Emerging and Re-Emerging Infections: Public Health Preparedness: Introduction to Infectious Outbreak Reporting and Containment

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Error!

Clinical Case:

You are the only Emergency Department attending in an urban teaching emergency department. A 28 year-old previously healthy female biologist presents with fever and rash of 1 day duration. She returned from Uganda 3 days ago, where she was in direct contact with green monkeys collecting DNA samples for academic research. Two days ago she developed a fever to 103 degrees Fahrenheit, sore throat and vomiting. Today she has had several very dark bowel movements, as reported by her boyfriend. Other than the recent travel, she has had no known sick contacts. The patient cannot recall any needlestick injuries.

Past medical history is only significant for an appendectomy at age 12. The patient is taking oral contraceptives and has no known drug allergies. She is a biologist for a major university and has frequent contact with monkeys, drawing blood for DNA analysis, most recently from wild monkeys from Central Africa.

Her vitals are as follows: BP 84/52, HR 132, T 104.4F, 94% saturation on room air. The patient appears very toxic and dry, in mild respiratory distress, diaphoretic and pale. Her demeanor is unusually apathetic.

HEENT: injected conjunctiva bilaterally with subconjunctival hemorrhages. Exudative tonsillitis. Prominent palatal petechiae and mild oozing around gum line.

CVS: Tachycardic, grade II/VI systolic ejection murmur at left upper sternal border. Thready though palpable peripheral pulses.

Lungs: Tachypneic, RR 44. Bibasilar rales.

Abdomen: Mildly distended, diffusely tender with guarding. Active bowel sounds. Heme positive dark stool.
Skin: Warm, very diaphoretic; centripetal maculopapular rash with hemorrhagic erythema on palms and soles.

While caring for the patient, the nurse notifies you that you have two urgent incoming phone calls on the line. Leaving the senior resident to continue aggressive resuscitation of your patient, you get on the line. EMS notifies you that they are transporting a 44 year-old non English-speaking diplomat who appears to be in DIC, with massive GI and gingival hemorrhage. Blood pressure is 60/palpable and the patient is "burning up". On the other line is a private internist sending into your emergency department two returned travelers with high fever and unusual rash. Both the EMS personnel and the private attending sound terrified, and are looking to you for advice and assistance.

Objectives:

1. To train clinicians to recognize sentinel cases and outbreak patterns
2. To introduce clinicians to sentinel outbreak reporting mechanisms.
3. To teach appropriate outbreak containment methods.
4. To provide an introduction to the basics of hospital, local, and national response plans.

Introduction:

In 1997 the United States spend 137 million dollars on biodefense. In 2000 funding increased to 1.5 billion dollars for military biodefense and an additional 1 billion dollars for domestic biological preparedness. Since September 11, 2001 and after the anthrax attacks that resulted in several deaths, Operation Bioshield has pledged $6 billion of federal funding over 10 years for the development of vaccines and treatments against potential bioterrorism agents[1].

Outbreak Detection

Most outbreaks present as "flu-like illness". The size of an outbreak is related to the virulence of the organism or agent, modes of transmission (i.e. contact vs. aerosol), and to the potential extent and mode of dissemination.

The following clinical features should alert clinicians to the possibility of a sentinel case for a contagious outbreak or bioterrorism-associated event, especially if seen in large numbers of patients or in an unexpected patient population, geographic location, or time of the year.

Gastroenteritis: salmonella, shigella
Pneumonia with sudden death in a healthy patient: pneumonic plague, SARS, anthrax
Widened mediastinum with fever: anthrax
Rash with synchronous vesicular or pustular lesions: smallpox
Acute neurologic illness with fever: botulism, viral hemorrhagic fever
Advancing cranial nerve impairment with progressive weakness: botulism[2]

Epidemiologic Criteria:

1. Severe disease in a healthy patient
2. Increased numbers of patients with fever, respiratory or gastrointestinal symptoms
3. Multiple patients presenting from a similar location with the same symptoms
4. Endemic disease at an unusual time of the year
5. Large numbers of rapidly fatal respiratory cases

6. Increasing numbers of ill or dead animals
7. Rapid rise and fall of the epidemic curve
8. Increased numbers of patients with sepsis, sepsis with coagulopathy, or fever with rash[3]

Syndromic Surveillance

In the response to a bioterrorism or contagious disease outbreak, time is critical in order to contain the outbreak and minimize potential spread to other individuals. Most agents with outbreak or bioterrorism potential present as "flu-like illness" and thus it would be extremely difficult to detect a low-level outbreak by traditional surveillance methods.

Syndromic Surveillance is the collection and analysis of statistical data on health trends. It aims to decrease the time to detection of an outbreak compared to traditional surveillance methods[4]. During the *syndrome grouping stage* data is collected and organized, i.e. using ICD-9 codes. Based on data collected over a defined period of time, during which there is no contagious disease or biological outbreak, a historical model can be built. In the *detection stage*, differences between predictions from the model and actual visits recorded are evaluated. Detection of a large outbreak is obvious, whereas a small outbreak is difficult. The basic syndromic surveillance model looks at the daily numbers of patients with flu-like symptoms and adds a hypothetical number of cases to mimic the pattern of an attack or outbreak. An excess of cases is chosen at which the alarm will be triggered.[5].

Syndromic surveillance systems have inherent trade-offs between sensitivity, timeliness, and false positive rates. The goal is to have a sensitive system but to minimize false alarms, as these will be costly both from an economic and time perspective. Syndromic surveillance encompasses a broad range of activities including monitoring illness syndromes or events. Alarms are triggered by "flags" that a statistical threshold has been reached. Such triggers are based on a certain number of markers, such as medication purchases or a diagnosis of "viral syndrome". In severe disease, hospital admissions and death more useful than early indicators of care. During the *clinician reporting stage* the individual clinician informs the local department of health[2].

The Healthy People 2010 national initiative calls for improved surveillance systems. To that end, various organizations have begun projects to develop such systems. The *Frontlines of Medicine Project* is a collaboration between emergency medicine, public health, law enforcement and informatics. The goal is to develop a non-proprietary open systems approach to reporting emergency department patient data that will be useful in syndromic detection. From a public health perspective, the CDC is developing the National Electronic Disease Surveillance System (NEDSS)[6].

Syndromic Surveillance Methods

Proposed syndromic surveillance systems vary in their methodology and complexity. Data can be collected in several fashions: i.e. hospital data from a 24 hour period, a moving daily average with increased weight of recent data, cumulative deviations from a constant expected value, or an expected daily value adjusted for seasonal variation in flu-like symptoms. The more statistically sophisticated methods have been predicted to increase the detection of a slow attack[4].

Integration of syndromic surveillance into the public health system is crucial. Traditional surveillance sets off alarms but limits the clinician's role in outbreak reporting. Physicians and other healthcare providers are essential for active syndromic surveillance and reporting to public health officials, conducting epidemiological investigations, and the use of information technology. Information technology facilitates real time detection, the communication between various entities (i.e. labs and clinicians), and the use of database systems for epidemiologic intelligence[4]. The clinician's role in outbreak detection is the determination of "credible risk" by both epidemiologic and clinical criteria, the arrangement of rapid and efficient laboratory evaluation, and the immediate notification of public health authorities[7].

In a study by *Foldy et. Al.*, a proposed online-based syndromic surveillance system was evaluated during two periods of potential bioterrorism. Patient visits meeting syndromic criteria and total visits were reported daily during those periods on a secured website and downloaded by public health staff. Syndromic trends were analyzed and displayed on site in a real-time fashion. The system was found to allow for rapid implementation of multi-site data collection restricted to emergency department triage, which could be valuable in the detection of an outbreak[8].

Epidemiologic Trends in Outbreaks:

From Fred M. Burkles, Jr. Mass Casualty Management of a Large Scale Bioterrorism Event: An Epidemiologic Approach that Shapes Triage Decisions. *Emergency Clinics of North America* 20(2), May 2002.

In a **common source epidemic**, the population at risk was exposed at a single point in time. Cases occur after the minimum incubation period and continue for a duration determined by the incubation time of those infected. The epidemic ends after this period, since there is no secondary spread of the toxin or pathogen[9].

Propagative or progressive epidemics involve uncontrolled person-to-person transmission of a pathogen from a common source or the presence of a pathogen over a period, as might be expected with smallpox and pneumonic plague. Secondary cases occur, leading to irregular peaks illustrating the number of infected, exposed and susceptible sources.

In a **classic epidemic**, typical for a human reservoir aerosol-borne disease, the gradual buildup of cases does not originate from a common source of exposure and occurs more slowly. This leads to a wave-shaped phenomenon at the start of the epidemic, which represents generations of transmission. [9]

Model for Outbreak Epidemiology: SEIRV

- S: susceptible: individuals who are healthy but are at risk for being exposed
- E: exposed: individuals who have been exposed to the agent and may become ill
- I: infective : individuals that are contagious
- R: removed: individuals who are no longer contagious or at risk, either by immunization, recovery, or death
- V: individuals who have been vaccinated successfully[10]

Emerging Infections: Why should we care?

The Institute of Medicine 1992 Report *Microbial Threats to Health: Energence, Detection and Response* outlined 5 factors that predispose to the emergence and spread of infectious disease. These are the factors that public health and governments need to address in order to decrease the risk of emerging and re-emerging infections causing widespread illness.

1. **Change in physical environment**: climate and weather changes affecting the ecology of vectors, animal reservoirs and the transmissibility of microbes
2. **Human behavorial activities**: global travel, land use, contact with animal reservoirs, globalization of food supply, increasing crowding, reforestation, irrigation
3. **Social/political/economi**c: war and famine leading to population movements, broken down public health infrastructure
4. **Bioterrorism**
5. **Increased use of antimicrobials and pesticides increasing resistance**[11],[12]

Outbreak Reporting:

Various national and international networks have been developed to facilitate national and world-wide recognition of infectious outbreaks.

- **EMERGency IDNET**: emergency department sentinel network for emerging infections
- **IDSA EIN**: Infectious Diseases Society of America Epidemic Intelligence Network
- **Geosentine**l: sentinel network of traveller's clinics used by CDC to analyze trends and develop travel advisories
- **LRN: Lab Research Network**: a network of national laboratories who goal is to enhance surge capacity for responding to oubreaks of unusual size and severity
- **National Nosocomial Infections Surveillance System**
- **Emerging Infections Journal**

PROMED: International Society of Infectious Disease program for monitoring infectious diseases. Promed maintains an email list of registrants at www.promedmail.org. Front line clinicians or public health staff report puzzling or unusual infections on the website. A team of experts reviews these reports as well as news reports and posts notices to registrants.

GOARN: WHO Global Outbreak Alert and Response Network (110 interlinked networks). This network systematically collects new outbreak reports and rumors and is responsible for outbreak verification as well as the communication and coordination of the international response to an outbreak.

Global Public Health Intelligence Network: GPHIN

GPHIN is an internet based "early warning" system for Health Canada and WHO that searches news reports and websites in six languages.

US DOD Global Emerging Infections Surveillance

Department of Defense infectious disease surveillance network that partners with US and foreign public and private agencies.

I**ntREPID**: a multidisciplinary team of government and academic scientists participate in this network. The system uses data from NASA's Earth Observing System (EOS) with the goal to build an early warning system based on climatic changes that may indicate early effects on ecologic systems that could increase the transmission of existing pathogenic organisms or the development of emerging zoonotic infections.

Zoo Network: detect zoonotic infections, based out of Cornell university. Analyzes laboratory specimens from zoo animals for the early detection of zoonotic infections.

International Emerging Infections Program of the CDC:
The goal of the this program is in prevention and control of emerging infections, training of public health officials and clinicians in outbreak detection and control, and the application of research and proven public health tools to the detection and control of emerging infections[11, 12.]

From Outbreak Reporting to Containment: Can we Learn?

In 1995 an Ebola outbreak in Congo led to 240 mortalities in 4 months. Due to geographic conditions and a broken down public health infrastructure, outbreak reporting was significantly delayed. Poor infection control practices and the lack of sterilization promoted hospital transmission of the illness, leading to multiple healthcare worker deaths. The provision of disinfectant and personal protective equipment led to eventual containment. In a subsequent Ebola outbreak in the Congo in 1997, it took 19 days to outbreak awareness and an additional 49 days to international assistance. The remote location of these outbreaks and their high mortality make detection and reporting a continued challenge[11].

Lessons from SARS

The Institute of Medicine released a report titled 2004 *Learning from SARS: Preparing for the Next Disease Outbreak,* in an effort to outline how public health can prepare for a future contagious disease outbreak.

SARS is a novel coronavirus that in late 2002 caused an estimated overall 80 billion dollar economic impact due to its effects on travel and tourism and business activities. A very efficient response by WHO, GOARN, GPHIN and Promed mail led to rapid communication, collaboration, assistance and scientific research once the outbreak was reported. On March 26 the Ontario provincial emergency decreased transfer to arriving hospitals, instituted control measures, and created specific SARS units. In Singapore a10 day quarantine was instituted for all SARS contacts, as well as screening of all airport and seaport arrivals for fever[13].
During the SARS outbreak, the following model was employed. For infected patients the goals were detection, isolation, and containment. For uninfected patients, monitoring and protection for transmission of the contagious disease were critical. The affected area hospitals converted patient rooms into isolation rooms, and established of "hot-wards" or SARS units that were designated as infectious zones. Designated ambulance services were created. For staffing needs and rest, back up teams and functional units were formed[14].

Outbreak Containment

Containment of a contagious outbreak requires sentinel case confirmation, epidemiologic surveillance and investigation, rapid agent detection and confirmation, and careful lab specimen handling, testing and referral. It requires a rapid response via activation and notification of a pre-existing outbreak containment plan and the use of a sophisticated national call-down communication system: the CDC HAN (Health Alert Network)[15],[16].

Containment of the outbreak involves several steps, including isolation of infectious patients, quarantine measures if recommended by local health authorities, and environmental controls to prevent transmission. The exposure of large numbers of individuals to biological agents or to infectious individuals may require mass prophylaxis, if the agent to which they were exposed can be prevented and/or treated by pharmaceuticals such as vaccines or antibiotics. This mass prophylaxis requires pre-assembled stockpiles ready for distribution. Similarly large numbers of ill patients as well as "worried well" would require the availability surge sites and the use of public information campaigns to educate people on signs and symptoms of illness and recommended courses of action. In a healthcare system in which there is a pre-existing shortage of nursing and other staff, staffing needs could require the use of credentialed volunteers. The panic and psychological impact caused by an outbreak or biological attack would greatly strain existing community and mental health resources[15,16].

<u>Laboratory Capabilities:</u>

Level A: Minimal identification
Level B: Identification, confirmation and susceptibility testing
Level C: Molecular techniques
Level D: CDC/DOD labs with advanced techniques and special surge capacity[17]

***Biosafety Levels*:**

BSL-1 labs are used to study agents not known to consistently cause disease in healthy adults. They follow basic safety procedures and require no special equipment or design features.

BSL-2 labs are used to study moderate-risk agents that pose a danger if accidentally inhaled, swallowed or exposed to the skin. Safety measures include the use of gloves and eyewear as well as handwashing sinks and waste decontamination facilities.

BSL-3 labs are used to study agents that can be transmitted through the air and cause potentially lethal infection. Researchers perform lab manipulations in a gas-tight enclosure. Other safety features include clothing decontamination, sealed windows, and specialized ventilation systems.

BSL-4 labs are used to study agents that pose a high risk of life-threatening disease for which no vaccine or therapy is available. Lab personnel are required to wear full-body, air-supplied suits and to shower when exiting the facility. The labs incorporate all BSL 3 features and occupy safe, isolated zones within a larger building.
More information is available in Biosafety in Microbiological and Biomedical Laboratories, a publication prepared by the National Institutes of Health and Centers for Disease Control and Prevention[18].

Surge Capacity:

Public health surge capacity refers to the ability of public health infrastructure to accommodate the evaluation and treatment of unexpectedly large numbers of patients, whether from a contagious disease outbreak or from a mass casualty or natural disaster. *Healthcare and facility based surge capacity* refers to the local ability to significantly increase the ability to care for patients. This capacity is usually limited, as the financial constraints that healthcare institutions currently operate under prohibit the warehousing of expensing stockpiles and equipment, and staffing is already short. Alternate sites of care could be “flat spaces” such as lobbies, waiting rooms, conference rooms, stadiums, or mobile units. In previous epidemics such as pandemic flu and smallpox outbreaks, auxiliary hospitals were used. Surge capacity should not be confused with *surge capability*, which refers to an institution’s ability to care for patients requiring specific interventions not normally available at that site (i.e. burn centers)[19].

Hospital Emergency Incident Command System (HEICS)

Based on the Incident Command Structure developed by firefighters to respond to mass casualties, HEICS incorporates a bioterrorism or contagious outbreak plan into existing internal operations in an "all hazards" approach. The Incident Command Structure has one Incident Commander designated as the leadership and authority for an event. Sub-chiefs are designated responsible for logistics, operations, finance, and planning. HEICS provides a common organizational structure to coordinate response to mass casualty event or outbreak[20].

Hospital Response Plans:

Based on the *CDC Bioterrorism Readiness Plan: A Template for Healthcare Facilities.* A contagious disease outbreak plan should be ready pre-event. It is activated on syndrome-based criteria and takes into account infection control, isolation precautions, patient placement, patient transport, cleaning, disinfection, sterilization, discharge management, post-mortem care, post-exposure management, triage of large scale exposures and suspected exposures, and psychological aspects and counseling[21].

Hospital response plans should include the following components:

Activation/Notification: Administration serves as leadership and authority, all public information released via media relations, with infection control responsible for epidemiologic investigations and control measures

Facility Protection: Security should be responsible for the lockdown state of the hospital with controlled entry and exit points and a controlled, unidirectional flow of patients. Separate external triage sites should be established for staff (for symptom review and fever checks) and patients (to determine who is high risk for contagion versus the worried well or those with other non-outbreak related chief complaints).

Decontamination: In the event of a contagious disease outbreak or the release of a biological agent, self-decontamination is usually sufficient. If the agent is still on the person, decontamination via shower is necessary. There is no indication for the use of bleach solutions.

Supplies/logistics: hospitals will need to review and have available necessary pharmaceuticals, personal protective equipment and ventilators. Infection control will be responsible for a coordinated review of all inpatient antimicrobial use with pharmacy services and to discontinue needed pharmaceuticals for other alternatives whenever feasible.

Alternative care sites: Increasing surge capacity within the healthcare facility occurs by expedient discharge of patients from the emergency department and inpatient wards and the cancellation of elective cases. It also requires a review to determine which patients may be taken off isolation or cohorted together.

Staff education/training: As part of emergency preparedness, the hospital or organization will be responsible for including training and practice drills on contagious disease outbreak or bioterrorism events as part of routine mass casualty protocols and drills.

Coordination and communication: Timely communication and cooperation between EMS and the Fire Department, police, government, and the media is necessary and should be stated in the plan[22].

Outbreak Containment: State and Federal Response

Local and State authorities are responsible for the first response to an outbreak. The Department of Health and Human Services' role is to identify and apply containment for epidemics. The Federal Emergency Management Association coordinates federal assistance should local and state resources be overwhelmed.

Under the National Medical Disaster system (NDMS), multiple Disaster Medical Assistance Teams (DMATs) can be deployed from various locations, some with expertise in specific areas, i.e. pediatrics, chemical weapons, etc. One DMAT is located in Northern Virginia and has provided assistance in the Oklahoma City Bombing and the earthquakes in Turkey.

During an outbreak the CDC will provide epidemiologic and laboratory expertise and the recommendation of control measures and prophylactic regimens.

The CDC and DHS maintain 8 Strategic National Stockpile "pushpacks" in several locations across the country, the contents and location of which are classified. Such a pushpack may be deployed upon State request if pharmaceuticals and/or other supplies are needed in a biological disaster. The pushpacks are slated to arrive within 12 hours, and would then be divided and distributed depending on the need in point of distribution centers (PODs). Should further or more specific supplies (i.e. ventilators, specific antibiotics) be necessary, Vendor Managed Inventory (VMI) is available within 24-36 hours[23].

HICPAC Infection Control Guidelines

These infection control guidelines were first established by CDC in 1991 as part of occupational safety for healthcare workers.

Standard precautions: should be used when the healthcare provider expects exposure to blood and body fluids. Personal protective equipment (PPE) is to be used, including a gown, gloves, and mask with eye protection if splash anticipated.

Contact isolation: PPE is required for all healthcare worker interactions, and patients are to be in private rooms, with the use of dedicated patient equipment and patient transport occurring only if necessary.

Droplet: this level is designated for microbes less than 5 micrometers in diameter, that are transmissible at less than 3 feet distance. Health care providers are to use PPE including masks at all times while providing patient care.

Airborne: for small infectious particles. PPE including N95/PAPR should be worn at all times and the patient should remain in a private negative pressure isolation room with 6-12 air changes per hour[24].

Clinical Case (continued)

A tentative diagnosis of viral hemorrhagic fever is made. The patients are placed in airborne isolation rooms and cohorted with the healthcare providers providing their care. The healthcare providers wear full PPE including PAPR. You call Infectious Disease on Call and Hospital Administration for activation of the Contagious Disease Outbreak Plan. You notify the DC DOH emergency hotline and the CDC for recommendations and assistance in containment of the outbreak and contact tracing. Identification and confirmation of Ebola serotype made by the USAMRIID BSL 4 laboratory located in Fort Detrick, Maryland.

Viral Hemorrhagic Fever: Filoviruses

Marburg and Ebola are members of the family of filoviruses (single stranded RNA viruses) that cause severe hemorrhagic illnesses. The family is endemic to Central Africa. The Marburg virus was first identified in Germany in 1967 in lab-workers who had been exposed to infected green monkeys. In 1989, the Ebola-Reston virus was discovered imported monkeys, which led to the institution of strict quarantine measures for imported animals. Fortunately, the virus, although very lethal to the affected monkeys, was not very pathogenic to humans. The story is chronicled in the book “The Hot Zone” by Richard Preston. Multiple outbreaks of Ebola have occurred since 1977, popularized by the movie “Outbreak” starring Dustin Hoffman and Rene Russo. There are four Ebola serotypes, with Ebola Zaire having 88% mortality.

The incubation period for the filoviruses is 4-5 days, with the sudden onset of high fever, sore throat, fatigue, and headache. The longest reported incubation period for is 21 days. Most patients get a non-pruritic maculo-papular centripetal rash that desquamates after one week. GI, skin and mucous membrane hemorrhages can be severe. Leukopenia, thrombocytopenia, transaminitis are common laboratory findings. Mortality results from hemorrhage and hypovolemic shock. The viral hemorrhagic fevers can initially be confused with other illnesses, and the differential diagnosis includes yellow fever, dengue, meningococcemia, leptospirosis, and ITP. Diagnosis is made by indirect immunofluorescence or ELISA; advanced techniques include PCR. Supportive therapy is the only treatment. Although army scientists are working on an Ebola vaccine, none is yet available[25].

Current guidelines for viral hemorrhagic fever recommend contact isolation precautions. Although airborne transmission cannot be ruled out, it appears to be very rare. PAPR provides slightly better filtration than N95 mask but is 500 times more expensive and increases the risk of needlestick injury due to its bulkiness Supportive treatment includes IV fluids, pressors if needed, the use of blood products, and ventilator use as needed. An experimental IND is available for ribavirin in arenavirus infections (i.e. Lassa fever) only[26].

Outbreak Preparedness: Goals for Clinicians

Clinicians need to be aware of credible risk and epidemiologic criteria for sentinel cases. They should be familiar with their hospital and community outbreak plansand how to report a suspected or unusual infectious illness. Basic principles of isolation, occupational health, and cohorting should be followed in an outbreak. Being active in hospital and local community disaster planning and staying informed of local, state and national biological preparedness policies are the best methods for being prepared for an outbreak of an emerging infection (i.e. Ebola or SARS) or re-emerging infection (i.e. tuberculosis or polio) or bioterrorism event (i.e.smallpox).

Resources:

- CDC Bioterrorism Website www.bt.cdc.gov
- Johns Hopkins Center for Civilian Biodefense Studies www.hopkins-defense.org
- US Army Medical Research Institute for Infectious Diseases www.usamriid.army.mil

Books of Interest

1. Joseph B. McCormick and Susan Fisher-Hoch with Leslie Ann Horvitz. Level 4 Virus Hunters of the CDC. Barnes and Noble Books: New York, New York, 1996.
2. Laurie Garrett. The Coming Plague. Newly Emerging Diseases in a World Out of Balance. Penguin Books: New York, New York, 1994.
3. Laurie Garrett. Betrayal of Trust. The Collapse of Global Public Health. Hyperion: New York, 2000.
4. Richard Preston. The Hot Zone. Random House, Inc: New York, 1994.
5. Christopher Wills. Yellow Fever. Black Goddess. The Coevolution of People and Plagues.
6. Germ Warriors. Stories of Men and Women Fighting the World's Worst Plagues. Ed. Clint Willis.

References

[1] David R. Franz and Russ Zajtchuk. Bioterrorism: Understanding the threat, preparation and medical response. *Disease-A-Month* 48(8), August 2002.
[2] James W. Buehler et. Al. Syndromic Surveillance and Bioterrorism-related epidemics. *Emerging Infectious Diseases*, October 2003
[3] Rega. Bioterrorism: A statistical manual to identify and treat diseases of bioterrorism. Mascap Inc, Ohio, 2000.
[4] Michael Stoto et. Al. The RAND Center for Domestic and International Health Securtiy. Syndromic Surveillance: Is it worth the effort? *Chance* 17(1), 2004, 19-24.
[5] Ben Y. Reise and Kenneth D. Mandl. Syndromic Surveillance: the effects of syndrome grouping on model accuracy and outbreak Detection. *Annals of Emergency Medicine* 44(3(), September 2004.
[6] Edward N. Barthell et. al. Syndromic Surveillance: The Frontiers of Medicine project: a proposal For the standardization communication of ED data for public health uses including syndromic Surveillance. *Annals of Emergency Medicine* 39(4), April 2002.
[7] Peter Katona. Bioterrorism Preparedness: A generic blueprint for health departments, Hospitals and physicians. *Infectious Diseases in Clinical Practice* 11(3), 2004, March/April 2002.
[8] Seth Foldy et. Al. Syndromic Surveillance Using Regional Emergency Medicine Internet. *Annals of Emergency Medicine* 44(3), September 2004.
[9] Fred M. Burkles, Jr. Mass Casualty Management of a Large Scale Bioterrorism Event: An Epidemiologic Approach that Shapes Triage Decisions. *Emergency Clinics of North America* 20(2), May 2002.
[10] KE Nelson. Infectious Disease Epidemiology: Theory and Practice. Aspen Publishers, 2001, p. 119-69.
[11] Centers for Disease Control and Prevention. Preventing Emerging Infectious Diseases. A Strategy for the 21st century.
[12] Global Emerging Crisis in Infectious Diseases. Challenges for the 21st century. *The Pfizer Journal.* V(2), 2004.
[13] Joshua Lederberg et. Al. Emerging Infections: Microbial threats to health in the United Sates. Institute of Medicine, 1992.
[14] Lessons Learned from SARS: Management of an Emerging Infectious Disease from a Military Perspective. ww.mindef.gov.sg
[15] 1.Peter Katona. Bioterrorism Preparedness: A generic blueprint for health departments, Hospitals and physicians. *Infectious Diseases in Clinical Practice* 11(3), 2004, March/April 2002.
[16] Lynn K. Flowers et. Al. Bioterrorism Preparedness II: The Community and EMS Systems. *Emergency Medicine Clinics of North America* 20(2), May 2002.
[17] Fred M. Henretig. Medical Management of the Suspected Victim of Bioterrorism:An algorithmic approach to the undifferentiated patient. *Emergency Medicine Clinics of North America* 20(2), May 2002.
[18] NIAID Biodefense Research website. http://www2.niaid.nih.gov/biodefense/public/biolab.htm
[19] John Hick et. Al. Health Care Facility and Community Strategies for Patient Surge Capacity. *Annals of Emergency Medicine* Volume 44 • Number 3 • September 2004
[20] Peter T. Pons and Stephen V. Catrill. Mass Casualty Management: A Coordinated Response. *Critical Decisions in Emergency Medicine*, November 2003.
[21] Centers for Disease Control and Prevention. APIC Bioterrorism Task Force. CDC Hospital Infections program bioterrorism working Group.
[22] Carl Shulz et. Al. Bioterrorism Preparedness I: The Emergency Department and Hospital. *Emergency Medicine Clinics of North America* 20(2), May 2002.
[23] Jerry L. Mothershead et. Al. Bioterrorism Preparedness III: State and Federal and Response. *Emergency Medicine Clinics of North America* 20(2), May 2002.
[24] http://www.cdc.gov/ncidod/hip/HICPAC/publications.htm
[25] Omar Lupi and Stephen K.Tyring. Tropical Dermatology: viral tropical Diseases. *Journal of the American Academy of Dermatology* 49 (6), December 2003.
[26] Luciana Borio et. Al. Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management. *JAMA* 287(18), May 8, 2002.