Oral--digestive tract	100	3+
Coxiella burnetii	Q Fever	Air--respiratory tract	low	3+
Coccidioides immitis	Valley Fever	Air--respiratory tract	1	4+
Variola virus	Smallpox	Air--respiratory tract	35	3+
Venezuelan Equine Encephalitis	Encephalitis	Air--respiratory tract direct contact--skin	70	1+
Ebola/Marburg viruses	Ebola	Direct contact--skin, mucus membrane	85	2+

Table 3. Infectious Doses and Incubation Periods of Diseases Caused by Biological Weapons

Agent	Infective dose (Aerosol)	Incubation period
Anthrax	8,000 to 50,000 spores	1-5 days
Brucellosis	10-100 organisms	5-60 days (occasionally months)
Plague	100-500 organisms	23 days
Q fever	1-10 organisms	10-40 days
Tularemia	10-50 organisms	2-10 days
Smallpox	Assumed low (10-100 organisms)	7-17 days
Viral encephalitides	10-100 organisms	Venezuelan equine encephalitis, 2-6 days Eastern equine encephalitis/Western Equine encephalitis, 7-14 days
Viral hemorrhagic fevers	1-10 organisms	4-21 days
Botulinum toxin	0.001 ug/kg (type A)	1-5 days
Staphylococcal enterotoxin B	30ng/person (incapacitating); 1.7 ug/person (lethal)	1-6 hours

In a packed ballpark tensed with excitement, the home team was up by two runs with two outs in the top of the ninth. Nobody paid the slightest attention to a truck that stopped briefly outside the park. Even if anyone had seen it, they could not have known that during its brief stop, the truck had released an aerosolized cloud of anthrax spores that were now wafting over the crowd on a balmy breeze.

Two days later, the people presented at local hospital emergency departments with nasal congestion and fever. The illness was initially diagnosed as influenza. But in succeeding days, more and more people became ill. Then deaths began to be reported. Finally, five days after the exposure occurred, a hospital laboratory identified anthrax as the cause of the outbreak and antibiotic treatment was begun in those who had been exposed. Even so, utilizing this epidemic model of the 20,000 people estimated to have been at the ball game, 4,000 died.(12) Regardless of the epidemic models used, the casualties and fatalities from a bioterrorism attack are enormous.

Terrorism's intent is to make laws unworkable and to create a climate of collapse. The realization that a biological attack could occur is a type of terrorism that could be a lethal form of intimidation. Most disturbingly, bio-agents can be used to threaten civilian populations and create mass panic. The estimates of casualties produced as a result of the hypothetical scenarios would cause havoc to a metropolitan region's government and health care system. In 1997, the economic impact of a bioterrorist aerosol attack on a city of 100,000 was estimated at $477 million for brucellosis to more than $26 billion for anthrax.(20)

Government Defense Preparations

Major cities in the United States and around the world are virtually indefensible to a biological weapon terrorist attack. The terrorists' goals are to have maximum casualties after an assault; therefore, metropolitan areas are at the highest risk.(23) The heightened concern of how well-prepared the U.S. is to respond to a major incidence has led to many studies. The findings are not very encouraging. However, the U.S. government is attempting to take actions to deter or prevent bioterrorism on its soil. An amendment of the 1997 Defense Authorization Act addressed the lack of preparedness by calling for better training, equipment, and coordination among emergency response personnel to deal with a terrorist incidence involving a weapon of mass destruction.

Until recently, the U.S. policy focused almost exclusively on preventing the acquisition and the use of biological weapons by other nations. It relied on three major strategies: First, it entered into a series of treaties and other international agreements designed to achieve biological disarmament and to prevent the proliferation of biological arms to countries that did not yet possess them. Second, it imposed economic and diplomatic sanctions on governments that persisted in their efforts to develop a biological arsenal. Third, it created an extensive system of export controls to prevent the transfer to other countries of U.S. goods and technologies that could be used in the development of biological weapons.

These U.S. strategies originated in 1972 when it and more than 70 other nations entered into an agreement known as the Biological Weapons and Toxin Convention (BWC). In BWC's article I, the signatory nations pledged that their respective

governments would refrain from developing, stockpiling, or acquiring any biological or toxic weapon. In addition, in Article IV, the nations pledged that their governments should take all necessary steps to prevent the development or retention of biological weapons by any party within their respective jurisdictions. But in response to the regional aggressive nations (North Korea, Libya, Syria, Iraq, and Iran) of the late 1980's, the United States initiated an aggressive arms-control policy to prevent them from acquiring biological arms and other weapons of mass destruction.(13)

Congress amended the Export Administration Act of 1979 in an attempt to prevent U.S. companies and individuals from exporting to prohibited countries any goods or technologies that would "directly and substantially assist" a government or group in developing or delivering a biological weapon. Any violator of this law who knowingly exported to prohibited country materials used for biological weapons was subject to civil and criminal penalties, including imprisonment of up to ten years.

Congress passed the Chemical and Biological Weapons Control Act of 1991 to establish an elaborate system of economic sanctions and export controls to curb the proliferation of biological arms. International companies that knowingly exported any goods or technologies used in the development of biological weapons to countries designated as terrorist states or prohibited nations would have the imposition of sanctions.

In the mid-1990's, the U.S. Congress passed three major statues in an effort to prevent the use of biological weapons by domestic and international terrorists as well as by nations. In addition, in 1996, Congress established the framework for a comprehensive

regulatory regime to control the domestic use of hazardous toxins and infectious agents. Under this regime, the Centers of Disease Control and Prevention (CDC) regulate the transfer and use of more than 30 toxins, bacteria, and viruses posing significant risks to the public health and safety (see Table 4).

To cover the threat within the border of the United States, the Anti-Terrorism Act of 1996 was passed to be used in conjunction with the Biological Weapons Act of 1989. In these statues, Congress attempted to reduce the dangers of bioterrorism in three ways. First, impose severe criminal penalties on the possession, manufacture, or use of biological weapons. Second, it authorized the federal government to seize any pathogens or material used to develop a biological weapon or its delivery system. Third, it created a regulatory system for controlling the use and transfer of hazardous biological agents.(13)

In 1997, the CDC's new regulations governing hazardous biological agents went into effect. The CDC sought to accomplish four major goals: (1) the identification of biological agents that are potentially hazardous to the public; (2) The creation of procedures for monitoring the acquisition and transfer of the restricted agents; (3) the establishment of safeguards for the transportation of the restricted agents; and (4) the creation of a system for alerting authorities when an improper attempt is made to acquire a restricted agent.

Table 4: CDC's List of Restricted Agents

The Centers for Disease Control and Prevention List of Restricted Agents

Viruses
- Crimean-Congo Hemorrhagic fever virus
- Eastern equine encephalitis virus
- Equine morbillivirus
- Lassa fever virus
- Marburg virus
- Rift Valley fever virus
- South American hemorrhagic fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)
- Tick-borne encephalitis complex viruses
- Variola major virus (smallpox)
- Venezuelan equine encephalitis virus
- Viruses causing hantavirus pulmonary syndrome
- Yellow fever virus
- Exemptions: Vaccine strains of viral agents
  (Junin virus strain candid #1, Rift Valley fever virus strain MP-12, Venezuelan equine encephalitis virus strain TC-83, and yellow fever virus strain 17-D)

Bacteria
- Bacillus anthracis
- Brucella abortus, Brucella melitansis, Brucella suis
- Burkholderia (Pseudomonas) mallei
- Clostridium botulinum
- Francisella tularensis
- Yersinia pestis
- Exemptions: vaccine strains as described in Title 9 CFR, 78.1

Rickettsiae
- Coxiella burnetii
- Rickettsia prowazekii
- Rickettsia rickettsii

Fungi
- Coccidioides immitis

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

T-2 toxin

Exemptions: Toxins for medical use, inactivated for use as vaccines, or toxin preparations for biomedical research use at a median lethal dose for vertebrates of more than 100ng/kg; national standard toxins required for biologic potency testing as described tin Title 9 CFR Part 113.

To achieve these goals, the CDC regulations first identified 24 infectious agents and 12 toxins that pose a significant risk to public health. The current list includes twelve types of viruses and seven bacteria as well as recombinant organisms and any genetic elements from any of the listed agents that produce or encode a factor associated with a disease.

The procedures for identifying all facilities possessing such agents and those appropriate safeguards are in place at each facility are under regulation of the CDC. The regulations provide that any university, research institution, private company or individual that requires any restricted agent (or that wants to acquire any agent) must register with the federal government. Each facility must have designated a "responsible facility individual" who will certify that the facility and its laboratory operations meet the appropriate bio-safety level requirements operations for working with the specific agent.

The CDC regulations established procedures for tracking the transfer of restricted agents between facilities. Prior to such a transfer, the shipping and receiving facilities must complete an "official transfer form" that identifies its registration numbers, the name of the restricted agent, and the proposed use and amount of the agent. A copy of the form must be maintained in a central repository that, while not publicly accessible, is available to both federal and local law enforcement authorities.(31)

Further provisions were made that the responsible facility official at the requesting facility must certify that the requesting researcher is officially affiliated with the facility and that the laboratory meets the appropriate biosafety level requirements.

Similarly, the regulations require the responsible facility hold a valid registration number indicating an appropriate bio-safety level capability.

Certain clinical uses of restricted agents were identified and are exempt from regulatory scheme. Under these exemptions, a clinical specimen containing a restricted agent is not subject to regulation if the specimen is intended for diagnostic reference, including research use. Also, regulations exempt any attenuated strains of restricted agents that have been approved for human vaccination purposes by the Food and Drug Administration. The regulations do apply, however, to all other attenuated, avirulent, or less pathogenic strains of the restricted agents.

Finally, regulations are enforceable by criminal penalties. In particular, an individual who knowingly makes a false statement on any of the forms required for the registration of facilities or for the transfer of restricted agents is subject to a fine or imprisonment of up to five years. However, an individual who knowingly violates other provisions of the regulations is subject to a fine of $250,000 and imprisonment of up to one year.

The CDC's National Center of Infectious Disease two top concerns is anthrax, a tough bacillus, and the variola virus that causes smallpox. Anthrax is treatable with antibiotics if detected quickly, but it is hard to spot an early infection and it kills quickly. Anthrax usually is not transmitted from person to person. Smallpox, on the other hand, is highly contagious and would cut a devastating swath through unvaccinated urban populations. Health and Human Services is planning to spend an initial $51 million on a stockpile of drugs and vaccines.

Smallpox poses an unusually serious threat, in part, because virtually everyone is now susceptible, vaccination having stopped worldwide 20 or more years ago as a result of the eradication of the disease. Because of waning immunity, it is probable that no more than 20% of the population is protected. Among the unprotected, case-fatality rates after infection with smallpox are 30%. There is no treatment. Virus, in aerosol form, can survive for 24 hours or more and is highly infectious even at low dosages.(8)

For anthrax, there are no civilian vaccine stocks at all. The Defense Department for the troops purchased supplies, and the sole factory that makes the vaccine is shut for renovation. CDC officials agree that it will be necessary to develop a new anthrax vaccine soon. Bringing new trial vaccines through a series of clinical trials will be costly. New vaccines may be ready by 2005; but in the meantime, anthrax will be dealt with by stockpiling antibiotics by the CDC.(14)

In Biological Terrorism, fear will understandably be great as people watch fellow citizens fall ill and possible die in large numbers due to the bio-agent. The greatest characteristic of terrorism is the fear among public that results from acts of violence.(22) Plans for dealing with hysteria among the potentially exposed and the disruption that would result in that area's health care delivery systems are now being addressed in our nation's 120 largest cities and should be completed by the end of 1999. Under this plan, the Department of Defense is funding the Public Health Service to assist local government in the initial planning and development of teams and related systems, procurements, and training of selected personnel.(27) Approximately 120,000 private sector beds are now set aside for the possible casualties from an attack in preenrolled

hospitals in major metropolitan areas. Other beds are available from hospitals operated by the Department of Defense.

Emergency Medical Personnel and First-Responders

If a biological agent was released into a community covertly, the first-responders would be unsuspecting medical personnel in clinics and emergency departments. Patients over several days to weeks would present to these facilities with vague symptoms. On the other hand, if a terrorist released a lethal chemical agent, the first-responders -- firefighters, police, and paramedics -- would arrive on the scene. Local hospitals and health care workers would bear the immediate burden of treating casualties.

While most municipalities have special hazardous material teams (HAZMAT) equipped with full-body protective suits and self-contained breathing apparatus, nevertheless, such teams are generally not trained or equipped to detect, identify, or handle chemical warfare agents, which, depending on purity, may be significantly more toxic than industrial chemicals. During the sarin incidence on the Tokyo subway, for example, the Tokyo Fire Department sent a total of 1,364 personnel to the 16 affected subway stations and other locations. Of these first-responders, 135 (about 10%) were themselves injured by direct or indirect exposure to the poisonous gas.

In the event of a covert biological terroristic attack, the probability of many casualties will be tremendous. With an unnoticed release of a biological agent, local resources would be central to any successful response to the biological agent. There is presently an urgent need of local hospitals and public health systems to have a capability

to rapidly detect unusual disease outbreaks and begin prompt effective treatment of large numbers of exposed individuals.

State governors can call up the National Guard to provide medical, decontamination, transportation, and other support services unavailable from other sources. There are 43 National Guard and U.S. Army Reserve component forces around the country. However, most National Guard Units require between 12 to 24 hours to mobilize to an armory and prepare to deploy to an incident site.(15)

During the initial hours after a covert incidence and until the actors eventually reveal that a biological agent was released, the unsuspecting exposed population will carry on with the daily activities of living. Consequently, in a susceptible and mobile society, the release of a contagious disease agent may result in severe secondary and tertiary spread. Depending on the causative agent released, the incubation period will vary. In the case of smallpox, the infected person's incubation period can range from 7 to 17 days and during this time, the individual can transmit this virus to many others.

A smallpox outbreak in which as few as 50 to 100 people were infected could burden the resources of many communities. The importance of health providers in communicating vague and unusual patient symptoms as well as recent travel histories to public health departments will be critical as the ill seek medical care for their symptoms.(11)

Military Medical Personnel and Hazardous Material Teams

The Department of Defense would participate in the federal response to an incidence of biological or chemical terrorism by providing technical assistance, bomb disposal, decontamination, security, and other services to federal, state, and local authorities. A defense-coordinating officer would be appointed as the on-scene representative to coordinate military support requirements with the Federal Emergency Management Agency, FEMA, and other federal agencies. Because the Posse Comitatus Act (Title 18, Section 1385, of the U.S. Code) strictly limits the use of military forces to execute civil and criminal law, the Department of Defense support to states and local authorities must be provided by military and civilian personnel who are not armed. They cannot engage in domestic law enforcement activities unless properly authorized by the President.

On notification of a chemical or biological terrorist incidence at or near a military facility, the Chemical/Biological Incident Response Force (CBIRF) would deploy to the affected site by the most expeditious means possible. The U.S. Marine Corp activated this force on April 4, 1996. This unit is based at Camp Lejeune, North Carolina, and consists of approximately 350 U.S. Navy and Marine Corps personnel divided into six elements: command and control, reconnaissance, decontamination, medical, security, and service support. The medical element of six medical officers and seventeen marine corpsmen would enter the contaminated area and provide immediate lifesaving medical treatment to those who were injured and exposed.(15)

The Department of Defense in 1996 also established a "rapid assessment and initial detection" unit in each of the ten Federal Emergency Management Agency (FEMA) regions after admitting its shortcomings in its ability to provide assistance to local emergency agencies in the event of biochemical attack. The Defense Department began biological protection efforts that year by immunizing military reservists (and all active duty military personnel) against anthrax, botulism, Q fever, plague, and tularemia. The stockpiling of antibiotics and vaccines (including those for anthrax and smallpox) are also underway. (17)

Each RAID team consists of 22 full-time National Guard members. In addition to being trained for combat readiness, the teams are designated first-responders to any domestic attack. The team members would determine the nature of the attack (biological, chemical, radiological, or other), assess casualties and damage, and seek to learn the exact agent(s) used.

To aid in detection of a biological aerosolized cloud, the Naval Research Laboratory, Georgetown University, Geocenters, Kaman Sciences, and Nova have designed a system that integrates an air sampler and an automated fluidics system with an antibody-based fiber-optic biosensor. A radio transceiver and a remotely piloted unmanned air vehicle (UAV) employs the system into the area of concern. It is capable of collecting aerosolized bacteria, identifying them, and transmitting the data to the operator.(18)

The Present Surveillance System

Surveillance and rapid response to identify disease threats are at the core of preventive medicine. A well-designed and well-implemented infections disease surveillance program can provide a means to detect unusual clusters of disease, document the geographic spread of an outbreak, and estimate the magnitude of the problem. The system should be able to describe the natural history of the disease, identify factors responsible for emergence, facilitate laboratory and epidemiological research, and assess the success of specific intervention efforts.

Surveillance can take many forms, from complex international networks involving sophisticated laboratory and epidemiological investigations, to small, community-based programs or a single astute clinician. To detect unusual disease outbreaks or the appearance of a new infectious agent, a formal surveillance system should be instituted in which public health workers actively seek out cases of disease and report their findings regularly to a central data collection point.

In the United States, surveillance of infectious diseases is a passive process. It relies on physicians, hospitals, and other health care providers to report cases to state and local organizations that are responsible for disease surveillance. The Centers for Disease Control (CDC) works in cooperation with the states in monitoring the domestic incidence of specific infectious (see Table 5). Each state has its own regulations regarding the reporting of specific diseases.

Reporting of diseases on the list is voluntary, with the exception of the diseases that require quarantine: yellow fever, cholera, diphtheria, infectious tuberculosis, plague,

suspected smallpox, and viral hemorrhagic fevers. The list of nationally notifiable diseases is maintained and revised as needed by the Council of State and Territorial Epidemiologists in collaboration with the CDC.

Reportable disease data are provided to the CDC on a weekly basis by state health departments, New York City, the District of Columbia, Puerto Rico, the Virgin Islands, Guam, American Samoa, and the Commomwealth of the Northern Mariana Islands. Since 1984, disease reporting has been accomplished through a computer-based telecommunications system.(16)

The current system is not real-time like the stock exchange that gives buyers and sellers a minute-to-hour gauge of stock values. With the advances in computers and with the ease of the Internet epidemiologists, public health, and medical professionals for effective surveillance could have a stock market of infectious diagnoses daily from clinicians. The present system is a passive process where health professionals notify public health departments of infectious diseases diagnosed within a given timespan as indicated by that state's law or the Centers for Disease Control in Atlanta.

Table 5. Diseases Currently Reportable to the Centers for Disease Control

Acquired immunodificency syndrome
Amebiasis
Anthrax
Aseptic meningitis
Botulism, food borne
Botulism, infant
Botulism, wound
Botulism, unspecified
Brucellosis
Chancroid
Cholera
Congenital rubella syndrome
Diphtheria
Encephalitis, post chickenpox
Encephalitis, post mumps
Encephalitis, other
Encephalitis, primary
Gonorrhea
Granuloma inguinale
Hansen disease
Hepatitis A
Hepatitis B
Hepatitis, non-A, non-B
Hepatitis, unspecified
Legionellosis
Leptospirosis
Lyme disease
Lymphogranuloma venereum
Malaria
Measles
Meningococcal infections
Mumps
Pertussis
Plague
Poliomyelitis, paralytic
Psittacosis
Rabies, animal
Rabies, human
Rheumatic fever
Rocky Mountain spotted fever
Rubella
Salmonellosis
Shigellosis
Syphilis, all stages
Syphilis, primary and secondary
Syphilis, congenital
Tetanus
Toxic shock syndrome
Trichinosis
Tuberculosis
Tularemia
Typhoid fever
Yellow fever

The existence of an organized surveillance system makes it possible to convey information and facilitate an appropriate public health response (see Table 6). There is currently the National Electronic Telecommunication System for Surveillance (NETSS) that links all state health departments by computer for routine collection, analysis, and dissemination of data on notifiable health conditions. With the availability of the Internet secured sites can be made to link local departments and health providers (i.e., hospitals, clinics and research facilities) to CDC for expedited data input. In linking as many medical facilities to the surveillance network as possible an unified standard of data collection will assist CDC and other mandated agencies the necessary information to prevent or reduce threats to public health.

Table 6. The Uses of Surveillance

- Detection of epidemics
- Quantitative estimates of the magnitude of a health problem
- Documentation of the distribution and spread of a health event
- Facilitating epidemiologic and laboratory research
- Testing hypotheses
- Portrayal of the natural history of disease
- Evaluation of control and prevention measures
- Monitoring of changes in infectious agents
- Monitoring of isolation activities
- Detection of changes in health practices
- Planning

METHODS

Epidemiological Mathematical Models

Epidemiological modeling of bioterroristic events can predict the severity of casualties and fatalities after an assault. Using the World Health Organization's hypothetical casualties' estimates after the environmental release of different biological agents, a simple mathematical formula was derived that considers a pathogen's infectious rate (see appendix), and lethality rate (see Table 7 and appendix). This equation also considers parameters such as population exposure size and the atmospheric conditions at the time of release of an aerosolized agent in estimating the amount of fatalities. In considering all variables, the equation for estimating infectious respiratory disease fatalities *PR* is:

$$PR = B \times LR \times EnS \times N \qquad \text{(equation 1)}$$

B is the variable for infection rate (also known as the attack rate). *LR* is the variable for lethality rate.(11) *EnS* is the variable for the environmental conditions during the release of the biological aerosolized agent (see Table 8), and *N* is the estimated population exposed during the terrorism.

In using this mathematical model, the number of casualties and fatalities (see appendix) can be estimated with the assumption that all members of this hypothetical population received an infective dose. In applying the known values of various respiratory pathogens into the equation, an estimate of fatalities can be estimated. For those agents that can be spread through aerosol and are also contagious, a second equation will be used to provide a deterministic approximation of the resultant epidemic.

A third mathematical model will estimate the change in the infectious rate at a given time in a vulnerable and untreated exposed population.

Those agents that are considered to be the most likely bioweapons (anthrax, plague, tularemia, Q fever, and smallpox) in a terrorist attack will be calculated to estimate the quantity of fatalities after a biological assault.

In this hypothetical scenario, 50 kilograms of anthrax spores are released from an aircraft 2 kilometers upwind from a population center of 500,000 unprotected people in ideal meteorological conditions. The aerosol cloud traveled greater than 20 kilometers downwind to cover the entire city. Utilizing equation 1 and inputting the infectious and lethality rates for anthrax, the estimated number of fatalities would be 95,625 people.

$$PR = B \times LR \times EnS \times N \quad \text{(equation 1)}$$

$$PR = .45 \times .85 \times 0.5 \times 500{,}000 = 95{,}625$$

The number of casualties (deaths plus injured) can be estimated using the following equation:

$$Cs = B \times EnS \times N \quad \text{(equation 2)}$$

The estimated number of casualties after the release of anthrax during the previously stated conditions would be 112,500 people.

With all conditions of environment and population size being held constant, the number of casualties, if 50 kg of tularemia is released from an aircraft over a city of unprotected people that is assumed to have received an infective dose, may be calculated:

$$PR = B \times LR \times EnS \times N$$

$$PR = .32 \times .40 \times 0.5 \times 500{,}000 = 32{,}000$$

The total number of casualties after a tularemia attack may be calculated:

$$Cs = B \times EnS \times N$$

$$Cs = .32 \times 0.5 \times 500{,}000 = 80{,}000$$

In analyzing the values specific for the biological pathogen *Yesinia pestis*, the causative agent of pneumonic plague, the estimated number of fatalities in a city of 500,000 unprotected people is 160,000 out of a total of 200,000 casualties.

$$PR = B \times LR \times EnS \times N$$

$$PR = .80 \times .80 \times 0.5 \times 500{,}000 = 160{,}000$$

Coxiella burnetii, the causative agent of the disease known as Q fever is generally not fatal; however, its infection rate of 20 percent in a susceptible population will be overwhelming nevertheless. Inputting Q fever's values into the model results in casualties estimates of 50,000 with approximately 500 deaths.

$$PR = .20 \times .01 \times 0.5 \times 500{,}000 = 500 \text{ fatalities}$$

$$Cs = .20 \times 0.5 \times 500{,}000 = 50{,}000 \text{ casualties}$$

For smallpox the estimated casualties and fatalities using this simple mathematical model would be devastating as well. There would be 70,000 fatalities out of 200,000 casualties.

$$PR = .80 \times .35 \times 0.5 \times 500{,}000 = 70{,}000$$

The *PR* equation gave the estimated quantity of fatalities in a city of 500,000 susceptible individuals after receiving an infective dose of aerosolized smallpox as 70,000.

Now the contagious factor of smallpox will be considered in another hypothetical scenario. In this instance a viral epidemic mathematical model demonstrating the contagious spread of the smallpox virus after the initial exposure and infection of spectators in attendance at a sporting event in the city of Fort Worth.(30)

The Fort Worth University Titans are hosting the University of Texar Longheads for the annual homecoming football classic. The stadium is filled to capacity with excited fans that are anticipating a victory for the home team. Scheduled for the half-time performance is a spectacular fireworks show. This was to be the largest fireworks show in the city's history. However, one of the many canisters was filled with a concentration of smallpox to infect everyone throughout the stadium.

At the conclusion of the first half, the Fort Worth Titans were leading the powerhouse Texar Longheads. The fireworks seemed more spectacular as a result of the home team possible victory. The final rounds of fireworks sparkled in the sky. The canister of smallpox fired a fine mist of infectious particles throughout the stadium and into the near surroundings. Approximately 52,000 became infected out of the 65,000 persons estimated to have been in the vicinity of the stadium. The initial infected persons that were in attendance at the game approximates about 10.5 percent of the city's population. In the epidemic viral model variables such as the initial fraction of infected population, the fraction of the population susceptible, and the probability of the each infected person coming into contact with five susceptible persons during the 7- to 17-day incubation period of smallpox is considered (see APPENDIX A and B).

A deterministic approximation model demonstrates the spread of smallpox throughout a susceptible population after the introduction of ten infectives from the city of Fort Worth who were in attendance at the homecoming football classic.

Deterministic Approximation Analysis Equation:

$$i(t) = \frac{io\,(1 - p')}{io + (1 - p' - io)e^{-(B'-S)t'}}$$

i is the independent variable and it is equal to the fraction of infected population. *io* is the initial fraction of the population infected. At a given time the fraction of the population infected can be calculated using this deterministic equation.(21) The variable *p'* is the average ratio of the rate at which the infectives will be cured (see Table 7).

$p' = S/B$

S = cure rate

B = infection rate

*$p > 1$ No epidemic

*$p < 1$ Epidemic

In this demonstration, ten infected persons with smallpox are vacationing in a rural town of 6,000. The town was celebrating its 100^{th} birthday. Virtually the entire town attended the event. The mood was festive and there was much intermingling.

In using the values for smallpox in the formula, the model indicates that approximately 10 percent of the population will be infected within 30 time units (see appendix).

Using the values for smallpox (see Table 7) in the following equation, one can estimate the infection rate change at a given time through this population of 6,000:

$$\frac{di}{dt} = Bi\,(1-i) - Si$$

For results, see APPENDIX C and D.

Table 7. Respiratory Infectious Agents' Infectious rates, Lethal Rates and Natural Cure Rates

Disease	Infectious Rate (*B*)	Lethal Rate (LR)	Natural Cure Rate (*S*)
Anthrax	.45	.85	.15
Plague	.80	.80	.20
Q fever	.20	<.01	>.99
Tularemia	.32	.40	.60
Smallpox*	.80^	.35	.65

*A contagious disease
^For the U.S. population susceptibility is estimated to range from 80 to 100 %

Table 8. Environmental Status During the Release of Aerosol Containing an Infective Dose of a Respiratory Pathogen

Environment in which agent is released via aerolization	Rating
Virtually a closed or "perfect" environment (ie., ventilation system of a mall, center or building)	1.0
Ideal environment (early morning or late evenings with wind speeds less than 5 miles per hour and no rain)	0.5
Less than Ideal environment	0.25

Discussion and Conclusions

Epidemic Modeling of a bioterroristic event estimates large numbers of casualties and fatalities after an assault in the civilian population. The military is at a reduced risk due to the Department of Defense actively immunizing reserve and active personnel. However, civilian medical personnel (doctors, nurses, paramedics and medical support) will suffer casualties. This would further impact the severity of the terrorist-induced epidemic. The accuracies of these mathematical predictions can only be confirmed by real-life scenarios by allowing the disease to spread throughout the vulnerable population. However, to obtain a fraction of the casualties predicted by the models requires much improvement in the nation's public health infrastructure. Various authorities have made recommendations to reduce the impact of bioterrorism in this country. The urgency to establish an improved infrastructure to prevent and reduce the number of causalities after a biological terroristic attack is now high on the national agenda.

The establishment of stockpiles of medical equipment, nerve agent antidotes, and broad-spectrum antibiotic and antiviral drugs in major metropolitan areas is now underway for the civilian population. This will ensure the prompt treatment of casualties in the event of an incidence of chemical or biological terrorism. The Public Health Service is assisting local governments in the initial planning and development of teams and related systems, initiation of special equipment procurements, and training of selected personnel. The Food and Drug Administration is directing the procurement of special antidotes and pharmaceuticals.

It is important that public information campaigns be prepared in advance of a terrorist incidence. This will minimize the spread of chemical contamination or infectious disease by reducing panic among the people in the contaminated area. The media announcements -- television, radio, and Internet -- during the incidence should inform the citizens about the nature of the threat, the likely symptoms, and what should be done to minimize exposure or seek treatment.

Procedures are in development so that urgent lifesaving operations by first-responders can proceed without destroying crucial pieces of evidence or disrupting the chain of custody of evidence needed for successful criminal prosecution. The possible forensic responsibilities of first-responders should receive appropriate consideration when collecting data and preparing for future action that will determine responsibility for the attack. Saving human lives and ensuring the safety of the investigators and emergency workers should take precedence.

Development and distribution of chemical and biological agent detection equipment for first-responders as well as provisions for individual protective gear should be implemented. The detection instruments should be relatively inexpensive, portable, and user-friendly systems that can detect and identify the released agents. The protective gear should provide supportive care with ventilators during treatment. Mass casualty decontamination systems should be readily available in the case of an incidence.

Critical cooperation of state and local public health officials, emergency department personnel, and national organizations such as the CDC is necessary so as to be able to alert the FBI about suspicious outbreaks of disease that might be linked to

biological terrorism. This improved epidemiological surveillance system will require all states to hire additional field epidemiologists.

Biologists, especially those in medicine and public health, are critical to confronting the problems posed by biological weapons, as are physicists in dealing with nuclear threats and chemists with chemical weapons. During 1998, steps were taken to facilitate such involvement. In 1999 Congress appropriated $133 million to Health and Human Services for countering biological and chemical threats, $51 million of which was for an emergency stockpile of antibiotics and vaccines. Most of the funds were allocated to the CDC, primarily for the strengthening of the infectious disease surveillance network and for enhancing the capacity of federal and state laboratories.(8)

In addition, primary care practitioners must be required to take continuing education courses in infectious diseases so as to become familiar with the signs and symptoms of the most likely biological terrorism agents. There should be intensified training of emergency room physicians and nurses. Infectious disease specialists and hospital epidemiologists must be required to receive continuous education credits in case recognition and in steps to take if a suspicious case is detected.

Laboratory directors and key staff designated with responsibilities for lab diagnosis should receive training in specimen handling and decontamination of diagnostic equipment. Moreover, state and local health officers and epidemiologists should receive required training in, among other things, detection, surveillance, and management of epidemic disease. Efforts are underway to access and enhance the capabilities of the state and local health department laboratories to fulfill the need for

rapid analysis. Planning for laboratory testing should be part of bioterrorism preparedness by state and local public health, law enforcement, and first-responder authorities in consultation with federal officials.

The psychological state of the community should be a concern of public health and medical officials. Consequently, governmental and private agencies are developing detailed strategies for responding to a biological terrorist attack that includes consideration of the psychological and societal impact of such an attack. Inattention to the phenomenon of terror and its consequences for individuals, institutions, and society jeopardize the efficacy of disaster relief efforts. Leaders, scientists, and media should develop protocols covering a broad range of scenarios that communicate accurate information about the risk and diminish rumors.(22)

These primary prevention efforts will be critical in preventing panic and demoralization in the attacked community. Planning and preparation for biological attacks and their attendant psychological consequences can diminish the terrorist's ability to achieve their overall goal -- the induction of terror! Education of the public and institutional preparedness can reduce the horror of terrorism. Such preparation efforts should be given high priority.

Realistic training for biological attacks should include the probability of large numbers of psychological casualties. Training exercises have been designed to teach cooperation and coordination between organizations as well as first-responders and hospital staff. Hospital accrediting bodies should encourage medical facilities to incorporate biological scenarios into their annual training.

"Preparations to combat bioterrorism will carry, as a bonus, widespread benefits to health," said Margaret Hamburg, MD, Health and Human Services' assistant secretary for planning and evaluation. "The things we need to do to adequately prepare for bioterrorist events have broad value across a range of infectious diseases," she noted. "The good news is that if we advance our public health infrastructure to make it truly robust and functioning, if we forge links between public health and medicine, we will also be protecting the health of this nation and the world against a range of naturally occurring infectious diseases."(12)

The public health response to bioterrorism requires communication and coordination with first-responders and law enforcement officials. State and local health departments should work with these groups to ensure that local disaster preparedness plans address bioterrorism, define the roles of each agency, including protection of first-responders; and are tested through simulations. Even though the FBI has jurisdiction for the bioterrorism response, the bureau recognizes the need to conduct epidemiological investigations, define at-risk groups, and rapidly implement potentially life-saving medical and public health responses.

Public health officials, working with law enforcement and first-response personnel, should determine the need for decontamination and postexposure prophylaxis. They should collect contact information for potentially exposed persons for notification of laboratory results or other follow-up. Potentially exposed persons should be given information about the signs and symptoms of illnesses associated with the biologic agent and about whom to contact and where to go should they develop illness.(9)

Physicians and other health providers will be in the front line for remediation in the wake of biological weapon attack. They should be alert to any constellation of disease that might be the harbinger of new outbreak. Clinicians would of course funnel their reports to local and state and, in turn, to the national Centers for Disease Control and Prevention.(25)

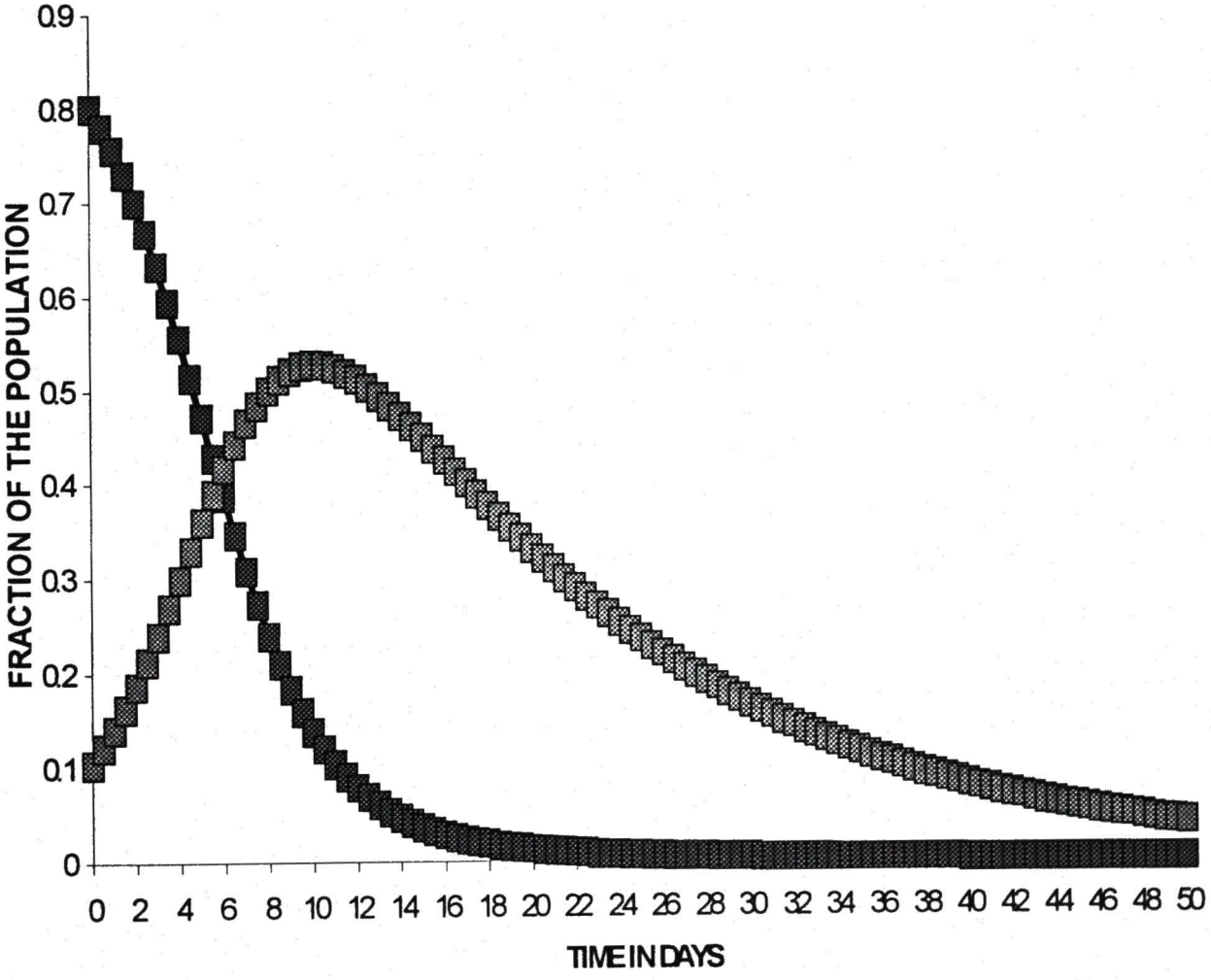
Besides their personal contribution, health providers are in the best position to assess the readiness of local health services, police, and firefighter first-responders to deal with health emergencies. This is the same apparatus needed to deal with natural disease outbreaks. In view of the rapid dispersal of people via jet aircraft, that coordination needs to be extended to a global venue and this scarcely exists in the present time. Epidemiological modeling of an bioterrorism event predicts that high casualties would occur without coordination of the public health infrastructure system linking public health departments, health providers, the CDC, and first-responders. The preparations that are being made by public health and medical authorities is going in the right direction in reducing and thus controlling bioterrorism.

APPENDIX A

Contagious Spread of Smallpox Among Ft. Worth Citizens After Sporting Event and Worksheet Excerpt

APPENDIX A

Fraction of Ft. Worth Citizens Susceptible and Infected with Smallpox



EPIDEMIC MODEL WORKSHEET FOR SMALLPOX AFTER SPORTING EVENT IN FORT WORTH, TX (HYPOTHETICAL)

ALPHA =	**P TRANSMISSION / INFECTIOUS CONTACT**	**=**	**0.1**
BETA =	**CONTACTS / DAY**	**=**	**5**
KAPPA =	**ALPHA * BETA**	**=**	**0.5 /DAY**
CHANGE TIME SCALE			**0.5 DAY**
NEW KAPPA =			**0.25**
INFECTIOUS PERIOD =			**14 DAY**
INFECTIOUS PER (NEW TIME UNITS) =			**28**
GAMMA		**=**	**0.035714**
INITIAL POP FRACTION INFECTED		**=**	**0.105**
INITIAL POP FRACTION SUSEPTIBLE		**=**	**0.8**

NOTE: BOXED NUMBERS ARE MODEL PARAMETERS THAT CAN BE CHANGED

EPIDEMIC MODEL WORKSHEET FOR SMALLPOX AFTER SPORTING EVENT IN FORT WORTH, TX (HYPOTHETICAL) ABSTRACT

TIME (NEW)	TIME (DAYS)	SUSEPTIBLES	INFECTIOUS	RECOVERED
0	0	#REF!	#REF!	0
1	0.5	0.779	0.12225	0.00375
2	1	0.755191813	0.141692116	0.008116071
3	1.5	0.728440631	0.163382865	0.013176504
4	2	0.698686952	0.187301442	0.019011606
5	2.5	0.665970683	0.213328373	0.025700944
6	3	0.630453073	0.241227113	0.033319814
7	3.5	0.592432479	0.270632453	0.041935068
8	4	0.552349615	0.301049872	0.051600513
9	4.5	0.51077842	0.331869286	0.062352294
10	5	0.468400503	0.362394729	0.074204769
11	5.5	0.425964035	0.391888528	0.087147437
12	6	0.38423143	0.419625114	0.101143456
13	6.5	0.343923141	0.444946792	0.116130067
14	7	0.305666266	0.46731271	0.132021024
15	7.5	0.269955833	0.486333403	0.148710764
16	8	0.237133699	0.501786487	0.166079814
17	8.5	0.207386077	0.513613163	0.18400076
18	9	0.180757022	0.52189889	0.202344087
19	9.5	0.1571728	0.526843867	0.220983333
20	10	0.136471419	0.528729396	0.239799186
21	10.5	0.118432306	0.527885316	0.258682378
22	11	0.102802637	0.524661937	0.277535425
23	11.5	0.089318479	0.519408169	0.296273352
24	12	0.077720292	0.512456064	0.314823644
25	12.5	0.067763234	0.504111121	0.333125646
26	13	0.059223184	0.494647202	0.351129614
27	13.5	0.051899538	0.484304876	0.368795586
28	14	0.045615738	0.473292073	0.386092189
29	14.5	0.040218347	0.461786177	0.402995477
30	15	0.035575277	0.449936882	0.41948784
31	15.5	0.03157362	0.437869365	0.435557015
32	1Error! Reference source not found.6	0.02811734	0.425687454	0.451195206

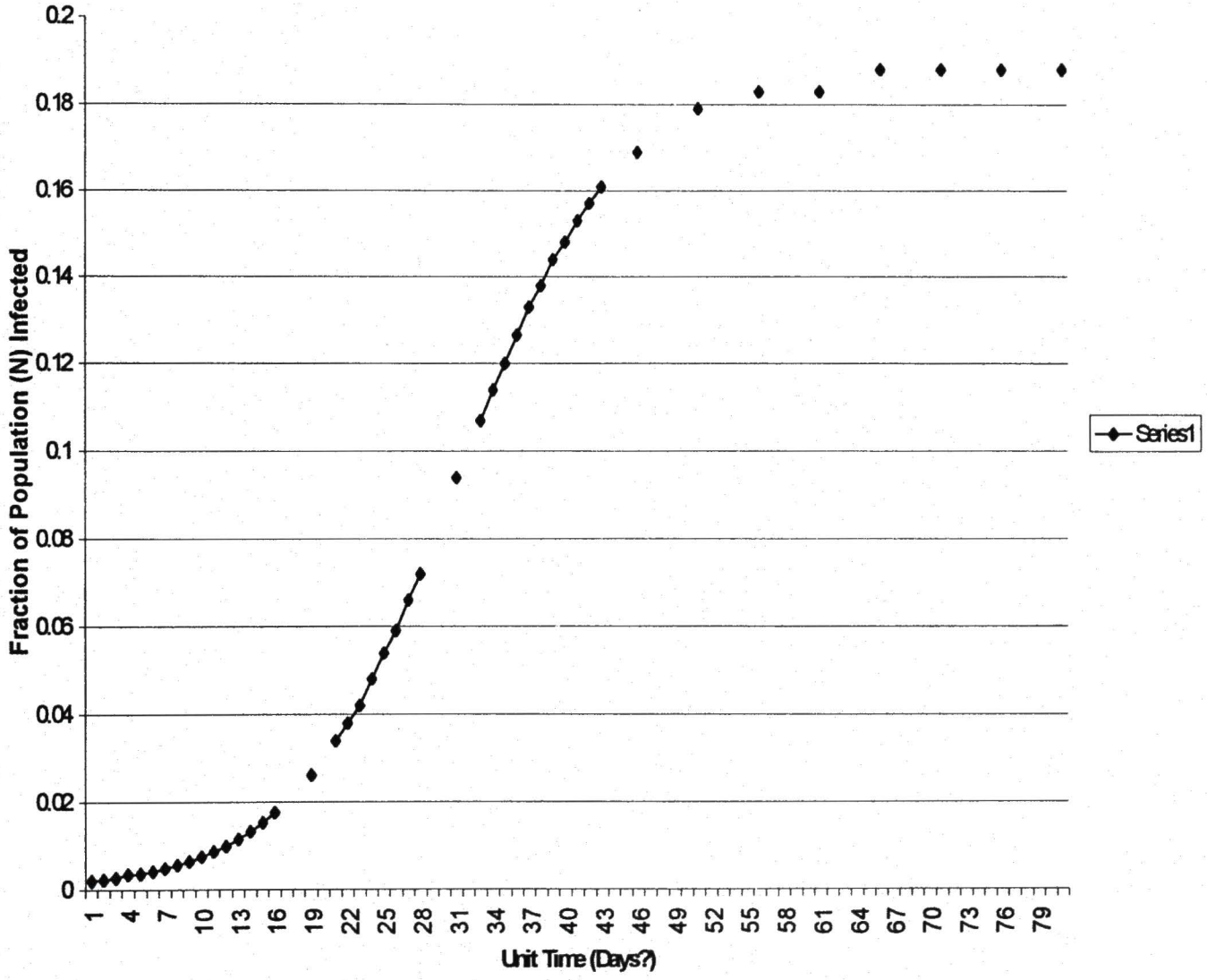
33	16.5	0.02512504	0.41347663	0.46639833
34	17	0.022527886	0.401306762	0.481165352
35	17.5	0.020267738	0.389234526	0.495497737
36	18	0.018295512	0.377305519	0.50939897
37	18.5	0.016569762	0.365556071	0.522874167
38	19	0.015055468	0.354014791	0.535929741
39	19.5	0.013723004	0.34270387	0.548573126
40	20	0.012547272	0.331640178	0.56081255
41	20.5	0.011506977	0.320836181	0.572656842
42	21	0.010584013	0.310300709	0.584115277
43	21.5	0.009762957	0.300039598	0.595197445
44	22	0.009030638	0.290056216	0.605913145
45	22.5	0.00837579	0.280351914	0.616272296
46	23	0.007788748	0.270926388	0.626284864
47	23.5	0.007261204	0.26177799	0.635960807
48	24	0.006785998	0.252903982	0.645310021
49	24.5	0.006356946	0.244300748	0.654342306
50	25	0.005968695	0.235963973	0.663067332
51	25.5	0.005616595	0.227888788	0.671494617
52	26	0.005296606	0.220069892	0.679633502
53	26.5	0.0050052	0.212501659	0.687493141
54	27	0.004739296	0.205178217	0.695082486
55	27.5	0.004496196	0.198093524	0.70241028
56	28	0.004273529	0.191241422	0.709485048
57	28.5	0.004069211	0.18461569	0.716315099
58	29	0.0038814	0.178210083	0.722908517
59	29.5	0.003708474	0.172018363	0.729273163
60	30	0.003548993	0.166034332	0.735416676
61	30.5	0.003401679	0.160251848	0.741346473
62	31	0.003265398	0.154664849	0.747069753
63	31.5	0.003139137	0.149267365	0.752593498
64	32	0.003021995	0.14405353	0.757924475
65	32.5	0.002913162	0.139017593	0.763069244
66	33	0.002811917	0.134153925	0.768034158
67	33.5	0.00271761	0.12945702	0.77282537
68	34	0.002629656	0.124921509	0.777448835
69	34.5	0.002547531	0.120542151	0.781910317
70	35	0.00247076	0.116313846	0.786215394
71	35.5	0.002398914	0.112231626	0.79036946

APPENDIX B

Fraction of Population Infected with Contagious Smallpox at Unit Time

APPENDIX B

Fraction of Exposed Population in Small Town with Smallpox, i(t)

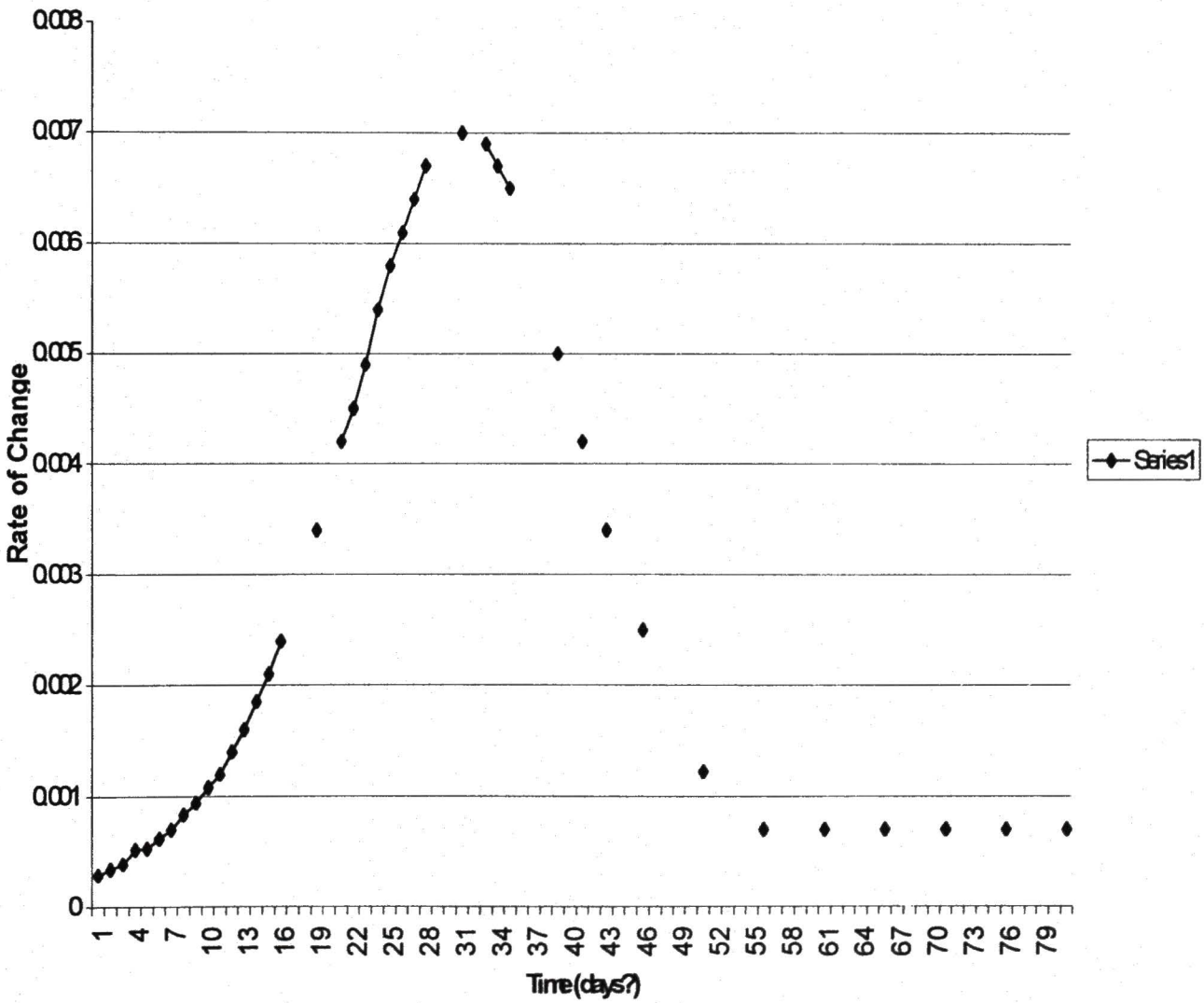


APPENDIX C

Infection Rate Change for Smallpox at Unit Time

APPENDIX C

Infection Rate Change for Smallpox at Unit Time



REFERENCES

1. Saltier MS and DD Trunkey Terrorism in America: An Evolving Threat Archives of Surgery 1997;132:1059-1066

2. Levinson WE and E Jawetz Medical Microbiology and Immunology 3rd Edition Norwalk: Appleton and Lange 1994

3. Franz DR and et al. Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents JAMA 1997;278:399-411

4. Robertson AG and LJ Robertson From Asps to Allegations: Biological Warfare In History Military Medicine, Volume 160, August 1995

5. Sanford JP. Biological Weapons Medical Grand Rounds, University of Texas Southwestern Medical Center at Dallas, October 5, 1995

6. Christopher GW and et al. Biological Warfare: A Historical Perspective JAMA 1997;278:412-417

7. Perry WJ. The New Threat From Nuclear, Biological , and Chemical Weapons

8. Henderson DA The Looming Threat of Bioterrorism Science Volume 283, 26 February 1999

9. Bioterrorism Alleging Use of Anthrax and Interim Guidelines for Management-U.S., 1998 JAMA 1999;281.9:787-789

10. Pile JC and et al. Anthrax as a Potential Biological Warfare Agent Archives for Internal Medicine, Volume 158, March 1998

11. Atlas RM The Medical Threat of Biological Weapons Critical Reviews in Microbiology, 24(3):157-168 (1998)

12. Marwick C Scary Scenarios Spark Action at Bioterrorism Symposium JAMA 1999;281:1071-1073

13. Ferguson JR. Biological Weapons and U.S. Law JAMA 1997;278:357-360

14. Marshall E Bioterror Defense Initiative Injects Shot of Cash Science Volume 283, 26 February 1999

15. Tucker JB National Health and Medical Services Response to Incidents of Chemical and Biological Terrorism JAMA 1997;278:362-368

16. Teutsh SM and RE Churchhill Principles and Practice of Public Health Surveillance

New York: Oxford University Press 1994

17. Gunby P RAID Teams to Respond to Terrorism Threat JAMA 1998:279:1855

18. Red alert—biosensor identifies bacteria in the air Analytical Chemistry News & Features, October 1, 1998

19. Kadlec RP et al. Biological Weapons Control: Prospects And Implications for the Future JAMA 1997:278:351-356

20. McGovern TW and et al. Cutaneous Manifestations of Biological Warfare and Related Threat Agents Arch Dermatology/Vol 135, March 1999

21. Deterministic Approximation Modeling http://www.av.ibm.com/Inside/thelab

22. Holloway HC et al. The Threat of Biological Weapons: Prophylaxis and Mitigation of Psychological and Social Consequences JAMA 1997;278:425-427

23. Mobley JA Biological Warfare in the Twentieth Century: Lessons from the Past, Challenges for the Future Military Medicine, Volume 160, November 1995

24. Lederberg J. and et al. Emerging Infections: Microbial Threats to Health in the United States Washington D.C.: National Academy Press 1992

25. Lederberg J. Infectious Disease and Biological Weapons: Prophylaxis and Mitigation JAMA 1997;283:435-436

26. The Federation of American Scientists Working Group on Biological Weapons Verification Report, April 1996

27. Stephenson J Pentagon-Funded Research Takes Aim at Agents of Biological Warfare JAMA 1997;278:373-375

28. Osterholm M Biological Terrorism: Use of Biological Agents to Intentionally Produce Disease or Intoxication in Susceptible Populations to Meet Terrorists Aims Video Conference 1998, Minnesota Department of Health

29. Laino C Bioterrorism: 'a very real scenario' http://www.msnbc.com/news/241715

30. SDSU Summer Science Bridge-Mathematical Modeling: Epidemic Viral Model http://www.scibridge.sdsu.edu/coursemats/introsci/mathmodeling/

31. Pearson GS The Complementary Role of Environmental and Security Biological Control Regimes in the 21st Century JAMA 1997;278:369-372