THE NATURE OF THE BIOTERRORISM THREAT

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ABSTRACT

This analysis provides an overview of the nature of the bioterrorism threat. It identifies potential CDC Class A biological agents that are likely candidates for use in a terrorist incident and describes the known sources of vulnerability. The paper also summarizes S&T resources/needs and assesses response options for achieving effective biodefense against terrorist threats.

INTRODUCTION

The shocking events of September 11, 2001, and the deliberate release of anthrax spores that occurred shortly thereafter have increased awareness of the dangers of terrorist attacks. Of all the actions that could be undertaken by terrorists, perhaps none has more potential for causing massive civilian casualties through asymmetric warfare than does the use of biological agents. Although most microorganisms that cause disease or produce toxins (i.e., viruses, bacteria, fungal spores, and toxins) may be used as biological weapons, some are more likely candidates for use in bioterrorism incidents because they are extremely infectious and exhibit high mortality or debilitating morbidity rates. Moreover, given the likelihood of delay in diagnosing some diseases caused by deliberate exposure, biological agents are a potent weapon in the hands of terrorists (1 - 4).

The growing threat of bioterrorism is based on four key and disturbing facts. First, the number of nations and groups possessing or seeking to acquire a biological agent capability is increasing. Second, biological agents with increasing lethality are possible with genetic engineering. Third, detection of biological agent development is difficult because much of the technology has legitimate dual-use applications in medicine and agriculture. And, unlike chemical or radiological/nuclear events, detection of a biological release may be delayed for days until individuals first display symptoms which are diagnosed accurately. Forth, and perhaps most troubling, bioterrorism has happen in the United States.

Computer modeling and field exercises have become the primary tools for simulating terrorist incidents and analyzing the consequences of terrorist attacks in order to evaluate options for minimizing casualties. This analysis provides an overview of the threat bioterrorism poses by identifying potential biological agents and describing sources of known vulnerability. The paper also summarizes S&T resources/needs and assesses response options for achieving effective biodefense.

POTENTIAL AGENTS

Potential bioterrorism agents such as anthrax, plague, small pox, and tularemia have been classified as Category A Select Agents because they are capable of rapidly producing large numbers of deaths, significant societal disruption, and widespread terror within civilian populations (2, 5-6). For example, early symptoms of inhalation anthrax mimic influenza and, if infection is established prior to accurate diagnosis, therapeutic intervention becomes ineffective with mortality rates approaching 90% (7). The World Health Organization (WHO) estimates that 50 kg of anthrax spores released upwind of an urban area with a population of 500,000 people would result in massive casualties – approximately 95,000 deaths and 125,000 hospitalizations (8). Similarly, projections by the Centers for Disease Control and

Prevention (CDC) suggest that a terrorist release of anthrax spores from a small aircraft over a suburb might expose 100,000 people, cause 30,000 deaths, and cost over $25 billion in economic damages (9).

The CDC listing of Select Agents currently has identified 36 select agents and their disease related genes as being dangerous to human health because of their potential for use in biowarfare/bioterorism. Individual biological agents are assigned to either Category A, Category B, or Category C based on the select agent's capability to cause substantial harm to humans with those classified as Category A being the most dangerous. Because of concerns about the possible use of these agents, the USA Patriot Act of 2001 and the Bioterrorism Preparedness Act of 2002 place restrictions on the possession of select agents or delivery systems within the United States. As a result, the CDC list is the logical starting point for identifying potential bioterrorism agents.

The list of CDC Category A Agents provided in Table 1 includes: anthrax (*Bacillus anthracis*); tularemia (*Francisella tularensis*); plague (*Yersinia pestis*); botulism (*Clostridium botulinum* toxin); smallpox (variola major); and viral hemorrhagic fevers (filoviruses [e.g., Ebola, Marburg] and arenaviruses [e.g., Lassa, Machupo]). Many of those agents are particularly virulent and resilient, can be readily cultivated, possibly 'weaponized', stored, transported, and released as aerosols using a variety of delivery systems, including primitive ones, which makes them extremely attractive for use in a bioterrorism incident.

Identifying the agents used in previous bioterrorism or biowarfare incidents provides additional insights into those agents that are likely to be used in future terrorist attacks. In considering potential bioterrorism threats, given the advances in genomics and molecular biology, it also is necessary to recognize that known agents or possibly previously unknown agents may be rendered antibiotic or toxin inhibitor resistant and become impervious to defenses.

SOURCES OF KNOWN VULNERABILITY

Human health and agricultural systems, including the food supply, represent the targets for bioterrorism. Vulnerability to bioterrorism stems from several sources. Some are related to the specific agent used, others to the ease of production and/or dissemination, some to the characteristics of civilian as opposed to military populations, and others to the magnitude of consequences.

No distinct signature may be readily detected to alert medical and security authorities to dispersion until individuals present symptoms to trained clinicians. For example, the initial symptoms of inhalation anthrax (i.e., flu-like symptoms and fever) mirror those of influenza. Figure 1 reveals that other select agents (tularemia, Staphylococcal eneterotoxin B, and Q-fever) similarly mimic colds and the flu for a larger percentage of the population.

Vaccines can provide immunity but are agent-specific, have side effects, and require time (ranging up to several months) before immunity develops. Antibiotics can provide immediate protection as therapeutics against bacterial agents but must be taken daily, may have side effects, and are not effective against resistant bacterial strains or toxins. For example, inhalation anthrax, tularemia, and Q-fever can be treated with antibiotics, although treatment for anthrax is only effective prior to the production of toxins. No antibiotic treatment currently is available for Staphylococcal eneterotoxin B (SEB). In addition, given the advances in genomics, agents may be bio-engineered to create antibiotic resistance. Many of the agents are rugged and durable with an LD_{50} (i.e., the lethal exposure level for 50 % of exposed humans) that produces substantial mortality, especially among individuals with immature or weakened immune systems.

Military populations are relatively homogeneous and consist of adults with reasonably robust immune systems. In addition, because the military can compel individuals to receive vaccines as active countermeasures, biowarfare countermeasure programs emphasize prophylaxis for the most likely agents supplemented with therapeutics for other agents. Unlike military populations, civilian populations are heterogeneous and include young children as well as adults with more vulnerable immune systems (i.e., the elderly and immune-suppressed individuals). Voluntary compliance with medical treatment and post-incident therapeutics is an established norm. As a result, this makes the vulnerabilities inherently larger when bioterrorism is targeted against civilians. Moreover, the dread feature of bioterrorism with its non-specific targeting of individuals (an inherent feature of terrorism) maximizes psychological impact even when actual casualties are low. As a result, hoaxes may create impacts such as psychosis even when actual deployments are not executed by terrorists.

Table 1. CDC Category A Select Agents

Biological Agent	Incubation Period (days)	Mean Lethality (%)	Contagious	Transmission	Reservoirs
Anthrax *(Bacillus anthracis)*	Inhalation 1-6 days Gastro-intestinal 2-5 days	Inhalation 80-100% Gastrointestinal 25 - 75%	No	Spores	Soil
Botulinum *(Clostridium botulinum* toxin*)*	< 1 days	< 10 %	No	Food, natural outbreaks (infants), rarely from infected wounds	Soil
Ebola (Viral hemorrhagic fever -- filovirus)	3 - 18 days	22 - 90 %	Yes, typically with direct contact	Unknown	Zoonotic, but species unknown
Lassa (Viral hemorrhagic fever -- arenavirus)	5 - 6 days	15 %	Yes, through direct contact	Urine & droppings (aerosol, ingestion, direct, contact)	Rodents of the genus Mastomys
Marburg (Viral hemorrhagic fever -- filovirus)	3 - 9 days		Yes	Unknown	Zoonotic, species vary
Plauge *(Yersinia pestis)*	2 - 6 days	50-90% if untreated, ≈15% if treated	Yes in pneumonic form	Fleas (bubonic), Aerosol (pneumonic)	Rodent most common
Smallpox *(variola major)*	7 - 17 days	≈ 30% for most cases up to 100% for some rarer forms	Yes, until scabs resolve	Direct contact, airborne in rare cases	Laboratory stockpiles
Tularemia *(Francisella tularensis)*	4 - 7 days	Ulceroglandular 5% Pneumonic 30 - 40%	No	Infected animals, bite of infected insects or other arthropod	Mostly rabbits and hares

Source: (10-15)

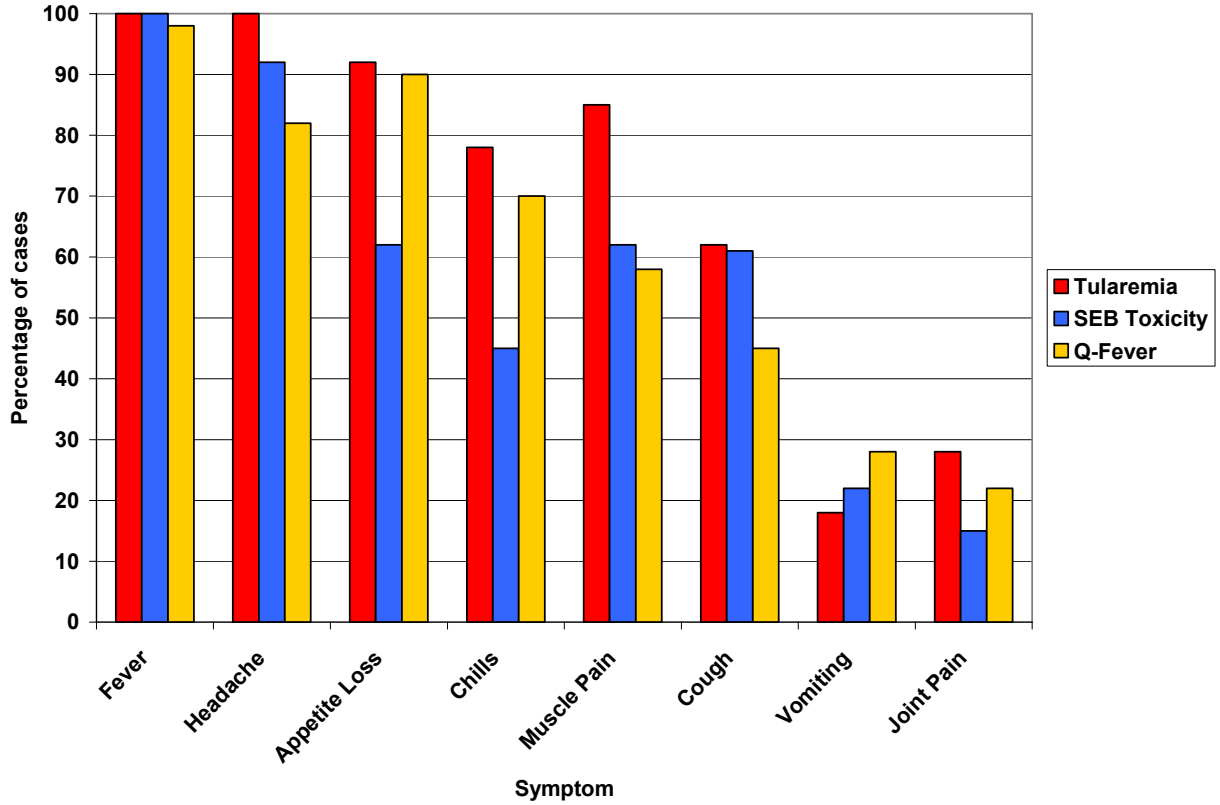

Fig. 1. Relative Frequency of Early Influenza-like Symptoms for Biological Agents

S&T RESOURCES AND NEEDS

Responding effectively to the bioterrorism threat will require focusing research capabilities and resources on detection, diagnosis, prevention, and consequence management. It is worth noting that most of the core agencies of the newly created Department of Homeland Security (DHS) lack significant biomedical S&T research, acquisition, and deployment experience. Key exceptions are the elements transferred from the U.S. Department of Energy's (DOE) National Nuclear Security Administration, DOE's Environmental Measurements Laboratory, and the U.S. Department of Agriculture's Plum Island research facility. DHS faces significant challenges in the biological agent arena including:

- Sharing technical information with industry and universities (the research and national security communities are likely to disagree over whether access to information should be restricted or classified)
- Resolving serious, legitimate dilemmas about what should in fact be published; balancing the needs for open publication with appreciation of risks
- Creating an architecture for defining the S&T program and managing its execution
- Developing rapid signature diagnostics for identifying exposures to specific biological agents
- Integrating the diagnostics, vaccines, and therapeutics developed by the biodefense research program conducted under the auspices of the National Institutes of Health (NIH) within the Department of Health and Human Services (HHS) into the overall, national counterterrorism strategy

In June 2002, the Office of Management and Budget (OMB) released its annual report to Congress on combating terrorism which included a breakout of funding for S&T (16). With the emergence of widespread concern about bioterrorism directed against the civilian population, significant increases have occurred in funding from FY 2001 through FY 2003. In FY 2001, approximately $600 million was appropriated for counterterrorism R&D. Figure 2 reveals that the majority of funds were allocated to the U.S. Department of Defense (DoD). After September 11 and the anthrax letters, funding was increased substantially with NIH assuming the role of lead agency for biodefense S&T; NIH funding rose from $50 million in FY 2001 to $275 million in FY 2002. In the FY 2002 budget, including the emergency supplemental enacted after September 11, funds for counter-terrorism S&T activities were increased to $1.2 billion. The FY 2003 budget proposed by President Bush would further increase funding to approximately $2.9 billion, primarily because of a nearly 5-fold increase in NIH funding to $1.7 billion in FY 2003.

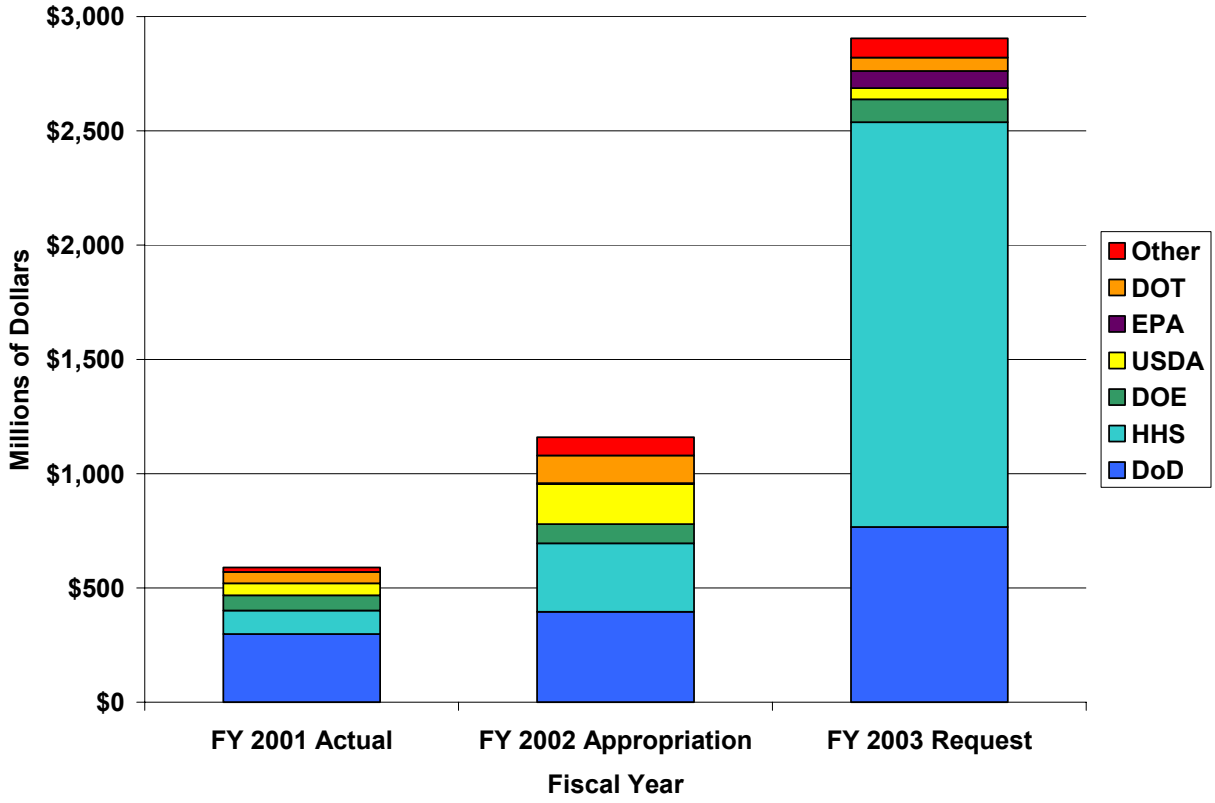

Fig. 2. Federal Counterterrorism S&T Funding by Agency Budget Authority, $ Millions (note that the 'Other' category includes NSF, NIST, Department of Justice, and Department of the Treasury)

As the breakout of federal S&T funding illustrates, by its very nature, counter-terrorism research crosses the boundaries of traditional disciplinary-based research. Responding to bioterrorism will require development of effective real-time, agent-specific detection systems to identify releases. When releases are not detected initially, medical surveillance systems will be needed to support diagnosis to minimize the spread of contagious, infectious diseases. Vaccines and novel therapeutics, including toxin inhibitors, will be needed to either prevent or reduce the severity of effects from exposure to bioterrorism agents. In addition, because bioterrorism is a psychological as well as physical threat, developing understanding of how humans respond to bioterrorism is needed in order to aid first-responders, other service providers,

and policy makers in shaping consequence management strategies. As a result, expertise will be needed from an array of disciplines including biomedical science, medical services, biology, chemistry, physics, engineering, information science, engineering, systems analysis, and the behavioral sciences.

RESPONSE OPTIONS

Achieving an effective defense against bioterrorism is one of the major challenges confronting DHS. DHS will need to successfully integrate a series of steps to meet this challenge:

- Accurately predict major threats.
- Take pre-emptive measures
- Devise countermeasures
- Sustain commitment

Response options can be categorized as either pre-emptive or counter-measures. Pre-emptive measures are aimed at preventing or deterring a bioterrorism incident. Developing prophylactic vaccines or toxin inhibitors are examples of pre-emptive measures aimed at the general population or specific subgroups such as first responders or medical personnel. Counter-measures include detection as the initial stage in a post-incident response and encompass activities such as medical surveillance, diagnosis, and treatment modalities. In reality, the response to the threat of bioterrorism will include both pre-emption and *ex post facto* counter-measures.

REFERENCES

1. S. M. Block "The growing threat of biological weapons," *American Scientist* 89: 28-37 (2001).

2. H.C. Lane, J.L. Montagne, and A.S. Fauci, "Bioterrorism," *Nat Med* 7: 1271-1273 (2001).

3. National Research Council, *Biological Threats and Terrorism*. Washington: National Academy Press (2002).

4. National Research Council, *Chemical and Biological Terrorism*. Washington: National Academy Press (1999).

5. National Institute for Allergy and Infectious Diseases, *The Counter-bioterrorism Research Agenda of the National Institute for Allergy and Infectious Diseases for CDC Category A Agents*. Bethesda, MD: National Institute for Allergy and Infectious Diseases (2002).

6. T.V Inglesby, *et al*. "Anthrax as a biological weapon," *Journal of the American Medical Association* 281: 1735-1745 (1999).

7. P.C. Hanna, and J.A. Ireland, "Understanding *Bacillus anthracis* pathogenisis," *Trends in Microbiology* 7: 180-182 (1999).

8. L. Baillie, "The development of new vaccines against *Bacillus anthracis*," *Journal of Applied Microbiology* 91: 609-613 (2001).

9. A.F. Kaufman, *et al*. "The economic impact of a bioterrorist attack," *Emerging Infectious Diseases* 3: 83-94 (1997).

10. J. Bennett. Cecil Textbook of Medicine. 20th ed. Saunders Press, Philadelphia, PA. (1996).

11. A. Granoff. Encyclopedia of Virology. 2nd edition. Academic Press. London, England (1999).

12. J. Louis. Toxicology Secrets. 1st edition. Philadelphia PA (2001).

13. U.S Army Medical Research Institute of Infectious Diseases. Medical Management of Biological Casualities Handbook. 4th ed. Maryland (2001).

14. Maryland Department of Health and Mental Hygiene. Potential Bioterrorism Agents. November, http://www.dhmh.state.md.us/labs/html/BT_potential_agents.html (2001).

15. CDC Bioterrorism Website. http://www.bt.cdc.gov/ (2002).

16. Office of Management and Budget, *Annual Report to Congress on Combating Terrorism.* Washington: U.S. Government Printing Office (2002).