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The Dangers of Smallpox in Modern Day Bioterrorism

Research Article

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Abstract

The United States is ill prepared to detect and deal with an outbreak of smallpox due to inherent security vulnerabilities. This article analyzes smallpox's mode of contraction and highlights its historical significance. It then examines the possibilities for disease re-emergence and evaluates American bio security programs and protocols to counteract that threat. The discussion then focuses on the probable modes of entry into the United States and makes recommendations on how to prevent or contain an outbreak. This discussion is important due to the escalating threat of terrorism and it may shed valuable light on how to focus bio defense efforts while simultaneously increasing public awareness of the smallpox threat.

Introduction

The virus, Variola major (VAMJ), which is also known as smallpox, has been in existence for hundreds of years and historically speaking is of significant importance due to its ability to incite epidemics with high mortality rates in unprepared populations. Smallpox has throughout the ages, repeatedly shown its applicability as a biological weapon and as an agent of biological terrorism. Fortunately, as of 1979, in one of the most successful public health campaigns of all time, through the use of mass vaccination and ring vaccination efforts, smallpox is theoretically eradicated. Although the only known isolates of VAMJ exist within secure labs at the Centers for Disease Control and Prevention (CDC) and the Russian equivalent State Research Center and Biotechnology (VECTOR) [1], does not altogether guarantee that the disease has not previously leaked to some other undesirable third party, making reemergence a grim possibility.

Misplaced biological weapons present a major conundrum for American society as we enjoy smallpox free lives, and not to mention, a life that for most civilians is absent of smallpox vaccine. Furthermore, as an increasing number of Americans settle in sprawling metropolitan areas, our close proximity with one another allows for exponential disease spread. Airport security is best equipped to detect individuals who are visibly sick and weapons, however due to the microscopic portable nature of viruses they can more readily avoid detection. Smallpox has a long incubation period of between 7 to 17 days, thus allowing for those not showing signs of disease to easily bypass security and land in the intended target country, bypass its security, and integrate themselves into densely populated areas. There are of course many other ways to get a virus into a country, including but not limited to: entry through sea, illegal border crossing, entry through human trafficking, mail services, entry through use of a motor vehicle, launching or floating items across the border, attaching disease vials to migratory animals, infecting unsuspecting persons, etc., all of which are subject to varying levels of security and surveillance. Therefore, an analysis of the smallpox virus and the United States' programs, protocols, and abilities that are designed to detect and treat it is of paramount importance.

Variola Major Information

The smallpox virus is comprised of two major species, Variola major and Variola minor. Of the two virus types, VAMJ has, by far the highest overall case fatality rate of ≥ 30% [2] and poses the largest threat to the public. Smallpox has a relatively long incubation period of roughly one to two weeks, and during this time frame infected individuals are both asymptomatic and non-virulent. This long incubation period acts as a double edged sword, as

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it gives infected individuals time to reach a doctor if they suspect infection, if an individual purposely self-infects or does not realize they are infected, this allows for an easy method of bypassing national security systems. Variola virus can be dispersed through a multitude of methods including but not limited to: contact with infected bedding and clothing, inhalation of coughs and or sneeze droplets, kissing, sexual intercourse, and direct touch of enanthem lesions.

One of the body's primary methods of developing an immune response to a viral infection is the production of a cytokine that activates macrophages called interferon-gamma. VAMJ very cleverly encodes for interferon-gamma binding protein [3], which literally binds to and immobilizes interferon-gamma and hence curtails the immune response. Once inside the body, the virus quickly spreads using the bloodstream as a means of transport. During the subclinical asymptomatic phase the disease begins replication in the lymph nodes and quickly leads to excessive cell lysis. Virions are spread throughout the bloodstream and enter various organ systems. At this point prodromal symptoms, such as headaches, body aches, emesis, sore throat and other symptoms, which are reminiscent of the flu or cold, first appear. During this phase the difficulty in differentiating between smallpox and other common viral infections can easily lead to health care neglect and further spread. Eventually the disease leads to open sores in the mouth, contaminating saliva with viral particles that significantly increases an individual's infectivity. A few days later slightly raised skin lesions that cover the body form and fill with opaque fluid, dead tissue, and millions of viral particles. These pustules are also infectious, but are not as concerning as droplet transmission due to the fact that by the time they become overly abundant an individual will most likely have sought medical attention. If the infected person lives, the pustules will scab-over and fall off leaving significant scarring, and in the case that one or more of the pustules happened to be located on that individual's eyelid, cornea, or conjunctiva could lead to infection and ultimately blindness.

The Grim History of Smallpox

Human disease likely attributable to Variola virus (VARV), the etiologic agent of smallpox, have been reported in human populations for more than 2,000 years and likely diverged from a rodent-borne Variola-like virus either 16,000 or 68,000 years ago [4]. From VARV came the more clinically severe VAMJ clade, which originated and spread from Asia either 400 or 1,600 years before present [4]. Throughout the ages smallpox has been burdensome to population health and has greatly influenced the world we live in today. For instance, it is responsible for the death of two ancient Japanese emperors, kings of Burma and Siam, an Egyptian pharaoh, and believed to have contributed to the downfall of Athens [5, 6]. It is widely acknowledged that smallpox was historically a widely disseminated disease spreading throughout Africa, Asia, Europe, North America, Japan, Australia, New Zealand, and Egypt. In a devastating display of its applicability as an agent of biological warfare, smallpox infected blankets were distributed to Native American warriors during the siege of Fort Pitt in the midst of the revolutionary war, the results were predictable and lead to widespread disease and infirmary [7]. Meanwhile in 17th and 18th century Britain a smallpox epidemic was burning out of control and was responsible in certain circumstances for killing up to 1/6th of the population's birth rate [8]. Fortunately, a brilliant physician named Edward Jenner formulated the idea of developing a vaccine through the use of the cowpox virus [9]. It was this ingenious discovery that ultimately led to hypothesized disease eradication in 1979, however the disease had already lead to an estimated 300-500 million deaths in the 20th century.

Dangers of Reemergence and Potential Sources of Virus Acquisition

Although smallpox is largely considered an eradicated disease, there are multitudes of ways that it can reemerge, and American society in general remains unprepared, unvaccinated, and unaware of this. It can be argued that the probabilities for disease reemergence outweigh the probability that it is truly extinct in the wild. Take for example the former Soviet Union's biological weapons program "Biopreparat," which despite signing the United Nations Biological Weapons Convention (BWC) multilateral agreement of 1972 [10], aggressively pursued the weaponization of pathogenic organisms for 19 years. The combination of over 40,000 employees, 43 laboratories [11], notoriously lax weapons depot management strategies, and significant downsizing and emigration after the collapse of the U.S.S.R. leads one to wonder, did any of the experimental organisms end up in the wrong hands? It is quite possible that one of Biopreparat's thousands of employees were able to smuggle a vial of smallpox virus out of the laboratory. Similar examples can be found in other biological weapons programs such as Japan's now non-existent World War II era "Unit 731." Unit 731 was based in modern day northeast China and was known to have experimented with smallpox. In 1945 as Russian forces advanced on the primary 731 facilities, and in their haste to destroy the evidence, there would likely have been plenty of potential for disease smuggling.

Developed countries like the United States who have biodefense programs such as the National Biodefense Analysis and Countermeasures Center (NBACC) may operate within the legal grey zones of the BWC, this tends toraise significant controversy [12]. Keeping this and the increasing threat of bioterrorism in mind, it is no surprise that after September 11, 2001 the United States armed forces set out with a goal to vaccinate half a million of its personnel against smallpox [13]. Ultimately the Department of Defense (DoD), while in the midst of analyzing the dangers of smallpox, came to the conclusion that the odds were high enough that half a million vaccinations was simply not enough, and by May 2007 had immunized over 1,200,000 of its personnel [14].

Another area of concern lies in the fact that an exact accounting of how long smallpox can survive outside a living host in the natural environment remains somewhat of a mystery. Evidence suggests that if certain conditions favoring the disease are met, then viral reanimation after exhaustive periods of dormancy are possible. For instance, viral particles that were freeze-dried at Liverpool University were re-animated after 20 years of storage [15]. Additionally anecdotal accounts indicate that in the year 1759 in Somerset England a coffin that contained the body of a smallpox victim who had died thirty years prior was accidently punctured and quickly led to an outbreak [15].

The possibility of a smallpox-harboring corpse that has been subject to consistent optimal environmental conditions, thus allowing the disease to lie dormant, is an area of concern. In fact,

VECTOR realized this and set out an expedition in 1991 that uncovered ancient thawing bodies in a remote region of Siberia, luckily the bodies proved to contain no viable smallpox viruses [16]. Possibly, somewhere in the world, there exists the remains of a smallpox victim whose preserved body is acting as a disease reservoir.

What is perhaps the most troubling scenario, is not the resurfacing of a lost smallpox weapons cache or an overlooked rural case, but instead the abundance of limitless information online pertaining to DNA sequencing of viral genomes and how to reverse engineer organisms through the use of artificial gene synthesis. In the early days of genomics, simple genome sequencing was a monumental challenge; however, molecular science is advancing its knowledge base exponentially. Now without even having a DNA parent strand as a guiding template, whole genomes can be constructed from scratch. There are a variety of companies that specialize in this area, and for a fee can construct any choice DNA sequence. To date, the only notable limitation to total gene synthesis is the associated cost [17]. Moreover, loose regulations of literature and an accompanied desire to publish research findings within the scientific community make data acquisition and scientific methodologies fair game for anyone willing to do a simple internet search. Dangerous viral genomes such as Spanish Influenza and VAMJ have long since been sequenced [18, 19] and the results are available for public viewing on websites such as the National Center for Biotechnology Information's website GeneBank [20]. Publication of literature regarding dangerous organism genomes should be blacked out to the public and preferentially be viewable to only select individuals within well-recognized governmental organizations such as the CDC, the DoD, the Department of Homeland Security (DHS), or the United States Medical Research Institute of Infectious Diseases (USAMRIID). With the expanding bioengineering knowledge base, the publicly viewable VAMJ genome sequence, and ironically the availability of similar viral organisms such as Edward Jenner's Vaccinia, someone with enough time and dedication may be able to artificially synthesize the smallpox genome and have it transferred it into a viable viral envelope, even though it is still currently difficult to ligate together molecules with genomes as long as VAMJ. In fact Vaccinia virus, which is a member of the poxvirus family, has already been constructed from synthetic DNA and cloned into an artificial bacterial chromosome [21]. In fact defectors from soviet bioweapons programs have stated that recombinant research was performed to create smallpox strains that were more virulent, contagious, and capable of evading vaccination than their wild type counterparts [22].

An Analysis of Key U.S. Biosecurity Programs

The BioWatch program, which was created in 2001 in response to domestic anthrax based mail-born terrorist attacks [23], is an early detection system designed to promptly identify dangerous airborne pathogens [24]. The program is overseen and ran by the DHS, which works in conjunction with the Environmental Protection Agency (EPA), the CDC, and the Federal Bureau of Investigation (FBI), all of which have specific roles in the program. The EPA is responsible for monitoring hidden air quality monitors, the CDC is responsible for testing samples, and the FBI is responsible for mounting a response to bioterrorist activities.

Unfortunately BioWatch has limitations. The exact scope of its coverage remains undisclosed; however, information suggests that the program currently operates in more than 30 cities [25], and it hopes to someday expand its coverage to as many as 120 cities [24], this indicates incomplete coverage. Furthermore as of 2012 there has been 149 false alarms due to the systems lack of sensitivity [25]. Other arguments against BioWatch's feasibility include but are not limited to: Concerns that the program is incapable of detecting indoor or underground releases, filters can potentially be avoided or tampered with, and improper filter placement [24]. Although BioWatch successfully detected Tularemia on two separate occasions in Houston and Washington D.C., there were no confirmed cases of anyone becoming ill from exposure [24, 26]. The BioWatch program has promise, to date it has many exploitable vulnerabilities and gaps in its coverage.

The Centers for Disease Control and Prevention Laboratory Response Network (CDC LRN) is a robust system of laboratories that work in conjunction with the CDC to detect biological agents [27, 28]. The 2003 Wisconsin Monkeypox outbreak provides a good example of the CDC LRN working to successfully detect human poxvirus infections [29]. Although the CDC LRN is extensive and precise, it relies on the laboratory diagnosis of biological pathogens which can take days. The long incubation period of VAMJ along with the extra time needed to run a confirmatory laboratory test allows a window of opportunity for an individual to either knowingly or unknowingly spread the disease.

The FBI's Weapons of Mass Destruction Directorate (WMDD) is a comprehensive program designed to deal with a WMD incident from prevention to response [30]. Furthermore; the program is designed to detect, deter, and dismantle WMD programs and thus incorporates elements of preparedness, counter measures, intelligence, and investigations and operations into its design. This program has had much success, as confirmed by one such case that led to the successful arrest of Roger Bergendorff, who was indicted for creating the regulated CDC toxin ricin [31]. Sadly the WMDD is not perfect, as indicated by the Boston Marathon Bombings of 2013 [32] and a series of close calls such as the Times Square car bombing attempt of 2010 [33].

Weapons of Mass Destruction Civil Support Teams (WMD-CST) are federally funded full time national guard units designed to rapidly respond to suspected WMD attacks, advise civilian responders on appropriate actions, and facilitate the arrival of additional military support [34]. The program consists of 57 teams of 22 members each that are strategically located near each U.S. state, territory, and Washington D.C [35]. WMD-CST's are unique in the respect that they perform their missions primarily under the command of governors of the states in which they are located; this aids their ability to mount a quick response [36]. This program has significant promise for post outbreak scenarios that require prompt management and containment. Although to date WMD-CST's have responded to over 70 chemical, biological, radiological, and nuclear (CBRN) incidents [35], it is still relatively new and has yet to prove itself in a real world scenario that requires the containment of VAMJ. Also it should be noted that WMD-CST's are in no way connected with counterterrorism activities, this is unfortunate, as their training could prove useful in the early detection of a VAMJ based attack.

Although the United States has multiple programs and methods

for identifying and managing biological attacks, as is the case in almost all programs, there are inherent weaknesses within each one. A well-planned attack could potentially exploit these weaknesses and bypass national security measures. The best way to manage bioterrorism without incurring excessive collateral damage is through effective pre-attack measures. The BioWatch program has great promise, but needs further fine-tuning to increase its sensitivity and feasibility. Meanwhile, the FBI's WMDD program has for the most part proven effective, however, there is always room for improvement and sadly some level of confidence is lost through the WMDD's previous shortcomings.

High Probability Modes of Entry into the United States

Post September 11, 2001 airport security has refocused its efforts to detect, deter, and screen for biological weapons. Nationally there is large-scale inter-agency collaboration between the DHS, the CDC, the FBI, local state health authorities, the civil aviation community, and first responders such as police and firefighters, in preparation for an aviation based attacks. However, at present, civil aviation remains ill-prepared to deal with biological threats [37]. In the event of an outbreak, plans are intact to create on site emergency operation centers and possibly mobile command posts. The CDC currently has 18 operational quarantine stations located near major airports, but these stations are not large enough to hold an airplane full of passengers [38] and there are far more than 18 American international airports. The fact that there is not a quarantine station in each international airport is an exploitable weakness and would essentially force quick mobilization of public health personnel to implement quarantine procedures should an outbreak occur. Regardless of some inherent weaknesses, airport screening has come a long way. Records of passengers, their home countries, their affiliations, and other biographical data may prove to be the most useful method for stopping this mode of attack. However, self-infected individuals with clean demographic records can easily bypass security screening stations, this is especially true in VAMJ's early asymptomatic stages. Even if an infected individual is not confident that they can bypass security, all they need do is loiter in busy parts of international airports and cough near people traveling to the United States. Needless to say, an analysis of how to detect infected individuals before they can traverse airport security is a critical concern that warrants consistent evaluation.

Entry through maritime means is another concern. Both the U.S. coast guard and U.S. Customs and Border Protection Agency (CBP) manage American port security. Under the 2002 Container Security Initiative (CSI), cargo containers that are deemed at high risk of containing WMD's may be detained in their original ports and examined by CBP agents [39, 40]. Additionally, the CBP created the Customs-Trade Partnership Against Terrorism (C-TPAT) program, which works in cooperation with over 10,000 companies globally to hinder terrorism by protecting the supply chain, identifying gaps in security, and implementing the best available security measures [41]. While the CSI and C-TPAT program's seem ideal for halting maritime biological terrorist attacks, an audit conducted by the DHS's Office of Inspector General (DHS OIG) came to the conclusion that the CBP could do more to mitigate threats posed by both biological and chemical weapons [42]. To date the CBP has not conducted a formal risk assessment to detect which pathways present the highest risk of carrying biological weapons in maritime cargo and the audit conducted by the DHS OIG also came to the conclusion that updated policies for focusing cargo container inspections are needed in order to avoid lapses in bio-agent detection [42]. Due to the fact that only around 4.1% of containers are examined annually [43], there is a very real chance of disease smuggling.

Besides cargo transport ships, other vessels can also be used as a means of disease transport. To curb this, the CDC has 20 quarantine stations located near major ports [44] and moreover contaminated ships may be ordered to drop anchor miles from shore and wait until health authorities can assess and manage the situation. Overall, methods of entry through port tend to take longer than air transportation and this gives government agencies and their partner's valuable time to recognize and deal with an outbreak before a ship and its passengers happen to make landfall. Nonetheless, securing maritime modes of entry is essential.

Perhaps the most troubling form of entry comes not from the air or the sea, but illegal land border crossings. According to the DHS, there were an estimated 5 million undocumented immigrants as of 1994 [45] with annual rate increase of about 275,500 persons per year. The aforementioned numbers are in relative agreement with the 2013 statistics, which estimate that currently 11.5 million illegal aliens reside in the United States [46]. This shows that the U.S. Immigration and Customs Enforcement Agency (ICE), which has 20,000 employees [47], has been unable to halt the immigration influx, and therefore it is highly likely that an individual could avoid detection and smuggle VAMJ in from the south. On another note, in 2010 former CBP commissioner Alan Bersin stated while in the midst of a hearing of the Senate Judiciary subcommittee on Immigration, Refugees, and Border Security that "In terms of terrorist threat, it's commonly accepted that the more significant threat comes from the U.S.-Canada border."48 Although in terms of immigration volume, the southern border presents the more significant problem, while in reference to extremist threat the northern border tends to attract higher rates of individuals on terrorist watch lists [48]. To make matters worse, the northern border is less heavily defended, there is no barrier, and it is much longer than its southern counterpart. Chances are high that a skilled woodsman could navigate through some remote part of Canada and into America uncontested.

Recommendations

It may well be within the best interest of the American government to consider investing funds into the creation of a new andimproved publicly available vaccine with a low side effects profile. In fact, according to one survey, 61 percent of Americans claimed that they would indeed want a smallpox vaccine should it become publicly available [49]. This may warrant further attention as according to the CDC's Smallpox Response Plan and Guidelines (SRPG), the United States currently has enough vaccine stockpiled to immunize every American [50]. Educating the public on the current vaccines safety profile, and then allowing civilians the choice to access these stocks may prove beneficial. If terrorists realize that the majority of American's are immunized against smallpox then the likelihood of them using itas a means of attack will be reduced. Even if smallpox were to be released on American soil, and even if the U.S. government did not manage

to immunize every single American, herd immunity could offer some level of protection.

Despite the method selected for use, post attack containment approaches that offer rapid mass protection have the potential to reduce the spread and impact of an outbreak and therefore deserve some level of consideration within the context of the US biodefense strategy and the SRPG.

It can be argued that airports are the most probable route of entry into the United States, and because of this it may be within the best interest of the Transit Security Administration (TSA) to create a standardized set of early response quarantine procedures for international airport terminals.

Sometimes the solution to a problem cannot be solved with only technological based measures, for instance, consider the scope of the America's border immigration problem. Almost anyone with enough will power can manage to cross the border and find his or her way to an American city. In order to reduce this problem, it may be within the government's best interest to re-locate a number of its National Guard bases to near border locations to reinforce ICE's efforts with their WMD-CST's. The combined collaboration between ICE and the military could help with detection and determent of biological weapons trafficking.

Programs designed to detect and halt terrorist attacks before they happen, such as the WMDD, are critical for preventing outbreaks and deserve consistent attention to ensure optimal functionality. BioWatch's early detection monitors show significant promise, and can assist other programs such as the LRN, CST's, and WMDD in formulating a quick disease diagnosis and timely response; therefore measures to perfect system performance is recommended.

Finally, creating well-known smallpox public education programstoteachpeople on how to spot the signs and symptoms of the disease would help with detection and determent. These programs have the added bonus of empoweringindividuals on how to properly report biological incidents, thus reducing the threat of a disease going unreported.

Conclusion

The threat of a smallpox-based attack is very real. Although security measures have come a long way since September 11, 2001, there are still many exploitable weaknesses in how effective security is at truly detecting, deterring, and managing biological weapons based attacks. Further evaluation of the problem along with a black and white post-attack contingency plan is recommended.

References

[1]. World Health Organization (2010) Advisory Group of Independent Experts to review the smallpox research programme (AGIES), Geneva, Switzerland.

[2]. Henderson DA, Inglesby TV, Bartlett JG (1999) Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA 281(22): 2127-2137.

[3]. Saint Louis University. How Poxviruses Such As Smallpox Evade The Immune System.Science Daily, 1 Feb. 2008. Web. 30 Jun. 2013.

[4]. Li Y, Carroll DS, Gardner SN (2007) On the origin of smallpox: Correlating variola phylogenics with historical smallpox records. Proc Natl Acad Sci 104(40): 15787-15792.

[5]. Hopkins DR (1983) In The Greatest Killer-Smallpox in History. University of Chicago Press, Chicago.

[6]. Fenner F, Henderson DA, Arita L (1989) Smallpox and its Eradication. (1st edn),World Health Organization, Geneva, Switzerland.

[7]. Fenn EA (2000) Biological Warfare in Eighteenth-Century North America: Beyond Jeffrey Amherst. J Am Hist 86(4): 1552-1580.

[8]. Behbehani AM (1983) The Smallpox Story: Life and Death of an Old Disease. Microbial Rev 47(4): 455-509.

[9]. Barquet N & Domingo P (1997) Smallpox: The Triumph over the Most Terrible of the Ministers of Death. Ann Intern Med 127(8): 635-642.

[10]. United Nations (2013) The Biological Weapons Agreement. UNODA, Geneva, Switzerland.

[11]. Biopreparat (1998) Available at: www.fas.org/nuke/guide/russia/agency/bw.htm.

[12]. Gronvall GK (2005) A New Role for Scientists in the Biological Weapons Convention. Nat Biotechnol 23(10): 1213-1216.

[13]. Fleck F (2003) Conference warns of danger of re-emergence of smallpox as weapon of bioterror. Bull World Health Organ 81(12): 917-918.

[14]. Military Vaccination Agency (2013) Smallpox Vaccination Safety Summary, Available at: www.smallpox.mil/event/SPSafetySum.asp (Accessed: 10th August 2013).

[15]. Razzell P (1976) Smallpox extinction: a note of caution. New Sci 71: 35.

[16]. Stone R (2002) Is live smallpox lurking in the Arctic? Science 295(5562): 2002.

[17]. Young L, Dong Q (2004) Two-step total gene synthesis method. Nucleic Acids Res 23(7): 1-6.

[18]. Tumpey TM, Basler CF, Aguilar PV (2005) Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus. Science 310(5745): 77-80.

[19]. Massung RF, Liu L, Qi J (1994) Analysis of the complete genome of smallpox variola major virus strain Bangladesh-1975. Virology 201(2): 215-240.

[20]. NCBI Reference Sequence (2000)Variola virus, complete genome.

[21]. Moss B, Domi A (2002) Cloning the vaccinia virus genome as a bacterial artificial chromosome in Escherichia coli and recovery of infectious virus in mammalian cells, Proc Natl Acad Sci 99(19): 12415-12420.

[22]. The University of Alabama at Birmingham (1995) Bioterrorism and Emerging Infections Education, Available at: www.bioterrorism.cme.uab.edu/CategoryA/Smallpox/smallpox.html (Accessed: 8th August 2013).

[23]. The Department of Justice (2010) Amerithrax Investigative Summary. Washington DC.

[24]. Shea D (2003) The BioWatch Program: Detection of Bioterrorism. Congressional Research Service, Washington, DC.

[25]. Willman D (2013) BioWatch's chief aim is off-target: US security officials say'. Los Angeles Times,USA.

[26]. Dvorak P (2005) Health Officials Vigilant for Illness After Sensors Detect Bacteria on Mall. The Washington Post.

[27]. Centers for Disease Control and Prevention (2012) Laboratory Network for Biological Terrorism.

[28]. Cieslak TJ, Christopher GW (2007) Medical Management of Potential Biological Casualties: A Stepwise Approach. Medical Aspects of Biological Warfare.1-22.

[29]. Reed KD, Melski JW, Graham MB, Regnery RL, Sotir MJ, et al., (2004) The Detection of Monkeypox in Humans in the Western Hemisphere. N Engl J Med 350(4): 342-350.

[30]. Federal Bureau of Investigation (2006) Key Programs.

[31]. Federal Bureau of Investigation (2008) Case Example.

[32]. United States District Court (2013) United States of America v. Dzhokhar Tsarnaev Criminal Complaint, State of Massachusetts, Washington Post.

[33]. Baker A, Rashbaum WK (2010) Police Find Car Bomb in Times Square. The New York Times.

[34]. Conflict 21 (2009) Weapons of Mass Destruction Civil Support Team.

[35]. National Guard (2013) Weapons of Mass Destruction (WMD) Civil Support Team (CST).

[36]. Cragin CL (2000) Defense Leaders Commentary: The Facts on WMD Civil Support Teams. American Forces Press Service, US Dept of Defense.

[37]. Raffel R (2003) Weapons of Mass Destruction and Civil Aviation Preparedness. FBI Law Enforcement Bulletin, FBI.

[38]. CDC Quarantine Station Frequently Asked Questions (2013).

[39]. Container Security Initiative CSI (2013).

[40]. Department of Homeland Security. (2013). CSI: Container Security Initiative.

[41]. US Customs and Border Protection (2013). CTPAT: Program Overview.

[42]. Department of Homeland Security Office of Inspector General (2009) CBP's Ability to Detect Biological and Chemical Threats in Maritime Cargo Containers, Washington D.C.: US Department of Homeland Security.

[43]. Bliss J (2012) US Backs Off All-Cargo Scanning Goal With Inspections at 4%, Bloomberg, 12th August.

[44]. Centers for Disease Control and Prevention (CDC). (2013). About Quarantine and Isolation.

[45]. Pro Con (2013) Illegal Alien Resident Population
[46]. Hoefer, M., Rytina, N., & Baker, B. (2013). Estimates of the Unauthorized Immigrant Population Residing in the United States: January 2011.
[47]. U.S. Immigration and Customs Enforcement. (2013). Careers.
[48]. Mora E (2011) Canadian Border Bigger Terror Threat than Mexico Border, Says Border Patrol Chief.
[49]. Bicknell WJ (2002) The Case for Voluntary Smallpox Vaccination. New England Journal of Medicine. 346(17): 1323-1325.
[50]. Centers for Disease Control and Prevention (2007) Smallpox Response Plan and Guidelines (Version 3.0).