Bioterrorism syndromic surveillance: A dual-use approach with direct application to the detection of infectious disease outbreaks

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Bioterrorism Syndromic Surveillance:
A Dual-Use Approach with Direct Application to the
Detection of Infectious Disease Outbreaks

by

Kristin Broome Uhde

A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
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Keywords: BioDefend, Epidemiology, Automated, Baseline, Alert, Syndromes

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DEDICATION

To God, for with whom all things are possible, to my Babycake Jochen who lovingly sacrificed all that he had to allow me to pursue my dreams, to Dad, Mom, Meredith, Tasso, family, and friends for their unconditional love and support.

In loving memory of Gunda Uhde, and those who lost their lives during the terrorist attacks of September 11, 2001.
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The threat of bioterrorism forces the public health infrastructure to focus attention on overall issues related to challenges posed by emerging and re-emerging infectious diseases. There is a crucial need to strengthen existing surveillance systems and to validate real-time approaches to surveillance that can provide timely alerts of epidemics whether they occur naturally or through a bioterrorism attack. The purpose of this study is to implement and evaluate a bioterrorism syndromic surveillance system called BioDefend™, to determine if the system could detect a potential epidemic/bioterrorism attack within 24-36 hours, more rapidly than it would be identified by routine health surveillance. This sentinel surveillance study was conducted in theme parks, theme park referral hospitals and clinics, and a military hospital and clinics in the Central Florida area. A six-month period of baseline data collection was completed at all surveillance sites for the purposes of serving as the comparison for the test period. The test period consisted of five months and served to validate the system. The baseline was also used to
identify normal illness trends and seasonality patterns so that thresholds could be established on which to determine significant syndromic aberrations. The web-based reporting system enabled near real-time data entry. The syndromic and demographic information then was processed in an automated analysis system to provide a mechanism for alerting surveillance sites when significant rises in reported syndromes and/or clinic/hospital daily visits exceeded the established thresholds. A pocket PC/phone device enabled staff to receive notification of alerts 24/7.

The surveillance system was evaluated by comparing regional, state, and national surveillance data to equivalent syndromic data reported from BioDefend™. After comparing these data, it was determined that the BioDefend™ system detected two epidemics of public health importance more than one month before they were identified through routine regional and state, regional, and national surveillance methods. The specific syndromes identified earlier than the State of Florida surveillance were “gastroenteritis” and “influenza-like illness.” This study has examined whether or not the BioDefend™ surveillance system is useful in the context of the above referenced surveillance sites, and whether it could serve as a national model for syndromic surveillance.
CHAPTER ONE: INTRODUCTION

Knowing is not enough; we must apply. Willing is not enough; we must do.

—Goethe

Introduction

Our communities need valid, cost-effective, public health surveillance systems that will rapidly identify potential bioterrorism attacks and infectious disease epidemics. Implementation of surveillance systems with “dual-use” capability to detect naturally occurring and intentional outbreaks related to bioterrorism would be a good use of resources. Existing surveillance efforts would benefit from an improved rapid identification process required to respond promptly to bioterrorism attacks and epidemics.

The Centers for Disease Control and Prevention define public health surveillance as, “the ongoing systematic collection, analysis, and interpretation of outcome-specific data for use in planning, implementation, and evaluation of public health practice (thacker, SB).” Information gathered from surveillance systems should be used to guide public health action, program planning, evaluation, and policy. Analysis of surveillance data is based on the reasoning process of looking at individual pieces to produce an overall general picture of illnesses in a population (1). In addition, surveillance systems have helped minimize illness and death by identifying emerging and re-emerging health problems, identifying at-risk populations, and detecting illness trends (2). Traditional
notifiable disease surveillance, or diagnosis-based surveillance, for infectious diseases is often slow and incomplete.

During the course of a disease, there is a time lapse between the exposure and the expression of symptoms. Another time lag occurs between the onset of symptoms and the diagnosis of the illness. It is important that these time lags are reduced in bioterrorism and infectious disease surveillance due to the shorter incubation period and thus minimizing the effective treatment period, as shown in Figure 1. When comparing the incubation period of chronic diseases, time is more likely measured in years (1). Capturing biological agent exposures in near real-time or at the first point of care could enable the detection of potential biological exposures earlier than would be expected with routine health surveillance.

![Figure 1. Disease Detection Graph](image-url)
Routine surveillance data is normally delayed, often taking hours, days, and weeks to be analyzed and reported to public health officials. This time lapse in reporting is not the only problem with routine surveillance; additional problems can arise with respect to the reliability of reporting. This reporting process is not only slow, but is often overlooked by providers, and has been estimated that less than 20% of providers comply with reporting notifiable diseases (1). Routine reporting procedures are currently not timely enough for the early detection of bioterrorism, therefore new surveillance methods for bioterrorism should be developed so that illnesses can be identified in the earliest stage and reported in near real-time, followed by automated analysis and alerting mechanisms to public health officials so that appropriate interventions can be initiated. Any delays in reporting a bioterrorism event could allow increased transmission and exposure in the community and globally.

Syndromic surveillance is not meant to replace existing notifiable disease surveillance, but should be used in addition, for the purposes of bioterrorism and infectious disease detection. Syndromic surveillance for purposes other than bioterrorism detection has been used for years, and simply refers to data that is gathered before diagnoses are made (3). For the purposes of this study, the first signs and symptoms of patients visiting theme parks and military personnel and their families have been categorized as syndromes for the intent of assessing the frequencies of these syndromes, establishing thresholds for reporting an event above the norm when compared to historical data, and reported to health officials.
Over the past few years, methods for identifying the first warning signs and symptoms of biological exposures have led to categorizing various symptom complexes into syndromes. In this study, classifying illnesses into eight to twelve different syndrome categories was based on information gathered from similar syndromic surveillance studies and from the biology, clinical manifestation, and epidemiology of selected pathogens, as well as seasonal risks. The syndrome definitions used are consistent with the likely presentation of a spectrum of potential biological agents to include those with influenza, respiratory, skin rashes, neurological symptoms, and/or gastroenteritis illnesses (4).

**PURPOSE OF RESEARCH**

The purpose of this study was to develop, implement, and evaluate a syndromic surveillance system to identify bioterrorism and infectious diseases of public health importance in high-risk facilities, some of which are likely to serve patients before they visit an emergency room. Two emergency departments were also included for a more complete analysis of the selected theme park and military sites. Patients are likely to show up at emergency rooms in the late stages of disease, when treatment might be too late or not possible. If the first signs of illness were detected at clinics or first aid stations at theme parks, the person would likely present with symptoms in the earlier stages of the disease, when treatment might be possible, and subsequent exposures prevented. The locations selected as surveillance sites for this pilot study are theme parks, theme park referral hospital/clinics, and military hospital/clinics in the Central Florida area.
Facilities considered at high-risk for biological attack or other pathogens, such as the theme parks, are logical points for early deployment of a detection system. If a bioterrorism attack occurred at a theme park, persons might present with the first signs of an illness to the first aid stations. The first aid stations or clinics are located within the theme parks for easy accessibility.

RESEARCH QUESTIONS AND HYPOTHESES

Can a syndromic surveillance system identify communicable diseases of public health importance before routine surveillance methods?

Hypothesis: Improving existing surveillance methodologies by incorporating near real-time reporting with automated analysis and notification mechanisms would reduce the detection time by weeks, days, or hours.

Is syndromic surveillance a reasonable approach for bioterrorism preparedness and should it be incorporated into the public health infrastructure even if the threat of bioterrorism disappears?

Hypothesis: Syndromic surveillance may be useful in identifying exposures from biological agents and other illnesses of public health importance early enough to prevent subsequent disease and death, which would make it worthy of incorporating into the public health and medical infrastructure in certain high-risk areas.
STUDY JUSTIFICATION

Bioterrorism Surveillance

The threat of bioterrorism highlights the need to detect disease outbreaks early. Rapid responses to these threats would ensure the public that local, state, and federal health agencies are working together to serve as a safety precaution for the nation’s health.

Recent findings from the National Academy of Science conducted a mimicked bioterrorism scenario evaluated by mathematical modeling. The results showed that a large-scale anthrax attack on a large U.S. city where one kilogram of anthrax spores were released from around 330 feet over a city of more than 10 million persons would cause 123,400 deaths with the current levels of preparedness (5). Only by increasing our preparedness level will the projected number of deaths be reduced.

Syndromic surveillance can serve as one level of protection. Intelligence officials have reported the possession of weapons of mass destruction by various countries, thus highlighting the need for bioterrorism preparedness and the added protection of syndromic surveillance. Preparation for intentional outbreaks will assist in the preparation of naturally occurring outbreaks (6).

Infectious Disease Surveillance

In 2003, the Centers for Disease Control and Prevention are awarding $918 million in bioterrorism grants (1). This time of increased attention and resources can be used to make lasting improvements to public health surveillance nationwide and perhaps
globally. The threat of emerging and re-emerging infectious diseases worldwide and the ability to travel globally has enabled the introduction of pathogens to countries that might have been previously free of them (7).

Using Florida’s Historical Experiences

Florida is considered a high-risk state for potential bio-threats, with the theme parks and Central Command. For this reason, Florida is a prime location to conduct a syndromic surveillance study, and could complement the state’s experience in planning hurricane preparedness strategies and responding to anthrax events of the recent past.

LIMITATIONS OF THE STUDY

This study was limited to specific surveillance sites that were considered high-risk facilities. Results from this study might not apply to other areas in Florida or the United States. It was not intended that this study be representative, but to provide a service for high-risk facilities. The theme parks serve a unique and heterogeneous population, as opposed to the military facility, which serves a more homogeneous population. Having a more representative sample would increase the statistical power and the rapidity of identifying actual harmful health events. However, the purpose of this study was not to obtain a representative sample, but to develop, implement, and evaluate a syndromic surveillance system that can be used in multiple settings, especially those at high-risk of a bioterrorism attack (8). Syndromic data from these sources were not previously collected and because they are major employers in the Central Florida area, could serve as an indicator of the health of the community.
The data were also limited to healthcare providers that had a good understanding of the syndrome definitions. At some surveillance sites, the staff turnover rate appeared higher than other locations.

The military hospital and five clinics serve only military personnel. Patients at the military facility included personnel traveling from other bases to be deployed, some of whom received pre- and post-deployment check-ups at a particular clinic.

It was planned to compare the number of daily visits at each site with the total daily entry counts reported to the system. Due to the lack of obtaining reports of daily clinic visits from the sites, estimating compliance was not possible, and was a limitation to this study. In addition, the daily number of patients varied at all sites, and there was likely some effect of uncontrollable factors on the data, including the war and the economy. There was also a constant shift in staff responsibilities, especially at the military facility on the data, which could have affected compliance. The number of theme park visitors varied over time, and park directors later confirmed that seasonal fluctuations in entries at Park A into the system were consistent with the overall number of park visitors, which varied by season, weather, economy, and by the fear of war and/or bio-threats.

RESEARCH DESIGN, STUDY POPULATION, DATA COLLECTION, AUTOMATED ANALYSIS AND NOTIFICATION

This study included four theme park first aid stations/clinics, one theme park referral hospital emergency room, one theme park referral clinic, and five military clinics within the military hospital. The baseline data collection period served as the comparison for the test period, and to determine syndromic aberrations above the normal range and as the
basis of reporting alerts to the sites. Due to the lack of electronic medical records or patient information systems at the selected sites, a simple data collection form was used at each facility so that providers could classify patients according to syndrome. A data entry staff person entered the data into a secure website in as near real-time as possible. Automated analysis methods were developed and used to detect syndromic aberrations as a basis for notifying public health staff to enable early detection and rapid response. When an aberration was detected, surveillance sites were contacted and encouraged to use routine procedures for notifying local/state health officials based on the severity and/or the frequency of illnesses that exceeded the pre-established threshold.

**CONCLUSION**

If we are to prevent illnesses and death from a bioterrorism attack and/or outbreak, it is important to incorporate surveillance systems that can utilize primary, secondary, and tertiary levels of prevention, including preventing the occurrence of disease, to stop or slow down the disease process, and/or to reduce secondary cases of illness. Syndromic surveillance systems for the purposes of bioterrorism detection should also be able to detect outbreaks on multiple levels, such as detecting the first or earliest reports of illness, any rise of a particular disease, identifying an existing epidemic/outbreak, and/or recognizing a spatial-temporal cluster (3).

Although current overlap exists among syndromic surveillance systems, no one system was identified that met all the criteria necessary for a successful and sustainable surveillance program, including a system that could be customized and easily integrated in a variety of settings. With the increased risk of bioterrorism, it is imperative that
surveillance systems designed for the purposes of bioterrorism identification can detect the initial cases of illness in a timely manner so that rapid investigation can enable public health action. If identified rapidly, early intervention could prevent the onset of serious complications among those exposed to anthrax. Figure 1 shows the small time frame of opportunity that is needed to treat individuals exposed to some biological agents. Early detection by only two days could increase the likelihood of treating those exposed before the treatment window expires. For this reason, a new system called BioDefend™ was developed, implemented, and evaluated in the selected surveillance sites in hopes that automated analysis could decrease the detection time of outbreaks/epidemics of public health importance.

Syndromic surveillance is only one part of bioterrorism preparedness, and when combined with other public health disciplines, including laboratory early detection methodologies and training/education programs, can provide a more complete means of identifying and responding to bioterrorism. Systems with dual-use and near real-time capabilities could also be useful in identifying health effects from environmental contamination/exposures such as increased air or water pollution. As detection times are reduced, the community-based system of collecting, identifying, reporting, and increasing awareness could serve as a model for bioterrorism preparedness.

We cannot directly assess the potential effectiveness of a syndromic surveillance system for the detection of bioterrorism, because such events are likely to be rare. However, these surveillance systems might be better evaluated using current emerging infectious diseases, such as the recent epidemic of severe acute respiratory syndrome
(SARS). With this new illness, we can see that national borders do not provide protection against pathogens. Margaret Hamburg, of the Institute of Medicine stated at a recent public briefing that, “one nation’s problem can soon become every nation’s problem,” and infectious diseases today are “endlessly resourceful” in adjusting to our well-connected “global village,” (9).

The threat of infectious diseases will not vanish, as substantial evidence shows their ability to resist antibiotics and mutate to remain virulent in the human population. Rapid mechanisms of detection are needed now and must be carefully integrated into public health and medical infrastructures so that they can be sustained over time. These systems can safeguard communities by combining state-of-the-art technology with disease detection strategies in order to keep up with emerging and re-emerging pathogens and their ability to survive circumstances (7).
CHAPTER TWO: LITERATURE REVIEW

BACKGROUND

In 1972 the Biological Weapons Convention assembled and 103 nations co-signed an agreement... “never to develop, produce, stockpile, or otherwise acquire or retain microbial or other biological agents or toxins, whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes; and weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.”

—Alibek, BioHazard

DETECTION OF OUTBREAKS USING DIFFERENT DISEASE SURVEILLANCE METHODOLOGIES

Bioterrorism is “the unlawful use, or threatened use, of microorganisms or toxins derived from living organisms to produce death or disease in humans, animals, or plants. The act is intended to create fear and/or intimidate governments or societies in the pursuit of political, religious, or ideological goals,” (10).

Some of the reasons that terrorists might choose to use biological agents over other weapons of mass destruction are because these attacks are most likely invisible, and the perpetrator is less likely identified compared to using explosive weapons. Biological agents are also attractive to terrorists because they are available, easy to produce, infective, can be lethal, and can be stabilized as a weaponized agent. They are also cheaper to use compared to nuclear or conventional weapons (11). Successfully weaponized biological agents have been reported and terrorists may escape more easily after an attack due to delayed incubation periods for various pathogens.
It has been proposed that biological weapons have been used long before history was recorded. Attackers placed toxins extracted from animals and plants, including fecal matter on the tips of arrows to kill enemies and animals. Biological agents were also used by dumping dead bodies and fecal matter into water sources to contaminate the enemy’s water supply. Military leaders employed bioterrorism as early as the 14th century by catapulting smallpox and bubonic plague-infected bodies over city walls to infect opposing forces. Europeans used smallpox-infected blankets against the American Indians, and during the Revolutionary War, General George Washington mandated that some colonists be immunized against smallpox for the purposes of intentionally infecting the opposition with the virus (12).

The increased availability of biological and chemical weapons and heightened expertise in weapon development technology could raise the risk of terrorist groups using them to launch an attack. In 1979, an incident occurred in the Soviet Union at the Sverdlovsk Institute of Microbiology and Virology. This institute manufactured biological agents for use as weapons, specifically a dry anthrax weapon for the Soviet arsenal. On one evening in 1979, a defective air filter in the building was removed and not replaced. That night, deadly anthrax spores were carried through the pipes, released into the evening air, and swept by the wind, infecting persons working the evening shift at a nearby ceramic-making plant that was located downwind from the weapons facility. Within a few days, many became ill, and within a week, virtually all of them died (13). Reports of the illness and death ranged from the sixties to the thousands, but no confirmed count has been made to date (14).
In 1995, the Japanese cult Aum Shinrikyo used sarin in the Tokyo subway. They placed sarin in soft-drink containers and lunch boxes on the floor of three different subway lines. Then they punched holes in the containers with umbrellas just before exiting the train during rush hour. Approximately 5,500 were injured during the attack. Not only were hospitals overflowing with patients, but 60% of victims suffered psychological complications, particularly post traumatic stress disorder for longer than six months after the attack. Some authors report that Japan had never experienced this form of terrorism and as a result of this attack, Japan received aid from the international community and has since developed its own disaster plan (15,16). The importance of this event showed that the healthcare system was overwhelmed with fearful persons that were miles away from the attack.

The anthrax attacks that caused 22 cases of illnesses and five deaths challenged the U.S. public health system in the fall of 2001. Endless resources and investigations were implemented immediately in response to the attacks, again great fear was instilled in the American people by this newly introduced agent into our population (17).

Routine infectious disease reporting and surveillance methodologies could help identify both types of outbreaks, those that occur naturally and those that are intentional. However, these methodologies can only be useful for identifying these events when health events are reported in near real-time (in this study, the term “near real-time” refers to the ability to identify illness patterns within six hours or less of a patient reporting to a healthcare facility with the first signs and symptoms of illnesses indicative of a biological
exposure). This real-time reporting capability could also be used to improve routine health surveillance methodologies.

Several efforts have been made to prohibit the use of biological warfare agents, such as the Geneva Protocol of 1925 and the Biological Weapons Convention of 1972. The latter prohibited the development, stockpiling, and retaining of any biological agents for any reason (18).

Although some of these initial efforts included around 103 countries, experts speculate that biological weapons still exist and are ready for use. Existing published evidence on exact biological agents is limited, although many believe that the Soviet bioweapons program continued after the signing of the Biological Weapons Convention in 1972. A former director of the bioweapons program reported that the Soviet program contained over 100-plus tons of anthrax stockpiled with a production capacity of over 1,000 tons per year, 20 tons of plague were stockpiled with a capacity to produce around 200 tons per year, and 20 tons of smallpox were stockpiled with a production capacity of about 100 tons per year. Additional reports suggested that the Soviet program could produce more than 1,000 tons annually of the plague, tularemia, anthrax and glanders at various facility locations. There are an estimated 25,000 missing employees of the Soviet bioweapons program, and after the breakup of the Soviet Union, many have feared that these weapons could have fallen into the hands of our enemies. (18).

In 1995 disclosures to United Nations Special Commission reported that Iraqi had a bioweapons program that produced around 19,000 liters (L) of botulinum toxin and weaponized 10,000L; produced 8,500L of anthrax spores with 6,500L weaponized; and
produced 2,200L of aflatoxin and weaponized 1,580L. They also field-tested three different anthrax stimulants, and researched and developed camel pox, rotavirus, enterovirus 70, various mycotoxins and aflotoxins. United States military reports suggested that natural and genetically-engineered strains of bioweapon development continued in the late 1980’s and early 1990’s. Some of these natural strains included Ebola, Lassa Fever, Bolivian Hemorrhagic Fever, Argentinean Hemorrhagic Fever, melioidosis, Japanese Encephalitis and Russian Spring-Summer Encephalitis. Suspected work on genetically engineered strains include antibiotic-resistant (AR) plague, AR anthrax, AR tularemia, AR glanders, sulfonamide-resistant glanders, smallpox with insertion of Venezuelan equine encephalitis genes, immune system-overcoming (IO) tularemia, IO anthrax, and IO plague. In the fall of 2001, media reports revealed that Iraq had ordered a million doses of the antidote atropine, potentially to protect their own army (16). Many of these biological weapons have no cure or treatment, thus making them prime agents for terrorists. It has also been reported that the use of bioweapons can cause chronic health problems, including mutagenesis, carcinogenesis from viral infections, teratogenesis, and the creation of new diseases (19). Other federal reports stated that several other countries have “probable” biological weapons programs, including China, Iran, North Korea, Libya, Syria, Taiwan, Cuba, Israel, and Egypt (18).

The World Health Organization noted the threat of biological weapons decades ago and stated that bioweapons were strategic, population-destroying devices (20). Today, we know that the technology used to build and disperse these weapons has advanced. Our capabilities to detect and respond to them should likewise advance. A recent study on
past and present weapons programs revealed about 30 countries that potentially possessed biological and chemical weapons. Table 1 shows the status of various weapon’s programs by country as reported by the Monterey Institute of International Studies (21).
<table>
<thead>
<tr>
<th>Country</th>
<th>Biological Program Status</th>
<th>Chemical Program Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>Research, but no evidence of production</td>
<td>Possible</td>
</tr>
<tr>
<td>Canada</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>China</td>
<td>Likely maintains offensive program</td>
<td>Probable</td>
</tr>
<tr>
<td>Cuba</td>
<td>-</td>
<td>Possible</td>
</tr>
<tr>
<td>Egypt</td>
<td>Likely maintains offensive program</td>
<td>Probable</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>-</td>
<td>Probable</td>
</tr>
<tr>
<td>France</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>Germany</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>India</td>
<td>Research, but no evidence of production</td>
<td>Former</td>
</tr>
<tr>
<td>Iran</td>
<td>Likely maintains offensive program</td>
<td>Known</td>
</tr>
<tr>
<td>Iraq</td>
<td>Previously active research &amp; production; potential</td>
<td>Known; Potential</td>
</tr>
<tr>
<td></td>
<td>reconstruction of programs</td>
<td>reconstruction program</td>
</tr>
<tr>
<td>Israel</td>
<td>Research, possible production</td>
<td>Probable</td>
</tr>
<tr>
<td>Italy</td>
<td>-</td>
<td>Former</td>
</tr>
<tr>
<td>Japan</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>Libya</td>
<td>Research, possible production</td>
<td>Known</td>
</tr>
<tr>
<td>Myanmar</td>
<td>-</td>
<td>Probable</td>
</tr>
<tr>
<td>North Korea</td>
<td>Research, possible production</td>
<td>Probable</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Possible</td>
<td>Probable</td>
</tr>
<tr>
<td>Russia</td>
<td>Research, some work beyond legitimate defense activity may continue</td>
<td>Probable</td>
</tr>
<tr>
<td>Soviet Union</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>South Africa</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>South Korea</td>
<td>-</td>
<td>Former</td>
</tr>
<tr>
<td>Sudan</td>
<td>Possible research program</td>
<td>Possible</td>
</tr>
<tr>
<td>Syria</td>
<td>Research, possible production</td>
<td>Probable</td>
</tr>
<tr>
<td>Taiwan</td>
<td>Possible research program</td>
<td>Probable</td>
</tr>
<tr>
<td>U.K.</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>U.S.A.</td>
<td>Former</td>
<td>Former</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>-</td>
<td>Possible</td>
</tr>
<tr>
<td>Yugoslavia, Federal Republic of (FRY)</td>
<td>None/Unknown</td>
<td>Former</td>
</tr>
</tbody>
</table>

Table 1. Reported Biological and Chemical Weapons Programs by Country from Monterey Institute of International Studies

The potential economic impact of a bioterrorism attack would be devastating. It would drain a vast majority of community, state, and federal resources, both human and financial, as seen by a model that addresses three agents, including Bacillus anthracis, Brucella melitensis, and Francisella tularensis. If 100,000 people were exposed to Brucella melitensis, the estimated cost burden is approximately $478 million. If the agent was Bacillus anthracis, the cost burden increases to $26 billion (22).

Based on these costs, Centers for Disease Control and Prevention researchers recommended a rapid implementation of a post-attack prophylaxis program as the most
important means to reduce human losses (22). Reducing exposures and transmission by way of early detection would more effectively minimize human and financial loss by preventing exposure rather than relying on after-attack treatments. Perhaps a combination of effective prevention and treatment is superior to either strategy alone.

From the first Gulf War to the current situation of U.S. military involvement in Iraq, some have expressed that the potential threat of biological weapons being used against military forces and civilian populations would increase, and could likely be part of the Iraqi response to U.S. forces (23). However, no weapons were used or found to date.

In response to events of September 11, 2001, the President signed an Executive Order Number 13228 instructing Americans to, “…coordinate development of monitoring protocols and equipment for use in detecting the release of biological, chemical, and radiological hazards,” as reported in Section 3D (24). More recently, the Homeland Security Act approved by Congress and signed by the President on November 25, 2002, involved over 30 federal agencies to establish the Department of Homeland Security to prevent terrorism aimed at the United States (25).

Findings reported in The Lancet suggested that the Public Health Security and Bioterrorism Response Act is the pulse of the U.S. response to bioterrorism. This act was implemented to create a unified national approach to identify the goals needed to respond to existing bio-threats, and are listed as such: tracking biological agents on U.S. soil; increasing existing knowledge about infectious disease surveillance; and improving the timeliness of reporting disease trends (26).
This is a critical time in our nation’s history as many public health disciplines have joined together to plan and respond to existing bio-threats through the use of various surveillance methodologies. The use of public health surveillance is needed for an effective response (27).

Surveillance for biological warfare agents is difficult due to their variable incubation periods and the nonspecific nature of the symptoms (28). Based on the nature and severity of the symptoms, the victim may delay seeking medical care from a primary health care provider. In a report from the Centers for Disease Control and Prevention regarding the anthrax attacks, six of seven cases described presented to clinics instead of an emergency department (4). It is likely that by the time patients present to an emergency department, it may be too late in the course of the disease to provide effective treatment. The growing threat of bioterrorism forces the public health infrastructure to focus attention on these challenges posed by bio-threats, as well as emerging and re-emerging infectious diseases.

With the current war on terrorism, public health officials should also consider the historical effect of war on the spread of infectious diseases. Results of the first Gulf War, led to the breakdown of water and sanitation, which was responsible for outbreaks of gastroenteritis, malaria, meningitis, brucellosis, measles, polio, hepatitis, typhoid, and other diseases (19).

We critically need to strengthen existing surveillance systems and to enhance innovative real-time approaches to surveillance that can provide timely alerts of epidemics whether they occur naturally or through an intentional attack (29). By
monitoring the earliest warning signs and symptoms of an outbreak or bioterrorism attack, surveillance systems like the one used in this study, could reduce the time it takes to identify a series of adverse health events when compared to the routine surveillance methods. This reduction in time to detection could significantly decrease morbidity and mortality in the event of a bioterrorism attack/epidemic (4).

**BIOTERRORISM SYNDROMIC SURVEILLANCE**

Bioterrorism syndromic surveillance is a type of surveillance used to track specific syndromes before a diagnosis is made that can serve as indicators of many infectious diseases and bioterrorism agent exposure in a specified population. Each syndrome is made up of a group of the first symptoms experienced when a person has been exposed to a bioterrorism agents and/or infectious disease. The case definitions used for many syndromic surveillance studies originated from the Centers for Disease Control and Prevention and the Department of Defense (4, 56).

The earliest symptoms of bioterrorism agent exposure will present as non-specific illnesses, such as respiratory tract infection with fever, influenza-like illness, gastroenteritis, and/or febrile illness. Several versions of syndrome listings are currently being used, and many are customized based on the needs of the population being surveled. Currently, there is no standard system or method that has been recommended for bioterrorism syndromic surveillance (1). Most syndromic surveillance projects have not been evaluated or published in peer-reviewed literature. Published peer-reviewed literature about bioterrorism syndromic surveillance is scarce, but based on discussions
with state and federal health professionals, routine bioterrorism syndromic surveillance in every hospital and clinic across the nation may not be appropriate or cost effective.

This type of active surveillance is not meant to replace existing methods of reporting notifiable disease, but to enhance or supplement diagnosis-based surveillance so that early detection can lead to earlier response. The importance of the dual-use nature of these systems can be seen with influenza surveillance in which the system does not identify a specific illness but identifies surges in influenza-like illnesses to use as a predictive means for determining influenza seasonal patterns, or as indicators of other diseases.

There are currently many discussions regarding the appropriate setting for surveillance, whether it is in an emergency room, clinic, or among special populations, such as the military and theme parks. Some believe that emergency rooms are the best places to launch surveillance, however, others argue that emergency rooms are too late to detect the first signs and symptoms. Often when people begin to experience flu-like symptoms are more likely to visit a clinic as opposed to the emergency department, where more severe patient tend to visit (30). This was seen during the anthrax cases in 2001, where six of the seven cases presented to clinics (4). Some believe that syndromic surveillance should be deployed only among special or high-risk populations, or other facilities at risk for a bioterrorist attack, such as military hospitals, VA hospitals, government facilities, and theme parks (8). Other discussions involve implementing surveillance among facilities that serve children and/or the elderly because these population can be more susceptible to illnesses and might be locations in which an event
would be detected early. Recent discussions and syndromic surveillance efforts are evolving that test whether or not multiple data sources of syndromic data can increase the likelihood of capturing true epidemics (30). Most agree that bioterrorism syndromic surveillance systems should be manned and housed by local and state health departments, and will be able to link to federal surveillance systems (31).

An effective response to an attack/epidemic requires and depends on rapid reporting and communications among public health agencies. Epidemiological principals are necessary components of syndromic surveillance systems, providing for interpretation of the data, meaningful feedback to the participating institutions, and to local, state, and federal public health agencies responsible for investigating epidemics/attacks. The current bioterrorism threat and its potential effect(s) on the population and the healthcare system are reason enough to aim to have syndromic surveillance data automatically analyzed and alerting capability around the clock (32).

Waiting until an emergency situation occurs is not the best time to implement methods of detection (32). A more logical and cost-effective method of responding to a bioterrorism threat is before an attack occurs. It is critical that public health officials have clear goals in which to plan, implement, and evaluate surveillance methodologies before an event occurs. If data from any surveillance program is incomplete and the system has been implemented and systems are only used during emergency situation, decision-making will likely be hasty, and lead to vast resources allocated to response rather than to prevent an event (27).
Implementing well-developed rapid surveillance mechanisms before an attack could be useful in establishing baseline illnesses and health risks patterns in a population so that thresholds can be established and serve as a comparison during an epidemic or bioterrorism attack. These early detection systems could serve as the foundation from which to identify, evaluate, and respond to bioterrorism and infectious disease events of public health importance.

Medical professionals have discussed other methods of bioterrorism syndromic surveillance, and some believe that only an astute physician will identify and report unusual illnesses to appropriate authorities. This may not be the case, especially as most U.S. physicians have not seen patients infected with many bioterrorism agents of concern. Furthermore, physicians do not have the means to identify illness patterns exposures that could be seen when syndromic data are aggregated, nor would they be able to identify illness clustering as can be automatically mapped in syndromic surveillance.

The results of a study published in the American Journal of Public Health showed that healthcare providers in emergency rooms reported that they did not feel prepared in the event of a biological and/or chemical attack (33). Bioterrorism syndromic surveillance, in combination with provider awareness, could reduce the time it takes to identify biothreats that otherwise might not be identified for hours, days, and perhaps weeks (7).

Training and education of healthcare providers should be an important component of any surveillance program. This type of training should incorporate methods for
recognizing the clinical presentation of bioterrorism agents through syndrome definitions, maintaining a high level of suspicion, recognizing unusual epidemiological trends, prevention and treatment of bioterrorism agents, and knowing how and where to report potential bioterrorism cases (11).

There have been numerous bioterrorism syndromic surveillance systems developed since September 11, 2001, but few have been published in peer-reviewed literature, or been formally evaluated. Syndromic surveillance has been implemented in emergency rooms, during special events, and among special populations. Data collection methods range from telephone and facsimile data transmission to web-based reporting systems. Some systems also claim to be bioterrorism syndromic surveillance systems and are based solely on diagnosis-related coding, which is by definition, not syndromic surveillance. Very few of these systems have real-time reporting capabilities and automated analysis. It is important to note that mere data collection is not surveillance, and systems that require staff to run statistical processes on data are not “real-time” and are not optimal for the purposes of rapidly detecting bioterrorism agent exposures (34).
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Importance of Criteria</th>
<th>RSVP- Relies on provider data entry of 6 syndromes and immediately sends alerts to the Dept. of Health Epidemiologist.</th>
<th>STARS- A web-based system that collects syndromic and demographic data and requires manual data analysis.</th>
<th>LEADERS- Web-based system used in special events.</th>
<th>ESSENCE- Developed for the military. Data extracted from diagnosis related codes and analysis conducted manually every 8 hours.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustable thresholds that are used to define syndromic aberrations</td>
<td>Unknown</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Reasonable cost</td>
<td>This is needed for sustainability</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>Outcome evaluation</td>
<td>Results should be published and the system evaluated</td>
<td>No</td>
<td>None</td>
<td>Yes (4)</td>
<td>Limited</td>
</tr>
<tr>
<td>Setting of system</td>
<td>Setting appropriate for system?</td>
<td>Hospitals and clinics</td>
<td>Emergency departments</td>
<td>Clinics and emergency dpts</td>
<td>Clinics and emergency departments</td>
</tr>
<tr>
<td>Technologically advanced system and capabilities</td>
<td>Unknown</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Compatibility with state and federal surveillance systems</td>
<td>It is important that systems can be fed into National surveillance programs</td>
<td>Unknown</td>
<td>No</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Spatial data distribution</td>
<td>Useful for mapping syndromic clusters</td>
<td>Yes</td>
<td>No</td>
<td>Limited</td>
<td>No</td>
</tr>
<tr>
<td>Adjustable thresholds (sensitivity and PVP)</td>
<td>This is important during flu season</td>
<td>Unknown</td>
<td>No</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>Automated analysis</td>
<td>This is necessary for near real-time BT detection.</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Automated alerts</td>
<td>Required for near real-time reporting of potential events.</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Timeliness of outbreak detection</td>
<td>Shown through evaluating surveillance experiences.</td>
<td>Unknown</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Baseline data collected</td>
<td>This is Important for establishing thresholds for reporting events.</td>
<td>Yes</td>
<td>Limited</td>
<td>Limited</td>
<td>Yes</td>
</tr>
<tr>
<td>User Friendly</td>
<td>Necessary for sustainability.</td>
<td>Yes</td>
<td>Somewhat</td>
<td>Somewhat</td>
<td>Unknown</td>
</tr>
<tr>
<td>System Customizability</td>
<td>Necessary for sustainability.</td>
<td>Yes</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>System Security</td>
<td>Data needs secured from hackers</td>
<td>Yes</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Table 2. Bioterrorism Syndromic Surveillance System Comparison
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Importance Of Criteria</th>
<th>RedBat-Scans symptoms from hospital databases and automatically calculates a score for each symptom to be categorized into one of ten syndromes.</th>
<th>RODS- Automatically collects and stores de-identified regional ER data. Analyzes, displays results.</th>
<th>EARS- Collects 911 calls, schools, ER, &amp; clinic data. Compares data to 7-day mean. Manual analysis.</th>
<th>SURVEIL™- Symptom data is collected and auto converted to ICD-9 codes. Manual analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustable thresholds used to define syndromic aberrations</td>
<td>Yes</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Reasonable cost</td>
<td>This is needed for sustainability</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Outcome evaluation</td>
<td>Results should be published and the system evaluated</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Limited</td>
</tr>
<tr>
<td>Setting of system</td>
<td>Is the design appropriate?</td>
<td>Emergency department</td>
<td>E.R. department, lab reports, and clinics</td>
<td>911 calls</td>
<td>E.R., clinics, and nurse call centers</td>
</tr>
<tr>
<td>Technologically advanced system</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Compatibility with state and federal systems.</td>
<td>It is important that systems can be fed to national &amp; state programs</td>
<td>Unknown</td>
<td>Yes</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
<tr>
<td>Spatial data distribution</td>
<td>Useful for mapping syndromic clusters</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Adjustable thresholds (sensitivity and PVP)</td>
<td>This is important during flu season</td>
<td>Yes</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Automated analysis</td>
<td>This is necessary for near real-time BT detection.</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Automated alerts</td>
<td>Required for near real-time reporting of potential events.</td>
<td>Unknown</td>
<td>Yes</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>Timeliness of outbreak detection</td>
<td>Shown through evaluating surveillance experiences.</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Baseline data collection</td>
<td>Important for thresholds for events.</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
<tr>
<td>User friendly</td>
<td>Necessary for sustainability.</td>
<td>Unknown</td>
<td>Minimal</td>
<td>Minimal</td>
<td>Unknown</td>
</tr>
<tr>
<td>System Customizability</td>
<td>Necessary for sustainability.</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Yes</td>
</tr>
<tr>
<td>System security</td>
<td>Syndromic and demographic data needs to be secured from hackers.</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Table 2. Bioterrorism Syndromic Surveillance System Comparison (Continued)
This is a comparative summary of several syndromic surveillance systems, some of which are commercial. This review of existing systems was conducted for the purpose of selecting the appropriate system for this study. There have been numerous systems developed since the September 2001 terrorist attacks. This review is not comprehensive, but is a good representation of systems available. The criteria for comparing the systems was selected and based on two papers published by the Centers for Disease Control and Prevention, and titled: Updated Guidelines for Evaluating Public Health Surveillance Systems; and the Draft Framework for Evaluating Syndromic Surveillance Systems. This comparison summary was written for the purposes of facilitating the comparison of different studies and systems to help public health agencies determine the best mechanisms of selecting appropriate surveillance systems (2, 3). Table 2 shows several systems compared using criteria defined in the Centers for Disease Control and Prevention publications.

Surveillance data are usually gathered one of two ways: 1) by collecting new data; and/or 2) by collecting existing data from electronic medical records or patient information systems (35). Determining the appropriate data collection method depends on the data that are available. The optimal means of data collection is to use a system that automatically abstracts and submits syndromic information from existing electronic medical records to a database (30). A common problem is that not all healthcare facilities have electronic information systems, therefore many surveillance efforts have focused on collecting new data by using paper forms completed by healthcare staff (30). This requires the provider to complete the syndromic and demographic information and a data
entry staff person to submit the forms into the database. Some systems automatically abstract data from diagnosis-related databases (36-38). This is not syndromic surveillance because syndromic surveillance by definition is data collected before a diagnosis is made, before data is coded (30). The coding of patient illnesses into diagnosis-related codes can take several days to several weeks, and is much too late for early identification of a bioterrorism attack (3, 30). The limitations of ICD-9 codes are that they were originally designed for billing purposes, and sometimes take a few days to a few weeks to be coded. Coding systems, such as the ICD-9 system uses specific diagnoses and they are not well-matched to the syndromes currently used in many bioterrorism surveillance efforts. The data should be available immediately or at best, in less than six hours, anything more than 12-24 hours is not timely enough to be useful for infectious disease outbreaks or a bioterrorism event.

A few syndromic surveillance systems described were viewed or used through interactive demonstrations; other system information was gathered from publicly available marketing systems documentation. There were many systems reviewed, but not all included in the comparison. The sample in Table 2 was chosen to show the variety in methods, data sources, and settings used for surveillance. Demonstrations were conducted on the following systems: the Lightweight Epidemiological Advanced Detection and Emergency Response System (LEADERS); the Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE); the Rapid Syndrome Validation Project (RSVP); Real-time Outbreak and Disease Surveillance (RODS); and the Syndromic Tracking and Reporting System (STARS) (36-
There were three other systems described in Table 3, but due to the lack of complete information about the systems, they will not be discussed in the text.

LEADERS was the syndromic surveillance system used during the September 11 attacks in New York City, the World Trade Organization Seattle Ministerial Conference, and during the Superbowl in 2001. This system is a commercial web-based system that provides medical surveillance and other emergency department software. This system was one of the first syndromic surveillance systems developed and deployed, and has been used in emergency departments. The system requires that medical personnel collect syndromes and demographic data for entry into a database. The system lacks flexibility, for example, data forms cannot be customized for individual sites. The reporting tool is standard, and can not be updated or improved. The system also lacks an automated analysis and alerting component, thus missing the real-time capability critical for the early detection of bioterrorism. This system does not use sufficient baseline data needed for determining accurate thresholds for reporting alerts. Without enough baseline data, too many false alarms, as was the case during the September 2001 deployment in New York City. These false alarms and resulting investigations have been associated with large costs, and overburdening public health officials (4). Essentially, this system is a database that requires staff to download the data and import it into a statistical software package for analysis to identify any aberrations in the data. The system is also costly, and too high to be sustained by local health department. These costs do not include staff required to analyze and interpret data, which has been reported that analyses are completed twice daily (43).
R.S.V.P. was developed by Sandia National Laboratory, and funded by the U.S. Department of Energy’s Chemical and Biological Weapons Non-Proliferation program. This system is used in emergency departments and clinics, and utilizes six syndromes that are assessed in the clinical setting. The primary purpose of this system is to aid the communications between public health officials and health care providers for the purposes of facilitating healthcare providers in the reporting of suspicious or unusual symptoms. Once syndromes are entered into the system, information about recent disease outbreaks is provided to healthcare providers (41, 44).

ESSENCE was developed by Johns Hopkins University Applied Physics Laboratory and sponsored by the Defense Advanced Research Projects Agency. It began as a surveillance system to detect a bioterrorism attack within the military population, but has expanded to include some civilian organizations. This system is not based on syndromes, but ICD-9 codes, and is therefore not considered to have the real-time capability required for bioterrorism early detection. Recent reports indicate that ESSENCE has been implemented in several countries outside the U.S. Additional non-traditional data sources have been added to the surveillance program. Increasing the types of surveillance data used to identify events should reduce the number of false positives. This system does not have automated data analysis, but reports indicate that data are analyzed every eight hours. By not having the analysis and alerting automated, it is not possible to detect events in near real-time. Baseline data are collected from historical data to serve as a comparison. The major limitations with this system are timeliness and quality of data (36, 37, 38).
The RODS system is a major statewide effort, involving health departments, medical centers, hospitals, and foundations in Pennsylvania. The system has automated analysis and alerting capability, but appears to be based on chief complaints and ICD-9 coding using medical information systems. An advantage of this system is that it also uses multiple data sources, has a spatial analysis component, and is compatible with the National Enhanced Disease Surveillance System and Health Level 7 (HL-7) messaging, thus making it possible for data to be fed into the federal surveillance system (39, 40).

STARS is a syndromic system modeled after LEADERS and developed by the Hillsborough County Health Department in Tampa, Florida for use in emergency departments. The system is very similar to LEADERS, in that it is basically a database for storing syndromic reports. STARS does not contain automated reporting, analysis, or alerting capabilities. As with LEADERS, STARS continues to place a high burden on the providers, for example, for every person that visits the emergency department, syndromic and demographic information must be completed by the provider. This burden of completing forms on all patients regardless of whether or not they have a syndrome is not practical (42).

The various bioterrorism syndromic surveillance systems currently being used incorporate a variety of data sources, both traditional and non-traditional. Table 3 is a list of several data sources that are currently being used (30, 44).
Table 3. Data Sources

Formal evaluation of many of the syndromic surveillance systems and the use of data sources have not yet been published. Surveillance of multiple data sources will increase the likelihood of not only detecting, but confirming an event. For example, if an increase in gastroenteritis was seen at local clinics and the emergency department, it might be confirmed with a laboratory data. By integrating more than one data source, the accuracy of reporting events should increase, thus reducing the human and financial resources spent on investigation and response (30).

Many of the systems use similar syndrome definitions, most of which were defined by federal agencies. A few surveillance system studies reported being compliant with federal surveillance systems, such as National Electronic Disease Surveillance System (50). There appeared to be a lack of the use of baseline data in surveillance efforts. Baseline data is important to establish thresholds for reporting alerts to public health officials. These thresholds need to be as accurate as possible so that the public health departments will not be overburdened with responding to false alarms.
We cannot wait for another bioterrorism attack to occur before we react. Taking the time now to plan, implement, and evaluate an effective response is crucial. The experience of deploying a surveillance system in the midst of a terrorist attack highlights many of the issues that could be resolved with advanced planning. Government officials should be commended for attempting this task during an emergency setting; however, the outcomes from the system deployed during the September 11, 2001 attacks may not be applicable in different settings, nor in situations that established surveillance programs with sufficient time for planning (4).

**NEW YORK CITY SYNDROMIC SURVEILLANCE EFFORT**

During the evening of September 11, 2001, after the terrorist attacks on the World Trade Center Towers, New York health officials, with the help of the Centers for Disease Control and Prevention health officials, decided to quickly implement a drop-in bioterrorism syndromic surveillance system for 30 days in order to help identify a potential secondary biological attack. The system was implemented in 15 hospital emergency departments, and to identify other health-related issues from the terrorist attacks on the towers. A data collection form was used to classify all patients into one of 12 syndromes. Seven, of which were indicative of bioterrorism agent exposure, four were syndromes associated with illnesses related to the attacks. A few days after implementing the system, training and orientation meetings were held for hospital staff, and up to three Centers for Disease Control and Prevention Epidemic Intelligence Service Officers were placed in each hospital. Data entry was conducted on-site, and follow-up investigations were conducted in response to alarms (4).
A low compliance of form completion was reported before the Epidemic Intelligence Service Officers were deployed. The system appeared to be overly sensitive, most likely due to the lack of baseline data. A total of 91 alerts were generated during the 30-day period. All of the alerts were from one of the following syndromes: gastrointestinal; respiratory; rash; neurological; and sepsis. There were 26 gastrointestinal-related alarms, and 25 respiratory-related alarms. These alarms were investigated, but none were suggestive of a bioterrorism attack or outbreak (4).

The results were one of the first documented uses of syndromic surveillance for the purpose of bioterrorism detection, and contributed in part to the improvement of systems currently in use. Due to the urgency of implementation, there was not a period of baseline data collection. The overly sensitivity of these results regarding the high frequency of false alarms showed the need for using baseline data to help minimize false alarms by establishing normal thresholds and identifying syndromic aberrations. The burden on providers, Epidemic Intelligence Service Officers, and technical staff was high, and the Centers for Disease Control and Prevention authors reported that the study probably would have not been possible without the addition of the Epidemic Intelligence Service Officers. This study probably would not be sustainable for these reasons. In addition, a completed data collection form was required for each patient in all 15 hospitals every day. Only 6.4% of the total reports were reported as syndromes, leaving about 94% of all data collection on patients with no syndrome. This is a tremendous burden when each form requires patient demographic information to be completed even when the patient did not have a reported syndrome. Manual data entry resulted in coding errors and helped
contribute, along with the lack of baseline data, to false alarms. It was also assumed that patients would present to emergency departments. Emergency rooms may not be the appropriate place for syndromic surveillance because the patients are likely to present in the latter stages of a disease, and may be too late for the system to serve as an early warning device. Clinics might be location where patients present during the beginning states of a disease. Of the seven patients diagnosed with anthrax during the October 2001 attack, six of them did not present to the emergency departments, but to clinics. Finally, authors reported that it was unknown whether this type of drop-in system could detect a biological attack faster than individual physician reports (4). Implementation the system was justified, given the perceived risk of terrorist attacks. Since this event, a new and improved automated system replaced the system used during the attacks. Continued research on bioterrorism syndromic surveillance, and the need to remove the personnel burden, to refine detection methods, and to ensure systems are designed that are flexible enough to be integrated into various settings (4).

An example of a more favorable scenario includes one in which the system was given a chance to be seeded into routine healthcare practices. The major limitations encountered in several surveillance systems are high cost, excessive labor, occurrence of false alarms, and the lack of baseline data, all of which likely contributed to the excessive amount of time and money needed to respond to false alarms (4).

The most effective strategy for staging an early detection system would be one that is tested and improved upon in multiple “every day” settings. Identification of the best methods and practices for the integration of a surveillance program into the existing
workflow of target healthcare settings is equally important to achieve lasting programs that are acceptable to the health care providers implementing them. Only after careful evaluation in both settings and under non-emergency scenarios will it be possible to determine where and how such surveillance systems may be best deployed.

The Centers for Disease Control and Prevention currently has a draft framework on how to evaluate bioterrorism syndromic surveillance systems, which is useful for evaluating syndromic surveillance systems (3). If syndromic surveillance systems are to continue improving, documenting early successes and evaluation is important. The Centers for Disease Control and Prevention article recommends that evaluation of systems should include the purpose, a description of the system, the target population, the goals, and how it works. The experiences of planning and implementing the system should also be described and a determination made regarding whether or not the system was useful, acceptable to the staff implementing it, generalizable for use in various settings, sufficiently stable enough to achieve consistent results, and whether it is cost effective. The detection of outbreaks should be described and based on the flexibility of the system to respond to changing risks, sensitivity of the system to capture true cases of illness, and the timeliness of reporting, analysis, alerting, and detection. The quality of the data should be assessed for representativeness, completeness, reliability, and consistency. Publications should include recommendations and conclusions based on their experiences in furthering and improving syndromic surveillance (3). To conclude, it is important for public health officials to recognize that mere data collection is not surveillance (51).
The first Gulf War experience emphasized the importance of health during military deployment. Recent research shows that health surveillance can be useful in the military to help identify health risks by using a baseline of health status before, during, and after deployment (52). Bioterrorism syndromic surveillance and military surveillance could be used together to enhance and facilitate the identification of health risks.

This type of surveillance have been predicted to be useful in detecting newly emerging diseases, such as the presence of Severe Acute Respiratory Syndrome. Additional uses include detecting seasonal variations, geographical clustering, and increases in hospital admissions/clinic visits, animal illnesses, and epidemiological links to a particular event (53).

Incorporating syndromic surveillance could strengthen the overall public health infrastructure and be an efficient and effective use of resources through early detection and a means to provide some level of protection against the consequences of an attack (53). Some useful epidemiological observations that can be used to help interpret and identify an attack using syndromic surveillance data include surges of patients to healthcare facilities, large numbers of illnesses in persons that attended a similar event, animal deaths, large numbers of illness or deaths among the old and the young, recent terrorist threats, illnesses normally treatable that are unresponsive to routine treatment, surges in illnesses with high morbidity and mortality, and/or unusual illnesses for a particular season or location (28).
Surveillance for Emerging Infectious Diseases

Surveillance of bioterrorism and infectious diseases overlaps in that their clinical presentation and routes of transmission are similar. Infectious diseases continue to be the leading cause of morbidity and mortality worldwide. Reports from the Institute of Medicine indicate that improvements to the public health infrastructure are needed globally in order to address the threat of infectious diseases. Illnesses such as HIV, multi-drug resistant tuberculosis, and viral hemorrhagic fevers serve as reminders that infectious diseases deserve continuous concern and care (54).

Due to the nature and overlap of bioterrorism agents and infectious diseases, a unified approach to dual-use surveillance methodologies should be addressed. Existing federal support for bioterrorism could also incorporate infectious disease surveillance and use funds as a means to improve upon existing successes and methods of surveillance that can be used for both purposes (7).

One of the main concerns in regard to infectious disease surveillance is that the reporting has not been as rapid as necessary for bioterrorism detection. If existing infectious disease surveillance and reporting practices are improved upon by eliminating the delay in reporting, reduction of the potential disease and death burden associated with a bioterrorism attack and/or outbreak of an infectious disease could be a result. The threat of a bioterrorism attack and/or infectious disease outbreaks extend beyond U.S. borders, and is now a worldwide problem.

A global response to terrorism would be optimal, and many countries including members of the European Union are planning response strategies. Many of these
countries are looking to the U.S. for best methods and practices for an effective response. Recent gaps in the European Union’s response to global threats have been identified as the need for, anticipation, support, and coordination of bioterrorism preparedness and communicable disease control programs (26).

In the age of working globally to advance the early detection of disease outbreaks, new methods of integrating technologies to allow for “real-time” surveillance is imperative. Research suggests the need to increase the role of computer networking in investigating unusual disease outbreaks and bioterrorism attacks worldwide. With the worldwide threat of infectious diseases and increased international travel, new opportunities to communicate globally could decrease the detection time of a bioterrorism attack (55).
CHAPTER THREE: METHODS

The reason for collecting, analyzing and disseminating information on a disease is to control that disease. Collection and analysis should not be allowed to consume resources if action does not follow.

—Foege W.H., Journal of Epidemiology

ORIGINS OF THE STUDY

In 2000, the University of South Florida, College of Public Health received a contract from the Department of Defense, U.S. Army Soldiers Biological and Chemical Command for research against biological threats. One sub-task of this contract was a research project on surveillance for bioterrorism. Two approaches were defined to include theme parks and schools. This paper summarizes the theme park syndromic surveillance research project. Over time, the study intended for the theme parks evolved to include other special populations that were considered high risk for potential biological threats (8). Theme parks, theme park referral hospitals and clinics, and a military hospital and clinics in the Central Florida area were invited to participate in this study.

STUDY DESIGN

This study summarizes one year of the active, sentinel surveillance system, including a six-month period of baseline data collection. The baseline data served as the comparison for the data collected during the test period. The baseline was also used to
establish thresholds for reporting events that occur at a frequency above normal, and to estimate seasonal patterns and illness trends among the participating sites. The test period served to validate the system. An overall mean was calculated, and a 30-day rolling mean was used to help reduce fluctuations in the data and to adjust for seasonal trends that might affect the analysis. Previous sentinel surveillance programs have been useful in providing information about strains, types, trends, and frequency of influenza in the community (10, 27).

**STUDY AREA AND POPULATION**

The surveillance sites were selected based on their risk of being a potential target of bioterrorism, their geographical proximity to the University, and their willingness to participate. The exact locations and names of the surveillance sites in this study will not be disclosed so that their identities will not be revealed. Government sources report that the theme parks and military facilities are at high risk for bio-threats (8). The parks are considered high-risk because they serve a diverse, global, and highly mobile population, and might be considered prime locations for terrorists to expose large groups of people to the biological agents. Due to varying incubation periods of biological pathogens, the identification of an attack might take time, especially at a theme park. Exposed persons may have returned to their respective countries and illnesses in multiple locations could mask the original exposure site. Therefore, patients might present to the theme park clinics with earlier and less severe symptoms compared to the time and severity of patients visiting an emergency department. Both types of healthcare settings were included to capture both situations.
Telephone and written communication was made to all participating institutions to assess their willingness to participate. The participating institutions were one military hospital and five clinics, two major theme parks, and one theme park referral hospital. For the purposes of maintaining site confidentiality, the theme parks will be called ‘Theme Park A’ and ‘Theme Park B’. The park referral hospital will be called ‘Hospital X’ and the military facility called Military Clinics A-E. These clinics include pediatrics, internal medicine, family practice, and the emergency department. About 75% of the patients served at the theme park referral hospital are guests and employees of local theme parks.

**STUDY CONDITIONS**

The names of each site cannot be disclosed due to verbal and/or written confidentiality agreements. Approval for the study was obtained by a study description protocol submitted to the University of South Florida’s Institutional Review Board. The study was considered exempt, indicating that the study subjects were not identifiable by the information obtained as a part of this study. A copy of the Institutional Review Board approval letter and study protocol was provided to each surveillance site.

**SOURCES OF DATA**

Theme Park A is composed of a main clinic/first aid station and is staffed with nurses, paramedics, and other healthcare staff to provide care for park guests and employees. They also make referrals and transport severely ill patients to a local hospital. For every patient that visited the clinic with an illness, a data collection form was
completed. All injury-related illnesses were excluded. The data collection forms contained demographic information, a choice of syndromes, and a “no syndrome” option. The providers completed demographic information only for patients with a syndrome. The data entry person at this site was also a healthcare provider within interest in the study and requested to be the designated data entry person and site coordinator. Data were entered in as near real-time as possible into the secure Internet site. A few back-up data entry staff persons were designated during the absence of the site coordinator.

**Theme Park B**

Theme Park B was composed of three clinics/first aid stations, and the data entry took place at the administration office. Data collection forms were transferred every few hours or at 4:00pm each day. An administrative staff person served as the site coordinator and data entry person.

**Military Facility**

The military facility/hospital included five clinics, each responsible for designating personnel to enter their data. The public health staff in the facility served as an additional data entry point to help the clinics with data collection responsibilities. Data collection forms were collected multiple times every day by public health staff so that all forms could be archived. The Public Health Commander served as the site coordinator. The data collection forms were uniform at all the military clinics, but differed from the other surveillance sites. A total of 12 syndromes were selected for this site, based on a mandate from the Office of a Military Surgeon General, which stated that the site should assess for
specified syndromes for the purposes of bioterrorism detection in real-time and in all points of patient care. Our surveillance system provided the facility with surveillance tools that met and exceeded the guidelines set forth in the mandate. At the time of implementation, the military had their own bioterrorism surveillance system called ESSENCE that was provided at no cost. However, our system was selected because the data were able to be collected and reported in near real-time. The military surveillance system was based on ICD-9 codes which could take several hours to several weeks to be coded, preventing the system from capturing syndromes reported in near real-time (56).

Hospital X.

Hospital X was the theme park referral hospital that provided care for theme park guests and employees. Data collection forms were similar to the parks, but an additional question assessed which, of any, theme parks the patient visited within the past two weeks. Forms were completed for every patient that visited the emergency department. An administrative staff person in the emergency department was responsible for data entry. Back-up data entry persons included two emergency department administrative staff, and two research coordinators. In the beginning of the study, the site coordinator was the emergency department director, and later due to staff turnover, became the research coordinator.
STUDY IMPLEMENTATION

Case Definitions

Each syndrome was defined by a group of symptoms that are considered early indicators of most infectious diseases of public health importance and biological agent exposures. One of the purposes of this study was to assess baseline levels of each of the syndromes for the purposes of determining thresholds, specific for each syndrome, to serve as the comparison for detecting events occurring above normal frequencies during the test period. During the initiation of this study, before September 11, 2001, few syndromic surveillance systems existed. The literature from these studies did not include a standard list of infectious diseases and bioterrorism agents that the syndromes could represent. The information on possible illnesses indicated by the syndromes was considered necessary for training healthcare providers in this study. A list of possible infectious diseases and biological agents that could be identified through the syndromes was compiled (See Table 4).

Two groups of syndromes were used; one specific for the military, and another for the theme parks. The syndrome list for all facilities except the military began as seven syndromes with a ‘No Syndrome’ option, but during the study an additional syndrome was added. The syndrome added was ‘influenza-like illness,’ and was added in August 2002, at both theme parks and Hospital X for the purposes of assessing for flu season and West Nile Virus. The syndrome list at the military facility included the influenza-like illness.
• Upper or lower respiratory tract infection with fever
  - SARS, Respiratory Syncytial Virus, Pertussis, Inhalational Anthrax, Inhalational Glanders, 2nd state of Hantavirus, Inhalational Ricin exposure, Pneumonic Plague, etc.

• Gastroenteritis
  - Plague, Tularemia, Hantavirus, Q Fever, E. coli, Giaria, Cryptosporidium, Shitgella, Oral Staphlococcus, Salmonella, Paralytic Shellfish Toxins, Rocky Mountain Spotted Fever, etc.

• Rash with fever
  - Smallpox, Glanders, Monkeypox, etc.

• Influenza-like illness
  - Smallpox, Anthrax, Brucellosis, Ebola, Hantavirus, Lassa Fever (most viral hemorrhagic fevers), 1st state of Q Fever, Tularemia, Influenza, West Nile Virus, Glanders, Rocky Mountain Spotted Fever, etc.

• Encephalitis, meningitis, or unexplained acute encephalopathy/delirium
  - West Nile Virus, Japanese Encephalitis, St. Louis Encephalitis, Meningitis, etc.

Table 4. Syndromes as Indicators of Infectious Diseases

Data collection forms were developed by the investigator and customized for each site based on the information already being collected, discussions with providers, managers, and data entry staff. Data collection paper and web forms were customized based on the changing needs of the facilities, and for the purposes of maintaining a low provider burden. The web forms were identical to the paper forms so that data entry would be easy. A copy of each site’s web form is shown in Appendix A.

Study Variables

The demographic information collected varied by site. At all facilities, the demographic information was only collected on ‘syndromic’ reports. For all ‘no
syndrome’ reports, only the ‘date of patient visit’ was collected. If the patient presented with a syndrome, a series of non-identifying information was collected, including a hospital-coded identification number, date and time of visit, date of onset, date of birth, gender, zip code, country of residence, and the last four digits of social security number. A unique patient identification number and/or letter combination was assigned by each surveillance site that could only be used by sites to link the number/letter combination to the patient medical record. During an alert/warning of a possible event, the investigator reported the illness and the patient identification number for the purposes of rapidly retrieving medical records. The patient identification number was meaningless to the investigator, but provided a mechanism for enabling a rapid response by providing the surveillance site staff a quick link from surveillance data to more-inclusive medical records at the site, and could be useful if retrospective treatment was required. This number could not be used to identify the patient by anyone except staff at that site.

The patient’s zip code was collected for future integration with a Geographic Information System to aid in data visualization, and cluster identification. Since it was possible that a patient could visit a theme park clinic and be transferred to Hospital X, making a double entry likely more for serious syndromes, the last four digits of patients’ social security numbers were collected and compared with the birth date and zip code to rule out duplicate reports of the same illness. For example, in the event that a patient visited a theme park clinic and was reported as having the sepsis syndrome, and transferred to Hospital X, the same patient would be reported twice. This would generate two alarms because of the severity of the syndrome and because all the sites had different
methods of assigning identification numbers, the system required a method of detecting
duplicate reports. Since the Health Insurance Portability and Accountability Act of 1996
(HIPAA) regulations went into affect on April 14, 2003, the last four digits of the social
security number have not been collected, and new methods of detecting duplicate reports
will be determined (57).

Site-Specific Variables Collected

The type of data collected varied by site. At Hospital X, there was a question added
to the data collection form that assessed whether or not the patient had visited a theme
park in the past two weeks, followed by a list of four main theme parks. At the military
facility, travel history was assessed for patients that had traveled outside the U.S. in the
past six months. At the theme parks, a question assessed for whether or not the patient
was transported to a hospital.

Data Collection Tool

Several variations of the data collection forms were used and continually updated as
requested by the surveillance sites (See Appendix A). Each form consisted of a short set
of instructions at the top of each page to ensure proper form completion. A phone number
of the site coordinator and the local health department were included at the bottom of the
form.

Introduction Meeting

Introductory Meetings were held with investigators and key personnel at each of the
sites, once they agreed to participate in the syndromic surveillance study. The site
planning staff usually included a director or executive-level staff member, clinic director, nurse, data entry staff person, and computer systems administrator. The study was presented and followed by a discussion of system integration strategies. Issues discussed were clinic and patient flow, system requirements, data collection, Internet accessibility, and any other concerns or questions from site staff. Copies of the presentation, study protocol, phone numbers for the investigator, and Institutional Review Board approval letters were provided to each site.

*Operations Meeting*

Once final corporate approval was obtained and staff members were ready to implement, the second meeting, the Operations Meeting, was held to plan and discuss final study implementation. A walk-through of most clinics helped determine best methods for integrating the system and to assess the current patient flow to identify insertion points for data collection forms, and the best method of transferring the forms for input. A designated basket marked ‘Health Surveillance Forms’ was identified, and was placed in a convenient location for providers for pick-up by the data entry person. The meeting concluded and the data entry person was given a user identification number and password to access the website, and received a brief training on data entry. The sites were provided with a hard copy and a floppy disc of the data collection tool. Colored paper of the site coordinators choosing was provided so that surveillance forms could be copied and easily identified from the other clinic forms. Study implementation began immediately or soon after the operations meeting was held.
Reporting Procedures

When patients visited a surveillance site, a data collection form was placed on top of, or in the patient chart. During the patient visit, the healthcare provider determined the status of the illness and classified the patient as syndromic or nonsyndromic by marking the appropriate checkbox. If the provider reported a patient with a syndrome, demographic information on the patient was collected. If the patient did not present with one of the syndromes, the provider simply checked a box marked ‘no syndrome,’ and the forms were placed in the box marked ‘Health Surveillance Forms’ for data entry. A data collection form was completed for every patient visit at each site (excluding injuries at the theme parks only).

Data Entry and Reporting Procedures

The data collection forms were ideally entered as they were placed in the designated boxes; however, most of the sites collected the forms from the clinics at various intervals throughout the day. The data entry process consisted of logging onto a secure website that required a user identification number and password. Once the website was accessed, a VeriSign™ Certificate confirmed that they were reporting data to the Center for Biological Defense only. Then the staff selected the data entry screen for data entry, the appropriate syndrome was selected and demographic information entered before submitting the record. The nonsyndromic reports were counted and one entry was made after selecting the nonsyndromic option, the system prompted the user to record the date and the number of no syndrome reports. This option was added a few months after study implementation after a surveillance site staff person requested a mechanism to make it
easier to report nonsyndromic data. This method was offered by DataSphere, LLC, and saved time.

Quality control was assessed at some clinics by comparing the total number of syndrome and no syndrome reports to daily clinic logs. This was only conducted a few times due to the difficulties and the amount of time it took for site staff to collect these numbers. The total number of daily reports should always equal the number of persons that visited each site that particular day, except for injury-related illnesses at the parks. This comparison was not possible for the theme parks because their daily clinic logs contained both illness and injury-related reports (without specifying illness or injury status), and for the purposes of this study, only illness-related data were collected.

Efforts were made to assure the consistency of the data obtained. The following actions were taken to support the reliability of the data: training of healthcare providers on syndrome definitions and reporting procedures, training of data entry personnel on form completion and data entry, training and feedback meetings every three months to ensure awareness and knowledge of syndromes and reporting procedures, site-specific newsletters, and continual updates on emerging diseases related to bioterrorism and infectious diseases.

**DATA MANAGEMENT**

The company that developed and maintained the software, and communicated with the investigator for rapid response to site technical requests was DataSphere, LLC. Data were entered into a secure database developed for the purposes of this study. The web forms were connected to a database so that when an authorized user logged onto the
website data could be securely submitted. All of the data were sent across public networks using 128-bit Secure Socket Layer encryption to protect the data by scrambling it during transmission, or making it meaningless if outside sources attempted to access the site. Data were stored in a Structured Query Language (SQL) Server database and resided on a Redundant Array of Inexpensive Disks (RAID) 5 data system to ensure that data were not lost due to hardware failure. Data back-ups were conducted daily to avoid data loss in the event of a system outage. The system was provided under an Application Service Provider (ASP) Software model to reduce costs and to ensure that data were backed up on a timely and routine schedule. The system enabled the option of providing a real-time copy of a given site’s data to a database server local to that facility so that the sites could keep their own data. A secure server then received the data, and as records were added to the database, a trigger initiated a query that calculated and compared the new syndromic data to the baseline for analysis. When the thresholds were exceeded, alerts and warnings were sent in near real-time to the investigator. When changes to the data were needed, such as a report was accidentally reported twice, system programmers edited the data only at the request of the investigator(s), and a record was kept of all changes to the data, along with the dates changes were made, and the user that requested them.

Data Storage

The data were stored in a standard method for a normalized relational database. While this format was not the same as the Center for Disease Control and Prevention’s National Electronic Disease Surveillance System
(NEDSS), customizable interfaces exist and are planned for future system use to provide mechanisms of data transfer to NEDSS, Health Level 7, and the State of Florida’s surveillance system called Merlin.

**Data Confidentiality**

Patient privacy and data confidentiality were maintained by limiting access only to personnel who needed direct access to the database. All other access to the database was completed through the system interface, which required each user to login using a username and password. A given username and password could access only the data designated for that user.

**Records Management**

All of the data were maintained within the system’s database and kept for the entire study period. Archiving was a possible feature provided primarily by the SQL Server, but was not needed in this study because the amount of data did not slow the performance of the system. If this were the case, as could be in the future, the database administrators will require specific policy changes requested, and the database management system software that would perform the task automatically.

**METHODS FOR ANALYSIS**

Once syndromic data were reported into the website, an automated analysis program was developed so that alerts and warnings could be issued in near real-time. The data from all surveillance sites were reported into the same system and accessed from a secure Internet site. This required a username and password, which was changed on several
occasions upon the investigator request. The Internet site housed several tabs that could be accessed to view different types of information. These tabs included an alert and warning list, a reporting page with customizable graphs and a syndrome frequency table, an entry detail list, and a notifications and device subscription listing, see Figures 2-6.

<table>
<thead>
<tr>
<th>Alert List</th>
<th>Graph</th>
<th>Entry Detail</th>
<th>Notifications</th>
<th>Devices</th>
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Figure 2. Alert and warning page from the reporting tool.
Figure 3. Syndrome frequencies and graph from the reporting tool.
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<td>US</td>
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<td></td>
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</tr>
</tbody>
</table>

Figure 4. Entry details from the reporting tool.
Add a New Alert Subscription

Please Select a Syndrome: RTI

Please Select a Facility:

Please Select a Rate of Standard Deviation: 0

(If you leave this set to the default value of zero, you will be notified each time the selected syndrome is reported at the facility that you select for this subscription. Otherwise, you will be notified when the syndrome reports reach your defined threshold.)

Please Select a Notification Device: Amy's E-mail

In order to receive notifications, you must register at least one notification device. This device can be a phone, PDA, computer, or any e-mail enabled device. You will not be able to subscribe to receive alerts until you register a device. To add devices, click on the "Add Devices" tab.

Add Subscription

Active Syndrome-Based Subscriptions

An alert will be sent each time a syndrome of the type specified in the subscription is reported at the selected facility.

<table>
<thead>
<tr>
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<th>Subscription ID</th>
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<th>Syndrome</th>
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<td>Syndrome</td>
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</table>

Figure 5. Notification web screen from the reporting tool.
Figure 6. Device registering page for receiving alerts and warnings, contained in the reporting tool.

**Automated Analysis**

The syndrome frequencies were graphed over time and were listed in a table below the graph (See Figure 3). The graphing tool allowed the investigator to view each syndrome and total entry counts for individual and aggregated sites. Each syndrome was graphed against the 30-day rolling mean, and one or two or three standard deviations above the mean. These thresholds are based on the assumption of normality of the moving average. These values are justified because of the Central Limit Theorem applied to the moving average (58, 59). When a syndrome frequency measured between two and
three standard deviations from the mean, the system issued a warning to the investigator. When a syndrome frequency measured over three standard deviations above the mean, the system issued an alert. For example, we selected two and three standard deviations above the mean as the threshold for issuing a alerts and warnings, and aberrations in the influenza-like illness data were found to were true outbreaks, which validated these thresholds. The system could provide syndromic data in the form of rates and/or frequencies, but due to the high variation in daily total entries, only frequency data were used. The denominator was defined as the total number of entry counts, including syndromic and nonsyndromic data. Automated alerts were issued when any one case of a more serious syndrome was reported, including ‘rash with fever,’ ‘sepsis or non-traumatic shock,’ ‘meningitis, encephalitis or unexplained acute encephalopathy/delirium,’ ‘botulism-like syndrome,’ and ‘unexplained death with history of fever.’ The option of reporting single cases of the more serious syndromes was provided to all surveillance sites, of which all chose to be notified during such an event. The option of changing the number of standard deviations could be completed within the notification page of the reporting tool, see Figure 5.

Not all of the alerts and warnings that the system issued were reported to the sites. For example, some reports were entered into the database twice which could compromise the alerts and warnings. Also, during flu season, more respiratory alerts were issued by the system. The reporting tool contained an alert and warning page listed by individual site alert and/or by combined sites that made up alerts/warnings.
**Graph**

The graphing tool allowed the investigator to view data in a user-friendly graph and tabular format by site or in the aggregate by specified dates, including syndromes graphed by week, month, all data, or custom graph, by rate or raw data. The total number of entry counts was another option and was used to measure the compliance of each site.

**Alerts and Warnings**

The alert and warning web page housed all alerts and warnings since study onset. An option was added that allowed the user to select any of the alerts or warnings. Once a specific alert/warning was selected, a report for that specific alert listed the data entry detail for each report, the facilities involved, the 60-day graph of the syndrome frequency, and a 60-day graph of total entry counts graphed against the means and standard deviations. The report also included information for contacting the site coordinators, and back-up secondary and tertiary contacts were listed in the event that the coordinators were not available. The demographic detail of each syndromic report that made up each alert facilitated rapid epidemiological links. Alerts/warnings could also be issued for increased and decreased total entry counts, however, due to the daily variation in total entry counts, not many of these alerts were issued, see Figure 2.

**Reporting Alerts and Warnings**

Once alerts and warnings were reported to surveillance sites, the sites were responsible for determining whether or not to report the health events to their local health department. The investigator reported alerts and warnings to the sites by phone or e-mail,
depending on the severity of the event. The site surveillance coordinator and the investigator usually worked together to confirm the event, first with data entry staff, then the coordinators initiated discussions with healthcare providers and made the final decision on whether or not to report the event to their local health department for further investigation.

*Entry Detail*

An entry detail tab on the reporting tool contained all case information on every syndrome that was reported to the system. This information included the site name, syndrome, patient identification number, specific clinic within each site, date of visit, date patient became ill, the date and time the syndrome was entered into the website, gender, birth date, zip code, country of residence, 60-day travel history (for military sites only), theme park guest or employee (if applicable), theme park(s) visited within the past two weeks (for theme park referral hospitals and clinics only), and theme park employee work location by department (if applicable). The theme park employee work location was a list provided by each theme park that helped further classify employees within the parks, including operations, culinary services, merchandising, animal training, zoological, engineering, maintenance, entertainment, administration, park services, warehouse, landscaping, and horticulture. This information was obtained for every syndromic case since the onset of the study period and can be accessed at any time from the investigator’s reporting tool.
Notifications

An alert subscription page, as seen in Figure 5, was added to the reporting tool and designed by DataSphere so that the number of standard deviations could be altered to adjust the sensitivity of alerts/warnings. A notification tool was added so the investigator in the form of text messages could receive alerts/warnings. These text messages were sent to electronic devices, such as pagers, mobile phones, and email, or other personal digital assistant, such as the pocket PC phone used in this study. These web-based tools provided the option of selecting the syndrome, site, standard deviation and/or notification device in which to receive alerts and warnings in near real-time. A list of every subscription by user could be viewed and deleted if the analysis parameters appeared to be too sensitive or not sensitive enough. These tools were useful in decreasing the sensitivity during times of known outbreaks, such as flu season, so that alerts would occur daily. This also provided a method for immediate alerts with one report of a serious syndrome, such as botulism-like syndrome.

Device

The ‘device’ page of the reporting tool shown in Figure 6 allowed the investigator to register a personal digital assistant that received email, such as pagers, mobile phones, and pocket PC phones in which to receive alert/warning notifications. The user specified the name, type, and address of the device.
System Changes/Adaptations

‘Influenza-like illness’ syndrome was added in August to assess for potential West Nile Virus and influenza season, and was integrated at the time for traditional influenza surveillance, October to May. This syndrome can also be an important indicator of early exposure to bioterrorism agents and other infectious diseases. Midway through the study, the reporting tool containing the alert and warning listing, entry detail list, notification list, and device listing was offered to the sites that had public health officials or epidemiologists on staff to help interpret data. Each facility that was offered access to their own reporting tool could only view their own data. The military facility and Hospital X were offered and accepted access to their data and the reporting tool.
CHAPTER FOUR: RESULTS

But we are at war now and this is not business-as-usual, we have to do things at a speed that has never been done before.

—Fauci

The entire study was planned for one year, including a six-month period of baseline data collection. The yearlong study period was decreased by five weeks due to changes in reporting requirements by the Health Insurance Portability and Accountability Act of 1996 (57). This analysis includes data reported from May 29, 2002 – April 13, 2003, with the baseline period running from May 29, 2002 – November 29, 2002. The test period was November 30, 2002 – April 13, 2003. The baseline period and test period were compared to determine thresholds for reporting syndromic alerts and/or warnings. This analysis includes data reported from first aid stations/clinics at two major theme parks, one theme park referral hospital emergency department, and one military hospital comprised of four clinics and one emergency department. For the purposes of confidentiality, the actual names of the surveillance sites are be reported, but are referred to as ‘Hospital X’, ‘Military Clinics A-E’, ‘Theme Park A,’ and ‘Theme Park B’.

Overall Data Analysis

The study was conducted for 47 weeks, with a total of 34,664 syndromic and non-syndromic total reports. The baseline study period consisted of 26 weeks, or 16,327 total entries, and the test period was conducted for of 21 weeks with 18,337 total entries.
**Syndromic Distribution**

A total of 2,296 syndromes (6.6% of all data) and 32,368 “no syndromes” (93.4% of all data) were reported. There were 693 syndromes reported during the baseline, and 1,603 reported during the test period. During the overall study, the syndromic distribution by site was composed of 1,351 reports from the military facility, and 673 reports from Hospital X, as seen in Figure 7. The theme park clinics reported fewer patients overall compared to the military facility and Hospital X.

![Syndromic Distribution by Facility](image)

*Figure 7. Syndromic Distribution by Facility*

**Overview of Syndromes Reported**

Figures 8-17 show graphs of each syndrome reported weekly for the overall study period. The most frequently reported syndromes triggering alerts and/or warnings were gastroenteritis, respiratory tract infection with fever, and influenza-like illness. A significant increase in gastroenteritis reports was identified on October 30, 2002, and
continued until April 29, 2003, as shown in Figure 10. There were few overall reports of fever of undetermined origin (this syndrome was only collected at the military facility), with more reports during the baseline period, shown in Figure 16. Respiratory tract infection with fever, influenza-like illness, and febrile illness (febrile illness collected only at the military facility) rapidly increased during the test period, as seen in Figures 8, 9, and 17. The respiratory tract infection with fever and influenza-like illness syndromes increased significantly on November 7 and 11, 2002. The febrile illness syndrome increased during the end of October 2002. Rash with fever reports were generally constant throughout the overall study period, peaking once during the baseline and once during the test period, but the numbers were small, as seen in Figure 11. Figure 12 shows contact dermatitis (a military-only syndrome) reports, which appeared to be reported in clusters, one during the baseline and another one during the test period, but the numbers were low. No reports of the “influenza” syndrome (a military-only syndrome) during the baseline period, and only a few were reported during the test period, as shown in Figure 13. The “influenza” syndrome was mandatory for the military to collect, but probably was not reported by providers because an accurate report of this syndrome would require a laboratory confirmation. This “influenza” syndrome was not assessed at any other facility.

Figure 14 shows the encephalitis/meningitis-like syndromic reports, which were mostly constant during the study period, with only ten total reports. There were only five cases of the non-traumatic shock/sepsis syndrome during the entire study period, and all five cases reported were during the test period, as can be seen in Figure 15. There were
five reports of death with fever and one botulism-like syndrome reported during the entire study period, all of which were misreported.

Figure 8. Respiratory tract infection with fever weekly reports.
Figure 9. Influenza-like illness weekly reports.
Figure 10. Gastroenteritis weekly reports.
Figure 11. Rash with fever weekly reports
Figure 12. Contact dermatitis weekly reports.
Figure 13. Influenza weekly reports.
Figure 14. Encephalitis/meningitis weekly reports.
Figure 15. Shock/sepsis weekly reports.
Figure 16. Fever of unknown origin weekly reports.
Figure 17. Febrile illness weekly reports.

Overall Entry Counts

The total number of entry counts (including syndromic and non-syndromic data) increased over time, and can be seen in Figure 18. Figure 19 shows the distribution of total entry counts by facility. Theme Park B reports were more consistent compared to the other sites. Hospital X’s participation increased over time, as did the military facility. Reporting from Theme Park A declined over time.
Figure 18. Total entry counts for all facilities, May 29, 2002- April 21, 2003

Figure 19. Total Entry Counts by Facility
Figure 20 shows the total number of entry counts (syndromic and nonsyndromic) reported from the military hospital by clinic. Clinics A and C had the highest number of total entries. Reporting in all the clinics was mandatory, but not enforced, except in Clinic A.

<table>
<thead>
<tr>
<th>Clinic</th>
<th>Total Entry Counts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Military Clinic A</td>
<td>8341</td>
</tr>
<tr>
<td>Military Clinic B</td>
<td>1529</td>
</tr>
<tr>
<td>Military Clinic C</td>
<td>4880</td>
</tr>
<tr>
<td>Military Clinic D</td>
<td>3344</td>
</tr>
<tr>
<td>Military Clinic E</td>
<td>74</td>
</tr>
</tbody>
</table>

Figure 20. Total Entry Counts

Figure 21 shows the total weekly entry counts for all facilities during the study period. Overall, reporting increased over time, and was highest during the second week of December. This graph shows the increase in compliance, which was probably attributed in part to customizing the system, providing feedback and training meetings and overall increased awareness of the study among providers.
Figure 21. Total Entry Counts by Week

Syndromic Frequencies

Figure 22 shows the percentages of each syndrome in proportion to all syndromic reports (2296). The most frequently reported syndromes for all sites combined during the overall study period, were gastroenteritis with 898 reports (39.11%), upper/lower respiratory tract infection with fever with 636 reports (27.7%), influenza-like illness at 386 reports (16.81%), and febrile illness with 208 reports (9.06% at military facility). The influenza-like illness was added in mid-September to be able to assess for West Nile Virus and flu season. There were 57 reports (2.48%) of fever of undetermined origin, 38 reports (1.66%) of rash with fever, 30 reports (1.31%) of contact dermatitis, 28 reports (1.22%) of influenza, 10 reports (0.44%) of encephalitis/meningitis, and 5 (0.22%) shock/sepsis reports.
Total Number of Syndromes Reported

- Encephalopathy: 0.44%
- Gastroenteritis: 39.11%
- Influenza-like Illness: 16.81%
- Respiratory Tract Infection: 27.70%
- Febrile Illness: 9.06%
- Fever Unknown Origin: 2.48%
- Influenza: 1.22%
- Shock/Sepsis: 0.22%
- Rash/Fever: 1.66%
- Contact Dermatitis: 1.31%

Figure 22. Total syndromes reported during overall study period.

DEMOGRAPHICS

The demographic information collected as a part of this study included age, gender, and zip code. This information was only gathered on patients that presented with a syndrome. In order to keep the provider burden low, no demographic information was collected on the ‘no syndrome’ reports, (93.4% of all data). In addition, it was decided that data entry persons spent too much time entering each “no syndrome” report. Therefore, all non-syndromic data were entered by clicking on the “no syndrome” option on the website, and typing in the total number of “no syndrome” reports for that period. These changes resulted in a significant decrease in the provider and data entry personnel workload since 93% of all reports were non-syndromic. Since the implementation of this study, other syndromic surveillance systems have implemented this feature, suggesting the impact that this study has had on other bioterrorism surveillance systems outside this
study. The theme park reports were divided into guest or employee categories, and for the employee reports, the department in which they worked was also assessed. Theme park A consisted of seven departments and Theme Park B had 10 departments.

Military Travel History

At the military facility, recent travel history was assessed for patients that presented with a syndrome for the purpose of serving as a potential epidemiological link in the event of a biological release during combat in other countries. A total of 186 patients reported recent travel outside the U.S., and some reports were classified. A complete listing of countries where patients at the military facility reported recent travel cannot be shown due to the sensitivity of the information, but the most frequently reported countries visited were Germany, Afghanistan, Puerto Rico, Mexico, and Qatar. No links or potential exposures were identified during this study with any one syndrome or country.

Hospital X’s Theme Park Visit History

Patients that presented with a syndrome at Hospital X were also asked if they had visited one of four major parks in the Central Florida area during the past two weeks. The most frequently visited parks visited were Disney World (97), Sea World (10), Universal Studios (7), and Busch Gardens (2). Busch Gardens is geographically located further from Hospital X than any of the other listed theme parks.
Country of Origin for Theme Parks & Hospital X Visitors

At both theme parks and Hospital X, the country of origin was reported for all patients with a reported syndrome. At Theme Park A, the most frequently reported country (excluding the U.S.) was the United Kingdom. For Theme Park B, the most frequently reported countries were United Kingdom and Puerto Rico. When combined, the overall most frequently reported countries of origin were the United Kingdom, Canada, and Puerto Rico, as seen in Table 5.
<table>
<thead>
<tr>
<th>Site</th>
<th>Country</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theme Park A</td>
<td>US</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>UK</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Costa Rica</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mexico</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Puerto Rico</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>105</td>
</tr>
<tr>
<td>Theme Park B</td>
<td>US</td>
<td>136</td>
</tr>
<tr>
<td></td>
<td>UK</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Puerto Rico</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Canada</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Colombia</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Denmark</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Germany</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Peru</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>167</td>
</tr>
<tr>
<td>Hospital X</td>
<td>US</td>
<td>618</td>
</tr>
<tr>
<td></td>
<td>UK</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Brazil</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Canada</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Costa Rica</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Japan</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mexico</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Puerto Rico</td>
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</tr>
<tr>
<td></td>
<td>Sri Lanka</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>673</td>
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</table>

<table>
<thead>
<tr>
<th>Totals</th>
<th>Country</th>
<th>Frequency</th>
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<tr>
<td></td>
<td>Brazil</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Canada</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Colombia</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Costa Rica</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Denmark</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Germany</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Peru</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Puerto Rico</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
<td>1</td>
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<td></td>
<td>UK</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>US</td>
<td>851</td>
</tr>
<tr>
<td></td>
<td>Sri Lanka</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Japan</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>945</td>
</tr>
</tbody>
</table>

| Site Totals  |         | 945       |

*Table 5. Country Listing of Visitors from Theme Park A, Theme Park B, & Hospital X*

**Age Distribution**

Birth date was assessed, but for the purposes of aggregating data in this analysis, birth dates were converted to age. Since it was probable that the theme parks served a younger population, two different analyses on age were performed, one for the adult age and another for youth (See Figures 24, 25). The age groups used in this analysis were
defined by standard age groups used in previous studies (60, 61). These age groups were consistently used for all sites.

As can be seen from Figure 23, there were significantly more reports in the 0-14 age group compared to the others. The next largest group was the 25-44 age group. When the 18 and under data were further stratified, there were significantly more reports in the 0-6 age group, as shown in Figure 25.

![Overall Age Distribution of Syndromic Data](image)

*Figure 23. Overall Age Distribution of Syndromic Data*
Overall Youth Age Distribution
Syndromic Data

Figure 24. Overall Youth Age Distribution Syndromic Data

Age Stratified by Facility

Figure 25 shows that when the syndromic data were stratified by age and facility, there were significantly more reports from the military in the 0-14 age group. There were fewest reports in the 65 and over age group.
Overall Age Distribution by Facility

Figure 25. Overall Age Distribution by Facility

Figure 26 shows the youth age stratified by facility. The military facility and Hospital X had more reports in the 0-6 age group.
Figure 26. Youth Age Distribution by Facility

Syndrome Stratified by Age

Figures 27 and 28 show syndromes stratified by the overall and youth age groups. The major differences were that the respiratory tract infection, gastroenteritis, influenza-like illness, rash with fever, febrile illness, and fever of undetermined origin syndromes were much higher in the 0-14 age group compared to other age groups. Gastroenteritis was also high for the 25-44 age group compared to other groups.
When syndromes were stratified by youth age group, the respiratory tract infection, gastroenteritis, influenza-like illness, febrile illness, fever of undetermined origin, and rash with fever syndromes were all much higher among the 0-6 age group compared to the other groups. The frequency of reports of the contact dermatitis, influenza, and encephalitis/meningitis-like syndromes were slightly higher among the 0-6 age group compared to the other groups. There were no shock/sepsis reports among any of the youth age groups.
**Figure 28. Youth Age Distribution by Syndrome**

**Syndromes Stratified by Baseline vs. Test Period by Site**

Appendix F contains supplemental graphs that accompany this text. The respiratory tract infection with fever, gastroenteritis, and influenza-like illness syndromes were higher during the test period than the baseline at the military facility and Hospital X. Rash with fever was higher during the test period at the military clinics, and Hospital X, and more frequent in the baseline at Theme Park A (probably due to a local outbreak of Fifth’s Disease that was detected by the surveillance system). Contact dermatitis was reported only at the military facility, and remained about the same in both periods. There were few overall reports of the encephalitis/meningitis-like syndrome, and no trend was seen during either period. All cases of the shock/sepsis-like syndrome were reported during the test period and were reported only at the military and Hospital X emergency.
departments. The influenza reports from the military facility were all reported during the
test period. Febrile illness reports from the military were consistently higher during the
test period compared to baseline. There were more reports of fever of undetermined
origin during the baseline period at the military facility compared to the test period, but
again, the numbers were very small.

*Syndrome Stratified by Month*

Appendix B contains supplemental graphs that correspond to this section.

Gastroenteritis reports were relatively steady until the end of October 2002, when
significant increases were detected and continued increasing until March 2003.
Respiratory tract infection and influenza-like illness reports were relatively consistent
until November 2002, when both began increasing, peaking in December and January.
Febrile illness reports increased steadily throughout the study, and were highest in
January. Rash with fever reports were highest during July 2002, and January 2003.
Contact dermatitis reports were similar, and peaked during May, June, and July 2002,
and again in mid-November thru mid-December, however, the number of reports was
small. Influenza reports peaked in February. Reports for fever of undetermined origin
were highest in May through July 2002, peaking in December 2002, and March 2003.
Overall, there were fewer reports of fever of undetermined origin than most of the other
syndromes. There was a small cluster of encephalitis/meningitis-like syndrome reports in
July. All the shock/sepsis syndromes were reported January through April 2003, with
most cases occurring during February and March 2003.
Gender

Of the 2,296 syndromic reports, the gender distribution was almost equal, with 49% male and 51% female, as shown in Figure 29. Gender was stratified by site and no significant differences were observed.

![Overall Gender Distribution](image)

**Figure 29. Overall Gender Distribution**

*Syndrome Stratified by Gender*

When syndromes were stratified by gender, there were no significant differences between males and females any syndrome except gastroenteritis, with more women reported than men (497, 401), as shown in Figure 30.
Figure 30. Gender Distribution by Syndrome

Syndromes Stratified by Site

Appendix C contains supplemental graphs that correspond to this section. Increases in the respiratory tract infection, gastroenteritis, influenza-like illness, rash with fever, shock/sepsis, and encephalitis/meningitis-like syndromes were all detected at the military facility clinics one month or more before increases were detected at Hospital X’s emergency department. Increases in gastroenteritis were detected at the clinics (theme park and military clinics) more than two months before increases were seen at both emergency departments (Hospital X and military).

Syndromes Stratified by Theme Parks A and B by Employee Department

Among employees of both theme parks, more syndromes were reported by three departments, including operations, culinary/food services, and merchandising; however,
these three departments were the largest overall distribution of employee departments at both parks. At Theme Park B, the three largest departments were food services (28% of employees), operations (22%), and merchandising (14%). When syndromes were grouped by department at Theme Park B, 38% of the syndromes were from employees that worked in the operations department, 25% in food services, and 11% in merchandising. At Theme Park A, the employee distribution across departments was 34%, culinary services 24%, and merchandising 14%. Thirty-four percent of syndromes were reported from operations, 30% from culinary services, and 14% from merchandising at Theme Park A. The similarities of syndrome reports at both parks appear to be consistent with the employee distribution, suggesting that this study has a representative sample of employees from both parks. See Appendix D for employee and syndromic distributions by departments at both parks.

Baseline Period Data Analysis

Baseline data collection was conducted during the first six months of the study, or 26 weeks, from May 29, 2002 – November 29, 2002. This baseline period was used to establish thresholds for defining alerts and warnings during the test period. During this period, there were 16,327 total reports, including 693 syndromes and 15,634 “no syndromes.” Of the total, 3,768 were reported from Hospital X, 7,859 from Military Clinics A-E, 231 from Theme Park A, and 4,469 from Theme Park B. The most frequently reported syndromes during the baseline period were gastroenteritis, respiratory tract infection, febrile illness, and influenza-like illness. Respiratory tract infection, gastroenteritis, influenza-like illness, and rash with fever were all reported more
frequently during the test period than at baseline. Please refer to Appendix E for supplemental graphs for this section.

Baseline Period at Military Facility

During the baseline period at the military facility, there were no cases of shock/sepsis reported. There were three cases of encephalitis/meningitis-like syndrome reported during June and July. When the baseline reports were compared to the test period, overall the baseline had fewer reports of every syndrome except for the encephalitis/meningitis-like syndrome and the fever of undetermined origin syndrome. Appendix F supplements all site-specific observations related to the baseline data analysis.

Baseline Period at Hospital X

Reports from Hospital X during the baseline period showed no reports of shock/sepsis, very few of the respiratory tract infection with fever syndrome, one report of rash with fever, few reports of influenza-like illness, low but relatively steady reports of gastroenteritis, and only one report of the encephalitis/meningitis-like syndrome. No one syndrome was reported more during the baseline than the test period. Hospital X had lower total entries during the baseline compared to the test period.

Baseline Period at Theme Park B

Only a few cases of respiratory tract infection with fever were reported during the baseline. Equal amounts of rash with fever were reported during the baseline and test
periods. There were no reports of the encephalitis/meningitis-like syndrome. No one syndrome was reported more during the baseline compared to the test period.

**Baseline Period at Theme Park A**

The baseline at Theme Park A showed few, but consistent reports of respiratory tract infection with fever. The rash with fever and gastroenteritis syndromes were reported more often during the baseline than during the test period.

**Test Period Data Analysis**

The test period was conducted for 20 weeks from November 30, 2002 – April 13, 2003. The total number of records reported during this period was 18,337, including 1,603 syndromes and 16,734 “no syndromes.” Of the total reports, 4,661 were reported from Hospital X, 10,949 from Military Clinics A-E, 170 from Theme Park A, and 2,557 from Theme Park B. The most frequently reported syndromes were gastroenteritis, respiratory tract infection, and influenza-like illness. Respiratory tract infection, gastroenteritis, and influenza-like illness, were more frequently reported during the test period, as shown in Figures 31-33. The influenza-like illness syndrome was more frequently reported during the test period, partly due to the late addition of this syndrome to the surveillance system. Rash with fever varied during the baseline and the test periods. The few cases of shock/sepsis were all reported during the test period. Appendix E contains additional graphs for this paragraph.
Figure 31. Baseline vs. Test Period Respiratory tract infection with fever Reported Weekly.
Figure 32. Baseline vs. test period gastroenteritis frequency reported weekly.

Figure 33. Baseline vs. test period influenza-like illness reported weekly.
Test Period for Military Facility

At the military facility, the respiratory tract infection with fever, gastroenteritis, influenza-like illness, rash with fever, shock/sepsis, influenza, and febrile illness syndromes were more frequently reported during test period compared to the baseline, see Figures 34-40). The gastroenteritis and influenza-like illness reports were the highest in December 2002, continuing through February 2003. All of the influenza syndrome were reported during the test period, and highest during February 2003. Febrile illness remained high during the test period, peaking in January 2003. The fever of undetermined origin reports were more frequent during the earlier part of the test period, from November through February 2003, but were lower during the baseline. Appendix F contains graphs for this section.
Figure 34. Baseline and test period reports of respiratory tract infection with fever reported from the military facility.
Figure 35. Baseline and test period reports of gastroenteritis reported from the military facility.
Figure 36. Baseline and test period reports of influenza-like illness reported from the military facility.
Figure 37. Baseline and test period reports of rash with fever reported from the military facility.
Figure 38. Baseline and test period reports of shock/sepsis reported from the military facility.
Figure 39. Baseline and test period reports of influenza reported from the military facility.
Figure 40. Baseline and test period reports of febrile illness reported from the military facility.

Test Period for Hospital X

At Hospital X, the respiratory tract infection with fever, gastroenteritis, influenza-like illness, rash with fever, encephalitis/meningitis, and shock/sepsis syndromes were reported more often during the test period than the baseline period, see Figures 41-46. The largest peak of the respiratory tract infection with fever syndrome occurred in February 2003. Gastroenteritis and influenza-like illness reports were highest during February and March 2003. There were few reports of rash with fever, encephalitis/meningitis, and shock/sepsis during the test period.
Figure 41. Baseline and test period reports of respiratory tract infection with fever reported from Hospital X.
Figure 42. Baseline and test period gastroenteritis reported from Hospital X.
"Influenza-like Illness" at Hospital X

Baseline vs. Test Period

Figure 43. Baseline and test period reports of influenza-like illness at Hospital X.
Figure 44. Baseline and test period reports of rash with fever at Hospital X.
Figure 45. Baseline and test period reports of encephalitis/meningitis syndrome at Hospital X.
Figure 46. Baseline and test period reports of shock/sepsis at Hospital X.

Test Period for Theme Park A

There was one large peak of the respiratory tract infection syndrome during March 2003, see Figure 47. Gastroenteritis reports increased during December and January, as can be seen in Figure 48. There were no other significant differences of syndromes reported during the test period. See Appendix F for graphs corresponding to this section.
Baseline vs. Test Period
"Respiratory Tract Infection w/ Fever"
at Theme Park A

Figure 47. Baseline and test period reports of respiratory tract infection with fever at Theme Park A.
Baseline vs. Test Period
"Gastroenteritis"
at Theme Park A

Figure 48. Baseline and test period reports of gastroenteritis at Theme Park A.

Test Period for Theme Park B

There were two significant increases of gastroenteritis during the test period during the months of January and April, see Figure 49. For additional graphs of Theme Park B, refer to Appendix F.
**Figure 49.** Baseline and test period reports of gastroenteritis at Theme Park B.

**EVALUATION OF SYSTEM**

The system was measured using the Centers for Disease Control and Prevention’s recommendations for evaluating syndromic surveillance systems. The criteria measured included identifying the purpose, the usefulness to stakeholders, and the operational procedures during the study implementation period (3).

Recruitment of surveillance sites was difficult before the September 11 attacks, probably due to the low perceived risk of a terrorist attack occurring in the U.S. The sites appeared to be more willing to participate after the attacks because the threat of a biological attack was likely perceived as real. Hospital X was the most difficult site to recruit, potentially because it was a busy emergency department. Of the sites that agreed
to participate, they reportedly did so in order to protect their guests, employees and community. The overall compliance with reporting increased throughout the study period. The purpose of the study was to serve as a ‘watchdog’ for identifying unusual illness patterns that could be indicators of biological agent exposure for high-risk facilities in the Central Florida area. The goal was achieved, as the system detected several clusters of illness in the community.

**Stakeholders**

The stakeholders at the sites reported being satisfied with the system and plan to continue syndromic surveillance utilizing the BioDefend™ system. Once training and feedback meetings were conducted for healthcare providers at the surveillance sites, it appeared that they had a better understanding of the need to report syndromic data. There was not much resistance to report data at the theme parks, but some resistance was encountered in one busy military clinic. Due to staff turnover at Hospital X, problems were encountered in reporting during the first half of the study, but as the issues were resolved, reporting increased. The overall support of this study by the sites was satisfactory in the beginning, improved over time, and increased training and feedback meetings were held.

**Significant Findings**

The alerts and warnings were divided into a five categories, including the following: individual facility alerts/warnings; syndromic increase at some or all of the sites called combined alerts/warnings; facility-requested alerts/warning of any one case of a serious
syndrome; and significant increases and/or decreases in the total number of entries at any one facility. See Tables 6 and 7 for the syndromic alert/warning report.
<table>
<thead>
<tr>
<th>Number</th>
<th>Date</th>
<th>Syndrome (confirmed frequency)</th>
<th>Useful Information for Epi Links</th>
<th>Action (See text for additional military actions)</th>
<th>Lessons Learned</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6/15/02</td>
<td>Gastroenteritis (5)</td>
<td>4 Employee, 1 guest; 2 employees were from the same department</td>
<td>Site investigation (SI), Medical Record Review (MRR), Provider Discussion (PD)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>7/10/02</td>
<td>Encephalitis/mening (1)</td>
<td>Employee</td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>7/16/02</td>
<td>Encephalitis/mening (1)</td>
<td>Child</td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>7/22/02</td>
<td>Rash with fever (4)</td>
<td>All children from outside U.S.</td>
<td>SI, MRR, PD</td>
<td>Later believed to be part of a local Fifth’s Disease outbreak among children.</td>
</tr>
<tr>
<td>5</td>
<td>7/23/02</td>
<td>Encephalitis/mening (1)</td>
<td>Visit from previous child from 7/16</td>
<td>MRR</td>
<td>Identification number entered incorrectly or system would have detected cases reported within the past 30 days.</td>
</tr>
<tr>
<td>6</td>
<td>8/13/02</td>
<td>Death with Fever (1)</td>
<td>Miss report</td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>8/14/02</td>
<td>Death with Fever (1)</td>
<td>Miss report</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>8/14/02</td>
<td>Botulism (1)</td>
<td>Miss report</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>8/21/02</td>
<td>Encephalitis/mening (1)</td>
<td>Child</td>
<td>SI, MRR, PD Case was later confirmed as viral meningitis.</td>
<td>System detected true case of meningitis in near real-time!!</td>
</tr>
<tr>
<td>10</td>
<td>8/24/02</td>
<td>Gastroenteritis (5)</td>
<td>3 Guests, 2 Employees; All cases under 18; 1 Reported motion sickness; 3 Vomiting; 1 from UK</td>
<td>SI, MRR, PD; Continued watching for more reports.</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>9/12/02</td>
<td>Rash with fever (1)</td>
<td></td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>10/1/02</td>
<td>Rash with fever (1)</td>
<td>Site called this report in &amp; referred patient to hospital. The nurse reported this as a potential measles case.</td>
<td>SI, MRR, PD; Patient referred to hospital. Investigator encouraged provider to follow-up and discussed measles as mandatory report to local health department.</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>11/13/02</td>
<td>Encephalitis/mening (1)</td>
<td></td>
<td>SI, MRR</td>
<td>Data were reported too late.</td>
</tr>
<tr>
<td>14</td>
<td>11/25/02</td>
<td>Encephalitis/mening (1)</td>
<td></td>
<td>SI, MRR</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>11/25/02</td>
<td>Respiratory tract infection with fever (5)</td>
<td>All under 18; All from 2 related clinics</td>
<td>SI, MRR, PD; Public health commander recommends all providers give flu shots to all or most patients.</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Alert and Warning Report: Baseline Period
<table>
<thead>
<tr>
<th>Date</th>
<th>Date</th>
<th>Condition</th>
<th>Case Details</th>
<th>Systematic, Monitoring, Reporting, Disease (S, MRR, PD)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>11/26/02</td>
<td>Gastroenteritis (4)</td>
<td>Five cases reported, but one reported twice.</td>
<td>S, MRR, PD</td>
<td>Site was alerted also on this day with more than its normal total entries. One double entry.</td>
</tr>
<tr>
<td>17</td>
<td>11/26/02</td>
<td>Respiratory tract infection (8)</td>
<td>3 reports within same zip code, mostly adults, one with recent travel history.</td>
<td>S, MRR, PD</td>
<td>Site was alerted also on this day with more than its normal total entries. Alerts 13 &amp; 14 could be attributed to increase in overall entries, or the increase in entries might be attributed to more patients reporting to the facility.</td>
</tr>
<tr>
<td>18</td>
<td>11/27/02</td>
<td>Gastroenteritis (6)</td>
<td>3 from same zip, 2 double entries, 2 from same family</td>
<td>S, MRR, PD</td>
<td>Two double entries. Notified facility of trouble with entering correct patient identification numbers.</td>
</tr>
<tr>
<td>19</td>
<td>11/27/02</td>
<td>Respiratory tract infection (7)</td>
<td>4 Children, 3 adults, most reports from same clinic.</td>
<td>Military public health officer sent email to all providers to give flu shots to all patients.</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>11/27/02</td>
<td>Gastroenteritis (9)</td>
<td>On 11/26, 6 cases reported when sites were combined.</td>
<td>Reported, outcome unknown.</td>
<td>Reporting alerts during baseline was difficult due to no set threshold to report an event.</td>
</tr>
</tbody>
</table>

*Table 6. Alert and Warning Report: Baseline Period (Continued)*
<table>
<thead>
<tr>
<th>Number</th>
<th>Date</th>
<th>Syndrome (confirmed frequency)</th>
<th>Facility</th>
<th>Useful Information for Epi Links</th>
<th>Action (See text for additional military actions)</th>
<th>Lessons Learned</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12/2/02</td>
<td>Respiratory tract infection (8)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td>SI, MRR, PD; Alert email sent to all providers.</td>
<td>An alert was also issued to this facility regarding increased entries.</td>
</tr>
<tr>
<td>2</td>
<td>12/3/02</td>
<td>Influenza-like illness (9)</td>
<td>Military</td>
<td>Mostly middle-aged.</td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>12/3/02</td>
<td>Gastroenteritis (7)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12/5/02</td>
<td>Encephalitis/meningitis (1)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>12/8/02</td>
<td>Gastroenteritis (3)</td>
<td>Park A</td>
<td>2 Employees, all female.</td>
<td>SI, MRR, PD</td>
<td>No major link apparent.</td>
</tr>
<tr>
<td>6</td>
<td>12/13/02</td>
<td>Rash with fever (1)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td>SI, MRR, PD; Site investigation showed all were employees, did not appear to be related.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>12/17/02</td>
<td>Gastroenteritis (6)</td>
<td>Combined</td>
<td>7 Reports, 1 double entry.</td>
<td>Reported, outcome unknown.</td>
<td>1 double entry.</td>
</tr>
<tr>
<td>8</td>
<td>12/20/02</td>
<td>Respiratory tract infection with fever (10)</td>
<td>Military</td>
<td>1 with recent travel history, 3 with same zip, mostly children.</td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>12/30/02</td>
<td>Influenza-like illness (5)</td>
<td>Military</td>
<td>1 with recent travel history.</td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>1/10/03</td>
<td>Gastroenteritis (8)</td>
<td>Combined</td>
<td>3 with recent travel history, two of which are same countries.</td>
<td>Reported, outcome unknown.</td>
<td>2 double entries.</td>
</tr>
<tr>
<td>11</td>
<td>1/10/03</td>
<td>Shock/sepsis (1)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1/10/03</td>
<td>Rash with fever (1)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>1/11/03</td>
<td>Rash with fever (1)</td>
<td>Military</td>
<td>SI, MRR, PD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>1/18/03</td>
<td>Death with fever (0)</td>
<td>Military</td>
<td>3 Cases reported, possible misreported from provider.</td>
<td>SI, MRR, PD</td>
<td>False positive, no actual deaths.</td>
</tr>
<tr>
<td>15</td>
<td>1/21/03</td>
<td>Respiratory tract infection (7)</td>
<td>Military</td>
<td>3 with same zip, most under 18.</td>
<td>SI, MRR, PD</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>1/22/03</td>
<td>Gastroenteritis (9)</td>
<td>Combined</td>
<td>2 reports with same zip.</td>
<td>Reported, outcomes unknown.</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Alert and Warning Report: Test Period.
<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
<th>Location</th>
<th>Details</th>
<th>Notification</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/01/03</td>
<td>Gastroenteritis (3)</td>
<td>Park B</td>
<td>2 emp, both food svcs, same zip, fem</td>
<td>SI, MRR, PD</td>
</tr>
<tr>
<td>23/01/03</td>
<td>Gastroenteritis (7)</td>
<td>Combined</td>
<td>3 employees from one park from same department; 1 with recent military travel</td>
<td>SI, MRR, PD</td>
</tr>
<tr>
<td>2/02/03</td>
<td>Encephalitis/meningitis (1)</td>
<td>Hospital X</td>
<td></td>
<td>Reported to site, outcome unknown.</td>
</tr>
<tr>
<td>2/05/03</td>
<td>Gastroenteritis (9)</td>
<td>Hospital X</td>
<td>4 recent park visitors (2 different parks), 6 were young</td>
<td>Reported to site, outcome unknown.</td>
</tr>
<tr>
<td>2/11/03</td>
<td>Respiratory tract infection with fever (12)</td>
<td>Combined</td>
<td>No apparent links.</td>
<td>Reported, unknown outcome.</td>
</tr>
<tr>
<td>2/12/03</td>
<td>Shock/sepsis (1)</td>
<td>Hospital X</td>
<td></td>
<td>SI, MRR.</td>
</tr>
<tr>
<td>2/16/03</td>
<td>Encephalitis/meningitis (1)</td>
<td>Hospital X</td>
<td></td>
<td>Reported to site, outcome unknown.</td>
</tr>
<tr>
<td>2/17/03</td>
<td>Gastroenteritis (11)</td>
<td>Hospital X</td>
<td>4 were previous park visitors at the same park.</td>
<td>Reported to site.</td>
</tr>
<tr>
<td>2/17/03</td>
<td>Gastroenteritis (13)</td>
<td>Combined</td>
<td></td>
<td>Reported to sites with most cases, outcome unknown.</td>
</tr>
<tr>
<td>2/18/03</td>
<td>Gastroenteritis (14)</td>
<td>Combined</td>
<td>Military &amp; hospital X reported most cases.</td>
<td>Reported to sites, outcome unknown.</td>
</tr>
<tr>
<td>2/27/03</td>
<td>Influenza-like illness (9)</td>
<td>Combined</td>
<td></td>
<td>Investigator sent alerts of recent increase in ILI &amp; GI with de-identified graph to sites, local health department, &amp; CDC.</td>
</tr>
<tr>
<td>3/1/03</td>
<td>Shock/sepsis (1)</td>
<td>Military</td>
<td></td>
<td>SI, MRR, PD</td>
</tr>
</tbody>
</table>

*Table 7. Alert and Warning Report: Test Period (Continued)*
<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
<th>Location</th>
<th>Additional Details</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/4/03</td>
<td>Gastroenteritis (14)</td>
<td>Combined</td>
<td>Reported, outcome unknown.</td>
<td></td>
</tr>
<tr>
<td>3/15/03</td>
<td>Shock/sepsis (1)</td>
<td>Hospital X</td>
<td>Reported, outcome unknown.</td>
<td></td>
</tr>
<tr>
<td>3/16/03</td>
<td>Influenza-like illness (9)</td>
<td>Combined</td>
<td>11 Reports, 2 cases double entered. Reported, outcome unknown. 11 cases reported, after identifying 2 double entries, 9 cases reported.</td>
<td></td>
</tr>
<tr>
<td>3/21/03</td>
<td>Shock/sepsis (1)</td>
<td>Hospital X</td>
<td>Not entered in near real-time. Reported, outcome unknown. Data too old to be useful for early detection of a bioterrorism attack.</td>
<td></td>
</tr>
<tr>
<td>3/22/03</td>
<td>Gastroenteritis (4)</td>
<td>Park B</td>
<td>3 Employees, 2 of these work in food services, 3 are females, all seen at same clinic within the same park. Reported to directors, outcome unknown.</td>
<td></td>
</tr>
<tr>
<td>3/22/03</td>
<td>Gastroenteritis (11)</td>
<td>Combined</td>
<td>No major links. Reported, outcome unknown.</td>
<td></td>
</tr>
<tr>
<td>3/25/03</td>
<td>Gastroenteritis (9)</td>
<td>Combined</td>
<td>10 Reports, one double entry. Reported, outcome unknown. One double entry.</td>
<td></td>
</tr>
<tr>
<td>4/4/03</td>
<td>Gastroenteritis (8)</td>
<td>Park B</td>
<td>3 employees, 1 from UK, 2 with same zip, cases reported from 2 clinics within same park. Reported, unknown outcome.</td>
<td></td>
</tr>
<tr>
<td>4/12/03</td>
<td>Respiratory tract infection with fever (3)</td>
<td>Park A</td>
<td>No links. Reported, unknown outcome. This was a big increase for this particular park, probably due to the recent SARS scare, and the SARS informational meeting with providers.</td>
<td></td>
</tr>
<tr>
<td>4/13/03</td>
<td>Encephalitis/meningitis (1)</td>
<td>Park B</td>
<td>Employee previously exposed to mononucleosis. Reported to directors, providers referred employee to healthcare facility. Symptoms reported here were similar to some symptoms reported with encephalitis, including headache, neck stiffness, fever, etc.</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Alert and Warning Report: Test Period (Continued)
Combined Alerts & Warnings

During the overall study period, there were 15 combined alerts/warnings, 11 of which were alerts and four were warnings. The most frequent syndromes that triggered combined alerts/warnings, were gastroenteritis (11), influenza-like illness (2), and respiratory tract infection with fever syndromes (2). The combined alerts included eight gastroenteritis and two influenza-like illnesses, with the combined warnings including three gastroenteritis, and one respiratory tract infection with fever. One combined alert of gastroenteritis occurred during the baseline study period and the other 14 during the test period.

Facility Specific Alerts & Warnings

The alerts issued to specific facilities during the baseline included four gastroenteritis alerts, two of which occurred at the military facility during November, and two at Theme Park A, one in June and one in August. There were three respiratory tract infections with fever alerts, all three reported at the military facility during the end of November 2002. The first respiratory alert at the military was among children, and the later respiratory alert was among mostly adults. There was one alert of rash with fever at Theme Park A during the month of July 2002, later confirmed as a local outbreak of Fifth’s Disease. Of the four reports of rash with fever, all were children, three from South America and one from the United Kingdom.

During the test period, there were four respiratory alerts and one warning. Three of the alerts and one warning occurred at the military facility during December and January,
and one at Park A during April 2003. Before the respiratory alert at Park A, a request for a training/education meeting was made to discuss the impact of SARS on surveillance. This alert could be attributed to better reporting of respiratory illnesses at Theme Park A.

There were seven gastroenteritis alerts during the test period, including three occurred at Park B, two at Hospital X, one at Park A, and one at the military facility, all during December – April. Two influenza-like illness alerts were issued for the military, both in December 2002. The combined facility alerts for influenza-like illness occurred in late February and mid-March, 2003.

The frequency of syndromes at Theme Park A and B was higher among employee departments that were considered “working areas” of the park where employees interacted with guests, compared to office/support positions in the back areas of the parks.

Facility-Requested Serious Syndrome Alerts

There were a total of 22 alerts, including 10 of the encephalitis/meningitis-like syndrome (six during baseline and four during the test period), five of the shock/sepsis syndrome (all during the test period), six rash with fever alerts (three during baseline and three during the test period), and three death with fever alerts, one of which contained three reports, but all were misreported. Four of the rash with fever alerts were issued to the military facility and two to the parks. Five of the encephalitis/meningitis-like syndrome alerts were issued to the military facility, three to Hospital X, and two to the parks. Three of the shock/sepsis alerts were issued to Hospital X, and two at the military
facility. There was one alert of botulism-like syndrome, but was a misreport by a provider at a theme park.

*Timeliness of Detection Among Clinics vs. Emergency Departments*

The combined alerts were issued for the respiratory tract infection syndrome, and the increase was seen at the clinics (military clinics B-E and all theme park clinics) five weeks before detected in the emergency departments (Hospital X and military emergency department), as can be seen in Figures 50-51. The more serious syndromes were more often reported at the emergency departments at the military facility and at Hospital X.

![Military and Theme Park Clinics Combined
"Respiratory Tract Infection"
Reported Weekly](image)

*Figure 50. Weekly frequency of respiratory tract infection reports from all clinics combined.*
Figure 51. Weekly frequency of respiratory tract infection reports from all emergency departments.

Timeliness of Detection Among Youth vs. Adults

Increases in respiratory tract infection reports were detected two weeks earlier in the less than 18 age group (week 25, in November) compared to the over 18 age group (week 27, in November), as seen in Figure 52. Increases in the gastroenteritis reports were also detected two weeks earlier in the youth age group (week 25) compared to the adult group (week 27, in November), as shown in Figure 53.
Overall Study Period
"Respiratory Tract Infection"
Adult vs. Youth

Figure 52. Respiratory tract infection with fever reports by adult and youth age groups.
Figure 53. Gastroenteritis reports stratified by adult and youth age groups.

Entry Count Alerts

Entry count alerts were issued when the total number of entries increased above normal at any of the sites. There were a total of 13 alerts for significant increases and decreases of entry counts. Eight alerts were issued to sites for decreased entry counts, and five alerts were issued for increased entries. Table 8 shows the entry count alert report.
Entry Count Alert Report for Overall Study Period

<table>
<thead>
<tr>
<th>Number</th>
<th>Date</th>
<th>Site</th>
<th>Issue</th>
<th>Action/Comment/Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8/6/02</td>
<td>Hospital X</td>
<td>Entries were low.</td>
<td>Reported to coordinator, and entries increased the next day.</td>
</tr>
<tr>
<td>2</td>
<td>8/7/02</td>
<td>Park A</td>
<td>Entries were low.</td>
<td>Reported to coordinator and she stated that overall park attendance was low.</td>
</tr>
<tr>
<td>3</td>
<td>9/12/02</td>
<td>Hospital X</td>
<td>Entries were high.</td>
<td>Backlogging data to catch up (data entry staff previously on vacation).</td>
</tr>
<tr>
<td>4</td>
<td>10/10/02</td>
<td>Hospital X</td>
<td>Entries were high.</td>
<td>Backlogging data. Appointed a secondary data entry staff.</td>
</tr>
<tr>
<td>5</td>
<td>11/18/02</td>
<td>Military</td>
<td>Entries were low.</td>
<td>Reported to coordinator.</td>
</tr>
<tr>
<td>6</td>
<td>11/21/02</td>
<td>Park A</td>
<td>Entries were low.</td>
<td>Park attendance was down, and very few patients were seen.</td>
</tr>
<tr>
<td>7</td>
<td>11/26/02</td>
<td>Military</td>
<td>Entries were high.</td>
<td>All clinics are better at reporting, more gastroenteritis and respiratory tract infections reported (2 alerts).</td>
</tr>
<tr>
<td>8</td>
<td>12/2/02</td>
<td>Military</td>
<td>Entries were high.</td>
<td>Alert to military facility about frequent reports of respiratory tract infection with fever syndrome.</td>
</tr>
<tr>
<td>9</td>
<td>12/23/02</td>
<td>Military</td>
<td>Entries were low at a few clinics.</td>
<td>Reported to site coordinator.</td>
</tr>
<tr>
<td>10</td>
<td>1/13/03</td>
<td>Military</td>
<td>Entries were low at a few clinics.</td>
<td>Reported to site coordinator.</td>
</tr>
<tr>
<td>11</td>
<td>1/14/03</td>
<td>Military</td>
<td>Entries were low at a few clinics.</td>
<td>Reported to site coordinator.</td>
</tr>
<tr>
<td>12</td>
<td>1/28/03</td>
<td>Military</td>
<td>Entries were high.</td>
<td>Alert for military with frequent reports of respiratory tract infection with fever syndrome.</td>
</tr>
<tr>
<td>13</td>
<td>3/17/03</td>
<td>Hospital X</td>
<td>Entries were low.</td>
<td>Patient volume was down.</td>
</tr>
</tbody>
</table>

Table 8. Entry count alert/warning report.

Low Entry Count Alerts

Low entry count alerts were issued to help maintain compliance. Four low entry count alerts were issued to the military facility, two to Hospital X, and two to Theme Park A. The decreased entry count alerts at Theme Park A was due to overall low park attendance, and was confirmed by a park director. The military facility received several low entry alerts January 2003, due to deployments related to the war in Iraq.

High Entry Count Alerts

The high entry count alerts corresponded to syndromic alerts related to the respiratory tract infection with fever and gastroenteritis. It is not known whether the syndromic alerts can be attributed to the increased total entries on those dates, or whether more people presented to the facility. Hospital X reported backlogging data twice
because the data entry staff person was on vacation. As a result, other people were
assigned to enter data in her absence.

Reporting Errors

There were six reporting errors, including five death with fever reports, all of which
were misreported by healthcare providers. There was one report of botulism-like
syndrome, also misreported by a healthcare provider at a theme park, who misunderstood
the case definition of botulism. There was one misreport of the encephalitis/meningitis-
like syndrome reported from the military facility. Entering duplicate reports appeared to
be more problematic than the misreports of syndromes. Although the system was built to
recognize when duplicate records were reported, when the number/letter combination
were reported in reverse order, the system was unable to determine when duplicates had
been reported. This was more problematic at the military facility compared to the other
sites because the patient identification letter/number combination was developed for the
purposes of this study, and was collected routinely, which made it difficult for providers
to remember the order in which the letters and numbers were placed.

Outbreak Detection

There were two significant outbreaks detected with the system. Significant increases
in gastroenteritis reports were detected on October 30, 2002, and continued increasing
through April 29, 2003, as shown in Figure 54. Influenza-like illness reports also
increased significantly on November 11, 2002 and continued until March 20, 2003, as
can be seen in Figure 55. Significant increases in the respiratory tract infection syndrome
were detected on November 7, 2002 and continued until March 11, 2003, as can be seen in Figure 56. A total of 10 individual reports of the encephalitis/meningitis-like syndrome were detected, two of which were among children under the age of 15 years. Another encephalitis/meningitis alert was issued to a clinic and was later confirmed by a laboratory test as viral meningitis. There were five individual shock/sepsis reports identified from the emergency departments. A rash with fever outbreak was detected at Theme Park A, and was later identified as a local outbreak of Fifth’s Disease among children. Of the cases that were reported to this system, all but one were international guests, all children, and all but one report was from South America, and one from the United Kingdom.

Figure 55. Daily influenza-like illnesses reports from all sites.

Figure 56. Daily respiratory tract infection with fever reports from all sites.
A gastroenteritis warning was issued to Theme Park B, and when the alert report was viewed, all were female, in their 40’s, living in the same zip code, and working in culinary services. During the baseline period in this study, reports of gastroenteritis at one park were detected, but were not significant. These reports could have been part of a national outbreak that originated at a Central Florida theme park that was not a part of this study. A salmonella outbreak of more than 300 persons was detected by the Minnesota Department of Health two months after it occurred. This particular park was hosting the transplant games, where persons that were recipients and organ donors and their families were in attendance, some of whom were immunocompromised. The Centers for Disease Control and Prevention conducted a retrospective investigation by emailing participants that had an email address to determine if anyone in their household had become ill after attending the theme park event. Around 300 persons responded that at least one person in their household was sick. About half of these had been receiving immunosuppressive therapies and some were hospitalized. If this particular park had implemented this surveillance system, the outbreak might have been detected earlier and might have provided early intervention for those ill (62).

**Comparisons with State, Regional, and National Data**

State, regional, and national data were used to compare significant increases of the gastroenteritis, respiratory tract infection with fever, and influenza-like illness syndromes. Significant increases of gastroenteritis reports were detected in this study on October 28, 2002, and continued through April 2003, as can be seen in Figure 54. The increase was significant because it was detected more than one month before identified
by the Florida Department of Health’s statewide Norovirus surveillance of institutional settings (e.g. long term care facilities, assisted living facilities). State officials reported the increase in Norovirus-positive specimens during the end of November and the beginning of December (Figure 57). By the time the report was available, it was February 2003, more than three months after it was identified using the BioDefend™ system (63).

At the same time as the increases in gastroenteritis reports in Florida and those observed in this study, the Centers for Disease Control and Prevention reported an increase in Norovirus among several states, including Washington and New York. The Washington study reported an increase in November-December. New Hampshire reported 35 outbreaks of similar gastroenteritis-related illnesses identified from clinics that were consistent with norovirus infection. In New Hampshire, emergency department syndromic surveillance detected increases in gastroenteritis reports in December 2002. In New York City, a total of 66 outbreaks were detected in November 2002, and were consistent with norovirus infection. Personal communications with Epidemic Intelligence Service Officers from the Centers for Disease Control and Prevention suggested that Norovirus activity was on the rise nationwide during this time of the increase in gastroenteritis reports detected in this study. The officials attributed this rise to an increase in community incidence of norovirus infection, as was suggested in New York City and New Hampshire. Also during this time, the Norovirus activity on cruise ships occurred in June – December 2002, with a flurry of activity in October. Two of the five outbreaks originated in Florida, and two included travel in Florida (64, 65).
Figure 57. Positive Norovirus Submissions Reported from Florida Department of Health

Figure 58. Florida Department of Health Influenza-Like Illness Surveillance Data
Figure 59. South Atlantic Region Influenza-Like Illness Surveillance Data for 2002-2003

Figure 60. National Summary of Influenza-Like Illness Surveillance Data for 2002-2003
Figure 61. National Summary of Influenza Isolates for 2002-2003 Influenza Isolates from the South Atlantic Region Reported by WHO/NREVSS Collaborating Laboratories 2002-2003 Season

Figure 62. South Atlantic Region Influenza Isolates for 2002-2003
As a result of the gastroenteritis increases, the surveillance sites were notified as well as public health officials at the county health departments, the state department of health, and the Centers for Disease Control and Prevention’s syndromic surveillance section and food borne surveillance sections.

Influenza-like illness sentinel surveillance data were used as a comparison for the data captured with the BioDefend™ system. Increases in the Florida Department of Health’s influenza-like illness sentinel surveillance system detected increases during the first week of January, 2003, more than one month after significant increases were detected in this study, as shown in Figure 58 (66). Data for influenza-like illness was also available for the South Atlantic Region, which included the states of Florida, Tennessee, Georgia, South Carolina, North Carolina, Virginia, West Virginia, and Maryland. The regional increases were detected during the last week of December 2002, again one month after detected in this study, as shown by Figure 59 (67). National influenza-like illness surveillance data reported by the Centers for Disease Control and Prevention also revealed significant increases above normal during the last week of December 2002, as can be seen in Figure 60 (68). In addition, influenza laboratory data from the National Respiratory and Enteric Virus Surveillance System detected increases in positive influenza specimens in December 2002, as shown in Figure 61 (69). Influenza isolates from the same laboratory specific for the South Atlantic Region showed increases during January 2003, again more than one month after detected in this study, as shown in Figure 62 (70).
Outbreak Response

When an alert/warning was detected by the system, the first step was for the investigator to determine if the cases appeared to be epidemiologically linked, specifically by looking at the alert/warning report details that included the zip code, age, gender, employee/guest, travel history, country of origin, and date of illness. Alerts and warnings were issued via phone call or email to the site coordinators. If the event appeared serious, repeated phone calls were made until a site coordinator or a secondary or tertiary contact was reached. In addition, an email was sent with the patient identification number, syndromic and demographic information of the reports. If the event appeared to be real, the site coordinator usually reviewed the medical records and tried to confirm the syndromic report by initiating discussions with the provider that treated the patient(s). The appropriate actions were determined by the sites. The final decision regarding the alert was made based on the outcome information from the syndrome report, medical record, provider discussion, any lab confirmation tests, and/or discussions between the investigator and site coordinator. The primary site coordinators worked in administration, public health director positions, or had the authority to determine the appropriate actions taken.

Health departments in the areas of the surveillance sites were notified of the study before implementation. To the best of our knowledge, there were no investigations conducted on the basis of alerts/warnings reported from this study by the health departments or the Centers for Disease Control and Prevention. The local health departments were contacted regarding the significant increases in the gastroenteritis and
influenza-like illness syndromes at all sites. This alert was also sent to the Epidemic Intelligence Service Officers in the syndromic surveillance and food borne outbreak branches of the Centers for Disease Control and Prevention.

The actions corresponding to alerts and warnings were divided into one of five categories; 1) site investigations, 2) health department investigations, 3) no investigation conducted, 4) false alarm, or 5) unknown. The surveillance sites were under no obligation to inform the investigator regarding the outcome of any investigation. If an investigation was conducted by either the site or health department, one of three events occurred; 1) nothing could be done about it, 2) an intervention was conducted, or 3) the event was not considered serious enough for an intervention.

Interventions/PH Actions Resulting from Alerts

At the military facility, the public health commander reported several interventions that resulted from being issued the alerts and warnings received from this study. Several informational bulletins were issued from the military public health units to all hospital and clinic staff about surveillance findings and recommendations. Significant alerts and/or findings were discussed in Medical Intelligence briefings to the hospital commander. In the individual clinics, time was set aside to discuss surveillance updates and related issues at staff meetings. Surveillance findings were shared with the Mobility Command Public Health Staff for dissemination to the entire national Command in their respective branch of service. The military findings from this study and the system will be presented at the national surveillance meeting for this particular branch of service in 2003. All other surveillance sites followed up on alerts and/or warnings by reviewing
medical records, provider discussions, infection control and/or discussion in regularly scheduled meetings. Hospital X used laboratory data to help confirm alerts. As a result of the influenza-like illness and respiratory tract infection alerts, the military public health unit sent specific orders to all providers stating that the flu shot be given to all patients. This email was sent out on November 25, 2002, and one month later the number of cases dropped at this facility only.

**Outcome Evaluation at the Military Facility**

Due to the increased workload on the investigator, an assistant was hired to help with site communication, reviewing data, continual system improvement and integration, and evaluating site procedures. This assistant conducted evaluations at the military facility to assess reporting procedures. The evaluator was a new employee to the Center for Biological Defense at the University of South Florida, and was not known among the site staff at the time of the evaluation. The goal of having an unknown person conduct the evaluation was for the purpose of having a more objective observation of the overall reporting process, awareness, and knowledge of the surveillance study. The primary issues encountered by the evaluator were the lack of knowledge of the study and reporting procedures among the staff. Her recommendations for improving reporting were to install the digital bridge to automatically retrieve data from their electronic patient information system, for the purposes of ensuring compliance. She also recommended incorporation of a system introduction and syndromic training meeting at each clinic to ensure the staff had a good understanding and knowledge of expectations, and so they had all the resources to make accurate reporting possible.


**Compliance**

Estimates of compliance were not obtained due to the difficulties sites had in reporting the daily number of visits in each clinic. Assessing the completeness of reporting was difficult due to the large variations in theme park attendance, which affected the number of visits to the first aid station/clinic and the referral hospital. Also, during this study, large numbers of military personnel were being deployed for war, which greatly affected compliance and the number of clinic visits.

Hospital X had lower overall reporting during the baseline period. This was partly due to administrative changes, and the lack of awareness of the study among healthcare providers and support staff. Once new administration staff was assigned to the study, reporting increased significantly.

For the theme parks, there were no clinic logs to show the number of persons seen per day that presented with an illness. Neither park could give estimates of the number of daily visits because they varied so much day-to-day by factors such as the weather, the economy, terrorist events from September 11, and other factors influencing theme park attendance. These factors also affected the referral hospital, Hospital X.

The military hospital/clinics were not able to give estimates of the average number of daily visits per clinic. Several events might have influenced the compliance during this study, including the deployment of staff to war.
Flexibility

An important requirement of the syndromic surveillance system selected for this study was the ability to continually modify the system for each site. Data collection forms, reporting procedures, and data parameters were customized for each site. This was imperative to the success of the study, and did not compromise the integrity or comparability of data between sites. Each surveillance site had unique needs and had specific requirements for integrating the system while keeping the burden on healthcare providers low.

Two aspects of the system allowed for rapid changes to be made to meet the needs of the sites, first the system was written using Microsoft.NET development tools and architecture. The use of these tools, along with modern programming techniques, allowed BioDefend™ to be written in a highly modular fashion where changes could be made to one module without affecting the other modules. Secondly, the procedures at DataSphere allowed requested changes to be made in a timely manner.

Timeliness

The timeliness of reporting (when a patient presented with symptoms to the time of data entry) was assessed for syndromic data and was measured by the log of the time the records were reported from the sites, and compared to the date and time of patient visits. Timeliness was assessed for combined and individual sites, as shown in Table 3. Data were categorized into less than six hours of the patient visit, between six and 12 hours,
12-24 hours, or over 24 hours. Table 9 shows the timeliness of reporting for the combined and individual site data. The facility with the most reports in the less than six-hour category was Park A. Park A also reported less patient visits overall compared to the other sites, perhaps allowing more time for data reporting. The military facility had the second highest percentage of reports entered in less than six hours. It also appeared that smaller clinics that provided cared for fewer patients also reported data more timely compared to the emergency departments.

Of all syndromic data, 67.4% were reported more than 24 hours after the patient visit. During the baseline period, 18.6% of the data were reported within six hours of the patient visit, but declined to 9.1% during the test period. This decline in the timeliness of reporting could be a factor of increased reporting. At Hospital X, 93.6% of the data during the baseline and 78.1% during the test period were reported in excess of 24 hours following the patient visit. Although this suggests a slight improvement in the timeliness of reporting, automated data collection may be required in order to receive more timely data.
### Table 9. Timeliness of Reporting Syndromic Data

<table>
<thead>
<tr>
<th></th>
<th>Baseline Pd. (%)</th>
<th>Test Pd. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Sites</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6hrs</td>
<td>129 (18.6)</td>
<td>145 (9.1)</td>
</tr>
<tr>
<td>6-12 hrs</td>
<td>45 (6.5)</td>
<td>95 (5.9)</td>
</tr>
<tr>
<td>12-24 hrs</td>
<td>66 (9.5)</td>
<td>268 (16.7)</td>
</tr>
<tr>
<td>&gt; 24 hrs</td>
<td>453 (65.4)</td>
<td>1095 (68.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>693</td>
<td>1603</td>
</tr>
<tr>
<td><strong>Military Facility</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6hrs</td>
<td>105 (21.4)</td>
<td>106 (12.5)</td>
</tr>
<tr>
<td>6-12 hrs</td>
<td>26 (5.3)</td>
<td>52 (6.1)</td>
</tr>
<tr>
<td>12-24 hrs</td>
<td>45 (9.2)</td>
<td>157 (18.5)</td>
</tr>
<tr>
<td>&gt; 24 hrs</td>
<td>314 (64.1)</td>
<td>536 (63.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>490</td>
<td>851</td>
</tr>
<tr>
<td><strong>Hospital X</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6hrs</td>
<td>0 (0)</td>
<td>16 (2.6)</td>
</tr>
<tr>
<td>6-12 hrs</td>
<td>0 (0)</td>
<td>31 (4.9)</td>
</tr>
<tr>
<td>12-24 hrs</td>
<td>3 (6.3)</td>
<td>90 (14.4)</td>
</tr>
<tr>
<td>&gt; 24 hrs</td>
<td>44 (93.6)</td>
<td>489 (78.1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>47</td>
<td>626</td>
</tr>
<tr>
<td><strong>Theme Park B</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6hrs</td>
<td>4 (4.9)</td>
<td>10 (11.8)</td>
</tr>
<tr>
<td>6-12 hrs</td>
<td>1 (1.2)</td>
<td>4 (4.7)</td>
</tr>
<tr>
<td>12-24 hrs</td>
<td>15 (18.3)</td>
<td>17 (20)</td>
</tr>
<tr>
<td>&gt; 24 hrs</td>
<td>62 (75.6)</td>
<td>54 (63.5)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>82</td>
<td>85</td>
</tr>
<tr>
<td><strong>Theme Park A</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6hrs</td>
<td>20 (31.3)</td>
<td>13 (31.7)</td>
</tr>
<tr>
<td>6-12 hrs</td>
<td>8 (12.5)</td>
<td>8 (19.5)</td>
</tr>
<tr>
<td>12-24 hrs</td>
<td>3 (4.7)</td>
<td>4 (9.8)</td>
</tr>
<tr>
<td>&gt; 24 hrs</td>
<td>33 (51.6)</td>
<td>16 (39.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>64</td>
<td>41</td>
</tr>
</tbody>
</table>
DATA QUALITY

*International Data*

The country of origin was assessed for park visitors, as shown in the country listing in Table 10. Most persons were from the United States, and the most frequently reported countries of origin from the theme parks were the United Kingdom, Canada, and Columbia. Also, not shown in this analysis was the recent travel history (the past 30 days) for patients that presented with a syndrome at the military facility.

*Completeness of Data*

The most frequently missing data elements were the last four digits of the social security number, illness dates, zip codes, and birth dates. All other demographic information was required, and the system would not allow records to be submitted until these fields were complete.

EXPERIENCE

*Usefulness*

Perhaps one of the most important aspects of this study is a demonstration that the use of technology and automated analysis for the detection of outbreaks in near, real-time for public health surveillance is possible. The usefulness could perhaps be seen in the following scenario, as a patient enters the clinic with smallpox-like symptoms, the data is entered automatically while the patient is still in the clinic. With the ability to detect one severe illness in near, real-time, the patient could be quarantined until lab confirmation.
was completed, thus reducing community exposures and transmission and perhaps halting the introduction of the agent to the population at-risk. The system was useful for the military hospital/clinics as noted by the public health commander, reporting that this study helped bridge communications between the medical clinics and public health unit. The theme parks also reported that the system was useful, especially by having access to employee illnesses. They also reported that during the SARS outbreak, the system provided staff with more security and assurance of detecting a potential bioterrorism event early.

Acceptability

The surveillance system was accepted by all of the participating surveillance sites. Resistance was encountered from a few physicians at the military hospital, often physicians with little or no public health training or understanding of the usefulness of surveillance. Over time, as alerts were reported, trainings were held, acceptability among all sites continued to increase.

Generalizability

Although the results from this study do not apply to other geographical locations, the system itself could be replicated elsewhere. The BioDefend™ system could be used in a variety of settings using the same or similar methodologies described in this study.
Stability

There were three system outages during the study period, but were repaired within a few hours once programmers were notified of the error(s). The cause for the outages were due to faulty upgrade procedures on the software. No data were ever lost.

Simplicity

The data forms were easy to complete, especially for “no syndromes.” The forms and reporting procedures were customized for each site so that they would better integrate into routine practices at each site. The reporting procedures were also simple (62).

Cost

The cost of implementing this surveillance system using the BioDefend™ software developed by DataSphere in five military clinics, two theme parks, and one hospital was $27,400 (See Table 10). A breakdown of this total includes a one-time setup price of $13,000 plus the monthly fee of $1,200 per month for 12 months (totaling $14,400 per year) for a total of $27,400 for the entire study. The cost of an additional year would be $14,400. The initial set-up fee was $1,000 per facility and $200 per site (each site refers here to each specific clinic/first aid station within each facility). The reporting tool, or data analysis software was installed for the investigator and for sites interested in viewing their own data. The cost of the reporting tool varied depending on whether it was for the investigator (for viewing all data) or for a specific facility (to view site-specific data). The cost of the reporting tool for the investigator was $1,000 per user with a minimum
five users. The cost of the reporting tool for each facility was $1,000 with a minimum of two users.

<table>
<thead>
<tr>
<th>BioDefend™ Cost</th>
<th>Quantity</th>
<th>Facilities</th>
<th>Sites</th>
<th>Total Setup fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital Bridge</td>
<td></td>
<td>0</td>
<td>0</td>
<td>$5,000.00 per Facility</td>
</tr>
<tr>
<td>Initial Setup Services</td>
<td>4</td>
<td>10</td>
<td></td>
<td>6,000 $1,000.00 per Facility and $200 per site</td>
</tr>
<tr>
<td>Reporting for Investigator</td>
<td>1</td>
<td>0</td>
<td></td>
<td>5,000 $1,000.00 per user, minimum 5 users</td>
</tr>
<tr>
<td>Reporting for Facility</td>
<td>2</td>
<td>0</td>
<td></td>
<td>2,000 $1,000.00 per user, minimum 2 users</td>
</tr>
</tbody>
</table>

**One-Time Setup Total** $13,000

<table>
<thead>
<tr>
<th>BioDefend™ Cost</th>
<th>Quantity</th>
<th>Total</th>
<th>Monthly Fees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital Bridge</td>
<td>0</td>
<td>$0.00</td>
<td>$500.00 per site</td>
</tr>
<tr>
<td>Web entry form</td>
<td>4</td>
<td>$200.00</td>
<td>$50.00 per site</td>
</tr>
<tr>
<td>Reporting for Investigator</td>
<td>1</td>
<td>$500.00</td>
<td>$50.00 per reporting site</td>
</tr>
<tr>
<td>Reporting for Facility</td>
<td>2</td>
<td>$500.00</td>
<td>$250.00 per reporting site</td>
</tr>
</tbody>
</table>

**Total Monthly Fee** $14,400

| Overall Cost | $27,400 | For each additional study year $14,400.00 |

**Table 10. BioDefend™ Study Cost**

**Communication**

There was much communication between surveillance sites and the investigator during this study. Weekly discussions at most sites during the first few months of implementation aided in system customization, requirements, planning of training meetings, and to troubleshoot any issues related to surveillance. A phone number was
provided to all the sites in the event that there was a problem with the system or questions about study procedures or syndromes during anytime during the study period. This phone number was linked to a pocket PC phone maintained by the investigator to receive and report automated alerts and warnings in near real-time, and to view data. The pocket PC phone is shown in Figure 57, and is a hand-held phone and mini computer with wireless access to the Internet. Data could be viewed by accessing the system website and logging onto the reporting tool. Alerts were received in text messaging format with the syndrome, syndrome frequency, patient identification number, facility, clinic name, and contact numbers at the site(s).

Figure 63. Pocket PC phone
LIMITATIONS OF FORMAL HYPOTHESIS TESTING FOR SURVEILLANCE DATA

There are limitations of using surveillance data for hypothesis testing, such as the absence of cases and controls, and the lack of a controlled environment. However, the usefulness of this system in the early detection of an epidemic and/or biological attack is likely to outweigh the cost for response.

Research Question 1

Can a syndromic surveillance system identify communicable diseases of public health importance before routine surveillance methods?

Hypothesis

Incorporating near real-time reporting techniques with automated analysis and notification would reduce the detection time by hours, days, or weeks.

It is somewhat difficult to compare syndromic data to specific illness data due to the nonspecific nature of the syndromes. Detecting communicable diseases earlier with syndromic surveillance systems compared to with routine surveillance has been shown in this study with the early detection of the gastroenteritis and influenza-like illness syndromes more than one month before data from other state, regional, and national surveillance systems. The integration of state-of-the-art technology can enable the early detection of a bioterrorism attack or infection disease outbreak compared to traditional surveillance methodologies.

The best example of detecting a significant community-wide increase of a communicable disease in this study can be seen with the significant increase of
gastroenteritis reports on October 30, 2002, compared to state data that reported on February 13, 2003 that increases of positive Norovirus specimens were detected during the end of November, as shown in Figure 54 and 57. By the time the data were reported by the state, they were already old, and preventing further exposure was a greater challenge than if the outbreaks had been detected earlier. Although syndromic surveillance for the purposes of bioterrorism is a relatively new public health discipline, the potential for using syndromes as early indicators of community outbreaks, combined with state-of-the-art technology can rapidly decrease the time of detecting infectious diseases epidemics, whether spread naturally or intentionally by way of a bioterrorism attack (63).

By comparing the influenza-like illness data from state, regional, and national surveillance and laboratory data, the same early detection pattern with the BioDefend™ system was identified more than one month before detected in any of the other systems compared. On November 11, 2002, significant increases in influenza-like illness reports were detected in this study. The Florida Department of Health data detected increases in influenza-like illness reports (from institutional settings) during the first week of January 2003, almost two months after detected by the BioDefend™ system. The South Atlantic Region and national data did not detect the increases in their influenza-like illness data until the last week of December 2002, which was more than one month later than this study (66-70).
Research Question 2

Is syndromic surveillance a reasonable approach for bioterrorism preparedness and should it be incorporated into the public health infrastructure even if the threat of bioterrorism disappears?

Hypothesis

Syndromic surveillance may identify illnesses of public health importance early enough to reduce or prevent disease and death, which could make it worthy of incorporating into the public health and medical infrastructure.

Considering the federal dollars that have been spent on bioterrorism preparedness over the past two years, and how there is still much more information needed to identify the best methods and locations of early exposures, the best use of existing bioterrorism funds would be for early detection. Since it is not likely that we can prevent terrorist groups from making, storing, and/or using weapons of mass destruction, preventing a bioterrorism event is not practical, at least from the public health point of view. However, the best mechanism of prevention and preparedness is identification of the attack with near real-time reporting and notification of illnesses. In order to do this, we must have a good, accurate, and timely estimates of the normal frequency of infectious diseases occurring in the population of interest at any given time. In addition, real-time surveillance methods can only strengthen and improve existing surveillance of infectious diseases. The cost of implementing the BioDefend™ system is not high, especially given the cost of responding to an attack and/or epidemic. The BioDefend™ syndromic surveillance system used in this study can be implemented in most any setting in the
United States. It should also be noted that not only has this system been easily implemented, but the design is simple, flexible, and has also been accepted by the institutions currently using it.

We do not yet know the effect of having real-time frequencies of infectious diseases present in a population, but this knowledge should serve to prevent more illness and death from community outbreaks and a bioterrorism attack. By establishing normal thresholds of certain illnesses in a population, one can quickly know through the use of automated analysis when illnesses within that population increase above normal. Syndromic surveillance is a simple concept and can be readily implemented in most any healthcare facility. It is easy to implement and costs much less than responding to and treating 100,000 people exposed to anthrax or the plague. We know that the potential economic impact of a bioterrorism attack is extremely high, and would drain a vast majority of community, state, and federal resources, both human and financial. The cost of exposing 100,000 people to Bacillus anthracis is about $26 billion, and if another 100,000 people were exposed to Brucella melitensis, the estimated cost burden is approximately $478 million (5).

Based on these costs, authors from the Centers for Disease Control and Prevention have previously recommended rapid implementation of post attack prophylaxis programs as the most important means of reducing the human losses (11). Preventing transmissions and reducing exposures through early detection can better minimize human and financial losses compared to relying on after-attack treatments.
CHAPTER FIVE: CONCLUSIONS, RECOMMENDATIONS, AND IMPLICATIONS FOR PUBLIC HEALTH PRACTICE

Public health professionals with access to information on the health and environmental effects of war or militarism, and on factors that may cause war, have the capability – and we believe, the responsibility – to gather these data, to analyze them, and to make them widely available. Such data can be extremely useful, if used by health professionals and others in education and awareness-raising programs, in preventing war or preparation for war, or in causing a halt to a war that is taking place.

—Levy and Victor Sidel

SUMMARY

The most important findings in this study were the early detection of the gastroenteritis and influenza-like illness events detected more than one month before they were identified by routine state, regional, and national surveillance. Although the findings were unexpected, it is not surprising that by incorporating state-of-the-art technology that provides automated analysis and notification capabilities with public health surveillance can greatly decrease the detection time of infectious disease outbreaks. The goal of decreasing routine detection of outbreak by hours, days, or weeks was exceeded in this study. Not only were large community-wide outbreaks detected early, but also individual cases of serious illnesses of public health importance. The frequency of alerts and warnings in this study might have been more sensitive than ideal, however, due to the high-risk nature of the facilities, it was appropriate considering the timing of implementation. Other studies including the Boston Public Health Commission system issued 103 alerts during the year 2002, and 22 entry count alerts (35). They
system used in for 30 days in New York City after the terrorist attacks resulted in 91 alerts of five syndromes (68,546 total entries). This effort in New York showed parallel results to the findings in this study regarding the most frequently reported syndromes were respiratory and gastroenteritis (4). The Boston study did not report the total number of entries.

The importance of evaluating different syndromic surveillance systems is imperative in order to rapidly detect naturally-occurring and/or intentional outbreaks. Some of the system claimed to be real-time and automated when in fact, they were not. Many large and well-funded systems base real-time syndromic surveillance on using diagnosis data that takes days to weeks to be coded. Syndromic surveillance is not inclusive of diagnosis-related data, by definition, it is the early capture of data before a diagnosis is made. By using old data, the near real-time capabilities are not possible, yet many systems using these methodologies claim otherwise. Before money is spent using these systems, evaluations of outcome data and system effectiveness for real-time outbreak detection should be published. There also appeared to be a lack of overall flexibility of systems to be used in a variety of settings, and a lack of knowledge that baseline data is required for establishing accurate thresholds for reporting events. If systems are implemented that do not carefully consider these factors, it could lead to the medical and public health infrastructure overburdened with reporting and responding to false alarms.

The features of the BioDefend™ system, including customizability and the overall flexibility of the system, were a determining factor for facilities to participate. There were differences in every clinic involved in this study, and the system was customized at
every site. It was also necessary to provide training and feedback to the site staff to maintain reporting, and for general bioterrorism awareness and knowledge. This study also shows the importance of syndromic surveillance being a local issue, because the knowledge needed for successful implementation is lies within the local level. Although these systems can be implemented on a local level, it is still important that systems can be linked to state and federal surveillance systems.

During the study, several events occurred that could have affected the reporting of the system, such as SARS, West Nile Virus, influenza, and the War on Terrorism. These events prompted the addition of a new syndrome, thus showing the need for a system that can continually be updated as new health risks occur. BioDefend™ was developed because there was no single bioterrorism syndromic surveillance system available that met the requirements for this study and the sites.

This surveillance system had some early successes with detecting a local outbreak of Fifth’s Disease among children mostly from South America at a theme park, and individual more serious illnesses, such as 10 reports of the encephalitis/meningitis-like syndromes, one of which was a confirmed case of viral meningitis, and two were among children less that 15 years of age, and five reports of the shock/sepsis syndrome. The increase in upper and lower respiratory tract infection, febrile illness, and influenza-like illness served as a potential indicator of flu season. All these syndromes are important considering Florida’s recent history with the anthrax attacks of 2001, the cruise ship Norovirus epidemic, and West Nile Virus. Not only were these early successes important for the region, but also for state and federal institutions to know that routine surveillance
can be improved with the use of appropriate technology. The timing of the study also provided the surveillance sites with an added assurance of protection knowing that syndromic reports were being monitored on a larger scale during the War on Terrorism.

**STRENGTHS**

The automated analysis component of the system that enabled automated alerts and warnings worked well for reporting increases in near real-time to facilities. The combined alerts were important in detecting community-wide phenomena, which could indicate regional epidemics. Capturing the more serious syndromes at the time when patients first present to healthcare facilities can provide more time to effectively treat some illnesses, and provide immediate quarantine and isolation for highly infectious agents. This should prevent further exposure, illness, and death. The BioDefend™ system has proven to be useful and that it can be sustained in these settings. Other systems have shown that they can be implemented, but are not sustainable. The reporting increased throughout the study and timely feedback of data were provided to local, state, and federal public health officials.

The surveillance sites were chosen based on their high-risk of being a target of bioterrorism, and also because some of them served an international population. Capturing the country of origin of the patients that presented with a syndrome and the recent travel history of military personnel provided important epidemiological links.

The early successes of this study have already had at least one impact on other syndromic surveillance systems, such as eliminating demographic data for nonsyndromic reports. Recent similar system development efforts have aimed to replicate this system,
but have not been successful at automating analysis, notification, and providing the necessary security.

It was determined that the frequency of reported syndromes was highest among both park departments that were considered in the working areas or areas that employees interacted with guests, as opposed to office or support positions in the back areas of the parks. The theme parks were interested in determining whether or not there was a pattern among employee versus guest syndrome reports. Some believe that ill guests enter the parks, and a few weeks later, similar illnesses are seen among the employees. By assessing whether or not the patient was an employee or guest, and the department in which employees worked, this could be determined, and also could be early indicators of events that originate in specific departments.

Throughout the study, many requests from the site staff were made about SARS, the potential impact of this illness on their organizations, and requests for additional infectious disease and bioterrorism training. The feedback and training meetings were extremely important to discuss current issues and to troubleshoot any issues so that reporting would increase and be maintained. The site meetings were also a time to discuss community health risks and public health education. Some of the sites agreed to share their data in the best interest of the community, as long as there was assurance that the confidentiality of their patients and facility would be preserved. During the study, the system received ample press attention, and was recommended for “Best Practices” among one of the military branches and one hospital received positive feedback from Joint Commission, an accreditation organization for hospitals.
WEAKNESSES

The data were probably not representative of the Central Florida area, due to the special population implementation of the system, but it was not the intended to be representative. Although six months of baseline data were collected, one full year would have provided a more complete seasonal pattern of syndromes since illness can vary by geographical location and time of year.

Additional limitations include specific biases for similar surveillance studies, including medical surveillance (or detection), misclassification, selection, and aggregation biases. An example of a medical surveillance or detection bias in this study was the potential impact of the SARS epidemic, and because it was given close media attention from February to the present, providers may have more closely monitored patients with the respiratory syndrome, or might have misclassified syndromes because of the increased awareness of this particular syndrome, showing the possibilities of a misclassification bias (71, 72). A selection bias was possible because persons that visit a theme park could have differences from those that do not visit, and one might expect similar biases with the theme park referral hospital, and with the military facility. An aggregation bias could have occurred when data were combined, which might have indicated an association of two factors, but was not true for individuals. An example of this phenomena would be the rise in shock/sepsis among children at the pediatric clinic at the military facility. When the data from all sites was aggregated, it appeared that the increase in shock/sepsis occurred system-wide, but was only a factor of a pediatric clinic at one site that was reported all the cases (10). In this study, the aggregation bias was
limited due to the ability to view data by each site and by clinic. There are limitations with surveillance data, mostly because they are observational by nature, as opposed to designed studies such as a randomized controlled trial, in which it might be easier to measure outcome data with more assurance of associations (51).

The inability to measure compliance, accuracy of the data, sensitivity of alerts, and the lack of some data being reporting timely were all limitations affecting reliability in this study. The parameters for reporting alerts was possibly set too low, making the alerting system too sensitive. Part of the high sensitivity was due to possible lack of trends established during the six-month period of baseline data collection. One year or more baseline data could have improved the thresholds for reporting alerts. The parameters and thresholds established for reporting alerts were based not only on historical trends, but also by the seriousness of the syndrome. Although, due to the time period of the study implementation (post-September 11 and the War on Terrorism), the alerting system should have been more sensitive, and therefore was not a serious limitation.

**FUTURE DIRECTIONS**

The BioDefend™ system in the future will include the implementation of a digital bridge designed to automatically collect syndromic and demographic data from patient information systems, virtually eliminating issues of compliance, data entry, accuracy, and timeliness of reporting. This process will be implemented as follows: the provider views each medical record from a computer while the patient is in the room. A checkbox embedded in the patient record will require the provider to select a syndromic or non-
syndromic option by clicking on the appropriate box. The system will automatically retrieve the demographic information from the patient record and be reported in near real-time. This syndromic checkbox will be a mandatory field for the physician to complete before exiting the patient record. The difficulties with implementing the digital bridge is that it has been estimated that currently, only 5% of hospitals have completely automated medical records (1). The military facility will continue using the BioDefend™ system and will be the first site to implement the digital bridge and automated system. The integration of Emergency Medical Systems (EMS) that have electronic medical record systems into the study is also planned.

More statistical testing, mathematical modeling, and the identification of a gold standard to serve as, and to provide a comparison for various systems will help validate systems and gain support from policy makers for the integration of syndromic surveillance into high-risk facilities. Methods for measuring the reliability of providers classifying patients according to syndromes is planned to help validate the system. The thresholds for reporting alerts worked well in this study, but in the future these will be updated based on validation studies. Measurements to determine how many alerts were true alerts will be included in validation studies.

The integration of Geographic Information Systems (GIS) is planned for the next year, and will aid in data visualization, and serve as a useful tool to gain support from directors, policy makers, community members, and many others by showing maps of syndromic clusters of outbreaks detected with syndromic surveillance (73). Plans are
being made to ensure the system is compliant with state and federal surveillance systems, including the National Electronic Disease Surveillance System (NEDSS), and the state MERLIN surveillance system.

A future study is planned to look at employee and guest illnesses at the theme parks. It is possible that an epidemic could be masked by analyzing employees and guests together. By stratifying the data by employee and guest, might eliminate the chance of diluting an event. In addition, if a bioterrorism event occurred at another park, in another country, and/or at the airport, the system should be able to detect the event earlier among guests, before illnesses were transmitted to employees. The parks appear to be prime locations for potential early detection sites of infectious diseases/bioterrorism events due to not only their high-risk, but the concentrated area of international guests with diverse exposures, and various types of animals. Since fewer patients visit the theme park clinics, and often present with less severe symptoms than an emergency department, the theme parks could be settings in which an outbreaks could be identified more rapidly. However, the theme parks are not likely to have electronic medical records.

RECOMMENDATIONS

This study showed that the purpose of detecting an outbreak within hours, days, or weeks before routine surveillance was exceeded. Throughout the study, participation increased, where other systems have failed. The success of this system could be attributed to several factors, including the increased perceived risk of bioterrorism, the flexibility of the system, training, and feedback to participating staff. By incorporating state-of-the-art technology with surveillance studies, fewer investigators are needed.
because personal digital technology can provide a means for receiving notifications and reviewing data, offering more flexibility for investigators to spend time and money for training, investigation, and response. Training should be a necessary component to all syndromic surveillance systems for healthcare providers know how to identify biological agent exposures, and to be able to report them to their local health department (74). A training program that allows providers to collect continuing medical education credit should enhance participation.

There is also a need for more peer-reviewed literature and comparative evaluations on syndromic surveillance systems nationwide. Instead of allocating money for large federal surveillance efforts, money would be better placed in local areas of increased risk of bioterrorism attacks, and on systems that have shown effective evaluations. Congressman John Dingell reported that sick persons visit clinics and emergency departments, and not federal agencies or government contractors, and physicians receive help from local health departments, and this is where emphasis should be placed. Before having all-inclusive systems that collect multiple data sources, early successes with single data sources should be documented and published with detailed information on data sources, methods of analysis, and detection of real outbreaks. Congressman Dingel also warned against developing, “high-powered surveillance systems that provide daily reams of information that cannot be analyzed, are not useful, and wear people out. They will likely cost much and accomplish little,” (75).

High-risk facilities, such as theme parks, referral hospitals, and potential military targets should continue syndromic surveillance efforts. It would be useful to expand
surveillance to theme park referral clinics. If possible, syndromes are likely best collected automatically to eliminate reporting, timeliness, and accuracy burdens. It has been estimated that only about 5% of healthcare facilities have patient information systems (1). Current increased money allocated for bioterrorism should be used to assist high-risk facilities in implementing near real-time and automated syndromic surveillance systems like the one used in this study. The lack of facilities having patient information systems is not a valid reason to neglect syndromic surveillance responsibilities, but incorporating flexible systems can enable surveillance to be conducted with minimal burden to providers. A congressional act should be developed to mandate high-risk and military facilities in the United States and overseas to conduct near real-time syndromic surveillance for the detection of bioterrorism and infectious diseases. This is not likely to occur until there is a high-impact bioterrorism attack in the United States. Syndromic surveillance methodologies from this study can be used to improve the timeliness of traditional surveillance of infectious diseases. Multiple data sources should be incorporated to confirm alerts and provide rapid epidemiological links, and to increase the sensitivity of alerts and warnings. Before combining various data sources, systems should be carefully evaluated for effectiveness and outcomes published. These systems should provide more than mere data collection. Only systems that incorporate automated analysis and alerting methodologies will be capable of identifying outbreaks in near real-time and be sustainable. From experiences in this study, the optimal syndromic surveillance effort would be to implement the system in settings with patient information systems with a system that is flexible and customizable to changing health risks of the
population served. In addition, incorporating automated analysis and alert capabilities with visualization tools, such as Geographic Information Systems, should be a requirement in order to enable rapid detection. Systems must also be able to communicate with state, regional, and national public health surveillance systems so that response and actions will follow. Mere reporting is not surveillance, and in order for actions to follow findings, surveillance must be more than a storehouse for data (27).

**IMPLICATIONS FOR PUBLIC HEALTH, BIOTERRORISM, AND INFECTIOUS DISEASE SURVEILLANCE**

Implementation of syndromic surveillance among high-risk facilities can offer more rapid identification of infectious diseases and potential bioterrorism attacks earlier than would be detected with routine surveillance. These systems are not designed to replace existing notifiable disease reporting procedures, but if given the opportunity, could improve the timeliness and quality in which the data are reported. It has been estimated that the compliance of mandatory reporting of diseases from physicians is less than 20%, thus showing the need for improving the need for improved reporting or methods to make reporting easier (1). With the ever-increasing threat of bioterrorism, high-risk facilities must be prepared for rapid detection so that exposures and death will be minimal, and fewer healthcare resources will be exhausted on response. The early detection of bioterrorism events is imperative for the prevention of unnecessary exposure and transmission, but surveillance systems need to be more timely and sensitive (76). Prevention through careful planning is key for identifying index or early cases of infectious diseases. Early successes of syndromic surveillance systems should be
measured by the Centers for Disease Control and Prevention’s paper on evaluating syndromic surveillance systems for the detection of bioterrorism, and findings published in peer-reviewed literature. Syndromic data should follow a similar “gold standard,” and should be able to communicate with state and federal systems when necessary, without compromising patient or site confidentiality.

Syndromic surveillance should not be implemented at all healthcare facilities in the United States, but can be useful and provide added protection among sites that are potential targets of terrorist attacks during periods of high-risk. With increased spending for bioterrorism preparedness, syndromic surveillance can enhance existing infectious disease surveillance programs to foster a more rapid disease reporting system that will enable the early detection of epidemics and bioterrorism attacks, thus benefiting not only the public health system, but the global population. Perhaps it is best said by the former Director of the Centers for Disease Control and Prevention, Dr. Jeffery Koplan, “Either we are all protected or we are all at risk,” (77).
REFERENCES


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APPENDICES
APPENDIX A: DATA COLLECTION FORMS

Figure A1. Hospital X Data Entry Form

<table>
<thead>
<tr>
<th>A. Please select ONE syndrome from the following list that best represents the primary condition for the patient.</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Upper or lower respiratory tract infection with fever <em>(do not check unless both are present)</em></td>
</tr>
<tr>
<td>☐ Diarrhea/gastroenteritis (including vomiting, abdominal pain, or any other GI distress)</td>
</tr>
<tr>
<td>☐ Influenza-like illness</td>
</tr>
<tr>
<td>☐ Rash with fever <em>(do not check unless both are present)</em></td>
</tr>
<tr>
<td>☐ Sepsis or non-traumatic shock</td>
</tr>
<tr>
<td>☐ Meningitis, encephalitis, or unexplained acute encephalopathy/delirium</td>
</tr>
<tr>
<td>☐ Botulism-like syndrome (cranial nerve impairment and weakness)</td>
</tr>
<tr>
<td>☐ Unexplained death with history of fever</td>
</tr>
</tbody>
</table>

The following fields are to be filled out only if a syndrome was selected above.

<table>
<thead>
<tr>
<th>B. Patient's account number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Date of patient visit (mm/dd/yyyy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/31/2003</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D. Time of arrival (24hr format - hh:mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>E. Date of onset of illness (mm/dd/yyyy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>F. Date of Birth (mm/dd/yyyy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G. Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Select One</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H. Zip code of patient's residence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I. Patient's country of residence</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>J. Last four digits of patient's Social Security Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>K. Has the patient visited a theme park within the past 2 weeks?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Select One</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>L. If Yes, please check the parks visited during the past 2 weeks.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disney World</td>
</tr>
<tr>
<td>Universal Studios</td>
</tr>
<tr>
<td>Busch Gardens</td>
</tr>
</tbody>
</table>

Submit Form

THIS FORM IS NOT PART OF THE PATIENT'S PERMANENT RECORD
APPENDIX A (Continued)

A. Please select **one** syndrome from the following list that best represents the primary condition for the patient.

- Upper or lower respiratory tract infection with fever (*do not check unless both are present*)
- Diarrhea/gastroenteritis (including vomiting, abdominal pain, or any other GI distress)
- Influenza
- Influenza-like illness
- Febrile illness
- Fever of undetermined origin
- Contact dermatitis
- Rash with fever (*do not check unless both are present*)
- Sepsis or non-traumatic shock
- Meningitis, encephalitis, or unexplained acute encephalopathy/delirium
- Botulism-like syndrome (cranial nerve impairment and weakness)
- Unexplained death with history of fever

[No Syndrome] *Click here if none of the above syndromes are present*

The following fields are to be filled out only if a syndrome was selected above.

<table>
<thead>
<tr>
<th>Field</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Patient ID#</td>
<td></td>
</tr>
<tr>
<td>C. Date of patient visit</td>
<td>mm/dd/yyyy</td>
</tr>
<tr>
<td>D. Time of visit</td>
<td>24hr format - hh:mm</td>
</tr>
<tr>
<td>E. Date of onset of illness</td>
<td>mm/dd/yyyy</td>
</tr>
<tr>
<td>F. Date of Birth</td>
<td>mm/dd/yyyy</td>
</tr>
<tr>
<td>G. Gender</td>
<td>Select One</td>
</tr>
<tr>
<td>H. Zip code of patient</td>
<td>U.S. only</td>
</tr>
<tr>
<td>I. Patient's country of residence</td>
<td>United States</td>
</tr>
<tr>
<td>J. Last four digits of patient's Social Security Number</td>
<td>No</td>
</tr>
<tr>
<td>K. Has patient traveled outside the U.S. within last 30 days</td>
<td>No</td>
</tr>
<tr>
<td>L. Select country visited</td>
<td>Select One</td>
</tr>
</tbody>
</table>

Submit Form

**THIS FORM IS NOT PART OF THE PATIENT'S PERMANENT RECORD**

*Figure A2. Military Facility Data Entry Form*
A. Please select ONE syndrome from the following list that best represents the primary condition for the patient.

- Upper or lower respiratory tract infection with fever (do not check unless both are present)
- Diarrhea/gastroenteritis (including vomiting, abdominal pain, or any other GI distress)
- Influenza-like illness
- Rash with fever (do not check unless both are present)
- Sepsis or non-traumatic shock (muscle weakness, rash with little purple point bleedings beginning as pin pricks in skin growing larger and forming fresh bruises)
- Meningitis, encephalitis, or unexplained acute encephalopathy/delirium
  - **adults**: headache, neck & back stiffness, nausea & vomiting, difficulty looking into bright lights, confusion, sleepiness, high fever
  - **infants**: slow, inactive, irritable, vomiting, bulging fontanel, strange cry, convulsions, muscle spasms in the back
- Botulism-like syndrome (cranial nerve impairment and weakness)
  - **adults**: double or blurred vision, drooping eyelids, slurred speech, muscle weakness, difficulty swallowing, and/or dry mouth
  - **infants**: lethargic, feed poorly, constipated, weak cry and poor muscle tone
- Unexplained death with history of fever

The following fields are to be filled out only if a syndrome was selected above.

- **B.** Patient ID#
- **C.** Date of patient visit (mm/dd/yyyy) 5/31/2003
- **D.** Time of visit (24hr format - h:mm) 17:46
- **E.** Date of onset of illness (mm/dd/yyyy) 
- **F.** Date of Birth (mm/dd/yyyy) 
- **G.** Gender [Select One]
- **H.** Zip code of patient (U.S. only) 
- **I.** Patient's country of residence [Select One - United States]
- **J.** Last four digits of patient's Social Security Number 
- **K.** Was patient transported to an emergency room or hospital? [Select One - No]
- **L.** Is patient an employee? [Select One - Employee]
- **M.** Employee work location [Select One]

Submit Form

**This form is not part of the patient's permanent record**

*Figure A3. Theme Park A Data Entry Form*
APPENDIX A (Continued)

A. Please select **ONE** syndrome from the following list that best represents the primary condition for the patient.

- Upper or lower respiratory tract infection with fever (do not check unless both are present)
- Diarrhea/gastroenteritis (including vomiting, abdominal pain, or any other GI distress)
- Influenza-like illness
- Rash with fever (do not check unless both are present)
- Sepsis or non-traumatic shock
- Meningitis, encephalitis, or unexplained acute encephalopathy/delirium
- Botulism-like syndrome (cranial nerve impairment and weakness)
- Unexplained death with history of fever

[No Syndrome]  Click here if none of the above syndromes are present

<table>
<thead>
<tr>
<th>The following fields are to be filled out only if a syndrome was selected above.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B.</strong> Patient ID#</td>
</tr>
<tr>
<td><strong>C.</strong> Date of patient visit (mm/dd/yyyy)</td>
</tr>
<tr>
<td><strong>D.</strong> Time of visit (24hr format: hh:mm)</td>
</tr>
<tr>
<td><strong>E.</strong> Date of onset of illness (mm/dd/yyyy)</td>
</tr>
<tr>
<td><strong>F.</strong> Date of Birth (mm/dd/yyyy)</td>
</tr>
<tr>
<td><strong>G.</strong> Gender</td>
</tr>
<tr>
<td><strong>H.</strong> Zip code of patient (U.S. only)</td>
</tr>
<tr>
<td><strong>I.</strong> Patient's country of residence</td>
</tr>
<tr>
<td><strong>J.</strong> Last four digits of patient's Social Security Number</td>
</tr>
<tr>
<td><strong>K.</strong> Was patient transported to an emergency room or hospital?</td>
</tr>
<tr>
<td><strong>L.</strong> Is patient an employee?</td>
</tr>
<tr>
<td><strong>M.</strong> Employee work location</td>
</tr>
</tbody>
</table>

Submit Form

**THIS FORM IS NOT PART OF THE PATIENT'S PERMANENT RECORD**

Figure A4. Theme Park B Data Entry Form
Figure B1. Employee Distribution by Department, Theme Park A
Figure B2. Syndromic Distribution, Theme Park A Employees (7 Departments)
Employee Distribution by Department
Theme Park B

Figure B3. Employee Distribution by Department, Theme Park B
Figure B4. Syndromic Distribution, Theme Park B Employees (10 Departments)
Figure C1. Baseline vs. Test Period, “Contact Dermatitis” at Military Facility
Figure C2. Baseline vs. Test Period, “Encephalopathy/Meningitis” at Military Facility
Figure C3. Baseline vs. Test Period. “Fever Unknown Origin” at Military Facility
Figure C4. Baseline vs. Test Period, “Influenza-like Illness” at Theme Park A
Figure C5. Baseline vs. Test Period, “Rash with Fever” at Theme Park A
Figure C6. Baseline vs. Test Period, “Encephalopathy/Meningitis” at Theme Park A
Figure C7. Baseline vs. Test Period, “Respiratory Tract Infection w/ Fever” at Theme Park B
Figure C8. Baseline vs. Test Period, “Influenza-like Illness” at Theme Park B
Figure C9. Baseline vs. Test Period, “Rash with Fever” at Theme Park B
Baseline vs. Test Period
"Encephalopathy/Meningitis"
at Theme Park B

Figure C10. Baseline vs. Test Period, “Encephalopathy/Meningitis” at Theme Park B
Figure D1. Overall Study Period, “Respiratory Track Infection w/Fever” by Facility
APPENDIX D (Continued)

Overall Study Period
"Gastroenteritis"
by Facility

Figure D2. Overall Study Period, “Gastroenteritis” by Facility
Figure D3. Overall Study Period, “Influenza-like Illness” by Facility
Figure D4. Overall Study Period, “Rash with Fever” by Facility
Figure D5. Overall Study Period, “Contact Dermatitis” by Facility
APPENDIX D (Continued)

Overall Study Period
"Influenza"
by Facility

Figure D6. Overall Study Period, “Influenza” by Facility
Figure D7. Overall Study Period, “Encephalopathy/Meningitis” by Facility
APPENDIX D (Continued)

Overall Study Period
"Fever Unknown Origin"
by Facility

Figure D8. Overall Study Period, “Fever Unknown Origin” by Facility
Figure D9. Overall Study Period, “Febrile Illness” by Facility
Figure D10. Overall Study Period, “Shock/Sepsis” by Facility
Figure E1. Seasonal Variation Overall Study Period
"Respiratory Tract Infection w/Fever"
Figure E2. Seasonal Variation Overall Study Period “Gastroenteritis”
Figure E3. Seasonal Variation Overall Study Period “Influenza-like Illness”
Figure E4. Seasonal Variation Overall Study Period “Rash with Fever”
Figure E5. Seasonal Variation Overall Study Period “Contact Dermatitis”
Seasonal Variation
Overall Study Period
"Influenza"

Figure E6. Seasonal Variation Overall Study Period “Influenza”
Seasonal Variation  
Overall Study Period  
"Fever of Unknown Origin"

Figure E7. Seasonal Variation Overall Study Period “Fever of Unknown Origin”
### Seasonal Variation

**Overall Study Period**

"Febrile Illness"

<table>
<thead>
<tr>
<th>Month &amp; Week</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 1</td>
<td>200</td>
</tr>
<tr>
<td>June 5</td>
<td>2003</td>
</tr>
<tr>
<td>July 9</td>
<td>13</td>
</tr>
<tr>
<td>Aug 13</td>
<td>17</td>
</tr>
<tr>
<td>Sep 17</td>
<td>21</td>
</tr>
<tr>
<td>Oct 21</td>
<td>25</td>
</tr>
<tr>
<td>Nov 25</td>
<td>33</td>
</tr>
<tr>
<td>Dec 29</td>
<td>37</td>
</tr>
<tr>
<td>Jan 33</td>
<td>41</td>
</tr>
<tr>
<td>Feb 41</td>
<td>45</td>
</tr>
<tr>
<td>Mar 45</td>
<td>50</td>
</tr>
<tr>
<td>Apr 50</td>
<td>55</td>
</tr>
</tbody>
</table>

*Figure E8. Seasonal Variation Overall Study Period “Febrile Illness”*
Figure E9. Seasonal Variation Overall Study Period “Encephalopathy/Meningitis”
Seasonal Variation
Overall Study Period
"Non-Traumatic Shock/Sepsis"

Figure E10. Seasonal Variation Overall Study Period “Non-Traumatic Shock/Sepsis”
Figure F1.
Geographical Distribution of All Syndromic Data in the Central Florida Area, May 29, 2002 – April 13, 2003
Figure F2. Detailed Zoom of Figure F1
APPENDIX G: RESPIRATORY TRACT INFECTION WITH FEVER

Figure G1. Geographical Distribution of “Respiratory Tract Infection with Fever” in the Central Florida Area, May 29, 2002 – April 13, 2003.
Figure G2. Zoom of G1
Figure H1. Baseline vs Test Period: “Rash w/ Fever”
Figure H2. Baseline vs. Test Period: “Shock/Sepsis”
Figure H3. Baseline vs. Test Period: “Encephalopathy Meningitis”
APPENDIX I: DEFINITION OF TERMS

1. Aberration. Describes the deviation in data compared to the normal pattern of data.

2. Alert. Aberrations in the data that are three standard deviations or more above the 30-day rolling mean.

3. Application Service Provider (ASP). A business model where a company provides software applications over the Internet. The users of this software subscribe to the service for as long as they use the software, rather than buying a license and installing it on their own machines.


5. Automated alert. Generated by the BioDefend™ system as data is received, calculated, and compared to the normal threshold. Any deviation from the normal threshold that is measured at or above 3 standard deviations above the rolling 30-day mean is considered an alert.

6. Automated analysis. The automatic calculation and comparison of data against normal thresholds.

7. Automated warning. Generated by the BioDefend™ system as data is received, calculated, and compared to the normal threshold. Any deviation from the normal threshold that is measured between two and three standard deviations above the rolling 30-day mean is considered a warning.

8. Baseline. Data used to determine thresholds for reporting events above normal.

9. Bioterrorism. “The unlawful use, or threatened use, of microorganisms or toxins derived from living organisms to produce death or disease in humans, animals, or plants. The act is intended to create fear and/or intimidate governments or societies in the pursuit of political, religious, or ideological goals” (11).

10. Bioterrorism Syndromic Surveillance. A type of surveillance used to track specific syndromes that can potentially serve as indicators of most infectious diseases and bioterrorism agent exposure in a specified population (3).


12. Bio-weapon. A device used to deliver and disseminate biological agents that are designed to cause disease, death, or damage to the environment and humans (74).

13. Database Management System (DBMS). A program that enables the user to create relational data applications and allows the user to store, modify, and remove information from the database.
14. Dual-use. Having the ability to detect biological agent and infectious disease exposures within a single system.

15. Epidemic. Affecting a large population within a community or region with a disease in excess of the normal expectancy (10).


17. Geographic Information System (GIS). A software toolset that is linked to a database and temporally displays spatial data from the real world onto a map through the retrieval, analysis, manipulation, modeling, and storage of the data (64).

18. Health Insurance Portability and Accountability Act of 1996 (HIPAA). An act written for the purposes of preventing the distribution of identifiable health information such as patient identification number, address, phone number, zip code, birth date, and any other identifiable information from being used to identify patients (57).

19. International Classification of Diseases, 9th revision (ICD-9 codes). “The classification of specific conditions and groups of conditions determined by an internationally representative group of experts who advise the World Health Organization.” There are 21 chapters within the manual (10).

20. Near Real-Time. Data captured within minutes of being reported.

21. Outbreak. A localized increase of a disease of epidemic proportion within a small area, such as a village, town, or closed institution (10).

22. Predictive Value Positive. The amount of positive validity of reported cases, or outbreaks, that is under surveillance (3).

23. Public Health Surveillance. “The ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health” (1).

24. Redundant Array of Inexpensive Disks (RAID). Computer hardware that continually updates copies of data onto multiple disks for added security of the possible loss of data.

25. Rolling 30-day mean. Creates a series of averages from adjacent observations for the last 30 days and is used to model cycles in the data.

26. Sensitivity. “The proportion of cases, or outbreaks, existing in the jurisdiction that is detected by the system” (3).

27. Sentinel Surveillance. “Surveillance based on selected population samples chosen to represent the relevant experience of particular groups” (10).

28. Standard deviation. The square root of the variance of the total number of observations (71).
29. Structured Query Language (SQL). A standardized query language that allows the user to request information from the database.

30. Syndrome. A group of symptom complexes gathered before the diagnosis is made, and could be considered to be an early indicator of most infectious disease and biological agent exposures (10).

31. Theme Park Referral Hospital/Clinic. A hospital or clinic that provides care for guest and employees that is referred by the theme parks.

32. Warning. An aberration in the data between two and three standard deviations above the rolling 30-day mean.
ABOUT THE AUTHOR
Kristin Uhde was born in North Carolina in 1973, and raised in Tennessee. She received a Bachelor’s Degree in Biology at Hollins College in Virginia in 1996. She graduated from East Tennessee State University with a Masters in Public Health. Her research focused on the prevention of neural tube defects with folic acid, and received an award from King and Monarch Pharmaceuticals. Uhde was a Visiting Fellow at the Centers for Disease Control and Prevention where she published her research in the Morbidity and Mortality Weekly Report. In 2000, she pursued a doctoral degree in Tropical and Infectious Diseases at the University of South Florida. During this time, Uhde presented her research at several international conferences, and received the Sam Bell Endowed Scholarship for Research and Outstanding Student of the Year Award. While working on her degree, she was a Research Assistant at the Center for Biological Defense.