



Managing Casualties from a Biological Outbreak—

A Casualty Predictive Template



February 2006

Prepared by U.S. Army Edgewood Chemical and Biological Center's (ECBC)
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| 14. ABSTRACT The Military Improved Response Program (MIRP) developed and used a key tool named the casualty predictive templates to plan and identify challenges associated with responding to biological terrorist incidents involving large numbers of victims. Casualty predictive templates were created for anthrax, pneumonic plague, smallpox, botulinum, tularemia, Venezuelan equine encephalitis, staphylococcus enterotoxin B intoxication, and melioidosis. To date, there are few biological agent predictive casualty tools available for emergency planners to use. This document provides an overview of each biological agent and highlights key information that emergency planners must recognize when formulating their response to a biological outbreak. The template itself identifies the number of casualties for each stage of a disease, for a given population exposed, so that the medical infrastructure can anticipate the total number of those seeking medical aid for a particular day, as well as for the following several weeks. Additionally, this model will allow the reader to analyze the formulas imputed into the template, as well as access the Excel spreadsheets, for the purpose of generating population numbers specific to their jurisdiction. | | | | | |
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**MANAGING CASUALTIES FROM A
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A CASUALTY PREDICTIVE TEMPLATE**

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PREFACE

The work described in this report was authorized under Contract No. SP0700-00-D-3180 Task no. 211, Delivery Order 0159. This work was started in May 1998 and completed in February 2006.

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And

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Drs. Wood and Gorman provided professional expertise in reviewing the Casualty Predictive Template document. Their input has helped the MIRP identify the many caveats required to formulate a realistic casualty predictive tool, and to incorporate the most current information about biological agents.

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EXECUTIVE SUMMARY

In 1998 the Military Improved Response Program (MIRP) developed and used key tools namely the casualty predictive templates to identify challenges associated with responding to biological terrorist incidents involving large numbers of victims. Prior to this time, there was little data, theoretical or actual, that adequately depicted the magnitude of an intentional biological outbreak. Moreover, if data was available, it was not compiled in a manner that easily assisted emergency planners formulate their response effort.

The purpose of this document is to support disaster planning efforts by providing planners a casualty predictive tool that identifies the potential number of casualties from exposure to various biological agents of concern. The document provides an overview of each biological agent and highlights key information that emergency planners must recognize to formulate their response, in addition to depicting the number of potential casualties, based on a given exposed population, the number of asymptomatic potentially exposed casualties (also referred to as the worried well), and the death toll for each given day of an outbreak. Emergency planners can use this data as a foundation for estimating how the current medical infrastructure must adapt, as well as identify the number and type of personnel required and the quantity and type of resources needed to manage large numbers of casualties. Since each biological agent has different characteristics, the MIRP developed a predictive casualty template for several of the major biological agents of concern- anthrax, tularemia, pneumonic plague, smallpox, botulinum, Venezuelan equine encephalitis, staphylococcus enterotoxin B intoxication, and melioidosis.

The document is further complimented by associated interactive Excel spreadsheets. These interactive spreadsheets allow the reader to modify the existing infected population with numbers specific to their jurisdiction, as well as to analyze and modify the formulas imputed into the template, to depict a more realistic situation for their jurisdiction. Additionally, having access to the actual Excel files will allow planners to modify the tool as new information becomes available.

Though initially this tool served the internal purposes of the MIRP, the developers of this document determined it should be finalized and posted on the Edgewood Chemical Biological Center (ECBC) Web site <http://www.ecbc.army.mil/hld/ip/index.htm> as a separate document, to include the interactive Excel spreadsheet model, so that all emergency planners had access to it to enhance their disaster planning efforts.

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INTRODUCTION

1.0 INTRODUCTION

The Domestic Preparedness Program, created under Title XIV of the National Defense Authorization Act of 1996 (Public Law 104-201, September 23, 1996), directed the Department of Defense (DoD) to develop training and equipment programs to support civilian agencies' response to weapons of mass destruction (WMD) events. The Department of the Army, as the Executive Agency for Chemical and Biological Defense, was tasked oversight, and the Edgewood Chemical Biological Center (ECBC) was assigned the responsibility of developing and implementing the program to include the development of supporting materials.

Prior to the full transfer of civilian preparedness responsibilities to the Department of Justice in 2000, ECBC developed a number of domestic preparedness initiatives through the Improved Response Program (later referred to as the Military Improved Response Program [MIRP]). The MIRP is one of several domestic preparedness programs that conducted scientific research, workshops, and technical investigations to enhance the abilities of emergency responders to safely and effectively respond to terrorist incidents involving chemical or biological warfare agents.

In 1998, MIRP established the Biological Weapons Improved Response Program to identify, evaluate, and demonstrate the best practical approaches to improve response to terrorist incidents involving biological weapons (BW). Composed of representatives of such federal agencies as the Departments of Health and Human Services (HHS), Energy (DOE), Agriculture (USDA), the Federal Emergency Management Agency (FEMA), the Federal Bureau of Investigation (FBI) and the Environmental Protection Agency (EPA), other federal and state experts, local responders, and technical experts, the MIRP team completed an assessment that outlined BW response problems. Following this effort, the MIRP formulated an integrated emergency management approach and response to a BW incident.

To more fully understand the breadth and scope of a BW incident, the MIRP developed and used a key tool namely the casualty predictive templates. These casualty predictive templates were critical to planning and identifying the challenges associated with responding to an event involving large numbers of victims. However, the development of an accurate tool was a challenge, as there was little worldwide data on responding to intentional outbreaks of biological pathogens or toxins to substantiate theoretical calculations. To assist the MIRP team in developing a more realistic and effective emergency management tool, ECBC collaborated with professionals from the Centers for Disease Control and Prevention (CDC), the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), and other subject matter experts, herein referred to as the developers, to devise a series of casualty predictive templates for biological diseases of greatest concern.

1.1 CASUALTY PREDICTIVE TEMPLATE

Casualty predictive templates were created for anthrax, tularemia, pneumonic plague, smallpox, botulinum toxin, Venezuelan equine encephalitis, staphylococcus enterotoxin B intoxication, and melioidosis. For each biological agent, the following areas were described:

- **Overview** - provides the name of the biological agent and corresponding disease, describes bio-terror agent characteristics, presents general treatment modalities to include relevant immunizations or vaccinations, and identifies personal protective equipment requirements.
- **Clinical features** - describes the incubation period, physical signs and symptoms, methods of diagnosis and mortality rate.
- **Template assumptions** - describes the developers assumptions associated with the formulas applied for each biological agent of concern by specifically addressing distribution of illness, fatality rate, secondary case rate, worried but well cases, effects of community prophylaxis, and institution of containment measures.
- **Casualty predictive calculations** - defines the formulas applied for each significant aspect of the outbreak by “rows” (e.g., Row A, B, C, etc.). These rows correspond with the casualty predictive template and are associated with the template assumptions for each agent.
- **Static casualty predictive template (as a table)** - reveals the number of casualties infected for each stage of the outbreak, as well as provides numbers of worried well, fatalities, and cumulative numbers of persons seeking care for each day, based on the formulas described in the casualty predictive calculations section. Since the casualty distribution of a biological outbreak is agent dependent, the template depicts the initial casualty spike and decline only; thus, for some templates, spikes and declines occur during a 21-day period and for other biological agents a 30 day period or greater is applied. [***Note- The casualty predictive template table is intended to be viewed on an 11x17 inch paper. The reader is encouraged to open the Excel spreadsheet using this paper size to properly and wholly review the details for each outbreak presented.]
- **Interactive casualty predictive template (as an Excel spreadsheet)** - a corresponding electronic Excel spreadsheet will be made available to the reader through the U.S. Army Edgewood Chemical Biological Center (ECBC) website <http://www.ecbc.army.mil/hld/ip/reports.htm> for those interested in manually adjusting the Excel spreadsheet equations to estimate realistic numbers for their jurisdiction. Planners are encouraged to modify the “population infected” for each biological outbreak. Moreover, emergency planners are encouraged to modify the Excel equations, as research becomes available to more accurately define casualty distribution rates

See appendix A for further details regarding how to modify the Excel spreadsheets.

1.1.1 Template Accuracy

Creating accurate predictive models is difficult. In general, the spread of a biological agent (terrorist related or naturally occurring) depends on the occurrence of multiple variables, sometimes occurring in a particular sequence. A predictive tool is not always able to mimic these variables or able to weigh the influence of multiple variables accurately. The accuracy of such predictive tools is thereby constrained by the developers' assumptions.

One such assumption is that this casualty predictive template does not discuss how biological agents are introduced into the community. The developers instead made general assumptions regarding those infected for the purpose of delineating a starting point for emergency planning. For each agent the developers assumed 5,000 people would become infected.

Additionally, the MIRP's casualty predictive template simplifies biological agent exposure by making general assumptions regarding the population exposed, distribution of presenting illness, fatality rate, second generation cases, worried-but-well cases (defined as patients that are presently asymptomatic but were possibly exposed to the biological agent), effects of community prophylaxis measures, and institution of possible containment measures. For all the bio agents, the developers assumed patients were infected with traditional forms of the agent and did not assume the agent was genetically altered rendering it resistant to antibiotic treatment. Thus, the developers made assumptions regarding these variables to formulate equations and predict the resulting number of casualties and the effectiveness of medical treatment.

To help substantiate the formulas applied to these assumptions, the developers used modeling and simulation tools and the Gaussian distribution. One particular tool used to determine the potential spread of a biological outbreak was the "Hazard Prediction and Assessment Capability" software created by Oak Ridge National Laboratory. Though this particular software actualizes the spread of nuclear material, it takes into account similar parameters, such as population density, material fallout concentrations, and wind direction, which would similarly influence an intentional spread of an aerosolized biological agent. Additionally, by applying the Gaussian distribution, also known as the normal distribution, the developers were able to formulate the most realistic numbers of those likely to present with an illness following a biological outbreak.

In some instances there was little real world data from which to formulate realistic predictions. In those instances the developers needed to devise an alternate method to formulate spreadsheet calculations. Estimating the number and distribution of worried well patients for example, was particularly challenging. Instead of using static ratios of worried well casualties to confirmed numbers of casualties, the developers based their calculations on three parameters- a high fatality rate or spike in the number of fatalities reported each day, the infectivity of the agent and its ability to transmit between humans (contagiousness), and a patient's ability to easily recognize acute onset of physical signs or symptoms related to the disease. To estimate the number of worried well for a

biological outbreak the developers instituted the highest ratio of worried well casualties to actual patients when all three parameters were present. When a biological outbreak did not exemplify all parameters or only some of the aforementioned characteristics, then moderate or low ratios were applied.

To date, there are few biological agent predictive casualty tools available for emergency planners to use. Most tools exist in the form of static tables and do not allow the reader to manipulate the general population numbers to more fully realize the potential casualty rate; additionally, such tools do not divulge the supporting formulas from which their findings are derived. This model will allow the reader to analyze the formulas imputed into the template, as well as access the Excel spreadsheet for the purpose of generating population numbers specific to their jurisdiction.

1.1.2 Template Applications

Updated in 2005, these templates may prove useful to emergency managers and planners. The casualty predictive template is intended to be used for a variety of purposes:

- ***As an educational tool.*** Community leaders, public safety officers, emergency managers, and leaders of public health, healthcare operations, and ancillary services may find it useful to study the template to identify the breadth and scope of the consequences for a particular type of outbreak within their community. The template is scalable – meaning planners can use their own initial entry value other than what is identified in the templates, to reflect populations more compatible for their geographic area.
- ***As a planning tool.*** The demands on a community, and particularly its healthcare resources, will be immense and require timely action to control and contain the continued spread of a biological outbreak. Performing epidemiological projections, during the initial phase of an outbreak, may facilitate resource mobilization in advance of actual requirements and may subsequently have a positive impact on minimizing overall community morbidity and mortality.
- ***As an exercise tool.*** Emergency planners, for all responding agencies, may find the template helpful when conducting an exercise. Exercise participants often need aids that divulge details regarding the breadth and scope of an incident to appropriately develop a response plan fitting to the scenario/incident being presented.

1.1.3 Template Interpretation

Before applying data obtained from the casualty predictive templates, emergency planners should understand how to read and interpret them. Each casualty predictive template corresponds to a preceding calculation table describing the formulas applied to that template. The calculation table identifies each row by a letter that directly corresponds to the same lettered row in the template. Each row of the table and the template identify key aspects of the disease, namely-casualties that are infected,

casualties presenting with early and late signs and symptoms, casualties that require medical care in hospital or can recover at home, the number of worried well, the number of fatalities, and the cumulative number of those seeking medical aid. Whereas the table provides the formula applied to each stage of the disease, the template predicts the number of casualties, based on the formula, over time.

In addition to depicting numbers over a period of days, the template will also identify the number of casualties infected, number of casualties presenting with illness as depicted in the distribution of presenting illness, and mortality rate. These factors are also associated with the preceding calculation section in a table.

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ANTHRAX

2.0 ANTHRAX OVERVIEW

Anthrax is caused by the *Bacillus anthracis* bacteria, which is a gram-positive, sporulating rod. These spores take an infective form and are very stable. They can remain viable for many years in soil and water and are resistant to degradation upon exposure to varying degrees of sunlight.¹

Anthrax is primarily a zoonotic disease that infects herbivores such as cattle, sheep, goats, and horses. Typically humans contract the disease when exposed to infected animals' hair, wool, hides, flesh, blood, bone meal and/or excreta. The bacteria can enter the body through the skin (e.g., direct exposure via scratches, wounds, or abrasions of the skin or by indirect exposure such as by being bitten by infected flies), the respiratory tract (e.g., breathing in the spores) or via the gastrointestinal tract (e.g., eating insufficiently cooked infected meat).

In general, authorities are most concerned with aerosolization of anthrax spores and resulting inhalational exposure cases; such exposures are more likely associated with potential terrorist acts. Additionally, inhalational anthrax is associated with higher mortality than other forms of anthrax disease.

Being infected with anthrax poses some difficult challenges. Historically, almost all inhalational anthrax cases in which treatment was initiated after patients were significantly symptomatic have been fatal, regardless of treatment provided.² Patients receiving appropriate antibiotics during the incubation period or when they first started experiencing symptoms of the infection have had a greater chance of survival. During the fall 2001 anthrax mailing attack, for example, patients exposed or potentially exposed were diagnosed and treated or received prophylactic (preventative) antibiotics early; very few patients died. The difficulty, however, is associated with identifying the outbreak early and then administering treatment and prophylaxis quickly. Unfortunately, initial patient symptoms mimic that of other common febrile illnesses which may not trigger an aggressive medical or public health response during the initial phase of symptom onset.

Resultantly, emergency planners are faced with the challenge to obtain and disperse post exposure prophylactic medication quickly once the attack has been recognized. Both military doctrine and public health policy developers recommend prophylaxis using ciprofloxacin or doxycycline as first line medication. Penicillin, though not generally recommended as first-line

¹ Guarner J, Jernigan JA, Shieh WJ, Tatti K, Flannagan LM, Stephens DS, Popovic T, Ashford DA, Perkins BA, Zaki SR; Inhalational Anthrax Pathology Working Group. Pathology and pathogenesis of bioterrorism-related inhalational anthrax. *Am J Pathol.* 2003 Aug;163(2):701-9.

² Dworkin MS, Ma X, Golash RG. Fear of bioterrorism and implications for public health preparedness. *Emerg Infect Dis.* 2003 Apr;9(4):503-5.

medication, tetracycline, erythromycin, or intravenous (IV) chloramphenicol may also be used as prophylactic medications.³ Patients must remain on medication and potentially receive aggressive supportive treatment and several medications for an extended period of time (up to 60 days)⁴, as is the case when treating symptomatic inhalational anthrax. Providing such care will place a heavy burden on the medical infrastructure.

A complicating factor when treating any bacterial infection such as *Bacillus anthracis* is that the agent can be altered genetically to render it resistant to antibiotics. Emergency and medical planners must be aware of this caveat as initial prophylactic measures may not mitigate the potential effects of an outbreak.

CDC's Strategic National Stockpile (SNS) contains both doxycycline and ciprofloxacin, with doxycycline as the primary prophylactic medication.

In addition to antibiotic treatment, patients can receive an anthrax immunization. The immunization series consists of six doses that take place within a regimented time frame, specifically at 0, 2, and 4 weeks, then 6, 12 and 18 months. Afterward, those inoculated should receive annual boosters to maintain immunity. As with all vaccines, the degree of protection is dependent upon the dose/concentration of the actual exposure. Patients suspected to have been exposed to anthrax should receive antibiotics and the vaccine to prevent the development of the disease.⁵

When caring for patients with anthrax, providers should wear personal protective equipment consistent with Standard Precautions guidelines to prevent exposure. There is no evidence of direct person-to-person spread of anthrax; therefore personnel do not need additional respiratory protection unless they enter known contaminated locations (e.g., the location where the agent was initially dispersed). Additional protective measures include thoroughly disinfecting instruments and patient areas with an anti-sporicidal disinfectant solution.

³ Tierney BC, Martin SW, Franzke LH, Marano N, Reissman DB, Louchart RD, Goff JA, Rosenstein NE, Sever JL, McNeil MM; Centers for Disease Control and Prevention's Anthrax Vaccine and Antimicrobial Availability Program. Serious adverse events among participants in the Centers for Disease Control and Prevention's Anthrax Vaccine and Antimicrobial Availability Program for persons at risk for bioterrorism-related inhalational anthrax. *Clin Infect Dis.* 2003 Oct 1;37(7):905-11. Epub 2003 Sep 12.

⁴ Tierney BC, Martin SW, Franzke LH, Marano N, Reissman DB, Louchart RD, Goff JA, Rosenstein NE, Sever JL, McNeil MM; Centers for Disease Control and Prevention's Anthrax Vaccine and Antimicrobial Availability Program. Serious adverse events among participants in the Centers for Disease Control and Prevention's Anthrax Vaccine and Antimicrobial Availability Program for persons at risk for bioterrorism-related inhalational anthrax. *Clin Infect Dis.* 2003 Oct 1;37(7):905-11. Epub 2003 Sep 12.

⁵ Tierney BC, Martin SW, Franzke LH, Marano N, Reissman DB, Louchart RD, Goff JA, Rosenstein NE, Sever JL, McNeil MM; Centers for Disease Control and Prevention's Anthrax Vaccine and Antimicrobial Availability Program. Serious adverse events among participants in the Centers for Disease Control and Prevention's Anthrax Vaccine and Antimicrobial Availability Program for persons at risk for bioterrorism-related inhalational anthrax. *Clin Infect Dis.* 2003 Oct 1;37(7):905-11. Epub 2003 Sep 12.

2.1 CLINICAL FEATURES

Anthrax presents in one of three distinct clinical syndromes in humans: cutaneous, gastrointestinal and inhalational disease. Cutaneous anthrax occurs most frequently on the hands and forearms and occasionally becomes a systemic infection. Gastrointestinal anthrax, although rare in humans, can also become a systemic infection. Inhalational anthrax presents the greatest concern, as it is most likely the result of an intentional aerosolized release, and is fatal if not treated immediately.

The incubation period for inhalational anthrax is typically 1–6 days, but can be as long as six weeks. The initial signs and symptoms are nonspecific. Patients experience high fever, malaise, and fatigue and may have a dry cough and/or mild chest discomfort. Initial symptoms can be followed by a short period of improvement (hours to 2–3 days), followed by the abrupt development of severe respiratory distress (dyspnea and stridor), profuse sweating (diaphoresis), and lack of tissue perfusion (cyanosis). Patients become septicemic and experience irreversible shock. Despite receiving treatment, patients often die within 24–36 hours after the onset of respiratory distress.⁶

In addition to these symptoms, there are specific signs medical professionals can use to help diagnosis anthrax.⁷

- A mildly elevated white blood cell count that will remain elevated until death.
- A widened mediastinum. In the majority of the cases, a patient chest x-ray or Computed Axial Tomography (CAT) scan will reveal a widened mediastinum, with or without pleural effusions, which may or may not have infiltrates.
- Positive gram stains and blood culture. Bacilli and toxins often appear late on day 2 or early on day 3 post-exposure.
- Organisms in the cerebrospinal fluid. In 50% of previously reported cases of inhalational anthrax, patients are found to have hemorrhagic meningitis.

Medical staff should focus on administering the aforementioned antibiotics in addition to providing symptomatic and supportive care. The key to survival is early administration of appropriate antibiotics coupled with aggressive treatment for shock and airway compromise.

⁶ Jernigan DB, Raghunathan PL, Bell BP, Brechner R, Bresnitz EA, Butler JC, Cetron M, Cohen M, Doyle T, Fischer M, Greene C, Griffith KS, Guarner J, Hadler JL, Hayslett JA, Meyer R, Petersen LR, Phillips M, Pinner R, Popovic T, Quinn CP, Reefhuis J, Reissman D, Rosenstein N, Schuchat A, Shieh WJ, Siegal L, Swerdlow DL, Tenover FC, Traeger M, Ward JW, Weisfuse I, Wiersma S, Yeskey K, Zaki S, Ashford DA, Perkins BA, Ostroff S, Hughes J, Fleming D, Koplan JP, Gerberding JL; National Anthrax Epidemiologic Investigation Team. Investigation of bioterrorism-related anthrax, United States, 2001: epidemiologic findings. *Emerg Infect Dis.* 2002 Oct;8(10):1019-28.

⁷ Jernigan DB, Raghunathan PL, Bell BP, Brechner R, Bresnitz EA, Butler JC, Cetron M, Cohen M, Doyle T, Fischer M, Greene C, Griffith KS, Guarner J, Hadler JL, Hayslett JA, Meyer R, Petersen LR, Phillips M, Pinner R, Popovic T, Quinn CP, Reefhuis J, Reissman D, Rosenstein N, Schuchat A, Shieh WJ, Siegal L, Swerdlow DL, Tenover FC, Traeger M, Ward JW, Weisfuse I, Wiersma S, Yeskey K, Zaki S, Ashford DA, Perkins BA, Ostroff S, Hughes J, Fleming D, Koplan JP, Gerberding JL; National Anthrax Epidemiologic Investigation Team. Investigation of bioterrorism-related anthrax, United States, 2001: epidemiologic findings. *Emerg Infect Dis.* 2002 Oct;8(10):1019-28.

The mortality of untreated cutaneous anthrax ranges up to 25 percent, while those that receive appropriate treatment are rarely fatal. In inhalational cases, untreated cases have a fatality rate of almost 100 percent, and treated cases vary depending on when treatment was initiated. The mortality of gastrointestinal anthrax is somewhat lower than untreated inhalational anthrax, yet it can be as high as 50% even in treated cases.

2.2 ANTHRAX CASUALTY PREDICTIVE TEMPLATE

The following casualty prediction template is intended to illustrate the potential impact of casualties on the medical infrastructure when approximately 5,000 people are infected with anthrax via aerosol exposure. Due to limited data on actual large-scale outbreaks of *B. anthracis* involving intentional aerosol spray release (the fall 2001 anthrax mail release was not the product of classic point or line spray release), the developers made a number of assumptions when developing this template. These assumptions, and the rationale used in developing the formula equations, are presented below.

2.2.1 Template Assumptions

- ***Distribution of presenting illness.*** Average incubation period is assumed to be three days, with severe symptoms beginning one day later.⁸ Those that are immunologically compromised, such as those who have an underlying illness, those at the extremes of the age continuum, or receive higher inoculums of pathogens, may have a short incubation period, perhaps as short as 24 hours. Conversely, those with robust immune systems, or have received smaller inoculums, may be asymptomatic for longer periods of time.
- ***Fatality rate.*** A fatality rate of 95% was used for this model.⁹ Fatality rates for anthrax are ultimately affected by early identification of the outbreak, diagnosis and treatment, and dependent on the availability and timely distribution of prophylactic medications. Although the case fatality rate of the fall 2001 anthrax mailing release was significantly less than the rate used for this model (45%), all patients in that particular outbreak experienced extraordinary clinical care that would likely not be available in a very large outbreak, during the initial phase of the response.
- ***Worried-but-well cases.*** The ratio of asymptomatic potentially exposed individuals (“worried well”) to actual casualties is expected to range from 3:1 to 10:1, based upon historical information from events like the sarin nerve agent attack in the Tokyo subway system in 1995. Subject matter experts have estimated that an intentional release of a pathogen in a community might result in even larger numbers of individuals seeking evaluation, treatment, or reassurance that range from 5 to 20

⁸ Inglesby TV, O'Toole T, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Friedlander AM, Gerberding J, Hauer J, Hughes J, McDade J, Osterholm MT, Parker G, Perl TM, Russell PK, Tonat K; Working Group on Civilian Biodefense. Anthrax as a biological weapon, 2002: updated recommendations for management. JAMA. 2002 May 1;287(17):2236-52. Review. Erratum in: JAMA 2002 Oct 16;288(15):1849.

⁹ Dworkin MS, Ma X, Golash RG. Fear of bioterrorism and implications for public health preparedness. Emerg Infect Dis. 2003 Apr;9(4):503-5.

times the actual number of casualties. For this template, the numbers of worried-but-well cases ranges from 0.75 to 3.0 times the number of new cases plus the number of fatalities. Although new cases would diminish rapidly, this template assumes that people would continue to seek care, particularly when the initial death toll is the highest and/or based on the community's perception that the medical system can mitigate the effects of the outbreak; thus providing the public concise, honest, and timely, information about the outbreak may dramatically reduce the number of worried well seeking care.

For all biological agents, emergency and medical planners can generally assume that patient survival will be inversely proportional to size of the outbreak and directly proportional to resources available to treat and prevent the disease.

- **Secondary Cases.** Inhalational anthrax is not known to have been transmitted between humans via the respiratory tract or blood and body fluids. For this reason this template will assume that there are no secondary cases of the disease.
- **Effects of community prophylaxis.** Institution of community prophylaxis will not commence until the fourth day after the attack. The developers made this determination based on the likely time required to identify the outbreak, diagnose initial cases, determine if the patient responds to treatment, determine of the cause of the outbreak, and determine the need to establish community prophylaxis; which probably would be about two days. Further delays, approximately 2 days, would occur due to the logistics involved with acquisition of pharmaceuticals, delivery to points of distribution, and institution of dispensing plans. Dispensing of prophylaxis to certain populations (e.g., homeless, disabled, house-bound, impoverished and/or those with language barriers or lacking transportation) may be delayed even further. Since, in this model, the vast majority of those primarily infected would have already developed severe symptoms before authorities institute community prophylaxis, there would be no early improvement on patient outcome as the result of community-wide prophylaxis. It is possible that communities with mature plans and ready access to major airfields for delivery of the Strategic National Stockpile (SNS) may reduce the time from exposure to prophylaxis than what this model depicts.

Strategic National Stockpile Initiative - The Cities Readiness Initiative stipulates cities must be able to provide prophylaxis for their entire populations within 48 hours of an event – this was mainly created for a large scale anthrax scenario and this practice is currently being applied in 21 cities in the United States.

- **Other containment measures.** No other containment measures were assumed in this model. In as much as inhalational anthrax is not readily transmissible through

human- to-human contact, other containment measures are believed to have little effect on the outcome of this outbreak.

2.2.2 Calculations

The following section outlines the calculations applied in developing the anthrax casualty predictive template. It also delineates the actual formula associated with each previously described assumption.

| Row | Definition | Formula |
|----------|--|--|
| A | Stage I - Incubation Period. | Initially 5,000, decreasing by numbers presenting at Stage II. Row A (previous day) – Row B (current day) |
| B | Stage II - Presenting Illness (Febrile syndrome). | Variable incubation period. See distribution at bottom of template. |
| C | Stage III - Acute Illness (Respiratory compromise and shock): Assumes 100% of Stage II Patients progress to Stage III. | Row B (previous day) |
| D | Stage IV _A - Chronic Recovery Requiring Care (5%). | Row D (previous day) + 0.05 x Row C (previous day) |
| E | Stage IV _B – Recovery at Home: Assumes 100% of surviving victims require skilled nursing care for at least 30 days after overt infection. | Not used in this template |
| F | Total Ill Today (Stage II, III, IV _A , IV _B). | Row B + Row C + Row D + Row E (current day) |
| G | Number of Worried Well Today: Assumes number of worried well rapidly climbs to 3 times number of new cases plus fatalities, stabilizes at this level, then declines gradually through the remainder of the outbreak. | Worried Well Factor (variable) x (Row B (previous day) + Row I (previous day)) |
| H | Total Seeking Medical Aid Today (Stage II and worried well). | Row B + Row G (current day) |

| Row | Definition | Formula |
|----------|--|--|
| I | Number of Fatalities Today (95%): Assumes 95% of victims progressing to Stage II die within 24 hours. | 0.95 x Row B (previous day) |
| J | Cumulative Number of Fatalities. | Row J (previous day) + Row I (current day) |
| K | Cumulative Number of Persons Seeking Medical Aid. | Row K (previous day) + Row H (current day) |

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TABLE 1 ANTHRAX CASUALTY PREDICTIVE TEMPLATE

| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 | |
|--|-------|-------|-------|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| A Stage I - Incubation Period (see distribution) | 5,000 | 4,650 | 3,300 | 1,400 | 700 | 400 | 150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting Illness (febrile syndrome) | 0 | 350 | 1,350 | 1,900 | 700 | 300 | 250 | 150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III - Acute Illness (respiratory compromise and shock) | 0 | 0 | 300 | 1,350 | 1,900 | 700 | 300 | 250 | 150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage IV _A - Chronic Recovery Requiring Care (5%) | 0 | 0 | 0 | 15 | 83 | 178 | 213 | 228 | 240 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 |
| E Stage IV _B - Recovery at Home | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| F Total Ill Today (Stage II, III, IV _A , IV _B) | 0 | 350 | 1,650 | 3,265 | 2,683 | 1,178 | 763 | 628 | 390 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 | 248 |
| G Number of Worried Well Today (see *note) | 0 | 0 | 1,400 | 4,370 | 5,948 | 6,315 | 2,745 | 1,305 | 713 | 428 | 321 | 240 | 180 | 135 | 101 | 76 | 57 | 0 | 0 | 0 | 0 | 0 |
| H Total Seeking Medical Aid Today (Stage II and WWW) | 0 | 350 | 2,750 | 6,270 | 6,648 | 6,615 | 2,995 | 1,455 | 713 | 428 | 321 | 240 | 180 | 135 | 101 | 76 | 57 | 0 | 0 | 0 | 0 | 0 |
| I Number of Fatalities Today (95%) | 0 | 0 | 50 | 285 | 1,283 | 1,805 | 665 | 285 | 238 | 143 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| J Cumulative Number of Fatalities | 0 | 0 | 50 | 335 | 1,618 | 3,423 | 4,088 | 4,373 | 4,610 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 | 4,753 |
| K Cumulative Number of Persons Seeking Medical Aid | 0 | 350 | 3,100 | 9,370 | 16,018 | 22,633 | 25,628 | 27,083 | 27,795 | 28,223 | 28,543 | 28,784 | 28,964 | 29,099 | 29,201 | 29,277 | 29,334 | 29,334 | 29,334 | 29,334 | 29,334 | 29,334 |

Day of Attack

Day First Ill Present

Distribution of Illness for Infected Persons

Worst Case Predictions if no Public Information Countermeasures are Instituted

Number of People Infected: 5,000
 Distribution of Presenting Illness: 7% 27% 38% 14% 6% 5% 3%
 Incident Mortality Rate: 95%

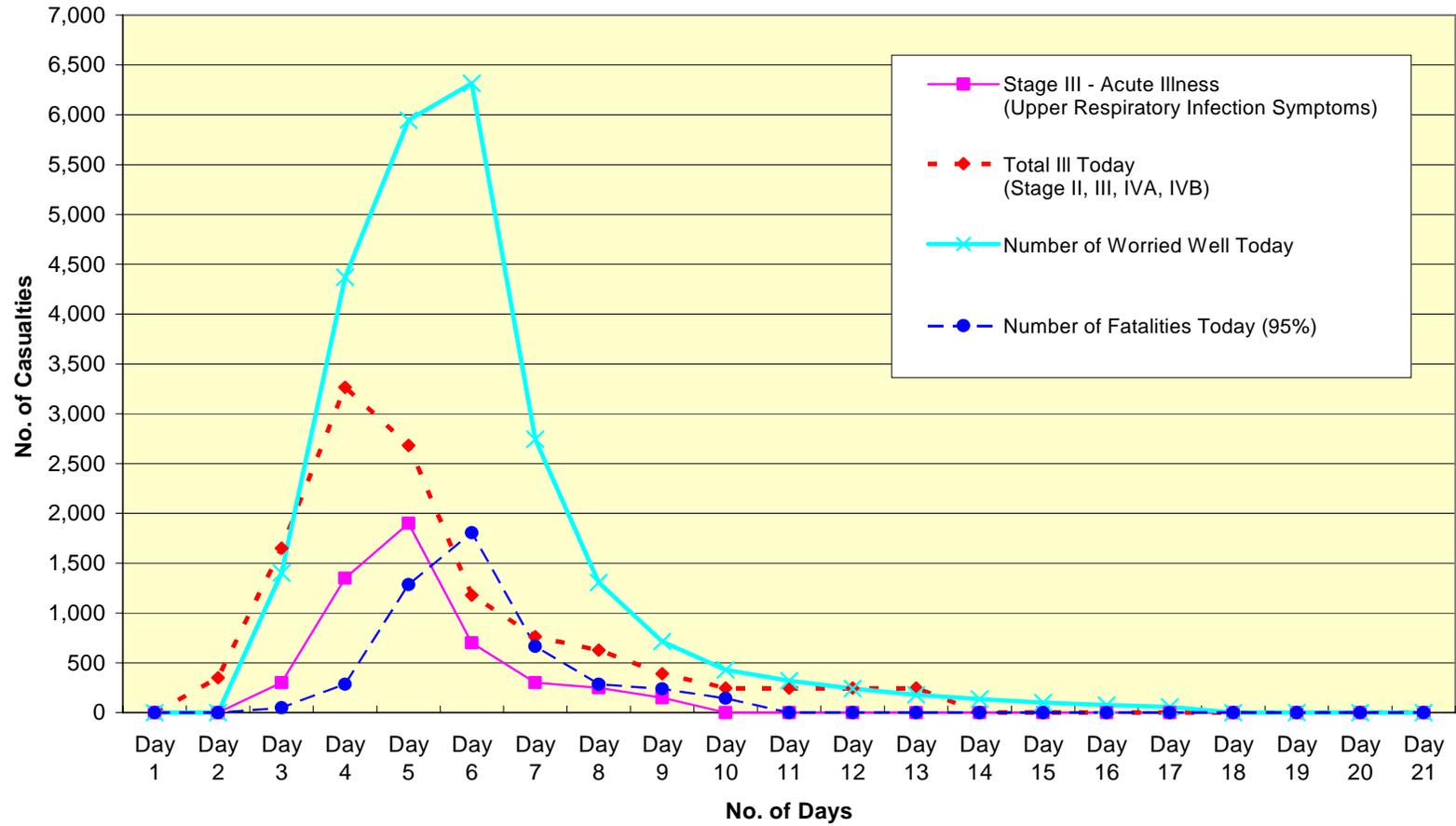
*Note: Day 3: The number of worried well = 1x the number that presents plus fatalities
 Day 4: The number of worried well = 2x the number that presents plus fatalities
 Days 5-10: The number of worried well = 3x the number that presents plus fatalities
 Days 11-17: The number of worried well = .75x the number that presents plus fatalities
 Day 18: The number of worried well drops to zero

Assumptions:

Distribution of presenting illness. Average incubation period is three days, with severe symptoms beginning day 4.
Worried-but-well cases. The ratio will range from 3:1 to 10:1. For most days, the numbers of worried-but-well cases ranges from 0.75 to 3.0 times the number of new cases plus the number of fatalities.
Secondary Cases. There are no secondary cases of the disease.
Effects of community prophylaxis. Will commence on the fourth day.
Other containment measures. No other containment measures were assumed.

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**FIGURE 1 ANTHRAX
CASUALTY PREDICTIVE DISTRIBUTION CHART**



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TULAREMIA

3.0 TULAREMIA OVERVIEW

Tularemia (also known as rabbit fever and deer fly fever) is caused by *francisella tularensis* (*F. tularensis*) a small, aerobic non-motile, gram-negative cocco-bacillus. It is a zoonotic disease that humans can acquire after their skin or mucous membranes contact infected tissues or body fluids of animals, or if they are bitten by infected ticks, deerflies, or mosquitoes. It is possible for people to contract the disease by inhaling bacteria-contaminated dust or ingesting contaminated foods or water, but this is not as common;¹⁰ thus, cases of typhoidal tularemia (tularemia septicemia) or tularemia pneumonia should raise suspicion of a terrorist-related infection.

F. tularensis can remain viable for weeks in water, soil, carcasses, and animal hides. It is resistant to decomposition for months in temperatures at or below freezing and can remain viable for years in frozen rabbit meat. It is, however, easily killed by heat and disinfectants.¹¹

The clinical presentation of tularemia may be severe, yet non-specific. Differential diagnoses (other diseases that share common symptomatology) include typhoid syndromes (meaning symptom clusters that include severe headache, generalized maculopapular rash, sustained high fever and/or progressive neurological signs), salmonella bacteremia, rickettsial diseases (e.g., Rocky Mountain spotted fever or typhus), malaria, and pneumonias (e.g., pneumonic plague or inhalational staphylococcal enterotoxin B [SEB]).¹²

Post-exposure prophylaxis medications (medications taken after exposure to the agent to prevent onset of disease) usually includes a two-week course of antibiotics, which is most effective if given within 24-hours of exposure (presuming it was an aerosol exposure and the strain is not antibiotic resistant). Typical antibiotics used to treat tularemia include doxycycline, tetracycline, ciprofloxacin, streptomycin, gentamicin, and chloramphenicol. Although practitioners can use any of these medications to treat tularemia they should be aware that streptomycin, the drug of choice, may not be readily available immediately following a large-scale attack and studies show

¹⁰ Dennis DT, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Friedlander AM, Hauer J, Layton M, Lillibridge SR, McDade JE, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Tonat K; Working Group on Civilian Biodefense. Tularemia as a biological weapon: medical and public health management. JAMA. 2001 Jun 6;285(21):2763-73.

¹¹ Dembek ZF, Buckman RL, Fowler SK, Hadler JL. Missed sentinel case of naturally occurring pneumonic tularemia outbreak: lessons for detection of bioterrorism. J Am Board Fam Pract. 2003 Jul-Aug;16(4):339-42.

¹² Dennis DT, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Friedlander AM, Hauer J, Layton M, Lillibridge SR, McDade JE, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Tonat K; Working Group on Civilian Biodefense. Tularemia as a biological weapon: medical and public health management. JAMA. 2001 Jun 6;285(21):2763-73.

that tetracycline, doxycycline, and chloramphenicol, are likely to result in relapse of the disease. In the end ciprofloxacin, may present the best antibiotic treatment alternative.

In general chemoprophylaxis is not recommended following potential natural exposures such as tick bites or rabbit or other animal exposures.¹³

There is a vaccine for tularemia which has demonstrated significant protection, but it is an investigational live-attenuated vaccine and not readily available to the public. As with all vaccines, the degree of protection is dependent on concentration of the challenge dose; hence even previously immunized casualties exposed to extremely high doses of *F. tularensis* may still contract the disease.¹⁴

All populations are susceptible to contracting the disease, and recovery is generally followed by permanent immunity.

Since there is no known human-to-human transmission, neither isolation nor quarantine is required. No additional personal protective equipment is required; however, providers should strictly adhere to Standard Precautions particularly when managing wound drainage/secretions, and especially when caring for lesions and handling/disinfecting soiled clothing, bedding, equipment, etc.¹⁵

3.1 CLINICAL FEATURES

Tularemia typically appears in one of six forms in humans: typhoidal, ulceroglandular, glandular, oculoglandular, oropharyngeal, and pneumonic. Typhoidal and pneumonic tularemia, the forms of disease most likely to occur following an intentional aerosol release, generally only make up 5-15% of natural occurring cases.¹⁶

The incubation period, which is dependent on the route of exposure and concentration of inoculum, varies between 2–21 days, with an average presentation between 3–5 days. In animal studies, high aerosol inocula can result in incubation periods as short as 36 hrs. Only 10 to 50 organisms are required to cause infection if inhaled or injected intradermally.

Typhoidal tularemia typically develops after inhalation of infectious aerosols but can occur after intradermal or gastrointestinal exposure. Patients experience fever, exhaustion, weight loss and cough (productive or non-productive). Although pneumonia is a common

¹³ Dennis DT, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Friedlander AM, Hauer J, Layton M, Lillibridge SR, McDade JE, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Tonat K; Working Group on Civilian Biodefense. Tularemia as a biological weapon: medical and public health management. *JAMA*. 2001 Jun 6;285(21):2763-73.

¹⁴ Eliasson H, Lindback J, Nuorti JP, Arneborn M, Giesecke J, Tegnell A. The 2000 tularemia outbreak: a case-control study of risk factors in disease-endemic and emergent areas, Sweden. *Emerg Infect Dis*. 2002 Sep;8(9):956-60.

¹⁵ Eliasson H, Lindback J, Nuorti JP, Arneborn M, Giesecke J, Tegnell A. The 2000 tularemia outbreak: a case-control study of risk factors in disease-endemic and emergent areas, Sweden. *Emerg Infect Dis*. 2002 Sep;8(9):956-60.

¹⁶ Stralin K, Eliasson H, Back E. An outbreak of primary pneumonic tularemia. *N Engl J Med*. 2002 Mar 28;346(13):1027-9

development for all types of tularemia, it occurs in 30-80% of typhoidal cases and can be quite severe.¹⁷

Those who contract pneumonic tularemia typically present with a severe, acute, atypical pneumonia. Pneumonia can occur as a direct result of inhaling organisms, or secondarily as a result of a bloodstream infection (bacteremia).

Medical professionals can diagnose the disease using radiological evidence, lab values, and blood cultures; however, there are limitations with each diagnostic measure. For example, only 50% of patients develop pneumonia that is detected by chest radiographs. Additionally, initial laboratory evaluations may be nonspecific early in the disease and only present limited findings later in the disease process. Cultures (which are typically taken from blood, ulcers, conjunctival and pharyngeal exudates, sputum, and gastric washings), can detect the bacteria even after the patient receives antibiotic therapy; but performing culture analysis requires special culture media and Biosafety Level 3 (BSL3) containment to prevent laboratory exposures. Moreover, serologic diagnosis (using bacterial agglutination or enzyme-linked immunosorbent assay [ELISA]) is usually negative the first week of the infection, positive the second week in only 50–70 percent of cases, but clearly detected between 4–8 weeks of infection.¹⁸ Thus, serology results are generally not helpful in early diagnosis of disease.

The fatality rate for those cases that contract tularemia naturally and receive appropriate antibiotic treatment is only 1–3%. When left untreated, however, the case fatality rate increases to 35% for typhoidal tularemia and can be even higher in pneumonic tularemia.¹⁹

3.2 TULAREMIA CASUALTY PREDICTIVE TEMPLATE

The following casualty predictive template is intended to illustrate the potential impact of casualties on the medical infrastructure when approximately 5,000 people are infected with *F. tularensis* via aerosol exposure. Since there is no data on large-scale outbreaks, the developers made a number of assumptions when developing this template. These assumptions, and the rationale used in developing the formula equations, are presented below.

3.2.1 Template Assumptions

- ***Distribution of presenting illness.*** Average incubation period is assumed to be four days for tularemia. Those with underlying illness, immunologically compromised, at the extremes of age, or exposed to higher doses of the bacterium, may have a shorter incubation period (as short as 2 days). Conversely, those with robust immune systems, or who have received smaller inoculums, may be asymptomatic for longer periods of time (up to 21 days). The template also assumes patients will only need to be treated within the hospital for 5 days, which may not be the case (patients that have fulminant pneumonia or septicemia forms of tularemia typically need up to three

¹⁷ Gill V, Cunha BA. Tularemia pneumonia. *Semin Respir Infect.* 1997 Mar;12(1):61-7.

¹⁸ Gill V, Cunha BA. Tularemia pneumonia. *Semin Respir Infect.* 1997 Mar;12(1):61-7.

¹⁹ Stralin K, Eliasson H, Back E. An outbreak of primary pneumonic tularemia. *N Engl J Med.* 2002 Mar 28;346(13):1027-9

weeks of hospitalization). Also the template assumes that patients sent home (Stage IVB of the table) will receive enough medication to sustain an additional five days of treatment and will survive without reentering the health care system.

- **Fatality rate.** A fatality rate of 10% was used for this model. Though it is plausible that only 1-3% of the population could die from tularemia, the initial fatality rate would be greater, due to early misdiagnosis or ineffective treatment, and later, the fatality rate would likely be greater than the 1-3% due to the limited availability of pharmaceuticals and supportive care treatments. Planners should keep in mind that an antibiotic-resistant strain of tularemia could result in a significantly higher mortality rate.
- **Secondary cases.** There are no secondary cases predicted with this template, as tularemia is not known to spread between humans.
- **Worried-but-well cases.** The developers selected to invoke variable ratios, ranging from 3:1 to 10:1, of asymptomatic, potentially exposed individuals (“worried well”) to actual casualties. Subject matter experts have estimated that an outbreak, resulting from an intentional bacterial release in a community, would result in large numbers of unexposed individuals seeking medical evaluation, treatment, or reassurance. During the fall 2001 anthrax mail release, worried-well case projections ranged between 5 to 20 times the actual numbers of casualties.²⁰

The variable ratios will function in the following manner. The number of worried well for Days 4–5 will equal three times the number of people that present with illness on the prior days. On Day 6, the number of worried well will be five times the number of people that present on Day 5. On Days 7–8, the number of worried well will equal ten times the number of people that present on the prior days. On Day 9, the number of worried well will be ten times the number of fatalities that occur on Day 8. On Days 10–13, the number of worried well will be five times the number of fatalities on the days prior, and on Days 14–18, the number of worried well will decrease by one-third the number of worried well the days prior. On Day 19 the number of worried well will drop to zero.

- **Effects of community prophylaxis.** This template assumes that community prophylaxis will not commence until the fourth day after the attack. The developers made this determination based on the likely time required to identify the outbreak, diagnose initial cases, determine the cause of the outbreak, and determine the need to establish community prophylaxis. Further delays would occur due to the logistics involved with acquisition of pharmaceuticals, delivery to points of distribution, and institution of dispensing plans. Dispensing of prophylaxis to certain populations (e.g., homeless, disabled, house-bound, impoverished and/or those with language barriers or lacking transportation) may be delayed even further. It is possible that

²⁰ Tucker, N. *Emergency Rooms Overrun by the ‘Worried by Well’* The Washington Post. Thursday, November 1, 2001; Page B01. Available at <http://www.washingtonpost.com/ac2/wp-dyn/A21059-2001Oct31?language=printer> [last visited 12 October 2003]

communities with mature plans and ready access to major airfields for delivery of the SNS may reduce the time from exposure to prophylaxis than what this model depicts.

- **Other containment measures.** Since this disease is not transmitted person-to-person, no other containment measures were assumed in developing this model. Instituting sanitation barrier measures, post-outbreak public health education, or other public health initiatives could significantly alter the dynamics of this outbreak.

3.2.2 Calculations

The following section outlines the calculations applied in developing the tularemia casualty predictive template. It also delineates the actual formula associated with each previously described assumption.

| Row | Definition | Formula |
|----------|--|--|
| A | Stage I – Incubation Period: Number of persons primarily infected but still asymptomatic. | Initially 5,000, decreasing by numbers presenting at Stage II. Row A (previous day) – Row B (current day) |
| B | Stage II – Presenting Illness (non-specific febrile syndrome): Number of persons primarily infected who present on the day in question with high fever, headache, body aches, and fatigue. | Incubation period of 4 days. See distribution at bottom of template. |
| C | Stage III - Acute Illness (septicemia and/or pneumonia): Total number of patients who have presented with the febrile syndrome on the day in question who have survived the day. All patients presumed to progress to this stage, 24 hours after initial symptoms. | Row B (previous day) + Row C (previous day) |
| D | Stage IV _A - Chronic Recovery. | Not used in this model |
| E | Stage IV _B - Recovery at Home. Presumes in-patient treatment required for 5 days. All surviving patients recover at home. | Row E (previous day) + Row A (5 previous days) – Row I (current day) |
| F | Total III Today (Stage II, III, IV _A , IV _B). Sum of these stages for the current day. | Row B + Row C + Row D + Row E (current day) |

| Row | Definition | Formula |
|----------|--|---|
| G | Number of Worried Well Today. Variable factor based on level of community disease. See distribution at bottom of template. | $(\text{Row I (day prior)} + \text{Row F (day prior)}) \times \text{Worried Well Factor}$ |
| H | Total Seeking Medical Aid Today. Total of worried well and actual ill for current day. | $\text{Row B} + \text{Row G (current day)}$ |
| I | Number of Fatalities Today. Fatalities begin 7 days after exposure. | $\text{Cell A (day 1)} \times \text{Fatality Rate X}$ |
| J | Cumulative Number of Fatalities. Current day's fatalities plus previous day's cumulative fatalities. | $\text{Row J (previous day)} + \text{Row I (current day)}$ |
| K | Cumulative Number of Persons Seeking Medical Aid. | $\text{Row K (previous day)} + \text{Row H (current day)}$ |

TABLE 2 TULAREMIA CASUALTY PREDICTIVE TEMPLATE

| Description | Distribution of Illness for Infected Persons | | | | | | | | | | | | | | | | | | | | |
|---|--|-------|-------|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 |
| A Stage I - Incubation Period (see distribution) | 5,000 | 5,000 | 4,850 | 2,300 | 500 | 150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting Illness (non-specific febrile syndrome) | 0 | 0 | 350 | 2,350 | 1,800 | 350 | 150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III - Acute Illness (septicemia and/or pneumonia) | 0 | 0 | 0 | 350 | 2,700 | 4,500 | 4,850 | 4,650 | 2,300 | 500 | 150 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage IV _A - Chronic Recovery | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| E Stage IV _B - Recovery at Home | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 220 | 2,330 | 4,025 | 4,355 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 |
| F Total Ill Today (Stage II, III, IV _A , IV _B) | 0 | 0 | 350 | 2,700 | 4,500 | 4,850 | 5,000 | 4,870 | 4,630 | 4,525 | 4,505 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 | 4,500 |
| G Number of Worried Well Today (see *note) | 0 | 0 | 0 | 1,050 | 7,050 | 9,000 | 3,500 | 1,500 | 1,300 | 1,200 | 525 | 100 | 25 | 17 | 11 | 7 | 5 | 3 | 0 | 0 | 0 |
| H Total Seeking Medical Aid Today | 0 | 0 | 350 | 3,400 | 8,850 | 9,350 | 3,650 | 1,500 | 1,300 | 1,200 | 525 | 100 | 25 | 17 | 11 | 7 | 5 | 3 | 0 | 0 | 0 |
| I Number of Fatalities Today (see mortality rate) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 130 | 240 | 105 | 20 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| J Cumulative Number of Fatalities | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 130 | 370 | 475 | 495 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |
| K Cumulative Number of Persons Seeking Medical Aid | 0 | 0 | 350 | 3,750 | 12,600 | 21,950 | 25,600 | 27,100 | 28,400 | 29,600 | 30,125 | 30,225 | 30,250 | 30,267 | 30,278 | 30,285 | 30,290 | 30,293 | 30,293 | 30,293 | 30,293 |

Worst Case Predictions if no Public Information Countermeasures are Instituted

Number of People Infected: 5,000

Distribution of Presenting Illness: 7% 47% 36% 7% 3%

Incident Mortality Rate: 10%

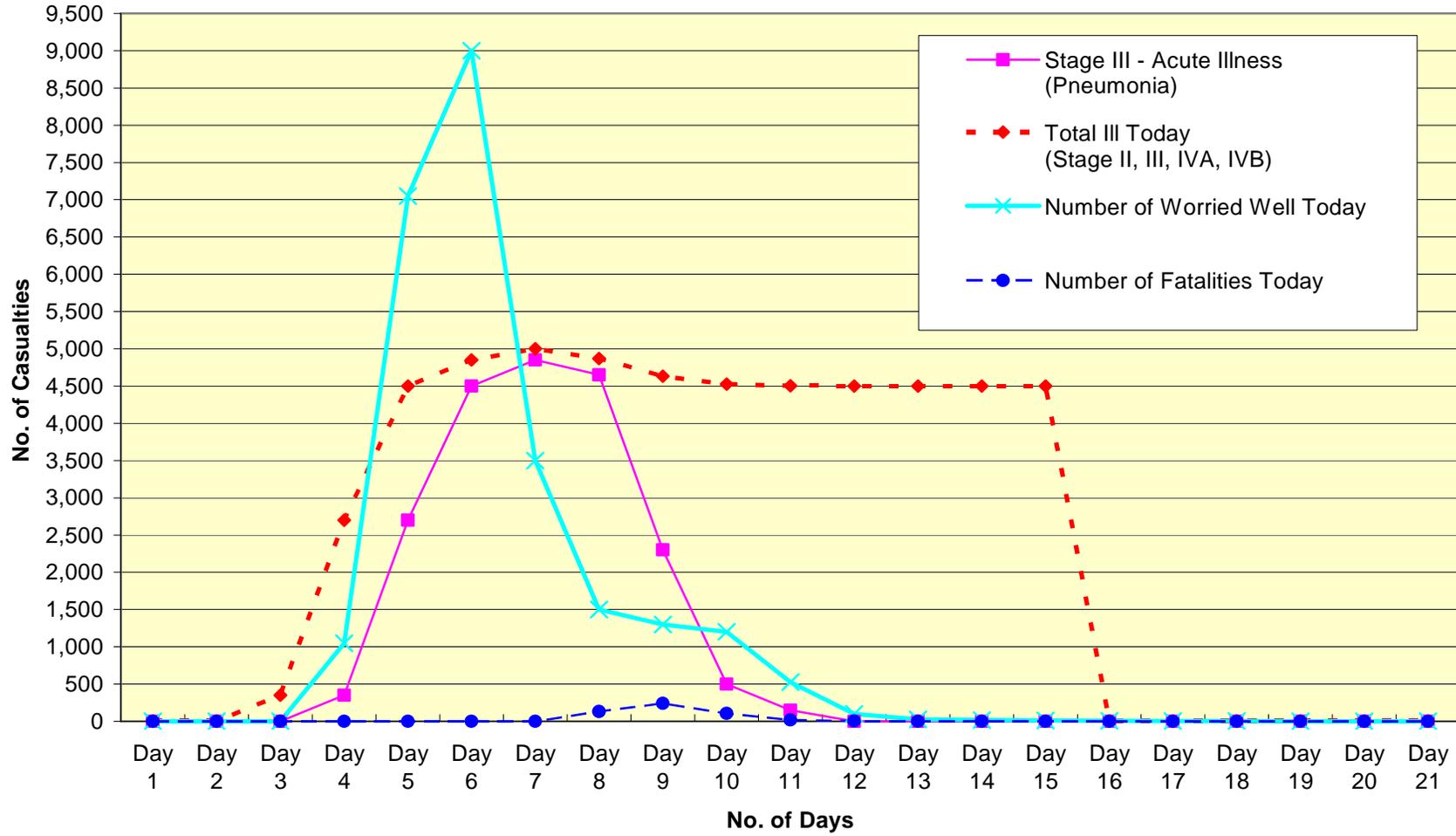
*Note: Days 4-5: The number of worried well = 3x the number that present the day prior
 Day 6: The number of worried well = 5x the number that present the day prior
 Days 7-8: The number of worried well = 10x the number that present the day prior
 Day 9: The number of worried well = 10x the number of fatalities the day prior
 Days 10-13: The number of worried well = 5x the number of fatalities the day prior
 Days 14-18: The number of worried well decreases by 1/3 the number of worried well the day prior

Assumptions:

Distribution of presenting illness. Average incubation period is four days.
Secondary cases. There are no secondary cases predicted.
Worried-but-well cases. The panel selected to invoke variable ratios, ranging from 3:1 to 10:1.
Effects of community prophylaxis. Will commence on the fourth day after awareness of the attack.
Other containment measures. No containment measures were assumed.

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**FIGURE 2 TULAREMIA
CASUALTY PREDICTION DISTRIBUTION CHART**



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PLAGUE

4.0 PLAGUE OVERVIEW

Plague, is caused by *Yersinia pestis* (*Y. pestis*), a rod-shaped, non-motile, non-sporulating, gram-negative bacterium.²¹ It is a zoonotic disease of rodents (e.g., rats, mice, ground squirrels) but can be transmitted to humans via a flea vector common to both rodents and man. In man, plague normally appears in three forms: bubonic (which occurs after being bitten by a *Y. pestis* infected flea), septicemic (which occurs when the bubonic plague progresses or after inhalational exposure, in which the plague bacillus enters the bloodstream), and pneumonic (which rarely occurs naturally and is the form most likely to occur following an intentional aerosol release).

Pneumonic plague poses a great concern, as it is contagious (can be transmitted person-to-person). Historically, primary caregivers that come in close contact (2 meters or less for prolonged periods) with severely ill, coughing patients, either at home or in the healthcare setting become infected. Person to person spread is more likely under crowded living conditions or during cold, humid weather.

Today, the disease exists worldwide and is endemic in the southwest United States (U.S.). All human populations are susceptible, and once a patient recovers from a *Y. pestis* infection, he/she is likely to experience temporary immunity.²²

The organism is relatively hardy, as it remains viable in water, moist soil, and grains for several weeks. At near freezing temperatures, it will remain alive for months to years but is totally degraded when exposed to 131° F (55° C) for 15 minutes. It also remains viable for some time in dry sputum, flea feces, and buried bodies but is sufficiently degraded if exposed to sunlight for several hours.²³

The choice of antibiotic for post exposure prophylaxis is doxycycline; however ciprofloxacin, tetracycline, and chloramphenicol may be acceptable antibiotic alternatives.²⁴

The antibiotic of choice for treatment of plague disease is streptomycin; but because this antibiotic may be difficult to obtain in large quantities in an outbreak setting, gentamicin is an

²¹ Centers for Disease Control and Prevention. Prevention of plague. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, 1996;45(RR-14):1-15.

²² Chanteau S, et al. Current epidemiology of human plague in Madagascar. *Microbes Infect.* 2000 Jan;2(1):25-31.

²³ Darling RG, Catlett CL, Huebner KD, Jarrett DG. Threats in bioterrorism. I: CDC category A agents. *Emerg Med Clin North Am.* 2002 May;20(2):273-309.

²⁴ Franz DR, et al. Clinical recognition and management of patients exposed to biological warfare agents. *JAMA.* 1997 Aug 6;278(5):399-411

alternative, but it has not been approved by the FDA for this use. Other antibiotics alternatives for treatment of symptomatic patients include doxycycline, tetracycline, and ciprofloxacin and for patients that have plague meningitis, Chloramphenicol is the typical antibiotic administered.

No vaccine is currently available for plague. A licensed vaccine was available in the U.S. from 1946 through November 1998; however it only offered protection against bubonic plague (not the pneumonic form).²⁵ Presently, the USAMRIID and other agencies are advancing on plague vaccines that have been proven effective in preventing pneumonic plague in mice.

Community containment measures that will mitigate person to person spread include using personal protective equipment (Droplet Precautions: surgical mask, eye protection, gown, and gloves), instituting laboratory safety practices, isolating pneumonic plague patients, and controlling vector and reservoir areas.²⁶ Other community containment measures include the following.

- Recommended infection control procedures include standard precautions for bubonic plague cases.
- Recommended infection control procedures for suspected pneumonic plague cases are standard precautions plus droplet precautions and respiratory isolation for at least 48 hours following the administration of antibiotic therapy or until patient sputum cultures are negative.
- Biosafety Level 2 (BSL-2) labs are required to conduct clinical assays; procedures producing aerosols or yielding significant quantities of organisms however, require BSL-3 containment.
- Community containment measures potentially include quarantine and vector (e.g., fleas) and reservoir (e.g., rodents) control if it is believed that they are contributing to the life cycle of the disease.

4.1 CLINICAL FEATURES

Bubonic plague has an incubation period of 2–10 days, followed by an acute and severe onset of nonspecific symptoms, such as high fever, malaise, headache, muscle tenderness, nausea, and abdominal pain. Simultaneous with or shortly after the onset of symptoms, the bubo develops—a swollen, very painful, infected lymph node. Buboes are normally seen in the femoral or inguinal lymph nodes and only pose an exposure risk to others if blood or body fluids drain from the site. The patient's liver and spleen are often tender and palpable. One quarter of patients will have various types of skin lesions, often at the site of the flea bite, and it is likely that untreated bubonic plague will progress to septicemic plague, as it occurs in approximately 80 percent of cases.²⁷

²⁵ Centers for Disease Control and Prevention. Prevention of plague. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, 1996;45(RR-14):1-15.

²⁶ Inglesby TV, et al. Plague as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

²⁷ Chanteau S, et al. Current epidemiology of human plague in Madagascar. Microbes Infect. 2000 Jan;2(1):25-31.

It is possible that plague septicemia can spread to the central nervous system, lungs (causing a pneumonia, or “secondary pneumonic plague”), and elsewhere in the body, resulting in necrosis and gangrene of the extremities. In rare instances plague septicemia can progress into disseminated intravascular coagulopathy (DIC) and cause meningitis (occurs in 6% of septicemic and pneumonic cases).²⁸

Pneumonic plague has an incubation period of 1 to 6 days, followed by abrupt onset of severe symptoms to include nausea, chills, headache, malaise, muscle tenderness, and abdominal pain. Typical signs include high fever, vomiting, diarrhea, and within 24 hours, pneumonia. Patients with plague pneumonia almost invariably develop a productive cough that has blood streaked or bloody sputum. Chest x-rays commonly reveal large bilateral infiltrates that can be patchy or consolidated. Laboratory findings include a leukocytosis, with a total white blood cells (WBC) count of 20,000 or greater, as well as elevated levels for blood urea nitrogen, creatinine, transaminases, and bilirubin. Pneumonic plague, which is denoted by physical signs of difficulty breathing, stridor, and poor tissue perfusion (cyanosis), can progress rapidly and result in respiratory failure and total circulatory collapse.²⁹

Mortality of untreated bubonic plague is approximately 60 percent, but reduces to less than five percent when effective treatment is administered promptly. For untreated pneumonic plague some sources identify a mortality rate of nearly 100 percent, especially when treatment is delayed beyond 18 hours of infection.³⁰ Data on actual cases in the U.S. during the past 50 years identify a 57 percent mortality rate (four of the seven pneumonic plague patients died). This number is corroborated by the 1989 Madagascar plague epidemic mortality rate, which was also 57 percent.³¹

4.2 PLAGUE CASUALTY PREDICTIVE TEMPLATE

The following casualty situation template is provided to illustrate the impact of casualties on the medical infrastructure when 5,000 people are infected with pneumonic plague. [The following template does not take into account bubonic or septicemic plague.] Due to the scant availability of data on actual outbreaks of pneumonic plague and the lack of any reported events involving intentional aerosol release of *Y. pestis*, the developers made a number of assumptions in developing this template. These assumptions, and the rationale used in developing the associated formula/equations, are presented below.

²⁸ Darling RG, Catlett CL, Huebner KD, Jarrett DG. Threats in bioterrorism. I: CDC category A agents. *Emerg Med Clin North Am.* 2002 May;20(2):273-309.

²⁹ Krishna G, Chitkara RK. Pneumonic plague. *Semin Respir Infect.* 2003 Sep;18(3):159-67.

³⁰ Krishna G, Chitkara RK. Pneumonic plague. *Semin Respir Infect.* 2003 Sep;18(3):159-67.

³¹ Chanteau S, et al. Current epidemiology of human plague in Madagascar. *Microbes Infect.* 2000 Jan;2(1):25-31.

4.2.1 Template Assumptions

- ***Distribution of presenting illness.*** Average incubation period is assumed to be two days for pneumonic plague.³² Those with underlying illness, immunologically compromised, at the extremes of age, or receiving higher pathogen inoculums, may have a shorter incubation period. Conversely, those with robust immune systems, or who have received smaller inoculums, may be asymptomatic for longer periods of time. For this template, the same incubation period was used for those secondarily exposed.
- ***Fatality rate.*** The vast majority of persons primarily infected would die, as the progression from the onset of symptoms until debilitation and ultimate death is often quite short. This high mortality rate is due to anticipated delays in diagnosis and administration of treatment, and a lack of sufficient medical resources during the initial days of the outbreak. As these delays diminish and effective treatment is administered promptly to secondary cases, and as outside resources become available, the mortality rate would lessen over time. The template attempts to depict this drop in the fatality rate by decreasing the fatality multiplier within the template during later stages of the outbreak (see formula row L).
- ***Secondary Cases.*** Each primary case is expected to infect 1.5 secondary cases. Once casualties become symptomatic, they are contagious and the disease can spread from person to person. Once the community becomes aware of the outbreak and public health officials institute simple infection control and containment strategies, the number of secondary cases of infection will decline dramatically.

There is some difficulty with accurately reflecting secondary cases in this equation. The equation assumes a basic reproductive ratio (R_0) of 1.3 based upon meta-analysis of previous epidemics of pneumonic plague (a R_0 between 1.0 and 5.0 indicates that the disease is transmissible).³³ This template equation however does not take into account those that may have taken prophylaxis medications, which decreases susceptibility of contracting the disease, nor does it attempt to figure out when the first generation R_0 values would fall below 1.0, which is usually an indication that further person to person spread will cease. Additionally, the developers did not address tertiary transmission by those secondarily infected to calculate third-generation cases.

- ***Worried-but-well cases.*** The ratio of asymptomatic potentially exposed individuals (“worried well”) to actual casualties will be assumed to be 10:1. Subject matter experts have estimated that the outbreak of a highly infectious disease that is transmissible between humans would result in large numbers of unexposed

³² Inglesby TV, et al. Plague as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA. 2000 May 3;283(17):2281-90.

³³ Keeling, M. “The mathematics of disease.” +Plus (on-line educational resource). Available at <http://plus.maths.org/issue14/features/diseases/index.html> [last visited 12 October 2003]

individuals seeking medical evaluation, treatment, or reassurance. During the fall 2001 anthrax mail release, worried well case projections ranged between 5 to 20 times the actual numbers of casualties.³⁴

- ***Effects of community prophylaxis.*** This template assumes that community prophylaxis will not commence until the fourth day after awareness of the attack. The developers made this determination based on the likely time required to identify the outbreak, diagnose initial cases, determine of the cause of the outbreak, and determine the need to establish community prophylaxis. Further delays could occur due to the logistics involved with acquisition of pharmaceuticals, delivery to points of distribution, and institution of dispensing plans. Dispensing of prophylaxis to certain populations (e.g., homeless, disabled, house-bound, impoverished and/or those with language barriers or lacking transportation) may be delayed even further. Since in this model, the vast majority of those primarily infected would have already developed severe symptoms before authorities would be able to institute community wide antibiotic prophylaxis, there would be no early improvement in patient outcome resulting from initiation of community-wide prophylaxis. It is possible that communities with mature plans and ready access to major airfields for delivery of the SNS may reduce the time from exposure to prophylaxis from what this model depicts.
- ***Other containment measures.*** No other containment measures were assumed in this model. Public health initiatives such as voluntary or involuntary quarantine, patient isolation, post-outbreak public health education, or population movement control were not taken into account when developing this predictive formula. Thus, instituting any or all of these measures could significantly alter the dynamics of the outbreak and lessen the number of overall cases.

4.2.2 Calculations

The following section outlines the calculations applied in developing the pneumonic plague casualty predictive template. It also delineates the actual formula associated with each previously described assumption.

³⁴ Tucker, N. *Emergency Rooms Overrun by the 'Worried by Well'* The Washington Post. Thursday, November 1, 2001; Page B01. Available at <http://www.washingtonpost.com/ac2/wp-dyn/A21059-2001Oct31?language=printer> [last visited 12 October 2003]

| Row | Definition | Formula |
|----------|--|--|
| A | Stage I (Primary) – Incubation Period: Number of persons primarily infected but still asymptomatic. | 5,000 |
| B | Stage II (Primary) – Presenting Illness (Fever, Chill, Headache, Pulmonary Hemorrhage): Number of persons primarily infected who present on the day in question with initial symptoms of pneumonic plague. | Based on variable incubation period. 24 hrs (10%) 48 hrs (80%) 72 hrs (10%) |
| C | Stage I (Secondary) - Incubation Period: Number of asymptomatic secondarily infected persons. | 1.5 x Row B (previous day) |
| D | Stage II (Secondary) - Presenting Illness: Number of persons secondarily infected who present on the day in question with initial symptoms of pneumonic plague. | 1.00 x Row C (previous day) |
| E | Total New Ill Today | Row B (current day) + Row D (current day) |
| F | Total Ill Today: Stage II less those who have died today. | Row E (current day) – Row L (current day) |
| G | Cumulative of Total Ill: Sum of previous day's Cumulative of Total Ill Today and current day's Total Ill Today. | Row F (current day) + Row G (previous day) |
| H | Stage III - Recovery at Home: Disease survivors who have recuperated sufficiently to continue convalescing in an out-patient setting. | Row F (from 9 days prior to current day) |
| I | Cumulative of Recovery: Sum of cumulative of Recovery from previous day and current day Stage III- Recovery at home. | Row I (previous day) + Row H (current day) |

| Row | Definition | Formula |
|----------|---|---|
| J | Number of Worried Well Today: Asymptomatic but potentially exposed casualties, or those with concerns but no symptoms. Multiple (10) of Total of New Ill Today from previous day. | 10 x Row E (previous day) |
| K | Total Seeking Medical Aid Today: Sum of Total New Ill Today (current day) and Worried Well Today (current day). | Row E (current day) + Row J (current day) |
| L | Number of Fatalities Today: Number of victims who have died during current day. | Based on variable fatality rate 90% (day2) 75% (day 3) 35% (day 4) 24% (day 5) 10% (day 6) Row E x fatality rate |
| M | Cumulative Number of Fatalities: Sum of fatalities from previous day and Number of Fatalities Today. | Row M (cumulative number of preceding days of those who died) |
| N | Cumulative Number of Persons Seeking Medical Aid: Cumulative sum of all persons who have sought care. | Row F (cumulative number of ill) + Row J (cumulative number of seeking care) |

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TABLE 3 PNEUMONIC PLAGUE CASUALTY PREDICTIVE TEMPLATE

| Description | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 |
|--|-------|-------|-------|--------|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| A Stage I (Primary) - Incubation Period (see distribution) | 5,000 | 4,500 | 500 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II (Primary) - Presenting Illness (Fever, Chills, Headache, Pulmonary Hemorrhage) | 0 | 500 | 4,000 | 500 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage I (Secondary) - Incubation Period | 0 | 0 | 750 | 6,000 | 750 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage II (Secondary) - Presenting Illness | 0 | 0 | 0 | 750 | 6,000 | 750 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| E Total New Ill Today | 0 | 500 | 4,000 | 1,250 | 6,000 | 750 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| F Total Ill Today (Stage II - Fatalities) | 0 | 50 | 1,000 | 813 | 4,500 | 675 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| G Cumulative of Total Ill | 0 | 50 | 1,050 | 1,863 | 6,363 | 7,038 | 7,038 | 7,038 | 7,038 | 7,038 | 6,988 | 5,988 | 5,175 | 675 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| H Stage III - Recovery at Home | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 50 | 1,000 | 813 | 4,500 | 675 | 0 | 0 | 0 | 0 | 0 | 0 |
| I Cumulative of Recovery | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 50 | 1,050 | 1,863 | 6,363 | 7,038 | 7,038 | 7,038 | 7,038 | 7,038 | 7,038 | 7,038 |
| J Number of Worried Well Today | 0 | 0 | 5,000 | 40,000 | 12,500 | 60,000 | 7,500 | 3,750 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| K Total Seeking Medical Aid Today | 0 | 500 | 9,000 | 41,250 | 18,500 | 60,750 | 7,500 | 3,750 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| L Number of Fatalities Today (see mortality rate) | 0 | 450 | 3,000 | 438 | 1,500 | 75 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M Cumulative Number of Fatalities | 0 | 450 | 3,450 | 3,888 | 5,388 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 | 5,463 |
| N Cumulative Number of Persons Seeking Medical Aid | 0 | 500 | 9,500 | 50,750 | 69,250 | 130,000 | 137,500 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 | 141,250 |

Number of People Infected: 5,000

Distribution of Presenting Illness (Primary): 10% 80% 10%

Distribution of Presenting Illness (Secondary): 100% 100% 100%

Incident Mortality Rate: 90% 75% 35% 25% 10%

Assumptions:

Distribution of presenting illness . Average incubation period is two days for both the primary and secondary generation.

Fatality rate . The vast majority will die during the initial outbreak but the rate will decrease during later stages of the outbreak.

Secondary Cases . Each primary case will infect three secondary cases.

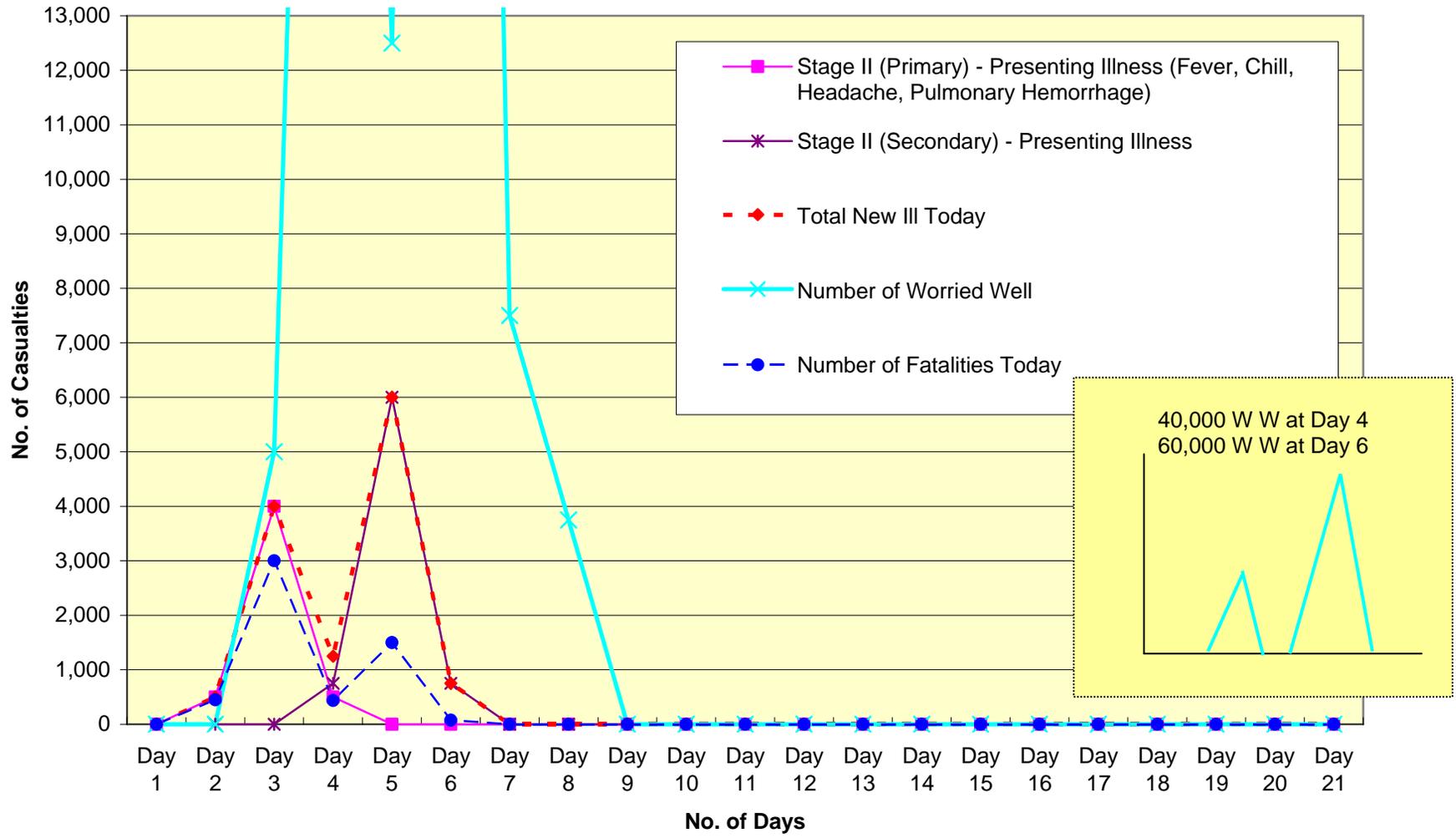
Worried-but-well cases . The ratio of worried well to actual casualties is 10:1.

Effects of community prophylaxis . Will commence on the fourth day after awareness of the attack.

Other containment measures . No other containment measures were assumed.

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FIGURE 3 PNEUMONIC PLAGUE CASUALTY PREDICTION DISTRIBUTION CHART



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SMALLPOX

5.0 SMALLPOX OVERVIEW

Smallpox is caused by the *Orthopoxvirus* variola, of which two strains have been identified: variola major and variola minor (a milder form of disease). Despite the global eradication of smallpox and continued availability of a vaccine (but not wide-scale administration), the possibility of releasing a weaponized version of variola continues to pose a military and civilian threat. Variola major is one of the biological agents of greatest concern due to the aerosol infectivity of the virus, which makes it highly contagious, the relative ease of large-scale production, and an increasingly *Orthopoxvirus*-naive populace.³⁵

Health and medical authorities must be prepared to quickly initiate isolation of contagious patients and quarantine of those potentially exposed following identification of smallpox disease. Patients infected with variola major can spread the infection from the time the rash erupts until scabs have separated. In very rare cases exposed persons can transmit the disease before manifesting a rash. It is recommended that patients secondarily exposed to smallpox be quarantined for 17 days so as to observe the development of a fever and to ensure that others are not inadvertently exposed.³⁶

Vaccinating patients with vaccinia vaccination and vaccinia immune globulin within 3-4 days (perhaps up to a week) of exposure is generally effective in either preventing or significantly ameliorating natural disease.³⁷ No specific antiviral therapy has proved effective in treating smallpox once symptoms develop.

Medical personnel that treat patients with smallpox must practice Airborne and Contact Precautions in addition to Standard Precautions. In addition to gloves, gown, and eye protection, providers should also wear powered air-purifying respirators (PAPRs) equipped with N-95 or high-efficiency particulate air (HEPA) filters.

5.1 CLINICAL FEATURES

The average incubation period of natural smallpox is 12 days, although it could range from 7–19 days following exposure. Intentional aerosol exposure of humans to variola could result in shortened incubation periods and develop into a more fulminant, severe disease. Acute clinical

³⁵ Legrand J, Viboud C, Boelle PY, Valleron AJ, Flahault A. Modelling responses to a smallpox epidemic taking into account uncertainty. *Epidemiol Infect.* 2004 Jan;132(1):19-25

³⁶ Ferguson NM, Keeling MJ, Edmunds WJ, Gani R, Grenfell BT, Anderson RM, Leach S. Planning for smallpox outbreaks. *Nature.* 2003 Oct 16;425(6959):681-5.

³⁷ Fulginiti VA, Papier A, Lane JM, Neff JM, Henderson DA. Smallpox vaccination: a review, part I. Background, vaccination technique, normal vaccination and revaccination, and expected normal reactions. *Clin Infect Dis.* 2003 Jul 15;37(2):241-50. Epub 2003 Jul 10.

manifestations include malaise, high fever, rigors, vomiting, headache, and backache; 15% of patients develop delirium.

A rash is a classic sign of smallpox however planners should not totally depend on this sign to make their diagnosis. Approximately 10% of light-skinned patients exhibit a mild rash during this initial stage. Then, 2 to 3 days after onset of fever, an erythematous, macular rash, appears. These skin lesions initially occur on the face, distal extremities, and then move centrally to the trunk. Lesions progress over the ensuing days from macules to papules, then vesicles and finally to pustules. Lesions are more abundant on the extremities and face. From 8 to 14 days after onset of the skin eruptions, the pustules form scabs that leave depressed depigmented scars upon healing.³⁸

Although the fully developed classic cutaneous eruption of smallpox is unique, earlier stages of the rash could be mistaken for varicella, impetigo, herpes-zoster or an allergic contact dermatitis.³⁹ Medical providers may have a challenging time diagnosing smallpox, as relatively mild cases seen in persons with partial immunity, as well as the more severe forms of disease (i.e., flat or hemorrhagic smallpox) do not always present in the expected manner.

The mortality rate of smallpox varies. Variola minor causes death in 1% of unvaccinated victims, while naturally occurring variola major has killed 30% of unvaccinated people and 3% of those vaccinated. Flat-type and hemorrhagic type smallpox can have higher percentages of mortality (up to 95%), and monkeypox, a naturally occurring relative of variola that is endemic to Africa, and is clinically indistinguishable from smallpox, has a lower mortality rate.⁴⁰ In all cases, higher mortality rates are seen in patients at the extremes of age, or who are immunocompromised or pregnant.

5.2 SMALLPOX CASUALTY PREDICTIVE TEMPLATE

The following smallpox casualty spreadsheet template is provided to illustrate the impact of 5,000 first-generation naturally infected smallpox patients on the medical infrastructure. No assumptions were made concerning how the initial population became exposed.

Due to variations in data on actual outbreaks of smallpox and the lack of any reported events involving intentional aerosol release of variola, the developers made a number of assumptions in developing this template. These assumptions, and the rationale used in developing the equations, are presented below.

³⁸ Zelicoff AP. An epidemiological analysis of the 1971 smallpox outbreak in Aralsk, Kazakhstan. *Crit Rev Microbiol.* 2003;29(2):97-108.

³⁹ Henderson DA, Inglesby TV, Bartlett JG, Ascher MS, Eitzen E, Jahrling PB, Hauer J, Layton M, McDade J, Osterholm MT, O'Toole T, Parker G, Perl T, Russell PK, Tonat K. Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. *JAMA.* 1999 Jun 9;281(22):2127-37.

⁴⁰ Fulginiti VA, Papier A, Lane JM, Neff JM, Henderson DA. Smallpox vaccination: a review, part II. Adverse events. *Clin Infect Dis.* 2003 Jul 15;37(2):251-71. Epub 2003 Jul 10.

5.2.1 Template Assumptions

- ***Distribution of presenting illness.*** For this template the incubation ranged between 7-17 days, with an average incubation period of 12 days for those initially as well as those secondarily exposed to smallpox. Those who are immunologically compromised, such as those who have an underlying illness, those at the extremes of the age continuum, or receive higher inoculums of pathogens, may have a shorter incubation period. Conversely, those with robust immune systems or have received smaller inoculums may be asymptomatic for longer periods of time.
- ***Fatality rate.*** The developers determined that 40% of persons primarily infected with smallpox would ultimately die. In some instances there may be a lack of sufficient medical resources to support large numbers of patients requiring extensive supportive care, particularly during the initial days of the outbreak. As the medical community is able to integrate outside resources, the mortality rate should subside. This is reflected in a decreasing fatality multiplier used in the template (see formula row L).
- ***Secondary cases.*** The developers determined that each primary case would infect three secondary cases. For typical cases of naturally-acquired smallpox, patients are profoundly ill before they become contagious thus the template assumes unimmunized primary caregivers, be they at home or within the hospital, will most likely be the ones to become infected. Once the community becomes aware of the outbreak and public health officials institute infection control and containment strategies, the number of secondary cases of infection will begin to decline.

There is some difficulty with accurately reflecting secondary cases in the equation. The equation assumes an R_0 based on exposing a population of only susceptible individuals to the infection. The equation does not take into account those who may have been vaccinated. Historically, during outbreaks, first generation R_0 values fall between 2.0 and 5.0.⁴¹ R_0 values as high as 11 have been reported, but this is rare for natural disease. Once the R_0 falls below 1.0, it is usually an indication that further person to person spread will cease. Additionally, in this template, the developers did not address tertiary transmission by those secondarily infected or calculate third-generation cases although a smallpox outbreak would likely generate third and fourth outbreak generations.

- ***Worried-but-well cases.*** This template applies a variable ratio that includes 1:1 to 10:1 regarding the number of asymptomatic-potentially-exposed individuals (“worried well”) to actual casualties. The developers estimate that the outbreak of a highly contagious disease in a community will result in large numbers of individuals seeking evaluation, treatment, or reassurance; the reality, however, is that many of them will have had little or minimal risk of exposure. Worried well projections for a bioterrorism event range from 5 to 20 times the actual number of casualties. The fall

⁴¹ Keeling, M. “The mathematics of disease.” +Plus (on-line educational resource). Available at <http://plus.maths.org/issue14/features/diseases/index.html> [last visited 12 October 2003]

2001 anthrax mailing incident reinforces this assumption, as there was several times the number of worried-but-well cases to actual casualties.

- ***Effects of community prophylaxis.*** The developers determined community prophylaxis will not commence until the eleventh day after the attack. Significant time would be lost between exposure (a 7 day incubation period was used), diagnosis of initial cases (first symptoms of smallpox are nonspecific and it is likely they won't be recognized as smallpox for 4-5 days after symptom onset), and confirmation of the cause of the outbreak.

Community prophylaxis could be further delayed than what is predicted due to the logistics of pharmaceutical or vaccine acquisition, delivery to points of distribution, and institution and execution of community dispensing plans. Moreover, delivering and administering vaccines or medications to particular populations (e.g., homeless, disabled, house-bound, impoverished and/or those with language barriers or lacking transportation) will likely require additional time. Only those communities with mature community prophylaxis plans and ready access to major airfields to receive delivery of the SNS are most likely to reduce the time from exposure to prophylaxis.

Emergency planners should keep in mind that this template outlines natural outbreak of smallpox. Many experts believe that the smallpox virus could be genetically engineered to render the existing vaccine minimally or even totally ineffective. Moreover, animal studies using genetically engineered aerosolized orthopox virus demonstrate a shortened incubation period of the disease and it rapidly progressing to fulminant pneumonia and shock before the development of a rash. The impact may be that patients become hyper-spreaders of the disease and die before being isolated, as medical professionals look for the distinguishing rash to determine the onset of contagiousness.

- ***Other containment measures.*** No containment measures were assumed in this model. If a jurisdiction did institute voluntary or mandatory quarantine, cordon sanitaria measures, post-outbreak public health education, or other public health initiatives, the number of infected patients and the dynamics of the outbreak could change considerably from the projected model outcome.

5.2.2 Calculations – Primary Generation

The following section outlines the calculations applied in developing the smallpox casualty predictive template for the primary generation of the outbreak. It also delineates the actual formula associated with each previously described assumption.

| Row | Definition | Formula |
|----------|---|--|
| A | Stage I – Incubation Period: Number of persons primarily infected but still asymptomatic. | 5,000 |
| B | Stage II – Presenting Illness: Number of persons primarily infected who present on the day in question with initial symptoms of malaise, fever, vomiting, and headache. | Based on variable incubation distribution ranging between Day 7 (0.1%) to Day 12 (22%) to Day 22 (0.1%) |
| C | Stage III – Acute Illness: Number of persons primarily infected who present on the day in question with acute illness and exhibit signs of lesions and rash. | Stage II (Row B) + 2 days |
| D | Stage IV _A – Chronic Illness and Recovering: Number of persons that have chronic signs and symptoms that require care but are recovering. | 37% Stage III (Row C previous day) |
| E | Stage IV _B – Recovering at Home: Disease survivors who have recuperated sufficiently to continue convalescing in an out-patient setting. | 63% Stage III (Row C previous day) |
| F | Total Ill Today: Stage II, III, IV _A , IV _B): Total number of patients that are ill today. | Stage II + III+ IV _A + IV _B (current day) |
| G | Number of Worried Well Today: Asymptomatic potentially exposed casualties, or those with concerns but no symptoms. Multiple (10) of Total of New Ill Today from previous day. | Variable ratio applied 3 x (Row B previous day) for the low ration on Day 8 to 10 x (Row B previous day for the high ration on Day 13. to 1 x (Row B previous day) on Day22 |
| H | Total Seeking Medical Aid Today: Sum of Total New Ill Today (current day) and Worried Well Today (current day). | Row F (current day) + Row G (current day) |
| I | Number of Fatalities Today: Number of victims who have died during current day. | 40% of Stage III (Row C) 8 days previous |

| Row | Definition | Formula |
|----------|---|--|
| J | Cumulative Number of Fatalities: Sum of fatalities from previous day and Number of Fatalities Today. | Row I (cumulative number of all previous days) |
| K | Cumulative Number of Persons Seeking Medical Aid: Cumulative sum of all persons who have sought care. | Row H (cumulative number of all previous days) |

TABLE 4 SMALLPOX (PRIMARY GENERATION) CASUALTY PREDICTIVE TEMPLATE

| Description | Day 1 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 | Day 22 | Day 23 | Day 24 | Day 25 | Day 26 | Day 27 | Day 28 | |
|---|-------|-------|-------|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| A Stage I - Incubation Period | 5,000 | 4,995 | 4,985 | 4,910 | 4,545 | 3,790 | 2,690 | 1,770 | 1,056 | 526 | 226 | 104 | 45 | 15 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting Illness (Malaise, Fever, Vomiting, Headache) | 0 | 5 | 10 | 75 | 365 | 755 | 1,100 | 920 | 714 | 530 | 300 | 122 | 59 | 30 | 10 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III - Acute Illness (Lesions, Rash) | 0 | 0 | 0 | 5 | 10 | 75 | 365 | 755 | 1,100 | 920 | 714 | 530 | 300 | 122 | 59 | 30 | 10 | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage IV _A - Chronic Recovery Requiring Care | 0 | 0 | 0 | 0 | 0 | 1 | 5 | 28 | 57 | 107 | 210 | 352 | 477 | 389 | 294 | 216 | 122 | 50 | 24 | 0 | 0 | 0 | 0 | 0 |
| E Stage IV _B - Recovery at Home | 0 | 0 | 0 | 0 | 3 | 6 | 47 | 230 | 476 | 693 | 580 | 450 | 334 | 189 | 77 | 37 | 19 | 6 | 3 | 0 | 0 | 0 | 0 | 0 |
| F Total Ill Today (Stage II, III, IV _A , IV _B) | 0 | 5 | 10 | 80 | 379 | 837 | 1,518 | 1,933 | 2,347 | 2,250 | 1,804 | 1,454 | 1,170 | 730 | 440 | 288 | 151 | 61 | 27 | 0 | 0 | 0 | 0 | 0 |
| G Number of Worried Well Today (see *note) | 0 | 0 | 15 | 30 | 450 | 2,190 | 7,550 | 11,000 | 4,600 | 3,570 | 1,590 | 900 | 366 | 118 | 60 | 10 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| H Total Seeking Medical Aid Today | 0 | 5 | 25 | 105 | 815 | 2,945 | 8,650 | 11,920 | 5,314 | 4,100 | 1,890 | 1,022 | 425 | 148 | 70 | 15 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| I Number of Fatalities Today (see mortality rate) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 4 | 30 | 146 | 302 | 440 | 368 | 286 | 212 | 120 | 49 | 24 | 24 |
| J Cumulative Number of Fatalities | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 6 | 36 | 182 | 484 | 924 | 1,292 | 1,578 | 1,790 | 1,910 | 1,958 | 1,982 | 1,982 |
| K Cumulative Number of Persons Seeking Medical Aid | 0 | 5 | 30 | 135 | 950 | 3,895 | 12,545 | 24,465 | 29,779 | 33,879 | 35,769 | 36,791 | 37,216 | 37,364 | 37,434 | 37,449 | 37,454 | 37,454 | 37,454 | 37,454 | 37,454 | 37,454 | 37,454 | 37,454 |

Number of People Infected: 5,000
 Distribution of Presenting Illness: 0.1% 0.2% 1.5% 7.3% 15.1% 22.0% 18.4% 14.3% 10.6% 6.0% 2.4% 1.2% 0.6% 0.2% 0.1%
 Incident Mortality Rate: 40%

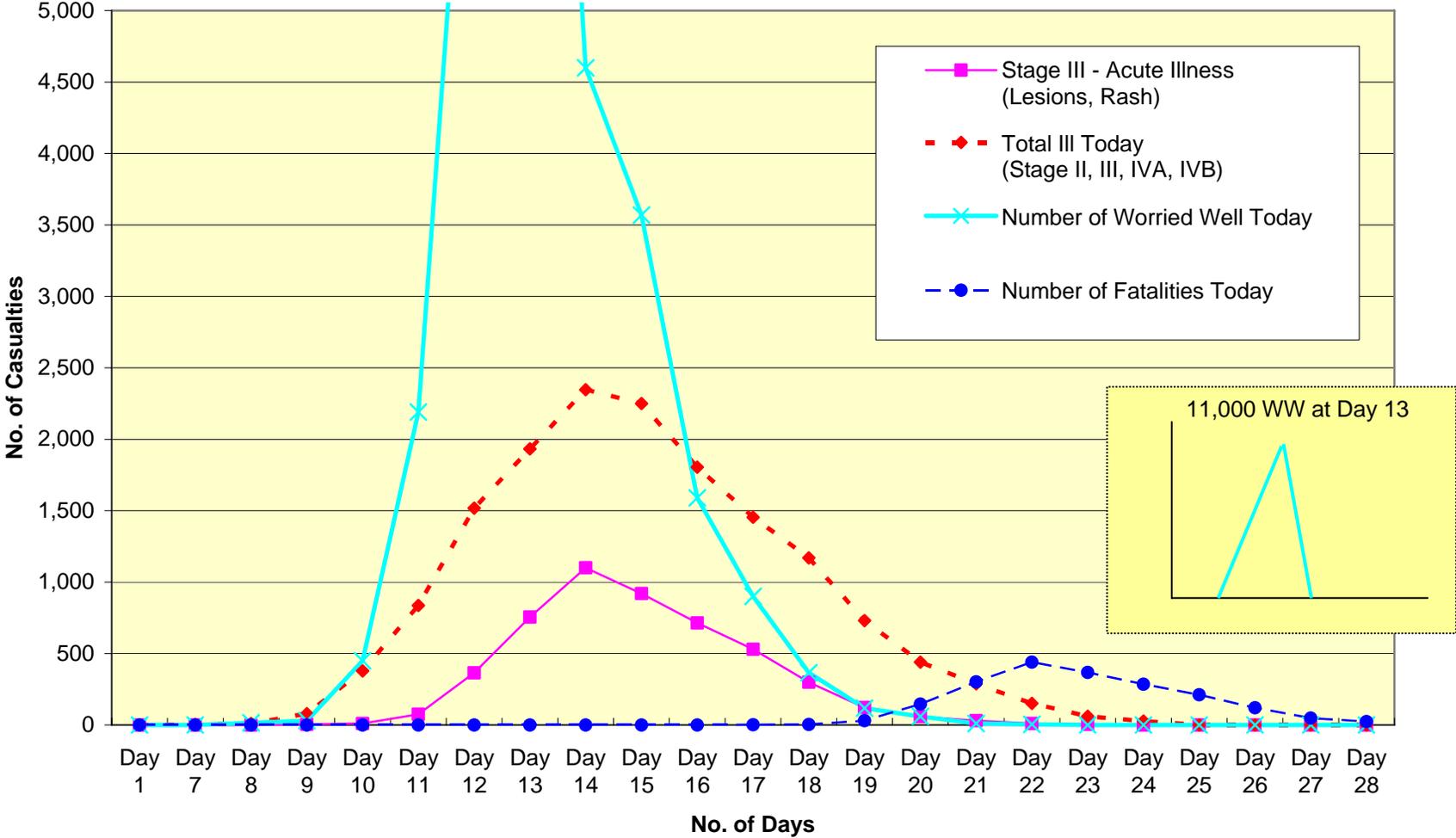
*Note: Days 8-9: The number of worried well = 3x the number that present the day prior
 Days 10-11: The number of worried well = 6x the number that present the day prior
 Days 12-13: The number of worried well = 10x the number that present the day prior
 Days 14-15: The number of worried well = 5x the number that present the day prior
 Days 16-18: The number of worried well = 3x the number that present the day prior
 Days 19-20: The number of worried well = 2x the number that present the day prior
 Days 21-22: The number of worried well = the number that present the day prior
 Day 23: The number of worried well drops to zero

Assumptions:

Distribution of presenting illness. Incubation will range between 7-17 days, with an average incubation period of 12 days.
Fatality rate. The vast majority of those primarily infected will die, but over time the fatality rate will diminish.
Secondary cases. Each primary case will infect three secondary cases.
Worried-but-well cases. A variable ratio between 1:1 to 10:1 is applied.
Effects of community prophylaxis. Will commence on the eleventh day
Other containment measures. No containment measures were assumed

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**FIGURE 4 SMALLPOX (PRIMARY GENERATION)
CASUALTY PREDICTION DISTRIBUTION CHART**



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5.2.3 Calculations- Secondary Generation

The following section outlines the calculations applied in developing the smallpox casualty predictive template for a secondary generation of the outbreak. It also delineates the actual formula associated with each previously described assumption.

****To understand the effects of the entire smallpox outbreak, emergency planners must add the corresponding day's casualty estimations for each category, for both the primary and secondary generation life cycles.*

| Row | Definition | Formula |
|----------|---|--|
| A | Stage I (Secondary) - Incubation Period: Number of asymptomatic secondarily infected persons. | 3.00 x Row A (Primary Generation) |
| B | Stage II (Secondary) - Presenting Illness: Number of persons secondarily infected who present on the day in question with initial symptoms of malaise, fever, vomiting, and headache. | Based on variable incubation distribution ranging between Day 15 (0.0%) to Day 23 (14.8%) to Day 29 (2.9%) |
| C | Stage III (Secondary)- Acute Illness Number of persons secondarily infected who present on the day in question with acute illness and exhibit signs of lesions and rash. | Stage II (Row B) + 2 days |
| D | Stage IV _A (Secondary) Chronic Recovery Requiring Care: Number of persons that have chronic signs and symptoms that require care but are recovering. | 37% Stage III (Row C previous day) |
| E | Stage IV _B - (Secondary) Recovery at Home: Disease survivors who have recuperated sufficiently to continue convalescing in an out-patient setting. | 63% Stage III (Row C previous day) |
| F | Total III Today (Secondary): Total New III Today | Stage II + III + IV _A + IV _B (current day) |

| Row | Definition | Formula |
|----------|--|--|
| G | Number of Worried Well Today (Secondary): Asymptomatic potentially exposed casualties, or those with concerns but no symptoms. | Variable ratio applied. Ranged from 3 x number of actual casualties from Row F (previous day) on Day 16 to 10 x actual casualties Row F (previous day) on Day 20 to zero on Day 31 |
| H | Total Seeking Medical Aid Today (Secondary): Sum of Total New Ill Today (current day) and Worried Well Today (current day). | Row F (current day) + Row G (current day) |
| I | Number of Fatalities Today (Secondary): Number of victims who have died during current day. | Based on variable fatality rate 20% Day 22 (Stage II Row C, 5 days previous) to 30% Day 30 (Stage II Row C, 8 day previous) |
| J | Cumulative Number of Fatalities (Secondary): Sum of fatalities from previous day and Number of Fatalities Today. | Row I (cumulative number of all previous days) |
| K | Cumulative Number of Persons Seeking Medical Aid (Secondary): Cumulative sum of all persons who have sought care. | Row H (cumulative number of all previous days) |

TABLE 5 SMALLPOX (SECONDARY GENERATION) CASUALTY PREDICTIVE TEMPLATE

| Description | Day 9 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 | Day 22 | Day 23 | Day 24 | Day 25 | Day 26 | Day 27 | Day 28 | Day 29 | Day 30 | Day 31 | Day 32 | Day 33 | Day 34 | Day 35 | Day 36 | |
|---|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| A Stage I - Incubation Period (see *note) | 15,000 | 14,995 | 14,975 | 14,855 | 14,584 | 13,942 | 12,880 | 11,231 | 9,166 | 6,939 | 4,759 | 3,007 | 1,712 | 904 | 430 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting Illness (Malaise, Fever, Vomiting, Headache) | 0 | 5 | 20 | 120 | 271 | 643 | 1,062 | 1,649 | 2,065 | 2,226 | 2,180 | 1,752 | 1,295 | 809 | 473 | 430 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III - Acute Illness (Lesions, Rash) | 0 | 0 | 0 | 5 | 20 | 120 | 271 | 643 | 1,062 | 1,649 | 2,065 | 2,226 | 2,180 | 1,752 | 1,295 | 809 | 473 | 430 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage IV _a - Chronic Recovery Requiring Care | 0 | 0 | 0 | 0 | 2 | 7 | 44 | 100 | 238 | 393 | 610 | 764 | 824 | 807 | 648 | 479 | 299 | 175 | 159 | 0 | 0 | 0 | 0 | 0 |
| E Stage IV _b - Recovery at Home | 0 | 0 | 0 | 0 | 3 | 13 | 75 | 171 | 405 | 669 | 1,039 | 1,301 | 1,403 | 1,373 | 1,104 | 816 | 509 | 298 | 271 | 0 | 0 | 0 | 0 | 0 |
| F Total Ill Today (Stage II, III, IV _a , IV _b) | 0 | 5 | 20 | 125 | 296 | 782 | 1,453 | 2,562 | 3,770 | 4,937 | 5,894 | 6,044 | 5,701 | 4,741 | 3,520 | 2,534 | 1,282 | 904 | 430 | 0 | 0 | 0 | 0 | 0 |
| G Number of Worried Well Today (see **note) | 0 | 0 | 15 | 60 | 719 | 1,627 | 6,426 | 10,620 | 8,243 | 10,327 | 6,679 | 6,540 | 5,257 | 2,590 | 1,617 | 473 | 430 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| H Total Seeking Medical Aid Today | 0 | 5 | 35 | 180 | 990 | 2,269 | 7,488 | 12,268 | 10,308 | 12,553 | 8,859 | 8,292 | 6,552 | 3,398 | 2,090 | 904 | 430 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| I Number of Fatalities Today | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 6 | 36 | 81 | 193 | 319 | 495 | 620 | 668 | 654 | 526 | 388 | 243 | 142 | 129 | |
| J Cumulative Number of Fatalities | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 7 | 43 | 125 | 318 | 636 | 1,131 | 1,750 | 2,418 | 3,072 | 3,598 | 3,986 | 4,229 | 4,371 | 4,500 | |
| K Cumulative Number of Persons Seeking Medical Aid | 0 | 5 | 40 | 220 | 1,210 | 3,479 | 10,967 | 23,235 | 33,543 | 46,097 | 54,955 | 63,247 | 69,799 | 73,198 | 75,288 | 76,192 | 76,622 | 76,622 | 76,622 | 76,622 | 76,622 | 76,622 | 76,622 | 76,622 |

Number of People Infected: 15,000
 Distribution of Presenting Illness: 0.0% 0.1% 0.8% 1.8% 4.3% 7.1% 11.0% 13.8% 14.8% 14.5% 11.7% 8.6% 5.4% 3.2% 2.9%
 Incident Mortality Rate: 30%

*Note: Day 9-14 represents the incubation period of the second generation of smallpox

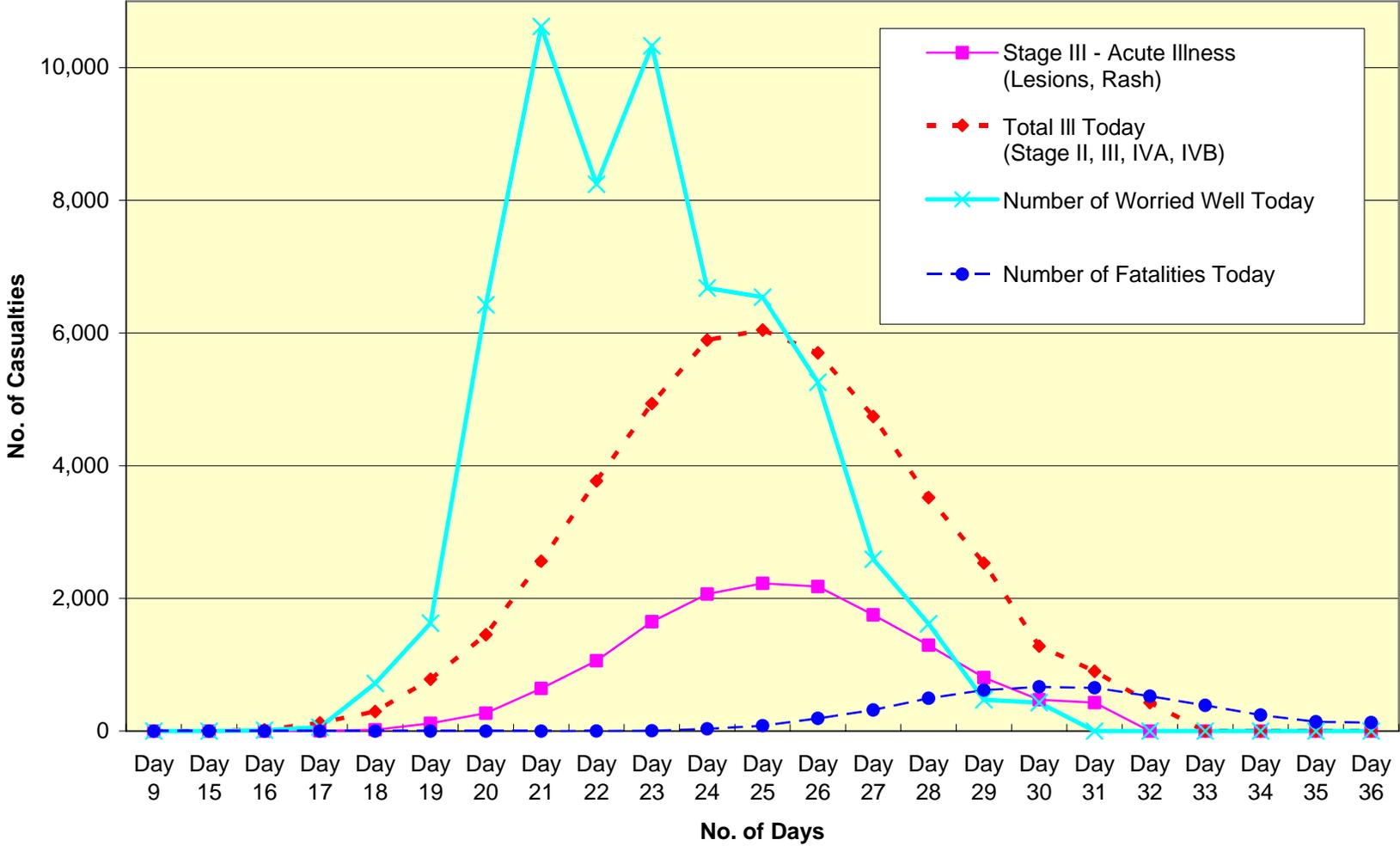
**Note: Days 16-17: The number of worried well = 3x the number that present the day prior
 Days 18-19: The number of worried well = 6x the number that present the day prior
 Days 20-21: The number of worried well = 10x the number that present the day prior
 Days 22-23: The number of worried well = 5x the number that present the day prior
 Days 24-26: The number of worried well = 3x the number that present the day prior
 Days 27-28: The number of worried well = 2x the number that present the day prior
 Days 29-30: The number of worried well = the number that present the day prior
 Day 31: The number of worried well drops to zero

Assumptions:

Distribution of presenting illness: Incubation will range between 7-17 days, with an average incubation period of 12 days.
Fatality rate: The vast majority of those primarily infected will die, but over time the fatality rate will diminish.
Secondary cases: Each primary case will infect three secondary cases.
Worried-but-well cases: A variable ratio between 1:1 to 10:1 is applied.
Effects of community prophylaxis: Will commence on the fourth day
Other containment measures: No containment measures were assumed

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**FIGURE 5 SMALLPOX (SECONDARY GENERATION)
CASUALTY PREDICTION DISTRIBUTION CHART**



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BOTULINUM

6.0 BOTULINUM OVERVIEW

Botulism is a clinical syndrome produced by botulinum toxins, which are neurotoxins⁴². Paradoxically, the most potent neurotoxins are medically used to treat spastic conditions (i.e., eye disorders, tetanus) and cosmetic conditions (e.g., facial wrinkles). Some of the characteristics that make botulinum toxin a potential biological weapon of choice are the ability to produce industrial-scale quantities with relative ease, the ability to aerosolize the agent, and the ability to use the neurotoxin to contaminate food and water supplies.⁴³

When botulinum is inhaled, these toxins produce a clinical picture identical to food borne intoxication. The neurotoxins produce muscular paralysis, which may take from 12 hours to several days to manifest, based on the exposure dose, and can ultimately lead to total respiratory failure and subsequent death.

Since survivors do not usually develop antibodies, as antibody development requires high doses and only a very small amount of toxin is necessary to produce clinical symptoms, patients are at risk for re-exposure.

Treating botulinum is limited. In terms of post-exposure treatment, as there are no prophylactic medications used to treat botulism, there is a licensed equine antitoxin available from the Centers for Disease Control and Prevention for cases of food borne botulism.⁴⁴ This product however, is limited in supply and, being a horse serum product, can lead to serum sickness.

For pre-exposure prophylaxis, there is a toxoid vaccine specific to *Clostridium botulinum* toxin types A, B, C, D, and E;⁴⁵ however, this vaccine is available in very limited quantities and is only under an investigational new drug (IND) status for pre-exposure use. Typically this vaccine should only be given to selected individuals or groups judged at high risk for exposure. The vaccine series is administered at 0, 2, and 12 weeks followed by a one- year booster and is considered 90% effective against type A botulinum toxin.

Antibiotics are not effective in preventing or treating botulism.

⁴² Shapiro RL, Hatheway C, Swerdlow DL. Botulism in the United States: a clinical and epidemiologic review. *Ann Intern Med.* 1998 Aug 1;129(3):221-8.

⁴³ Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Fine AD, Hauer J, Layton M, Lillibridge S, Osterholm MT, O'Toole T, Parker G, Perl TM, Russell PK, Swerdlow DL, Tonat K; Working Group on Civilian Biodefense. Botulinum toxin as a biological weapon: medical and public health management. *JAMA.* 2001 Feb 28;285(8):1059-70. Review. Erratum in: *JAMA* 2001 Apr 25;285(16):2081.

⁴⁴ Davis LE. Botulism. *Curr Treat Options Neurol.* 2003 Jan;5(1):23-31.

⁴⁵ Davis LE. Botulism. *Curr Treat Options Neurol.* 2003 Jan;5(1):23-31.

Planners must realize that botulism patients may require extensive medical support, consisting predominantly of ventilatory assistance, which can last weeks or even months, and treatment of secondary infections.

Botulism is not contagious, and thus adherence to Standard Precautions alone is sufficient when caring for patients with botulism.

6.1 CLINICAL FEATURES

The onset of symptoms of botulism can be seen between 12 to 36 hours following exposure, and it is directly proportional to the dose exposed. For example, incubation periods of 96 hours or more have been reported with ingestion of very low doses of toxin.⁴⁶

Patients may complain of blurred vision, dry mouth, and difficulty speaking and swallowing. Patients exhibit a normal mental status, as the toxins do not enter the central nervous system; thus patients have intact senses (pain, etc.) since sensory nerves are not affected.

Medical professionals can often diagnose botulinum based upon the patient's symptoms and signs. Cranial nerve palsies are prominent early, resulting in light sensitivity (photophobia), dilated pupils, difficulty speaking (dysarthria), difficulty enunciating words (dysphonia), and difficulty swallowing (dysphagia).⁴⁷ Flaccid skeletal muscle paralysis progresses in a symmetrical and descending (head-to-toe) manner. As the descending motor weakness reaches the accessory respiratory muscles and then the diaphragm, respiratory failure may occur abruptly. Progression from onset of symptoms to respiratory failure can occur in as little as 24 hours in cases of severe food borne botulinum.

Laboratory testing is generally not critical for making a diagnosis of botulism; however, there are tests that can detect the presence of these toxins (mouse neutralization bioassay), polymerase chain reaction (PCR), ELISA and electrochemiluminescence (ECL) tests.⁴⁸

Botulism can be treated with an antitoxin, if given early in the patient's course of treatment. Early administration of the antitoxin is critical, since the antitoxin can only neutralize the toxin when it is circulating in the body. Patient signs and symptoms are evidence that the toxin is present, however when symptom progression ceases, no circulating toxin remains, and the antitoxin will have no effect.⁴⁹ Antitoxin will not reverse existing paralysis, which can persist for many weeks and even months.

The mortality rate prior to 1950 for reported cases was 60%.⁵⁰ With improvements in medical care and respiratory support (e.g., tracheotomy, endotracheal intubation and ventilatory assistance), fatalities today are less than five percent. Intensive and prolonged care may be required for up to three months, followed by less intense care for up to a year.

⁴⁶ Cherington M. Clinical spectrum of botulism. *Muscle Nerve*. 1998 Jun;21(6):701-10.

⁴⁷ Cherington M. Clinical spectrum of botulism. *Muscle Nerve*. 1998 Jun;21(6):701-10.

⁴⁸ Hatheway CL. Botulism: the present status of the disease. *Curr Top Microbiol Immunol*. 1995;195:55-75.

⁴⁹ Shapiro RL, Hatheway C, Swerdlow DL. Botulism in the United States: a clinical and epidemiologic review. *Ann Intern Med*. 1998 Aug 1;129(3):221-8.

⁵⁰ Hatheway CL. Botulism: the present status of the disease. *Curr Top Microbiol Immunol*. 1995;195:55-75.

6.2 BOTULINUM CASUALTY PREDICTIVE TEMPLATE

The following casualty predictive template is intended to illustrate the potential impact of casualties on the medical infrastructure when approximately 5,000 people are infected with botulinum toxin via aerosol exposure. Since there is no data on large-scale outbreaks, the developers made a number of assumptions when developing this template. These assumptions, and the rationale used in developing the formula equations, are presented below.

6.2.1 Template Assumptions

- ***Distribution of presenting illness.*** Average incubation period is assumed to be two days for botulinum. Those exposed to higher doses of the toxin may have a shorter incubation period. Conversely, those who have received smaller inoculums may be asymptomatic for longer periods of time, up to 4 days. It was assumed, for this model, that a high concentration of toxin would be released, resulting in a disproportionate number of victims falling ill within the first 48 hours after exposure.
- ***Fatality rate.*** A variable fatality rate was used for this model. This model did not take into account the delivery of experimental medical treatment (e.g., IND pharmaceuticals) nor did it address exactly when or in what quantities ventilators would arrive to support patient respiratory needs.

The developers considered several factors when determining the fatality rate. Initially the mortality could be higher as the number of cases out number the availability of ventilators and medical personnel to manage them. As more equipment arrives, through the SNS and the hospital's medical supply contingency plans, there could then be a decrease in the mortality rate. Some hospitals may have plans to initially support patient airways manually with personnel taking shifts hand bagging patients; although this effort could prevent patient death, it is still possible patient death would occur days or weeks later due to a secondary infection related to aspiration.

Additional factors that influence the fatality rate depend upon accurate diagnosis and early administration of antitoxin.

- ***Secondary cases.*** Botulinum toxin is not transmitted person-to-person; therefore no secondary cases were addressed in this model.
- ***Worried-but-well cases.*** The ratio of asymptomatic potentially exposed individuals ("worried well") to actual casualties will be variable. Subject matter experts have estimated that an outbreak, resulting from an intentional release of a toxin in a community, would result in large numbers of unexposed individuals seeking medical evaluation, treatment, or reassurance. During the fall 2001 anthrax mail release,

worried-well case projections ranged between 5 to 20 times the actual numbers of casualties.⁵¹ In this model, ratios of 3:1 to 10:1 were used.

- **Effects of community prophylaxis.** The effects of prophylaxis were not included directly in this model.
- **Other containment measures.** Since this disease is not transmitted person-to-person, no other containment measures were assumed in developing this model.

6.2.2 Calculations

The following section outlines the calculations applied in developing the botulinum casualty predictive template. It also delineates the actual formula associated with each previously described assumption.

| Row | Definition | Formula |
|-----|---|--|
| A | Stage I – Incubation Period: Number of persons primarily infected but still asymptomatic. | Initial 5,000 casualties, then decreasing by numbers presenting at Stage II. Row A (previous day) – Row B (current day) |
| B | Stage II - Presenting Illness (Neurological Symptoms): Number of persons primarily infected who present on the day in question with initial symptoms resembling a generalized neurological illness. | Variable incubation period. See distribution at bottom of template. |
| C | Stage III - Illness not Requiring Ventilators. Set at 40%. | Row B (previous day) x 0.4 |
| D | Stage IV _A - Illness Requiring Ventilators. Variable, ranging from 35-56%. | Row B (previous day) x Variable |
| E | Stage IV _B - Recovery at Home: Patients who have recuperated sufficiently to be treated at home as outpatients. Set at 40% after 6 days in-patient treatment. | Row B (6 previous days) x 0.4 |

⁵¹ Tucker, N. *Emergency Rooms Overrun by the 'Worried by Well'* The Washington Post. Thursday, November 1, 2001; Page B01. Available at <http://www.washingtonpost.com/ac2/wp-dyn/A21059-2001Oct31?language=printer> [last visited 12 October 2003]

| Row | Definition | Formula |
|----------|--|---|
| F | Total Ill Today (Stage II, III, IV _A , IV _B). Sum of these stages for the current day. | Row B + Row C + Row D + Row E (current day) |
| G | Number of Worried Well Today. Variable factor based on public perception of the disease. See distribution at bottom of template. | Row B x Variable Factor (current day) |
| H | Total Seeking Medical Aid Today. Total of worried well and actual ill for current day. | Row B + Row G (current day) |
| I | Number of Fatalities Today. Variable but declining from 25% to 4%, due to more resources. Victims die after 1 day of disease. | Variable Factor x Row B (1 previous day) |
| J | Cumulative Number of Fatalities. Current day's fatalities plus previous day's cumulative fatalities. | Row J (previous day) + Row I (current day) |
| K | Cumulative Number of Persons Seeking Medical Aid. | Row K (previous day) + Row H (current day) |

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TABLE 6 BOTULINUM CASUALTY PREDICTIVE TEMPLATE

| Description | Distribution of Illness for Infected Persons | | | | | | | | | | | | | | | | | | | | |
|---|--|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 |
| A Stage I - Incubation Period (see distribution) | 5,000 | 4,500 | 1,500 | 500 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting Illness (Neurologic Symptoms) | 0 | 500 | 3,000 | 1,000 | 500 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III - Illness not Requiring Ventilators | 0 | 0 | 200 | 1,200 | 400 | 200 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage IV _A - Illness Requiring Ventilators | 0 | 0 | 175 | 1,500 | 560 | 280 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| E Stage IV _B - Recovery at Home | 0 | 0 | 0 | 0 | 0 | 0 | 200 | 1,200 | 400 | 200 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| F Total Ill Today (Stage II, III, IV _A , IV _B) | 0 | 500 | 3,375 | 3,700 | 1,460 | 480 | 200 | 1,200 | 400 | 200 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| G Number of Worried Well Today (see *note) | 0 | 1,500 | 15,000 | 10,000 | 2,500 | 1,500 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| H Total Seeking Medical Aid Today | 0 | 2,000 | 18,000 | 11,000 | 3,000 | 1,500 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| I Number of Fatalities Today | 0 | 0 | 125 | 300 | 40 | 20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| J Cumulative Number of Fatalities | 0 | 0 | 125 | 425 | 465 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 | 485 |
| K Cumulative Number of Persons Seeking Medical Aid | 0 | 2,000 | 20,000 | 31,000 | 34,000 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 | 35,500 |

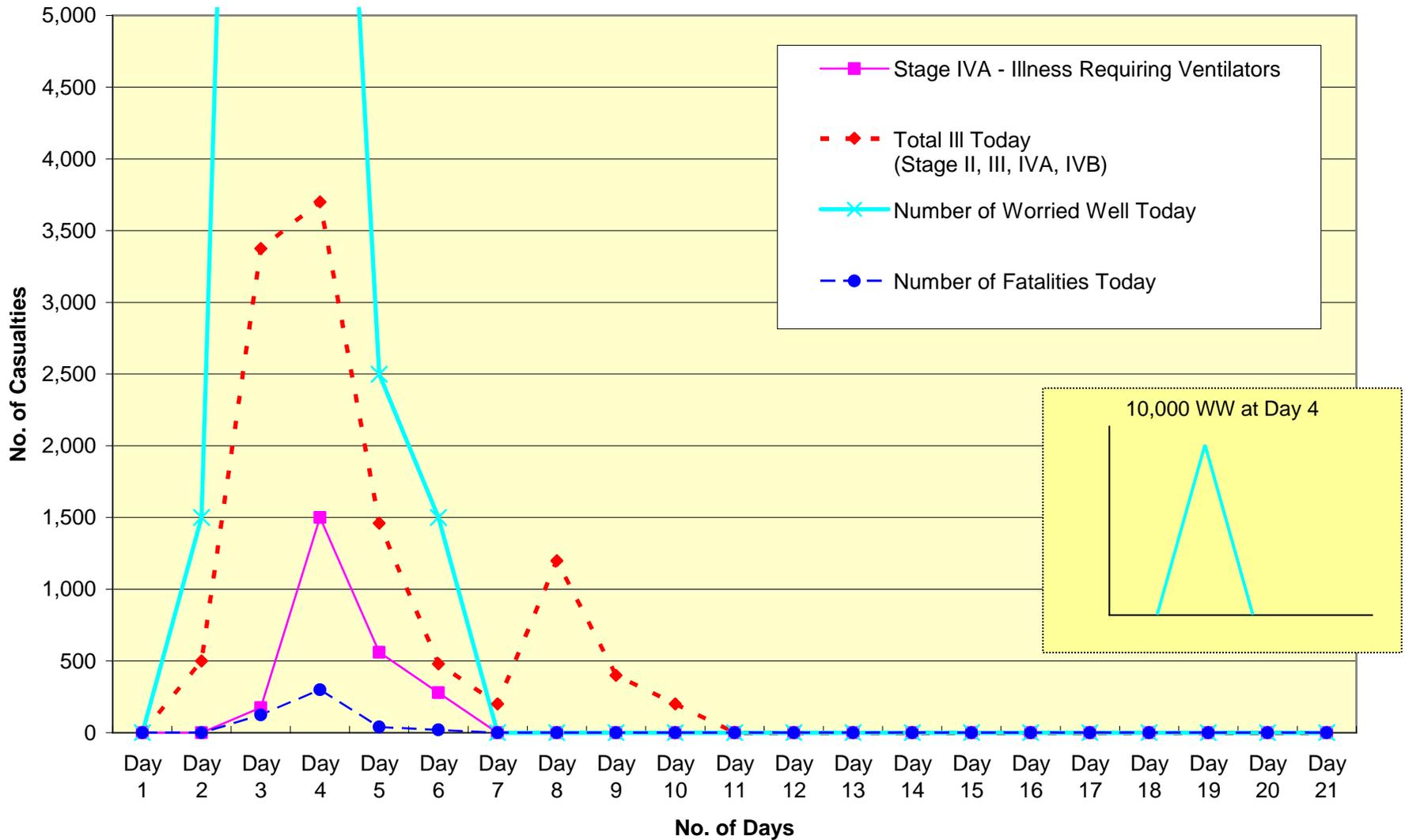
Number of People Infected: 5,000
 Distribution of Presenting Illness: 10% 60% 20% 10%
 Incident Mortality Rate: 25% 10% 4% 4%

*Note: Day 2: The number of worried well = 3x the number that present
 Day 3: The number of worried well = 5x the number that present
 Day 4: The number of worried well = 10x the number that present
 Day 5: The number of worried well = 5x the number that present
 Day 6: The number of worried well = 3x the number that present
 Day 7: The number of worried well drops to zero

Assumptions:
Distribution of presenting illness . Average incubation period will be two days
Fatality rate . The fatality rate will be high during the initial outbreak and will diminish over time.
Secondary cases . No secondary cases were assumed.
Worried-but-well cases . Ratios of 3:1 to 10:1 were applied.
Worried-but-well cases . Ratios of 3:1 to 10:1 were applied.
Effects of community prophylaxis . No community prophylaxis was assumed.
Other containment measures . No containment measures were assumed.

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**FIGURE 6 BOTULINUM
CASUALTY PREDICTION DISTRIBUTION CHART**



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STAPHYLOCOCCAL ENTEROTOXIN B (SEB)

7.0 STAPHYLOCOCCAL ENTEROTOXIN B OVERVIEW

Staphylococcal enterotoxin B (SEB) is one of many *Staphylococcus aureus* exotoxins that can produce human disease. The SEB toxin, most known for producing food poisoning in humans upon eating improperly cooked food that contains the toxin, is a biological agent of concern because it is moderately stable (it requires exposure to 100°C/212°F to inactivate the toxin) and can easily be used to sabotage food or small volume water supplies.⁵²

SEB can be inhaled or ingested and symptoms vary according to the route of entry. Even at very low exposure doses (100 times less than the lethal dose) patients experience abrupt and severe illness that leaves them incapacitated for several days.

Presently there is no human vaccine for immunization against SEB intoxication, but there are several vaccine candidates in development. Some preliminary animal studies have shown a reduction in mortality, but only when one particular vaccine is given within 4–8 hours after inhaling SEB.⁵³ Interestingly, most people have detectable antibody titers to SEB, however, immunity acquired through natural exposure to SEB is usually not sufficient to provide complete protection from an aerosol challenge.

Currently, treatment is limited to symptomatic and supportive care. Therapy primarily includes patient hydration and fever reduction, and in severe pulmonary edema cases ventilation support and the use of vasopressors and diuretics.

SEB intoxication is non-contagious. Medical personnel should adhere to Standard Precautions when taking care of SEB infected patients.

7.1 CLINICAL FEATURES

For inhalational SEB, symptoms begin 3–12 hours after exposure. General symptoms include sudden onset of fever, chills, headache, and muscle aches. Often patients experience a nonproductive cough, which can last up to four weeks, chest tightness, and difficulty breathing. Patients will have a fever that may last up to five days and range from 103 to 106

⁵² Greenfield RA, Brown BR, Hutchins JB, Iandolo JJ, Jackson R, Slater LN, Bronze MS. Microbiological, biological, and chemical weapons of warfare and terrorism. *Am J Med Sci.* 2002 Jun;323(6):326-40.

⁵³ Weng CF, Komisar JL, Hunt RE, Johnson AJ, Pitt ML, Ruble DL, Tseng J. Immediate responses of leukocytes, cytokines and glucocorticoid hormones in the blood circulation of monkeys following challenge with aerosolized staphylococcal enterotoxin B. *Int Immunol.* 1997 Dec;9(12):1825-36.

degrees Fahrenheit (or 39.4°- 41.1° Celsius).⁵⁴ Inhalational cases of SEB can be severe and result in acute pulmonary edema and respiratory failure. It is possible that aerosolized SEB could also cause gastrointestinal symptoms should patients inadvertently swallow toxin-containing mucus from the upper airway.

The gastrointestinal form of SEB also begins shortly after exposure, within 4–10 hours, and also includes general symptoms such as fever, chills, headache, and general muscle aches, but also nausea, vomiting, and diarrhea. The fever may last up to five days and range from 103 to 106 degrees Fahrenheit (or 39.4°- 41.1° Celsius).

Diagnosing SEB intoxication based solely upon clinical and epidemiologic features may initially be a challenge. The inhalational form of SEB intoxication can manifest signs and symptoms similar to several other respiratory pathogens such as common community-acquired pneumonias or influenza; many respiratory infections present with fever, non-productive cough, general muscle aches, and headache. One differential feature is that an intentional SEB attack would cause large numbers of patients to seek care over a very short period of time, probably within a single 24-hour period, whereas patients with naturally-acquired pneumonias or influenza would likely present over a more prolonged interval of time. Moreover, naturally occurring staphylococcal food poisoning cases would not present with pulmonary symptoms.

Physical examination in patients with SEB intoxication is often unremarkable. In some cases patients may present with postural hypotension, due to fluid loss, develop increased interstitial markings of the lung, such as atelectasis or overt pulmonary edema, or denote signs of Acute Respiratory Distress Syndrome (ARDS) upon chest x-ray.

Laboratory confirmation (i.e., ELISA, ECL, and PCR) of SEB intoxication is possible, as tests can look for antigen detection or *Staphylococcal* genes. SEB may not be detectable at the time symptoms occur via a serum specimen, but respiratory secretions and nasal swabs may depict the presence of the toxin within 24 hours of exposure, as most patients develop a significant antibody response to the toxin.⁵⁵

Most patients recover after the initial acute phase of the illness, which may last one to two weeks. Generally only a few cases of SEB, particularly those involving inhalational exposure to high doses of the toxin, will be fatal.

7.2 SEB CASUALTY PREDICTIVE TEMPLATE

The following casualty prediction template is intended to illustrate the potential impact of casualties on the medical infrastructure when approximately 5,000 people are infected with

⁵⁴ Ulrich RG, S Sidell, TJ Taylor, CL Wilhelmsen, DR Franz. Staphylococcal Enterotoxin B and Related Pyrogenic Toxins, in *Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare*, Second Edition, Eds. FR Sidell, ET Takafuji, DR Franz. Borden Press, Bethesda, MD 1997, pp. 621-30.

⁵⁵ Weng CF, Komisar JL, Hunt RE, Johnson AJ, Pitt ML, Ruble DL, Tseng J. Immediate responses of leukocytes, cytokines and glucocorticoid hormones in the blood circulation of monkeys following challenge with aerosolized staphylococcal enterotoxin B. *Int Immunol.* 1997 Dec;9(12):1825-36.

SEB toxin via aerosol exposure. Since there is no data on large-scale outbreaks, the developers made a number of assumptions when developing this template. These assumptions, and the rationale used in developing the formula equations, are presented below.

7.2.1 Template Assumptions

- ***Distribution of presenting illness.*** The developers determined that patients would be intentionally exposed to a high concentration of the SEB toxin via aerosol exposure. Thus the model will depict a disproportionate number of victims falling ill within the first six hours after exposure. The majority of the casualties is assumed to only require symptomatic and supportive care, and is expected to recover without extensive medical treatment. A considerable number of patients will begin recovering within 72 hours of onset of symptoms, with the vast majority recovering within five days. Ten percent of casualties, however, will become severely ill prior to recovery. Additionally, out of the 95% of casualties that recover, 1% will manifest pulmonary edema and will take up to four weeks to recover.

Those with underlying illness, who are immunologically compromised, at the extremes of age, or exposed to higher doses of the toxin, may have a shorter incubation period and more severe symptoms. Conversely, those with robust immune systems, or who have received smaller inoculums, may be asymptomatic for longer periods of time.

- ***Fatality rate.*** The developers assumed that 5% of those exposed will become severely ill and die within 72 hours of symptom onset. Though it is plausible that less than 5% of the population could die from SEB intoxication, the developers believed the initial fatality rate would be greater, due to early misdiagnosis and ineffective treatment, and later, due to the limited availability of skilled medical providers, ventilators, pharmaceuticals, and intensive care unit equipment and supplies.
- ***Secondary Cases.*** There are no secondary cases predicted with this template, as SEB is not spread between humans.
- ***Worried-but-well cases.*** In this model a variable calculation was used, 5:1 to 3:1, concerning asymptomatic potentially exposed individuals (“worried well”). Subject matter experts often hinge their worried well prediction on the number of fatalities, severity of the outbreak and the manifestation and/or onset of an outbreak. Since a SEB intoxication outbreak could be contained within the first 24 hours and very few people are predicted to die, the developers assumed that there would not be a significant number of asymptomatic individuals seeking medical evaluation. Emergency planners should note that this may not be an accurate prediction.
- ***Effects of community prophylaxis.*** No community prophylaxis measures were considered in this model, to include immunizing mass casualties with an experimental vaccination.

- **Other containment measures.** No containment measures were considered in this model, particularly since the spread of SEB toxins is not transmitted between humans.

7.2.2 Calculations

The following section outlines the calculations applied in developing the SEB casualty predictive template. It also delineates the actual formulas associated with each previously described assumption.

| Row | Definition | Formula |
|----------|--|---|
| A | Stage I - Latent Period: Persons intoxicated but asymptomatic. | Initially 5,000, decreasing by numbers presenting at Stage II. Row A (previous day) – Row B (current day) |
| B | Stage II - Presenting Illness (Fever, headache, malaise, GI, respiratory). | Variable, rapidly decreasing incubation period. See distribution at bottom of template. |
| C | Stage III _A - Ongoing Illness (Total): Total number ill, less those who have recovered or have died or are categorized as severely ill. | Total Exposed – Row I – Row H |
| D | Stage III _B - Severe Illness (Pulmonary edema). | 15% (Total Exposed) distributed over two days post exposure |
| E | Total Ill Today (Stage II, III _A , III _B). | Row B + Row C + Row D (current day) |
| F | Number of Worried Well | A variable rate starting with 5:1 during the first 3 days and then decreases to 3:1 from Day 4 – Day 7; afterward no worried well are expected. |
| G | Stage IV – Recovered. | 95% (Total Exposed), patient distribution over 5 days beginning 3 days post exposure (5%, 10%, 70%, 10%, 5%) |
| H | Number of Fatalities Today. | 5% (Total Exposed), distributed 80% first day post exposure, 20% second day post exposure |
| I | Cumulative Number of Fatalities | Row H (previous day) + Row G (current day) |

| Row | Definition | Formula |
|-----|---|--|
| J | Cumulative Number of Persons Recovered. | Row I (previous day) + Row F (current day) |

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TABLE 7 STAPHYLOCOCCAL ENTEROTOXIN B (SEB) CASUALTY PREDICTIVE TEMPLATE

Distribution of Illness for Infected Persons

| Description | Day 1 | | | | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 28 |
|---|--------|---------|---------|---------|-------|--------|--------|-------|-------|-------|-------|-------|--------|--------|
| | 6 Hrs. | 12 Hrs. | 18 Hrs. | 24 Hrs. | | | | | | | | | | |
| A Stage I - Latent Period (see distribution) | 1000 | 3000 | 750 | 250 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting Illness (Fever, Headache, Myalgia, GI, Resp.) | 0 | 1000 | 3000 | 750 | 250 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III _A - On Going Illness (Total) | 0 | 0 | 0 | 0 | 4,300 | 4,263 | 4,038 | 715 | 245 | 88 | 0 | 0 | 0 | 0 |
| D Stage III _B - Acute Illness (Pneumonia) | 0 | 0 | 0 | 0 | 250 | 250 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| E Stage IV - Chronic Recovery | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 5 | 33 | 5 | 2 | 0 | 0 | 0 |
| F Total Ill Today (Stage II, III _A , III _B , IV) | 0 | 0 | 0 | 0 | 4,800 | 4,513 | 4,040 | 720 | 278 | 93 | 48 | 48 | 48 | 0 |
| G Number of Worried Well Today | 0 | 0 | 0 | 0 | 4,750 | 23,750 | 14,250 | 1,250 | 750 | 750 | 0 | 0 | 0 | 0 |
| H Stage V - Recovered | 0 | 0 | 0 | 0 | 0 | 238 | 475 | 3,325 | 475 | 190 | 0 | 0 | 0 | 48 |
| I Number of Fatalities Today | 0 | 0 | 0 | 0 | 200 | 50 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| J Cumulative Number of Fatalities | 0 | 0 | 0 | 0 | 200 | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| K Cumulative Number of Persons Recovered | 0 | 0 | 0 | 0 | 0 | 238 | 713 | 4,038 | 4,513 | 4,703 | 4,703 | 4,703 | 4,703 | 4,750 |

Number of People Infected: 5,000
 Distribution of Presenting Illness: 20% 60% 15% 5%
 Incident Mortality Rate: 5%

Assumptions:

Distribution of presenting illness. Ten percent of casualties will become severely ill and one percent will manifest pulmonary edema.

Fatality rate. 5% of those exposed will become severely ill and die within 72 hours of symptom onset.

Secondary Cases. There are no secondary cases predicted.

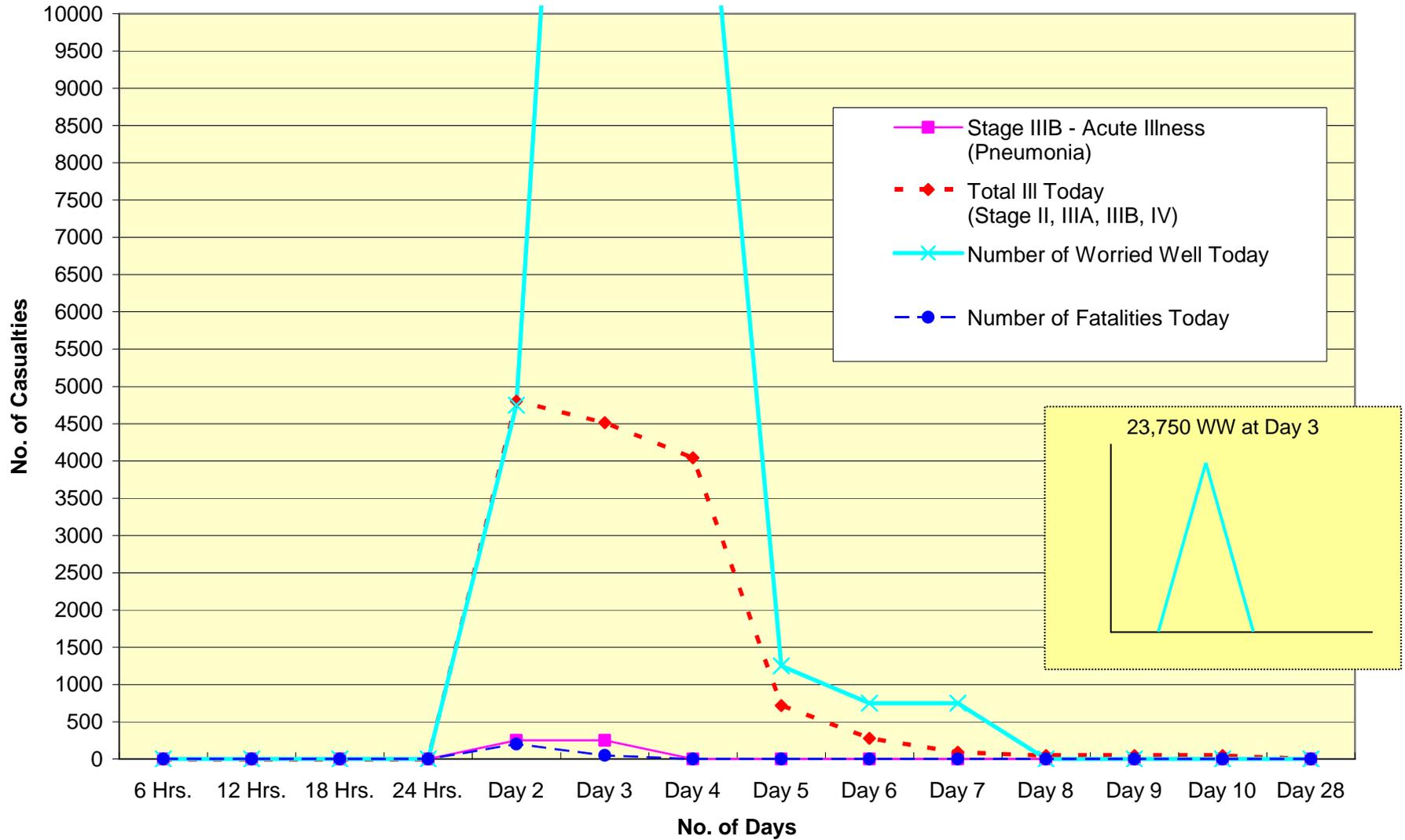
Worried-but-well cases. No calculation was done.

Effects of community prophylaxis. No community prophylaxis measures were considered.

Other containment measures. No containment measures were considered.

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**FIGURE 7 STAPHYLOCOCCAL ENTEROTOXIN B (SEB)
CASUALTY PREDICTION DISTRIBUTION CHART**



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VENEZUELAN EQUINE ENCEPHALITIS (VEE)

8.0 VENEZUELAN EQUINE ENCEPHALITIS OVERVIEW

Venezuelan equine encephalitis (VEE), endemic in northern South America, Trinidad, Central America, Mexico, and Florida, is a virus complex made up of a group of eight mosquito-borne viruses. These viruses can cause severe diseases in humans as well as specific equestrian animals (namely horses, mules, burros, and donkeys).⁵⁶ Patients usually contract the disease via mosquito bites and not through direct human or horse contact, although equine can become an amplifying host for the infectious vector (i.e., mosquitoes).⁵⁷

VEE is typically an acute, temporarily incapacitating, febrile illness. It does, however, have the potential to develop into a severe disease called encephalitis (inflammation of the brain). Though most naturally acquired cases are minor, studies indicate that there is a higher rate of morbidity and mortality associated with an intentional aerosol exposure of VEE. Such inhalational exposures can perhaps lead to a higher incidence of encephalitis, as the virus may travel along the olfactory nerve and spread directly to the central nervous system (CNS).⁵⁸

In addition to VEE potential to create severe illness, it is highly infectious. Humans only need to be exposed to very few organisms (10-100) to contract the disease. Neither the percentage of infected mosquitoes nor the aerosol concentration of the virus has to be high for VEE to be transmitted.⁵⁹

To date, there are no licensed VEE vaccines, but there are two IND human unlicensed vaccines. The first IND vaccine (designated TC-83) was developed in the 1960's and is a live, attenuated cell-culture-derived vaccine. This vaccine is not effective against all serotypes in the VEE complex, but it has been used to protect laboratory personnel. The second IND vaccine (designated C-84) is primarily used to boost the immunity of those who have not responded to the TC-83 vaccine.⁶⁰ As with all vaccines, one's protection is dependent on the magnitude of the challenge dose, as vaccine-induced protection could be overwhelmed by extremely high doses of the pathogen. Research is underway to produce a recombinant VEE vaccine.

⁵⁶ Rico-Hesse R. Venezuelan equine encephalomyelitis. *Vet Clin North Am Equine Pract.* 2000 Dec;16(3):553-63.

⁵⁷ Sidwell RW, Smee DF. Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control. *Antiviral Res.* 2003 Jan;57(1-2):101-11.

⁵⁸ ronze MS, Huycke MM, Machado LJ, Voskuhl GW, Greenfield RA. Viral agents as biological weapons and agents of bioterrorism. *Am J Med Sci.* 2002 Jun;323(6):316-25.

⁵⁹ ronze MS, Huycke MM, Machado LJ, Voskuhl GW, Greenfield RA. Viral agents as biological weapons and agents of bioterrorism. *Am J Med Sci.* 2002 Jun;323(6):316-25.

⁶⁰ Sidwell RW, Smee DF. Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control. *Antiviral Res.* 2003 Jan;57(1-2):101-11.

Since there is no specific treatment, medical professionals must focus on providing symptomatic and supportive care. Treatment may range from analgesics, fluid and electrolyte replacement, mitigation of secondary bacterial infections, and seizure precautions (i.e., administering anticonvulsants) for those who develop encephalitis.

Though VEE patients do not require isolation or quarantine, providers should institute simple practices to contain its spread. Use of disinfectants or exposure to heat (176° Fahrenheit/ 80° Celsius) will kill the virus complex.

Providers should institute Standard Precautions when treating VEE infected patients.⁶¹

8.1 CLINICAL FEATURES

Ninety to 100% of those exposed to VEE become infected, and nearly 100% of those infected develop overt signs and symptoms, usually within 1–6 days. The acute phase lasts 24–72 hours and patients usually experience chills, severe headache, sore throat, nausea, and muscle soreness, specifically with regard to the legs and lower back. Additional signs may include a spiking fever (100-105° F/38°C–40.5°C), photophobia, vomiting, cough, and diarrhea. Typically patients are incapacitated by malaise and fatigue for 1–2 weeks before making a full recovery.⁶²

During natural epidemics, approximately 4% of infected children (<15 years old) and less than 1% of adults, develop signs of severe CNS infection. Such patients may experience lethargy, somnolence, mild confusion, seizures, ataxia (defective muscular coordination), paralysis, or coma. Although it is rare for adults to develop severe disease, pregnant patients have a greater risk of suffering complications, as the virus may cause encephalitis in the fetus, placental damage, spontaneous abortion, or severe congenital anomalies.⁶³

Diagnosing VEE on clinical and epidemiological grounds is possible but may be a challenge. Providers should look for clues such as the occurrence of a small grouping of neurological cases or corresponding disease in equine animals. An aerosol attack could theoretically lead to an epidemic of febrile meningoencephalitis. In general, however, a VEE outbreak may initially mimic an influenza epidemic.

Accurately diagnosing VEE includes blood and serum culture analysis. In VEE, patients usually have a marked decrease in WBC and lymphocytes. Presumptive diagnosis may be made within 5–7 days after onset of illness, as the presence of the virus in the blood is high enough to detect (using an ELISA test) during the acute phase of the illness, but not when patients have encephalitis.⁶⁴ For encephalitis cases, patients may have increased

⁶¹ Watts DM, Lavera V, Callahan J, Rossi C, Oberste MS, Roehrig JT, Cropp CB, Karabatsos N, Smith JF, Gubler DJ, Wooster MT, Nelson WM, Hayes CG. Venezuelan equine encephalitis and Oropouche virus infections among Peruvian army troops in the Amazon region of Peru. *Am J Trop Med Hyg.* 1997 Jun;56(6):661-7.

⁶² Sidwell RW, Smee DF. Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control. *Antiviral Res.* 2003 Jan;57(1-2):101-11.

⁶³ Sidwell RW, Smee DF. Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control. *Antiviral Res.* 2003 Jan;57(1-2):101-11.

⁶⁴ Rico-Hesse R. Venezuelan equine encephalomyelitis. *Vet Clin North Am Equine Pract.* 2000 Dec;16(3):553-63.

cerebrospinal fluid pressure and the fluid may contain WBCs and reveal an elevated protein concentration. Confirmatory analysis using cell culture is possible for VEE but performing this test requires BSL 3 containment.⁶⁵

The overall case fatality rate for naturally occurring VEE is < 1%, although it is somewhat higher for those who are very young or aged. Patients that develop CNS infection have a higher mortality rate (35% fatality for children and 10% for adults).⁶⁶ Most patients recover from an infection and usually have long-term immunity to the infecting strain.

8.2 VEE CASUALTY PREDICTIVE TEMPLATE

The following casualty predictive template is intended to illustrate the potential impact of casualties on the medical infrastructure when approximately 5,000 people are infected with VEE via aerosol exposure. Data concerning large-scale outbreaks were reviewed, and the developers made some assumptions in developing this template. These assumptions, and the rationale used in developing the formula equations, are presented below.

8.2.1 Template Assumptions

- ***Distribution of presenting illness.*** The average incubation period of VEE in this model is assumed to be two days. The developers determined that patients would be exposed to a high concentration of viable virions via aerosol, resulting in a disproportionate number of victims falling ill by day 2 and 3 versus patients taking ill between 1-6 days following the incubation period of natural VEE. Ninety-two percent of infected patients would contract the mild form of VEE and thereby only require four days of in-patient treatment, followed by a full recovery at home. Only seven percent of patients would develop CNS symptoms, which would subsequently require prolonged in-patient treatment.

Those with underlying illness, immunologically compromised, at the extremes of age, or exposed to higher doses of the toxin, may have a shorter mean incubation period and more severe disease. Conversely, those with robust immune systems, or who have received smaller inoculums, may be asymptomatic for longer periods of time and have fewer severe complications.

- ***Fatality rate.*** A fatality rate of 1% was used for this model. Though it is plausible that the fatality rate could be less than 1% for the overall population exposed, the developers believed the initial fatality rate would be greater than normal, due to exposure to a more potent form of VEE than the natural form, and the lack of effective treatment, and later, due to the limited availability of bed space and medical

⁶⁵ Sidwell RW, Smee DF. Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control. *Antiviral Res.* 2003 Jan;57(1-2):101-11.

⁶⁶ Sidwell RW, Smee DF. Viruses of the Bunya- and Togaviridae families: potential as bioterrorism agents and means of control. *Antiviral Res.* 2003 Jan;57(1-2):101-11.

supplies. This model does not take into account the use of experimental vaccines to prevent onset of disease.

- **Secondary Cases.** No secondary cases were predicted with this template, as VEE is not known to spread between humans.
- **Worried-but-well cases.** In this model, variable ratios of 5:1 and 10:1 were applied for asymptomatic potentially exposed individuals (“worried well”) to actual casualties. This model depicts high numbers of worried well initially, with numbers tapering after day 20. The developers applied a worst case scenario, despite the containment of the outbreak (meaning no new presenting fatalities or cases), as they did not base their prediction on authorities potentially implementing public information countermeasures, which would reduce the number of worried-well cases.
- **Effects of community prophylaxis.** No community prophylaxis measures were considered in this model, as administering existing vaccines post-exposure are not effective.
- **Other containment measures.** No other containment measures were assumed in this model, particularly since VEE is not generally transmitted between humans.

8.2.2 Calculations

The following section outlines the calculations applied in developing the VEE casualty predictive template. It also delineates the actual formulas associated with each previously described assumption.

| Row | Definition | Formula |
|-----|--|--|
| A | Stage I – Incubation Period: Number of persons primarily infected but still asymptomatic. | Initially 5,000, decreasing by numbers presenting at Stage II. Row A (previous day) – Row B (current day) |
| B | Stage II – Presenting Illness (headache, photophobia, and malaise). Number of persons primarily infected who present on the day in question with flu-like illness. | Variable incubation period. See distribution at bottom of template. |

| Row | Definition | Formula |
|----------|--|---|
| C | Stage III - Acute Illness (nausea, vomiting, cough, sore throat, and diarrhea): Total number of patients who have presented with symptoms consistent with viral infection on the day in question who have survived the day. All patients presumed to progress to this stage 24 hours after initial symptoms. | $\text{Row B (previous day) + Row C (previous day) - Row B (4 previous days)*}$ *all victims transition to deceased, chronically ill, or recovering at home after four days. |
| D | Stage IV _A - Chronic Recovery Requiring Care (7% CNS Effects). Presumes a small percentage of victims require prolonged inpatient treatment and/or skilled nursing care. | $0.07 \times \text{Row B (4 previous days)} + \text{Row D (previous day)}$ All victims in this category remain for duration of chart |
| E | Stage IV _B - Recovery at Home (92%). Presumes in-patient treatment required for 4 days. All surviving patients recover at home. | $0.92 \times \text{Row B (4 previous days)} + \text{Row E (previous day)**}$ ** Presumes recovery at home for one week, then 25% of this population fully recovered each subsequent day |
| F | Total Ill Today (Stage II, III, IV _A , IV _B). Sum of these stages for the current day. | $\text{Row B} + \text{Row C} + \text{Row D} + \text{Row E (current day)}$ |
| G | Number of Worried Well Today. Variable factor based on level of community disease. See distribution at bottom of template. | $\text{Row B} \times 5 + \text{Row I} \times 10 \text{ (current day)}$ First day of outbreak, worried well = number in Stage II |
| H | Total Seeking Medical Aid Today. Total of worried well and actual ill for current day. | $\text{Row B} + \text{Row G (current day)}$ |
| I | Number of Fatalities Today (1%). Victims die after 4 days of disease. | $0.01 \times \text{Row B (4 previous days)}$ |
| J | Cumulative Number of Fatalities. Current day's fatalities plus previous day's cumulative fatalities | $\text{Row J (previous day)} + \text{Row I (current day)}$ |

| Row | Definition | Formula |
|-----|--|--|
| K | Cumulative Number of Persons Seeking Medical Aid | Row K (previous day) + Row H (current day) |

TABLE 8 VENEZUELAN EQUINE ENCEPHALITIS (VEE) CASUALTY PREDICTIVE TEMPLATE

| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 | |
|---|-------|-------|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| A Stage I - Incubation Period (see distribution) | 5,000 | 1,750 | 600 | 200 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| B Stage II - Presenting illness (headache, photophobia, and myalgias in the legs and lumbosacral area) | 0 | 0 | 3,250 | 1,150 | 400 | 200 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage III - Acute illness (Nausea, vomiting, cough, sore throat, and diarrhea) | 0 | 0 | 0 | 3,250 | 4,400 | 4,800 | 1,750 | 600 | 200 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage IV _a - Chronic Recovery Requiring Care (7% CNS Effects) | 0 | 0 | 0 | 0 | 0 | 0 | 228 | 308 | 336 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 | 350 |
| E Stage IV _b - Recovery at Home (92%) | 0 | 0 | 0 | 0 | 0 | 0 | 2,990 | 4,048 | 4,416 | 4,600 | 4,600 | 4,600 | 4,600 | 4,600 | 4,600 | 3,450 | 2,588 | 1,941 | 1,455 | 1,092 | 819 | |
| F Total Ill Today (Stage II, III, IV _a , IV _b) | 0 | 0 | 3,250 | 4,400 | 4,800 | 5,000 | 4,968 | 4,956 | 4,952 | 4,950 | 4,950 | 4,950 | 4,950 | 4,950 | 4,950 | 3,800 | 2,938 | 2,291 | 1,805 | 1,442 | 1,169 | |
| G Number of Worried Well Today | 0 | 0 | 3,250 | 5,750 | 2,000 | 1,000 | 325 | 115 | 40 | 20 | 16 | 13 | 10 | 8 | 7 | 5 | 4 | 0 | 0 | 0 | 0 | 0 |
| H Total Seeking Medical Aid Today (Stage II and WW) | 0 | 0 | 6,500 | 6,900 | 2,400 | 1,200 | 325 | 115 | 40 | 20 | 16 | 13 | 10 | 8 | 7 | 5 | 4 | 0 | 0 | 0 | 0 | 0 |
| I Number of Fatalities Today (1%) | 0 | 0 | 0 | 0 | 0 | 0 | 33 | 12 | 4 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| J Cumulative Number of Fatalities | 0 | 0 | 0 | 0 | 0 | 0 | 33 | 44 | 48 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| K Cumulative Number of Persons Seeking Medical Aid | 0 | 0 | 6,500 | 13,400 | 15,800 | 17,000 | 17,325 | 17,440 | 17,480 | 17,500 | 17,516 | 17,529 | 17,539 | 17,547 | 17,554 | 17,559 | 17,563 | 17,563 | 17,563 | 17,563 | 17,563 | 17,563 |

Worst Case Predictions if no Public Information Countermeasures are Instituted

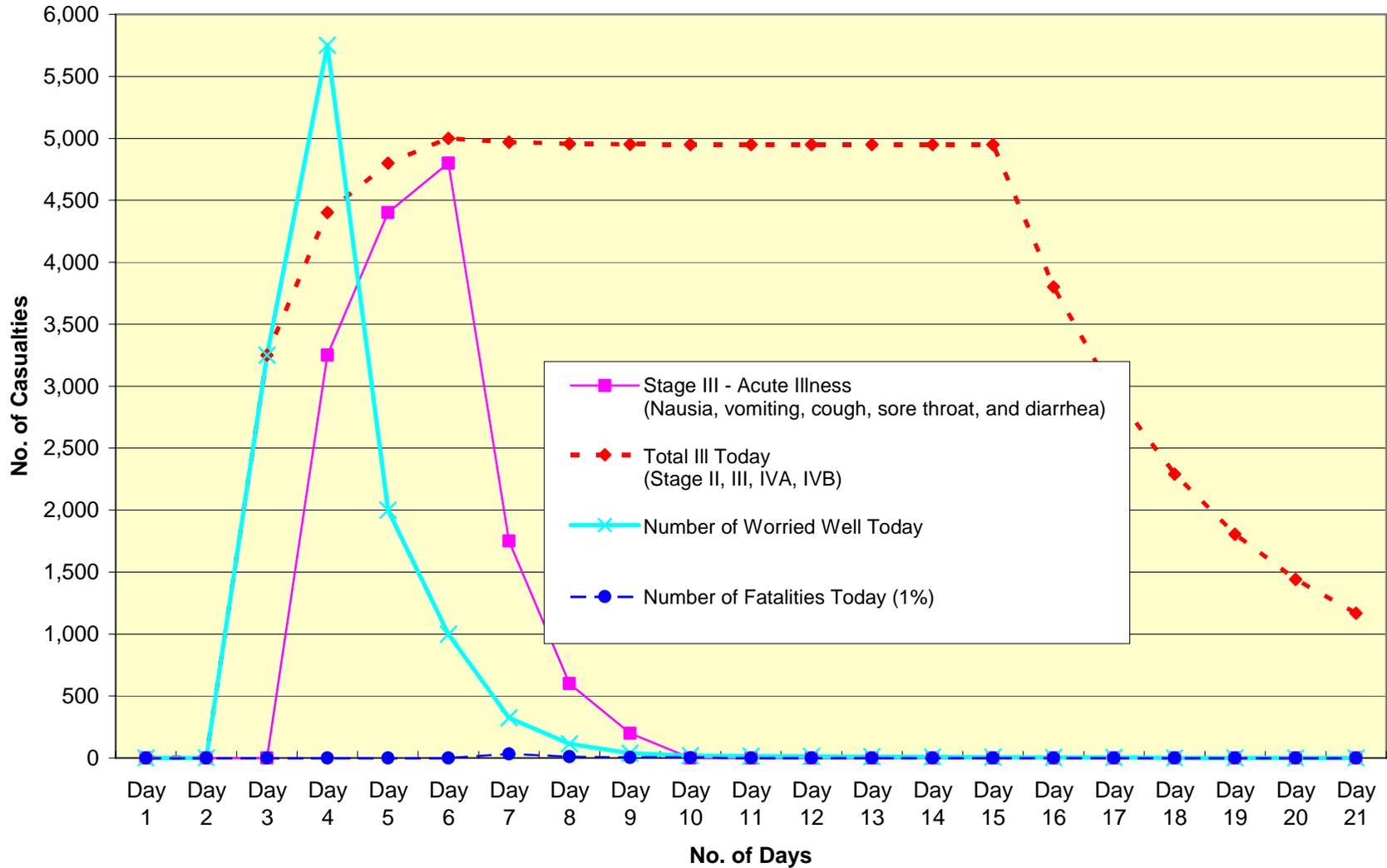
Number of People Infected: 5,000
 Distribution of Presenting Illness: 65% 23% 8% 4%
 Incident Mortality Rate: 1%

Assumptions:

Distribution of presenting illness. The average incubation period is one day.
Fatality rate. A fatality rate of 1% was used.
Secondary Cases. No secondary cases were predicted.
Worried-but-well cases. Variable ratios of 5:1 and 10:1 were applied.
Effects of community prophylaxis. No community prophylaxis measures were considered.
Other containment measures. No other containment measures were assumed.

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**FIGURE 8 VENEZUELAN EQUINE ENCEPHALITIS (VEE)
CASUALTY PREDICTION DISTRIBUTION CHART**



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MELIOIDOSIS

9.0 MELIOIDOSIS OVERVIEW

Melioidosis, *Burkholderia pseudomallei* (*B. pseudomallei*), is a gram-negative bacilli with a “safety-pin” appearance on microscopic examination. Such bacilli are common in many tropical and subtropical regions, such as Southeast Asia, northern Australia and northeastern Thailand. Typically the bacilli are found in contaminated water and soil where it can persist for many years.⁶⁷ Melioidosis, (similar to Glanders, *Burkholderia mallei* (*B. mallei*)) is classified as a BW agent because of its relatively high infectivity via aerosol, the severity of resulting disease, the lack of an effective vaccine, and the difficulty managing the disease with antibiotics.⁶⁸

For man (and animals) melioidosis is not known to spread person to person. The most common exposure occurs via environmental contact or inhalation of contaminated droplets, thus laboratory culture of the organism requires BSL 3 containment due to the aerosol infection risk posed by handling even standard cultures.⁶⁹ Emergency planners should be aware that multiple cases of melioidosis, in persons who have not recently traveled to regions of the world where it is endemic, should be considered presumptive evidence of a BW attack.

Naturally occurring melioidosis most commonly infects immunocompromised people, especially those with diabetes, chronic alcoholism, or cystic fibrosis. The organism can remain dormant in a normal host, only to become symptomatic years later when the individual becomes immunocompromised due to some other disease. Symptomatic melioidosis typically presents as an acute illness in several distinct forms, ranging from prostatic infection, acute, severe pneumonia, or septicemia. Some septicemic forms rapidly progress to melioidosis septic shock, which often leads to death within 24-48 hours of symptomatic onset.⁷⁰

Localized or less severe naturally-occurring melioidosis can be treated with broad spectrum oral antibiotics for 3 to 6 months. Relapse is common. More severe forms of the disease requires intravenous, broad spectrum antibiotics like ceftazidime or imipenem, plus trimethoprim/sulfamethoxazole for at least 14 days, then oral antibiotics for at least another 4-6 months.

⁶⁷ White NJ. Melioidosis. Lancet. 2003 May 17;361(9370):1715-22.

⁶⁸ Voskuhl GW, Cornea P, Bronze MS, Greenfield RA. Other bacterial diseases as a potential consequence of bioterrorism: Q fever, brucellosis, glanders, and melioidosis. J Okla State Med Assoc. 2003 May;96(5):214-7.

⁶⁹ Ip M, Osterberg LG, Chau PY, Raffin TA. Pulmonary melioidosis. Chest. 1995 Nov;108(5):1420-4.

⁷⁰ Chaowagul W, Suputtamongkol Y, Dance DA, Rajchanuvong A, Pattara-arechachai J, White NJ. Relapse in melioidosis: incidence and risk factors. J Infect Dis. 1993 Nov;168(5):1181-5.

After a known, intentional aerosol exposure, post exposure prophylaxis can be attempted with trimethoprim/sulfamethoxazole or doxycycline; however, the efficacy of such prophylaxis is unproven.

In some cases, medical personnel may need to drain abscesses⁷¹; instituting Standard Precautions are sufficient to prevent person-to-person transmission.

9.1 CLINICAL FEATURES

The incubation period for the inhaled version of the disease varies from 10–14 days, as denoted in the few reported laboratory exposure cases. The incubation period following an intentional aerosolization may be significantly shorter, and would likely depend on the inhaled dose and the agent's virulence; animal inhalation models of high dose melioidosis and glanders have both resulted in incubation periods as short as 1-4 days. Patients that have the pulmonary form may have suffered a direct inhalational exposure or the disease entered the lungs as a result of septicemia. Chest x-rays may show small nodules, consolidation, lung lesions, bilateral bronchopneumonia, or segmental or lobar pneumonia.⁷²

Should the septicemic form progress to septic shock, signs and symptoms may progress very rapidly. Patients will present with fever, rigors, sweats, muscle aches, shortness of breath, and chest pain associated with pneumonia. Physical examination may also include fever, tachycardia, hypotension, and a mildly enlarged liver or spleen.⁷³

The chronic form of melioidosis may not present with any immediate physical signs or symptoms and can remain dormant for decades. Melioidosis, like glanders, can present with abscesses in any organ.

Diagnosis is most commonly made by culturing blood or other body fluids. *B. pseudomallei* can be cultured and identified using standard bacteriological media, and blood cultures in acutely ill patients are often positive. Serology is not as useful, as it may not be positive until a week or more after symptom onset and the results are often confounded by a high background seroprevalence in patients who have lived in melioidosis endemic regions.⁷⁴ Leukocytosis is common; or, an abnormal decrease of WBC can be seen in some cases, but this may not occur unless the patient's condition is severe.⁷⁵

Although septicemic forms of melioidosis have mortality rates up to 90% (although this has dropped to 10% in N. Australia with the advent of aggressive therapies), the other types of the disease are generally nonfatal if appropriately treated.⁷⁶ Disaster planners must realize

⁷¹ Chaowagul W. Recent advances in the treatment of severe melioidosis. *Acta Trop.* 2000 Feb 5;74(2-3):133-7.

⁷² Ip M, Osterberg LG, Chau PY, Raffin TA. Pulmonary melioidosis. *Chest.* 1995 Nov;108(5):1420-4.

⁷³ M, Osterberg LG, Chau PY, Raffin TA. Pulmonary melioidosis. *Chest.* 1995 Nov;108(5):1420-4.

White NJ. Melioidosis. *Lancet.* 2003 May 17;361(9370):1715-22.

⁷⁴ Chaowagul W. Recent advances in the treatment of severe melioidosis. *Acta Trop.* 2000 Feb 5;74(2-3):133-7.

⁷⁵ Chaowagul W. Recent advances in the treatment of severe melioidosis. *Acta Trop.* 2000 Feb 5;74(2-3):133-7.

⁷⁶ Ip M, Osterberg LG, Chau PY, Raffin TA. Pulmonary melioidosis. *Chest.* 1995 Nov;108(5):1420-4.

that weaponized forms of melioidosis may be antibiotic resistant, which in turn profoundly increases the mortality rate.

9.2 MELIOIDOSIS CASUALTY PREDICTIVE TEMPLATE

The following casualty prediction template is intended to illustrate the potential impact of casualties on the medical infrastructure when approximately 5,000 people are infected with melioidosis via aerosol exposure. Additionally, it is assumed for those recovering at home, there will be adequate quantities of effective antibiotics available to support several months of treatment. These assumptions and others, and the rationale used in developing the formula equations, are presented below.

9.2.1 Template Assumptions

- ***Distribution of presenting illness.*** A variable incubation period was used for this template, as the incubation period for naturally acquired melioidosis is not known; what is known is the onset of melioidosis can vary with inoculum challenge dose and illness type. The developers assumed the majority of victims infected with the bacilli would remain asymptomatic and not seek care. For those that do seek medical attention, the developers speculated that signs and symptoms will begin appearing between day 3 to day 7 for septicemic shock, day 10 to day 15 days for non-disseminated septicemia, and day 20 to day 28 days for the localized form of the disease. Those with underlying illness, immunologically compromised, at the extremes of age, or exposed to higher doses of the bacilli, may have a shorter incubation period. Conversely, those with robust immune systems, or who have received smaller inoculums, may be asymptomatic for longer periods of time.
- ***Fatality rate.*** A variable fatality rate was used for this template. It was assumed that 60% of the people infected who become acutely symptomatic, presenting with septicemic shock, have a 50% fatality rate, 15% of the people infected present with non-disseminated septicemia, have a 20% fatality rate, and 25% of the people infected present with localized disease, have a 10% fatality rate. The developers applied high fatality rates as it is more probably that an intentional aerosol release would likely have higher inoculums. Time of death will also vary with the type of illness (i.e., death from septicemic shock occurs sooner than death from non-disseminated septicemia). Those that die from the localized form of the disease will likely not die within the 30-day window presented in this template.
- ***Secondary Cases.*** The developers determined no secondary cases would be predicted for this template. Although melioidosis can theoretically spread from person to person, there have not been any reported cases of airborne or droplet transmission. Of greater concern is exposure to infected secretions; however this can usually be contained when providers adhere to Standard Precautions.
- ***Worried-but-well cases.*** In this template, a low ratio (1:1) of asymptomatic potentially exposed individuals (“worried well”) cases to actual casualties was

predicted. The developers determined that a low mortality rate overall would not precipitate the same type of public fear/concern as would be expected for other biological outbreaks; this assumption, however, may not be entirely valid.

- ***Effects of community prophylaxis.*** The effects of community prophylaxis were not included in this template. It is possible that if the strain disseminated were susceptible to antibiotics, post-exposure prophylaxis will prevent the disease in exposed/asymptomatic patients, just as it has in animal models. In such instances health professions would need to determine what type of antibiotic or series of antibiotics would be effective and then execute community prophylaxis operations. Some additional delays may occur due to the logistics involved with acquisition of pharmaceuticals, delivery to points of distribution, and institution of dispensing plans. Dispensing of prophylaxis to certain populations (e.g., homeless, disabled, house-bound, impoverished and/or those with language barriers or lacking transportation) may be delayed even further. It is possible that communities with mature plans and ready access to major airfields for delivery of the SNS may reduce the time from exposure to prophylaxis than what this model depicts.
- ***Other containment measures.*** No other containment measures were assumed in this model. Since melioidosis is not known to be transmissible through casual human-to-human contact, it is also believed that alternate containment measures would have little effect on the overall outcome of this outbreak.

9.2.2 Calculations

The following section outlines the calculations applied in developing the melioidosis casualty predictive template. It also delineates the actual formulas associated with each previously described assumption.

| Row | Definition | Formula |
|-----|--|--|
| A | Stage I - Incubation Period. | 5,000 initial, decreasing by new presentations. Row A (previous day) – (Row B + Row C + Row D) (current day) |
| B | Stage II _A – Septicemic Shock (60%). | Gaussian distribution around incubation period of 5 days |
| C | Stage II _B - Non-Disseminated Septicemia (15%). | Gaussian distribution around incubation period of 11 days |
| D | Stage II _C – Localized (25%). | Gaussian distribution around incubation period of 24 days |
| E | Total Hospitalized Today. | Row B + Row C + Row D (current day) |

| Row | Definition | Formula |
|----------|--|---|
| F | Total No. of Cases in Hospitals (Stage II - Fatalities). | Row F (previous day) + Row E (current day) – Row G (current day) – Row K (current day) |
| G | Stage III - Recovery at Home Today. | Row D (current day) + Row C |
| H | Cumulative Number of Recovery at Home. | Row H (previous day) + Row G (current day) |
| I | Number of Worried Well Today. | Assumed 1:1 for this template |
| J | Total Seeking Medical Aid Today. | Row B + Row C + Row D + Row I (current day) |
| K | Number of Fatalities Today. | 0.5 x Row B (2 previous days) + 0.2 x Row C (11 previous days) + 0.1 x Row D (21 previous days) |
| L | Cumulative Number of Fatalities. | Row K (previous day) + Row K (current day) |
| M | Cumulative Number of Persons Seeking Medical Aid. | Row M (previous day) + Row J (current day) |

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TABLE 9 MELIOIDOSIS CASUALTY PREDICTIVE TEMPLATE

| Description | Day of Attack | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---------------|-------|-------|-------|-------|-------|-------|-------|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 11 | Day 12 | Day 13 | Day 14 | Day 15 | Day 16 | Day 17 | Day 18 | Day 19 | Day 20 | Day 21 | Day 22 | Day 23 | Day 24 | Day 25 | Day 26 | Day 27 | Day 28 | Day 29 | Day 30 |
| A Stage I - Incubation Period | 5,000 | 5,000 | 5,000 | 4,500 | 3,500 | 2,750 | 2,250 | 2,000 | 2,000 | 1,850 | 1,600 | 1,450 | 1,350 | 1,275 | 1,250 | 1,250 | 1,250 | 1,250 | 1,250 | 1,200 | 1,100 | 950 | 750 | 500 | 300 | 150 | 50 | 0 | 0 | 0 |
| B Stage II _A - Septicemic Shock | 0 | 0 | 0 | 500 | 1,000 | 750 | 500 | 250 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C Stage II _B - Non-Disseminated Septicemia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 150 | 250 | 150 | 100 | 75 | 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| D Stage II _C - Localized | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 50 | 100 | 150 | 200 | 250 | 200 | 150 | 100 | 50 | 0 | 0 |
| E Total Hospitalized Today | 0 | 0 | 0 | 500 | 1,000 | 750 | 500 | 250 | 0 | 150 | 250 | 150 | 100 | 75 | 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| F Total No. of Cases in Hospitals (Stage II - Fatalities) | 0 | 0 | 0 | 500 | 1,500 | 2,000 | 2,000 | 1,875 | 1,625 | 1,650 | 1,600 | 2,050 | 2,150 | 2,225 | 2,250 | 2,250 | 2,250 | 2,250 | 2,250 | 2,250 | 2,220 | 2,170 | 2,140 | 2,120 | 2,105 | 2,100 | 0 | 0 | 0 | 0 |
| G Stage III - Recovery at Home Today | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 420 | 700 | 420 | 280 | 210 | 70 | 0 | 0 | 0 | 0 |
| H Cumulative Number of Recovery at Home | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 50 | 570 | 1,420 | 2,040 | 2,570 | 2,980 | 3,200 | 3,300 | 3,350 | 3,350 | 3,350 |
| I Number of Worried Well Today | 0 | 0 | 0 | 500 | 1,000 | 750 | 500 | 250 | 0 | 150 | 250 | 150 | 100 | 75 | 25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| J Total Seeking Medical Aid Today | 0 | 0 | 0 | 1,000 | 2,000 | 1,500 | 1,000 | 500 | 0 | 300 | 500 | 300 | 200 | 150 | 50 | 0 | 0 | 0 | 0 | 50 | 100 | 150 | 200 | 250 | 200 | 150 | 100 | 50 | 0 | 0 |
| K Number of Fatalities Today | 0 | 0 | 0 | 0 | 0 | 250 | 500 | 375 | 250 | 125 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 30 | 50 | 30 | 20 | 15 | 5 | 0 | 0 | 0 | 0 | |
| L Cumulative Number of Fatalities | 0 | 0 | 0 | 0 | 0 | 250 | 750 | 1,125 | 1,375 | 1,500 | 1,500 | 1,500 | 1,500 | 1,500 | 1,500 | 1,500 | 1,500 | 1,500 | 1,500 | 1,530 | 1,580 | 1,610 | 1,630 | 1,645 | 1,650 | 1,650 | 1,650 | 1,650 | 1,650 | |
| M Cumulative Number of Persons Seeking Medical Aid | 0 | 0 | 0 | 1,000 | 3,000 | 4,500 | 5,500 | 6,000 | 6,000 | 6,300 | 6,800 | 7,100 | 7,300 | 7,450 | 7,500 | 7,500 | 7,500 | 7,500 | 7,500 | 7,550 | 7,650 | 7,800 | 8,000 | 8,250 | 8,450 | 8,600 | 8,700 | 8,750 | 8,750 | 8,750 |

Day First Ill Present

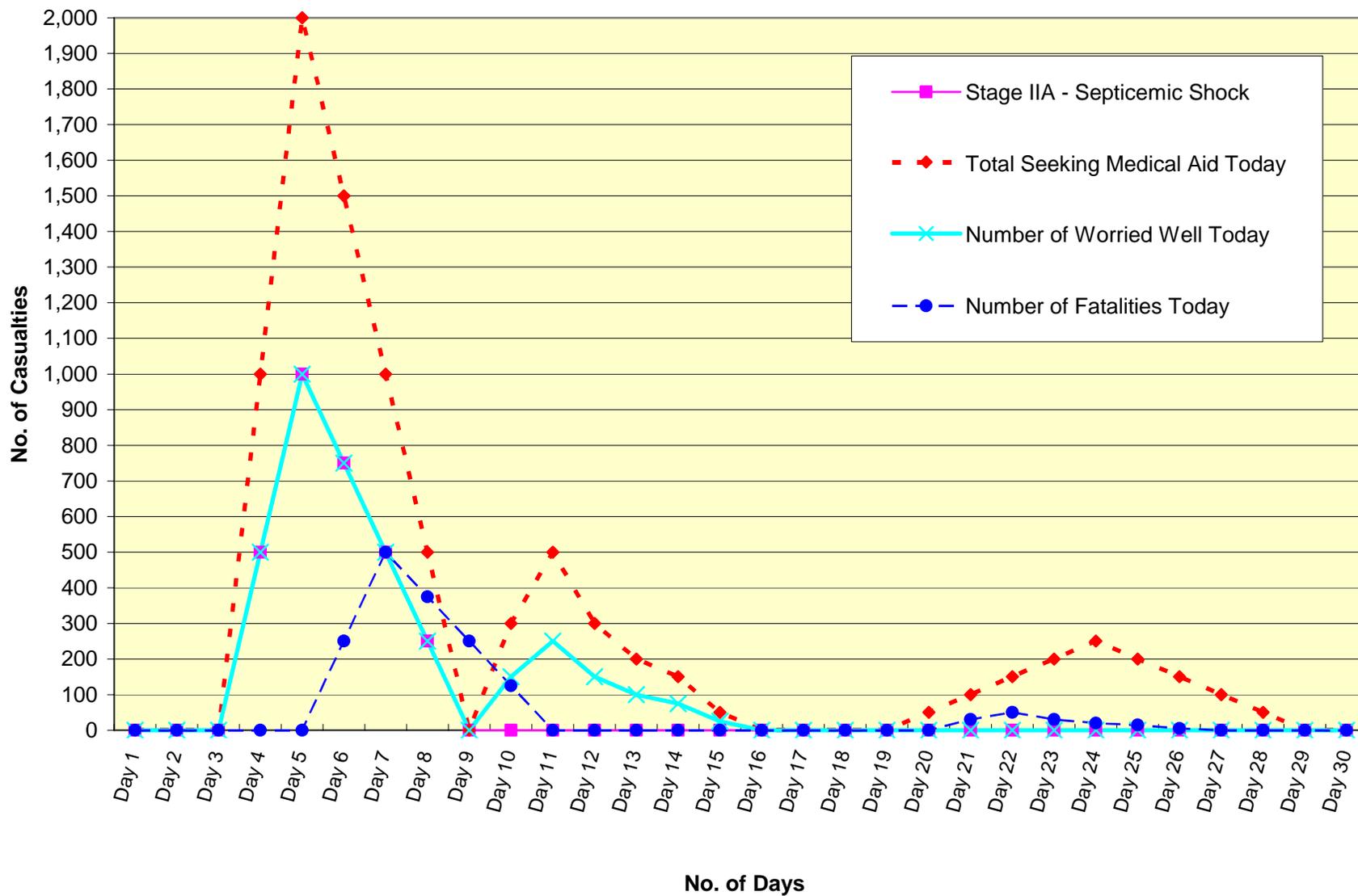
Day of Attack

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|-----|-----|-----|----|----|-----|-----|----|------|------|----|----|----|----|----|----|----|----|--|--|--|--|--|--|--|--|--|--|--|
| Number of People Infected: | 5,000 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Distribution of Presenting Septicemic Shock (80%): | 10% | 20% | 15% | 10% | 5% | | | | | | | | | | | | | | | | | | | | | | | | | |
| Distribution of Presenting Non-Disseminated Septicemia (15%): | | | | | | 3% | 5% | 3% | 2% | 1.5% | 0.5% | | | | | | | | | | | | | | | | | | | |
| Distribution of Presenting Localized (25%): | | | | | | | | | | | 1% | 2% | 3% | 4% | 5% | 4% | 3% | 2% | 1% | | | | | | | | | | | |
| Incident Mortality Rate (Disseminated Septicemia) (50%): | | | | | | 8% | 17% | 13% | 8% | 4% | | | | | | | | | | | | | | | | | | | | |
| Incident Mortality Rate (Non-Disseminated Septicemia) (20%): | | | | | | | | | | | 4% | 7% | 4% | 3% | 2% | 1% | | | | | | | | | | | | | | |
| Incident Mortality Rate (Localized): | 10 will die with Localized disease sometime in the next 1-2 months. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Assumptions:
Distribution of presenting illness. A variable incubation period was used.
 3 to 7 days for septicemic shock.
 10 to 15 days for non-disseminated septicemia.
 20 to 28 days for the localized form of the disease.
Fatality rate. A variable fatality rate was used for this template.
 60% of the people infected with septicemic shock have a 100% fatality rate.
 15% of the people infected with non-disseminated septicemia have a 20% fatality rate.
 25% of the people infected with localized disease have a 10% fatality rate.
Secondary Cases. No secondary cases are predicted.
Worried-but-well cases. No cases were predicted
Effects of community prophylaxis. Effects were not considered.
Other containment measures. No other containment measures were assumed.

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**FIGURE 9 MELIROIDOSIS
CASUALTY PREDICTION DISTRIBUTION CHART**



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CONCLUSION

10.0 CONCLUSION

The MIRP developed these casualty predictive templates initially, to more fully understand the breadth and scope of BW incidents to formulate response concepts of operation. The information contained within each template, combined with the ability to modify the templates to fit any jurisdiction population, however, has a broader application than the MIRP original use, as the templates have direct application for all emergency and medical planners.

The templates are intended to simplify biological agent exposure by providing the most critical information about each of the agents- anthrax, tularemia, pneumonic plague, smallpox, botulinum toxin, Venezuelan equine encephalitis, staphylococcus enterotoxin B intoxication, and melioidosis. Though information obtained solely from scientific peer review journals provides the most authoritative information, often it is too difficult to interpret the application of these writings to any other situation or person than those the document was originally intended. This report is intended to apply such writings to emergency planners.

These templates can assist emergency planners fabricate their response, but planners must realize that the MIRP made general assumptions regarding the population exposed, distribution of presenting illness, fatality rate, second generation cases, worried-but-well cases, effects of community prophylaxis measures, and institution of possible containment measures. The accuracy of this tool is therefore dependent on the similarity between these assumptions and particular parameters surrounding an actual biological outbreak.

The MIRP encourages planners to use this information to simplify their own planning efforts. Additionally, we recommend that planners modify the associated Casualty Predictive Template's Excel spreadsheets to either reflect their jurisdiction's population, as well as modify the calculations based on current relevant research.

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APPENDIX A

APPENDIX A- MODIFYING THE EXCEL SPREADSHEETS

1.1 INSTRUCTIONS & EXAMPLES

The Casualty Predictive Template’s Excel spreadsheets are an interactive disaster planning tool intended to depict the potential outcome of a biological outbreak. Emergency managers can modify specific predictive dependent parameters to more accurately reflect their jurisdiction. Additionally, the tool can be updated to reflect the most current information available that results from an actual outbreak or upon receiving relevant research findings to enhance the predictive accuracy of the tool.

There are three parameters the developers recommend the reader adjust—the number of people infected, the fatality rate, and the worried well rate. Planners that choose to modify the spreadsheet should have a working knowledge of Excel spreadsheets and realize that some parameters may only require the reader to adjust one data cell while others, require the reader to adjust the formula for each cell within the row category.

To modify the number of people infected, the reader must change the number in the cell entitled “*Number of People Infected.*” This cell is found near the bottom of the spreadsheet and has an original population estimation of 5,000 casualties, see Example 1. By modifying this parameter, the entire spreadsheet will automatically repopulate the number of casualties.

| | | | | | | |
|----------|--|-------|-------|--------|--------|-------|
| K | Cumulative Number of Persons Seeking Medical Aid | 0 | 6,500 | 13,400 | 15,800 | 1,700 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |
| | Distribution of Presenting Illness | 7% | 27% | 38% | 14% | 6% |

Example 1

To modify the fatality rate for anthrax, SEB, and VEE, the reader will need to change the equation for each cell within the row category. In the row entitled “*Number of Fatalities Today*” click the cell that has a value other than zero. A functional equation will appear in the formula bar of the Excel spreadsheet depicting the percentage of casualties for a particular day, such as $C7*0.01$, see Example 2. This formula multiplies the value at cell address C7, the number of persons in the incubation stage, by 0.01 or 1% of those in the incubation stage. Repeat the same steps for each cell in the row to depict an accurate fatality rate of an outbreak for your jurisdiction.

| | | | | | | |
|-----|--|----------|-----|-------|-------|--------|
| E15 | f_x | =C7*0.01 | | | | |
| I | Number of Fatalities Today | 0 | 0 | 50 | 285 | 1,283 |
| J | Cumulative Number of Fatalities | 0 | 0 | 335 | 1,618 | 3,423 |
| K | Cumulative Number of Persons Seeking Aid | 0 | 350 | 3,100 | 9,370 | 16,018 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |

Example 2

In other biological outbreaks such as tularemia, pneumonic plague, smallpox, botulinum, and melioidosis, modifying the fatality rate is simpler. Go to the “*Incident Mortality Rate*” near the bottom of the spreadsheet and adjust the percentages, see Example 3. This percentage relates to the total of newly identified ill for that day and can be modified to depict any percentage value the planner wishes to use.

| | | | | | | |
|---|--|-------|-------|--------|--------|-------|
| K | Cumulative Number of Persons Seeking Medical Aid | 0 | 6,500 | 13,400 | 15,800 | 1,700 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |
| | Distribution of Presenting Illness | 7% | 27% | 38% | 14% | 6% |
| | Incident Mortality Rate | 90% | 75% | 35% | 25% | 10% |

Example 3

Modifying the worried well rate is similar to modifying the fatality rate in that each cell in the row within the category must be changed to reflect your predications. In the row entitled “*Number of Worried Well Today*” click inside a cell with a value other than zero. Typically the number of worried well is based on a multiple number of casualties that present in the severe stage of the illness and a multiple number of fatalities for that day. Often times the assumptions for that particular biological agent will specifically address the worried well cycle rate. On Example 4, the rate starts as one times those presenting illness (E8) plus one times the number of fatalities today (E15). This rate escalates to 2 then 3 times the values in cells E8 and E15. As the number of those presenting illness declines, the worried well is calculated as ¾ or 75% of the number of fatalities from the previous day.

| | | | | | | |
|----------|---------------------------------|-----------------|----|-------|-------|-------|
| SUM | <i>fx</i> | =(E8*1)+(E15*1) | | | | |
| G | Number of Worried Well Today | 0 | 0 | 1,400 | 4,370 | 5,948 |
| H | Total Seeking Medical Aid Today | 0 | 35 | 2,750 | 6,270 | 6,648 |
| I | Number of Fatalities Today | 0 | 0 | 50 | 285 | 1,283 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |

Example 4

1.2 LIMITATIONS

As with any tool, there are inherent constraints. Those using or modifying the Excel spreadsheets should be aware of these constraints to avoid obtaining inaccurate or skewed data. For example, several data points are dependent on two or more equations that precede or occur after the cell in question. If a number in a particular cell is changed it may only adjust the values that cell is linked to versus modifying an entire category.

Modifying the “*distribution of presenting illness*” will affect several parameters, such as the number of casualties in each stage of infection, fatalities, secondary cases, worried well cases, and effects of community prophylaxis. Though the reader can change the percentages, these numbers were developed by a consensus of biological weapons of mass destruction experts, as they possessed working knowledge of the biological agents. Though not recommended, to modify the distribution, go to the “*Distribution of Presenting Illness*” row at the bottom of the spreadsheet. Each day corresponds with a percentage value that can be modified accordingly. Anytime the percentage is changed, the values for the entire row must equal 100% to accurately reflect the number of casualties (e.g., for anthrax 7% + 27% + 38% + 18% + 10% = 100%), see Example 5.

| | | | | | | |
|----------|--|-------|-------|--------|--------|-------|
| K | Cumulative Number of Persons Seeking Medical Aid | 0 | 6,500 | 13,400 | 15,800 | 1,700 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |
| | Distribution of Presenting Illness | 7% | 27% | 38% | 18% | 10% |

Example 5

Another limitation of the Excel spreadsheets was depicting the secondary generation of an outbreak. For some biological outbreaks, such as pneumonic plague, the primary and secondary generation of the outbreak is included in one spreadsheet. The reader has the benefit of identifying the total numbers of the outbreak simultaneously. To modify the secondary outbreak numbers, the reader must change the formula. For pneumonic plague, the developers assumed that one original case would infect three secondary cases. Thus the formula will read D7*3, see Example 6. Unlike the primary generation distribution that must equal 100%, instead the

secondary generation distribution will equal 100% for each day that there are secondary cases, as the secondary case calculations are not driven by the distribution percentage but by each row calculation, which for pneumonic plague is set to three.

| | | | | | | |
|----------|--|-------|-----|-------|--------|--------|
| E8 | <i>fx</i> | =D7*3 | | | | |
| B | Stage II (Primary) Presenting Illness | 0 | 500 | 4,000 | 500 | 0 |
| C | Stage I (Secondary) Incubation Period | 0 | 0 | 1,500 | 12,000 | 1,500 |
| D | Stage II (Secondary) Presenting Illness | 0 | 0 | 0 | 1,500 | 12,000 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |
| | Distribution of Presenting Illness Primary | 10% | 80% | 10% | | |
| | Distribution of Presenting Illness Secondary | | | 100% | 100% | 100% |

Example 6

For other outbreaks, such as smallpox, the secondary generation is depicted in a separate spreadsheet. Smallpox has a more complex disease cycle, which made it more difficult to portray in one spreadsheet without important information getting masked. Thus the primary and secondary generations of smallpox are reflected in two spreadsheets; however the secondary generation identifies the day of the outbreak as it corresponds to the progression of the outbreak for the primary generation. To figure out the total number of casualties and fatalities for the entire outbreak, the reader must add the totals from each generation for the day in question, see Example 7.

| Smallpox Primary Generation | | | | | | |
|-----------------------------|---------------------------------|-------|---|----|-----|-----|
| G | Number of Worried Well Today | 0 | 0 | 15 | 30 | 450 |
| H | Total Seeking Medical Aid Today | 0 | 5 | 25 | 105 | 815 |
| I | Number of Fatalities Today | 0 | 0 | 0 | 0 | 0 |
| | | | | | | |
| | Number of People Infected | 5,000 | | | | |

| Smallpox Secondary Generation | | | | | | |
|-------------------------------|---------------------------------|--------|---|----|-----|-----|
| G | Number of Worried Well Today | 0 | 0 | 15 | 60 | 719 |
| H | Total Seeking Medical Aid Today | 0 | 5 | 35 | 180 | 990 |
| I | Number of Fatalities Today | 0 | 0 | 0 | 0 | 0 |
| | | | | | | |
| | Number of People Infected | 15,000 | | | | |

| Total for Primary and Secondary Generations | | | | | | |
|---|---------------------------------|--------|----|----|-----|-------|
| | Number of Worried Well Today | 0 | 0 | 30 | 90 | 1,169 |
| | Total Seeking Medical Aid Today | 0 | 10 | 60 | 285 | 1,805 |
| | Number of Fatalities Today | 0 | 0 | 0 | 0 | 0 |
| | | | | | | |
| | Number of People Infected | 20,000 | | | | |

Example 7

Those wanting to modify the Excel spreadsheets should realize that there are other limitations to the tool. Specifically, the tool can not populate numbers for known variables by working backwards. For example, there is an

- Inability to drive the casualty numbers independent of the percentages;
- Inability to work backwards--meaning that planners know the actual values for some parameters and then try to work backwards to derive numbers for other parameters such as the total population infected;
- Inability to force the spreadsheet to calculate certain parameters that it was not intended to derive.

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APPENDIX B

APPENDIX B- LIST OF ACRONYMS

| | |
|----------|--|
| ACIP | Advisory Committee on Immunization Practices |
| ARDS | Acute Respiratory Distress Syndrome |
| BSL2 | Biosafety Level 2 |
| BSL3 | Biosafety Level 3 |
| BW | Biological Weapon |
| CAT | Computed Axial Tomography |
| CDC | Centers for Disease Control |
| CNS | Central Nervous System |
| DIC | Disseminated Intravascular Coagulopathy |
| DoD | Department of Defense |
| DOE | Department of Energy |
| ECBC | Edgewood Chemical Biological Command |
| ECL | Electrochemiluminescence |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| EPA | Environmental Protection Agency |
| FBI | Federal Bureau of Investigation |
| FEMA | Federal Emergency Management Agency |
| HEPA | High Efficiency Particulate Air |
| HHS | Health and Human Services |
| IND | Investigational New Drug |
| IV | Intravenous |
| MIRP | Military Improved Response Program |
| PAPR | Powered Air Purifying Respirators |
| PCR | Polymerase Chain Reaction |
| Ro | Reproductive Ratio |
| SEB | Staphylococcal Enterotoxin B |
| SNS | Strategic National Stockpile |
| U.S. | United States |
| USAMRIID | United States Army Medical Research Institute of Infectious Diseases |
| USDA | United States Department of Agriculture |
| VEE | Venezuelan Equine Encephalitis |
| WBC | White Blood Cells |
| WMD | Weapon of Mass Destruction |

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