Chapter 35

MEDICAL CHALLENGES IN CHEMICAL AND BIOLOGICAL DEFENSE FOR THE 21ST CENTURY

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INTRODUCTION

Biological and chemical warfare has long concerned military planners, strategists, and tacticians. Experiences in the Persian Gulf War (1990–1991), the rising concern over terrorist groups and their interest in weapons of mass destruction, and the continuing difficulties with curbing the proliferation of traditional chemical and biological weapons have resulted in continuing modifications in policies that would be employed in future scenarios. The use of such agents against the United States or its allies or both, including military and civilian populations, remains a distinct and perhaps increasing possibility.

Recent events in the world, including the terrorist attack with the nerve agent sarin in a subway in Tokyo, Japan, in March 1995, have demonstrated both the willingness of extremist organizations to use these agents and the ready availability of deadly agents. Biological organisms continue to be readily available throughout the world, obtainable in nature or through biological supply houses or medical laboratories. Dangerous chemicals already exist in local communities and in hardware and gardening shops.

The current threat posed by weapons of biological and chemical origin has been discussed extensively in previous chapters of this textbook. This chapter discusses three issues that will likely have a significant effect on chemical and biological defense in the next century:

- the global proliferation of biological weapons;
- the advances in technology, particularly biotechnology, that will affect the development of weapons and their countermeasures; and
- possible changes in the future use of chemical and biological weapons by the enemy that will make delivery of medical care even more challenging.

Efforts at counterproliferation will not be discussed in this chapter. This should not be construed as a reflection of its reduced importance, for limiting the proliferation of weapons of mass destruction continues to be a large effort of the United States government. Instead, emphasis is placed here on the issue of biotechnology, for this is the area where medical personnel will find the greatest controversy and conflict. For the interested reader who desires a more in-depth review of the subject of future prospects of biological weapons and proliferation, we refer you to two excellent sources: *Biological Weapons: Weapons of the Future?* and *Director's Series on Proliferation* (see Recommended Reading at the end of this chapter).

The potential exists for both (*a*) misuse of the biotechnology for refinement of current biological weapons and (*b*) development of new agents with added potency. The profound impact that biotechnology will continue to have on biological weapons and their countermeasures is of particular concern when put in the context of the worldwide deployability of military forces, the potential use of genetic engineering for both peaceful and sinister purposes, and continued attractiveness of biological warfare as an option by adversaries in future conflicts.

PROLIFERATION OF BIOLOGICAL WEAPONS

The limitation and eventual elimination of both chemical and biological weapons are two of the greatest challenges facing the international community. Unfortunately, proliferation of such weapons is continuing despite the best efforts of many nations, including the United States, to prevent proliferation.[1] Biological weaponry is the most worrisome issue because of the relative ease in developing and mass-producing potent agents, the continuing difficulties in identifying enemy capabilities and limiting their development, and the potential ability for adversaries to bioengineer and deliver new organisms using the latest advances in technology.

On 23 February 1993, following the Persian Gulf War and the breakup of the Soviet Union, a panel of the U.S. House of Representatives Committee on Armed Services submitted a special report,[2] *Special Inquiry of the House Armed Services Committee Into the Chemical and Biological Weapons Threat*. This report concluded that despite the decrease in absolute quantities of chemical weapons, the potential diversity and the frequency with which such weapons could be encountered were increasing. The threat had shifted to Third World scenarios, with deployed U.S. military forces facing new threats from chemical and biological weapons. Technological advances have increased the diversity of potential weapons of each variety. The report stated the following concern, which goes to the heart of the problems that the U.S. military medical departments will face in the 21st century:

> Genetic tailoring and the speed of technological innovation create opportunities for the creation of exotic new agents which may be difficult to detect or defend against.[2(p7)]

In addition, the report of the House of Representatives Special Committee alluded to 31 nations that either possess or have the ability to develop an offensive chemical weapons capability, and 11 nations that either possess or have the ability to develop an offensive biological weapons capability. The Special Committee realized that while it would be more difficult for a country to mass-produce classic chemical warfare agents in large quantities without detection, it would be very easy for a country or organized group to develop the technological capabilities to produce other agents.[2]

The former Soviet Union, long suspected of having an aggressive research and development program despite its participation in international agreements to curtail such development, has continued to be a major factor in the global threat. Covert programs continued, at least through 1992, despite open declarations to the contrary. With the dissolution of the Soviet Union, concern has been generated about the export of the scientific technology and weaponry beyond its borders. Cooperation between the Russian Federation and the United States is making progress in reducing this potentially dangerous situation.

North Korea, Iran, and Iraq are three examples of countries with biological warfare potential. North Korea has continued to have a program of cooperation with several countries in the Middle East, and the prospect of biological weapons being used on the Korean peninsula is a genuine concern. Iraq was known to have an active research, development, and weaponization program at the time of the Gulf War, although whether Saddam Hussein intended to use such weapons is controversial. If chemical weapons agreements are any indication of national compliance and intent, it should be noted that Iraq secretly constructed chemical warfare production plants and imported chemical warfare technology from the West in violation of the Geneva Protocol.[3] The use of chemical weapons on Kurdish forces has now been well documented.

The Persian Gulf War and continuing problems with Iraq resulted in the creation of a unique United Nations organization known as The United Nations Special Commission on Iraq (UNSCOM).[3] UNSCOM was established specifically by a United Nations Security Council resolution that spelled out conditions for cease-fire and the destruction, removal, or rendering harmless of chemical, biological, and nuclear weapons and ballistic missiles with a range greater than 150 km. UNSCOM unilaterally defined the terms for its inspections of Iraqi facilities and has continued to direct and support compliance inspections.

The United States has been active in its participation in international efforts to specifically control the spread of biological and chemical weapons. The Convention on the Prohibition of the Development, Production, and Stockpiling of Bacteriological and Toxin Weapons and their Destruction (also known as the Biological Weapons Convention) and the Chemical Weapons Convention have been discussed in detail in other publications,[4,5] as have various confidence-building measures,[5] which have met with limited success.

It should be noted that UNSCOM activities are not directly associated with the Biological Weapons and Chemical Weapons Convention agreements, although elimination of weapons of mass destruction continues to be a goal of most nations. It is plausible to assume that should international situations arise in the future regarding proliferents with biological warfare capabilities, the United Nations may again take actions similar to those it took with Iraq.

The “dual-use” issue, in which the technologies used to develop and produce biological or chemical weapons are very similar to those that would be needed for human and veterinary healthcare research and production and the agricultural industry, has created many challenges. The technologies involved in pesticide dispersal, for example, could easily be adapted for the delivery of aerosols containing biological agents. Verification inspections and confidence-building measures have had limited success, but efforts continue to strengthen the conventions.

BIOTECHNOLOGY

Since 1953, when James D. Watson and Francis Crick identified the genetic code contained in deoxyribonucleic acid (DNA), discoveries in the field of molecular genetics have skyrocketed. Breakthroughs in genetic engineering have allowed genes to be substantially altered and combined with other genes in ways that have benefited mankind tremendously. Over the last 30 years, for example, the number of recognized human genetic disorders has risen from fewer than 500 to more than 4,200, primarily as a result of the ability to sequence genes quickly and precisely.[6–8] Since 1990, gene therapy experiments have been approved involving numerous human studies aimed at 12 genetic disorders, including cystic fibrosis, severe combined immune deficiency, familial hypercholesterolemia, acquired immunodeficiency syndrome, and several cancers.

However, the progress in genetic engineering and molecular biology has raised serious ethical issues, such as man's apparent ability to freely manipulate nature without clear societal controls; the potentially dangerous effects of bioengineered organisms of plant and animal origin on the environment; the arbitrary use of human embryonic tissue in research; and the control, storage, and access of genetic information.[7,9] These controversies have arisen as scientific accomplishments have proceeded at a more accelerated pace than has society's ability to resolve such complex issues.

For the military, knowledge of man's specific genetic defects or vulnerabilities (or ways to create such defects) and the ability to modify microorganisms or toxins that would increase pathogenicity take on added concern. Biotechnology theoretically provides opportunities for adversaries to modify existing organisms with specific characteristics, such as increased virulence, infectivity, or stability. Modern advances also allow for the inexpensive production of large quantities of replicating microorganisms for weaponization through recombinant methodologies, and the possibility to create "new" agents for future warfare that bypass current preventive or therapeutic interventions. These could be accomplished through secretive research programs that are superimposed on open biomedical research efforts in pharmaceutical firms or government laboratories. Ironically, while such possibilities continue to generate fear, the same technological advances can and do contribute to the development of new medical countermeasures, such as new vaccines, drugs, and diagnostic tests.

Enhanced Pathogenicity

Splicing genes for virulence, infectivity, stability, or other factors into the genome of an existing organism is one possibility for manipulating potential biological warfare agents. Microorganisms are able to cause disease through a variety of mechanisms that may involve interactions at the cellular level or at target organs. An understanding of the basic mechanisms of action that determine or influence cellular attachment, penetration, and genetic alteration is critical in the redesign of microorganisms.

Infectivity

Although influenza A virus has not been known to be bioengineered as an offensive biological weapon, it serves as an example of opportunities for viral modification. Naturally occurring mutations that result in antigenic drifts and shifts suggest that with today's technology, man could achieve deliberately what nature is already accomplishing naturally. If we are to develop effective countermeasures, we must understand how a virus penetrates the host's natural defenses and modifies itself genetically to promote its spread and ultimate survivability.

Influenza A possesses a neuraminidase that cleaves the terminal neuraminic acid residue at the cell surface carbohydrates. This simple enzymatic action allows the virus to attach to the cell surface and penetrate the membrane. Once infection has occurred, the body gradually develops specific antibodies to the infecting viral strain. Humoral immunity could also be elicited through immunization with an attenuated strain or a nonreplicating portion of the influenza virus itself.

The infectivity of "new" influenza virus strains is based on the ability of such strains to evade the body's preexisting immune defenses. The virus's genes and their products—hemagglutinin and neuraminidase—are altered enough that the body perceives it to be a new virus. This antigenic change could theoretically occur through man-made genetic alterations. The concept for developing new biological weapons is a basic one: develop a virus that evades the protective immunological system, reaches a target organ or tissue quickly, and causes significant disease, disability, or death. Viruses that debilitate or cause chronic illnesses may be just as militarily significant as those that cause acute disease, depending on specific scenarios.

Paradoxically, it may be advantageous for a biologically weaponized virus to cause a severe protracted illness with high communicability rather than quick death with little opportunity for continued spread. The only factor that prevents this from becoming an easy option for adversaries is the aggressor's need to develop a protective vaccine against the modified virus for use in their troops.

The fact that new influenza vaccines are needed every year to provide protection against new or modified circulating strains of virus illustrates the difficulties in developing a long-lasting, immunologically based defense against such viruses.

Virulence

Several bacterial agents have virulence factors that would enhance their pathogenicity in man. Such additions to a highly infectious but less pathogenic strain could make the modified organisms more attractive candidates for offensive weapons. Countermeasures, including vaccines and antimicrobial drugs, must be developed with this possibility in mind to provide the broadest measure of protection.

Moreover, when used in combination, microorganisms have the potential to create a more severe disease state. Similarly, infection with one agent with a shorter incubation period that may weaken overall resistance may provide easier opportunities for infection with a second organism with greater morbidity and mortality. The ability of multiple organisms with different levels of virulence to confuse medical officers looking for a common etiology accentuates the need for sensitive and specific diagnostic tests to be available in the field setting. These diagnostic tests must be able to decipher genetic differences and differentiate endemic from nonendemic forms of microorganisms.

Genetic Recombination

The ability for some genes to transpose themselves on chromosomes, rearrange and combine with other genes in a manner that may result in radical phenotypic and genotypic changes in the original organism, or to form plasmids that may sit quiescently for the right moment to exert their effect, has been demonstrated in the laboratory. The ability for cancer-producing genes (oncogenes) to be produced through genetic insertion or to be "turned on" by enzymes produced by other genes has given rise to the now-proven theory that some cancers are caused by infectious agents.[7]

In addition, retroviruses that attach to and invade specific cells of the body, inserting themselves into host genes and disrupting the normal DNA, can create long-lasting changes in the host that may eventually weaken overall immunity to diseases. While such discoveries lend themselves well to a better understanding of the pathological processes, they also provide opportunities that may not be as readily apparent for the development of sinister weapons.

Immunity

It is now recognized that protection against respiratory challenge by pathogens may require that a certain level of mucosal immunity be maintained. Cytokines released by leukocytes and other cells are extremely important in the development of the immune response; they modulate the differentiation and division of hematopoietic stem cells, activate lymphocytes and phagocytes, and are very much involved in the development of humoral and cell-mediated immunity. An understanding of the importance of cytokines in the immunological process, as well as factors leading to immunopotentiation and immunosuppression, could be applied practically to enhancement of vaccine efficacy or the prevention of release of potentially dangerous substances in the body.

These are just a few of the current immunological challenges in research. Advances in our understanding of immunomodulation allow for breakthroughs in cancer therapy or immunodeficient states to be applied to the development of new protective strategies against a broad spectrum of biowarfare agents. We can only speculate that future medical interventions will incorporate new knowledge on such processes.

Antibiotic Resistance

It has been recognized for many years that the uncontrolled use of antibiotics will promote the selective development of certain resistant strains of many microorganisms. Bacterial agents may rely on a variety of mechanisms to increase their virulence or resistance to antibiotics: through more permanent chromosomal mediation; or through plasmids, independently replicating extrachromosomal DNA segments floating freely in the cytoplasm that are capable of being ejected when antibiotic pressures are absent. Modified biological agents with resistance factors may be unaffected by therapeutic and chemoprophylactic regimens directed against sensitive organisms.

Biotechnology allows for the introduction of factors into many replicating organisms that would promote resistance to antibiotics. With human pathogens, concerns center on bacterial, viral, rickettsial, and fungal agents capable of causing acute and chronic infections. An armamentarium of structurally different, broad-spectrum drugs, which have been developed to initiate their specific therapeutic effects via different mechanisms, will allow some circumvention of the resistance threat.

Bioengineered Toxin Production

Taking bacterial organisms one step further, the combination of a known pathogenic biological agent with genes for producing toxin from another organism spliced into it generates a series of potential issues, including the ability of the original organism to retain enough of its previous pathogenicity; and its ability to replicate, spread, and produce enough toxin to cause symptoms. Although this concept may sound intriguing, naturally occurring organisms that already produce toxins may achieve the same desired effect. Recent experiences with *Escherichia coli* 0157:H7 causing hemorrhagic colitis and a hemolytic uremic syndrome as a result of consumption of contaminated meat demonstrate the devastating effect that the presence of a shigalike toxin may have. Identification of specific pathogens and their toxins require current technologies, including polymerase chain reaction and gene probe technologies, to be readily available even in a field setting.

A more worrisome concept involves the hybridization of two or more genes, such as combining a toxin with a monoclonal or polyclonal antibody directed against specific target cells in the body. Oncological immunotherapy is based on this concept and is effective in treating several types of cancers. While cancer therapy may depend on strong affinity of molecules for specific receptors, biological defense may favor deactivation of receptors or blocking of attachment. Molecular modeling would be helpful in understanding this phenomenon.

Genetic Weaponry

"Genetic warfare" has been raised as an issue, whereby targeting of specific populations or individuals with specific genotypic characteristics could theoretically be accomplished. Fortunately, although several replicating agents and toxins can now be mass produced with relative ease, entirely different types of biological agents are still difficult to create. This may not be the case in the next century, where emerging pathogens will include biological agents.[7,10]

It has been postulated that "genetic weapons" might very well be developed in the wake of increased knowledge about the human genome and genetic diversity. We would hope that the development of genocidal agents is so repulsive a concept that it would never be accepted by the international community. Racial differences do exist with blood-group proteins and histocompatibility proteins, and genetic susceptibilities to specific diseases have been demonstrated. However, it has been estimated that only 0.1% to 1% of the human genome can clearly be associated with pure ethnic differences[10]; whether this diversity is enough for the development of tailored agents is an open question. And whether a nation would find it necessary to specifically pursue a course to develop such targeted offensive weaponry remains to be seen.

It is improbable that such weapons would pose a serious threat to the forces of this nation, since the population of the United States is more heterogeneous than more segregated homogeneous societies. It is unrealistic to consider this a real threat anytime soon.

The Human Genome Project

The Human Genome Project, begun in the mid 1980s, has as its goal to have genetically sequenced over 100,000 genes in the human genome by year 2005. The information will be placed in a gene bank for international access.[6,7,9] The Human Genome Organization (HUGO) was established to coordinate the human genomic analyses being performed internationally and to maintain the database repository of all sequence information. The purpose of the project is to provide information on the chemical structure of humans. This will allow for a better understanding of hereditary diseases, the immune response, and certain chronic diseases. An understanding of what constitutes a healthy state may tempt proponents of offensive warfare to develop agents that create a state of poor health in their enemies. This could be accomplished through minor alterations in genes that control enzymatic actions in the body or changes in genes that control other genes. Although legal patent issues appear to be the principal difficulty currently, nations that have provided data in the project will claim a right to have access to all information.

New Medical Countermeasures

Advances in technology now allow for more directed and coordinated approaches in vaccine development against biological warfare agents and endemic diseases. The development of combination vaccines that eliminate the need for multiple vaccinations is of practical importance to the military. But efforts to increase the immunogenicity of vaccines—in particular, recombinant subunit vaccines that have traditionally been associated with lower antibody titer responses than live attenuated vaccines—may result in the discovery of better adjuvants or slow-release formulations (eg, microencapsulation) that will result in highly satisfactory and long-lasting immunological responses. Reversion of attenuated strains is always a concern with live vaccines, although this has not been shown to be a significant problem up to now. Recombinant vector vaccines, including those against vaccinia, adenovirus, and *Salmonella,* also offer some safer prospects,[11,12] but when vaccines against specific biological warfare agents are developed, the soldier's immunological responses to other vaccines administered need to be considered.

It is impossible to provide protection against every conceivable agent, but it seems likely that future medical protective measures will need to be more broadly based if they are to provide the best protection against biowarfare agents in the future. Current and future research must evaluate how to best stimulate the immunological response that will protect against categories of agents, while at the same time ensuring that those agents highest on the threat list are adequately covered.

As mentioned earlier, an understanding of the role of the mucosal response is critical, especially for protection via the respiratory or gastrointestinal tracts, as well as the importance of the humoral versus the cell-mediated response. Antimicrobial drug supplementation may also provide added benefit for immediate or short-term protection.

The abilities to develop monoclonal antibodies against specific antigens and to be able to develop transgenic animal models to form chimeras have opened large windows of research opportunity.[7] For example, the ability to microinject human genes into the pronuclei of fertilized mouse eggs and replace original genetic segments permits sophisticated animal models to be developed that can be used in challenge studies with specific infectious agents. The ethical animal-rights issues associated with creating and using such chimeras in research are obvious, but the opportunities for medical advancement are equally certain. Although transgenic mice currently provide little to new weapons development, they may be extremely helpful in the development of effective countermeasures. Transgenic plant research, leading to the development of resistance to insects and plant diseases, is another extension of genetic research.

MILITARY SCENARIOS

The threat that chemical agents will be used by hostile forces continues to be a military concern. However, effective personal protective measures and environmental detection systems will likely provide satisfactory protection for the forces in nearly all perceived scenarios involving agents described in earlier chapters of this textbook. Carefully followed decontamination procedures will reduce the possibility of further injury and allow medical personnel to render appropriate care to casualties.

Scenarios of the future may be complicated by the possible use of multiple agents, or the delivery of chemical and replicating agents and / or their toxins that have been carefully matched, based on their stability and ability to generate specific symptoms. Health effects could be potentiated. Therefore, from a medical perspective, detection requires the availability of rapid diagnostic methods and procedures to assess illnesses that will be the result of multiple agents.

Stated another way, detecting the presence of one single agent may not be adequate, since detectors can detect only what they were designed to detect. The classic chemical agents described earlier in this textbook will be only part of the concern, for readily available, highly toxic, industrial compounds that are not under the same degree of international monitoring as well-recognized chemical warfare agents could be used as weapons.

The deployment of troops to foreign lands provides opportunities for biological and chemical incidents to occur. In 1993, the United States, along with 71 other countries belonging to the United Nations, contributed troops to over a dozen peacekeeping missions throughout the world. These deployments involved military medical elements from different countries, but many of the smaller nations, in particular, possess limited abilities to deal with a nuclear, biological, or chemical warfare situation. As of this writing (1996), no chemical or biological warfare incidents have occurred during such peacekeeping missions, although sabotage and terrorism have occurred.

Since the military has the greatest capability in this country to address chemical and biological warfare, the missions for the military have now included the domestic front. Military medical practitioners will very likely find it necessary to be familiar with the diagnosis, treatment, and prevention of injuries and illness caused by chemical and biological agents, for we will frequently be consulted for our expertise.

Biological warfare, in particular, is of great concern for the military for several reasons:

- Many potent agents are readily available. Theoretically, any microorganism or toxin capable of inflicting death or disease has the potential of being adapted for use as a biological weapon.
- Naturally occurring infectious agents could be used to generate epidemics among susceptible troops, creating confusing disease situations on the battlefield. Naturally occurring or deliberately disseminated spore-forming microbes could continue to persist in the environment, and some aerosolization might occur during military maneuvers; environmental detectors may not necessarily be able to differentiate between natural and man-generated contamination.
- Many classic agents can be mass-produced in a short time using very basic laboratory techniques. Large fermenters may not be necessary if a small amount of agent is all that is required.
- Theoretically, biological agents can be genetically altered to escape detection.
- Biological agents require no precursors for development, unlike chemical and nuclear agents, and a covert program is much more difficult to detect.

SUMMARY

The future requires that we carefully and continually assess the evolving threat from chemical and biological weapons. This can be predicted with certainty: the threat will change with time. As stronger countermeasures are developed by the United States and its allies, the employment of certain agents may become less appealing to adversaries on the battlefield. From that standpoint, medical countermeasures may be an effective deterrent. Biotechnology itself may be the threat of the future, and not specific agents, as adversaries may attempt to evade effective preventive measures with bioengineering. The employment of multiple chemical and biological agents is a very likely scenario of the future, thereby challenging the medical community to be much more proactive in its development of appropriate countermeasures.

The missions of the United States military are changing, and deployments will require a capability to address potential chemical and biological incidents on the domestic and international fronts. Military medical personnel must, therefore, be continually prepared to deal with such contingencies as we become an even more important asset to this nation's defense and healthcare structures.

REFERENCES

1. ter Haar B. *The Future of Biological Weapons*. New York, NY: Praeger; 1991.

2. House of Representatives, 102nd Cong, 2nd Sess. *Report of the Special Inquiry Into the Chemical and Biological Threat of the Committee on Armed Services*. Washington, DC: US Government Printing Office; 23 Feb 1993.

3. Spertzel RO, Wannemacher RW, Linden CD. *Global Proliferation—Dynamics, Acquisition, Strategies, and Responses*. Vol 4. In: *Biological Weapons Proliferation*. Alexandria, Va: Defense Nuclear Agency; September 1994. DNA Technical Report 93-129-V4.

4. Geissler E, ed. *Biological and Toxin Weapons Today*. Oxford, England: Stockholm International Peace Research Institute, Oxford University Press; 1986: 135–137.

5. Roberts B, ed. *Ratifying the Chemical Weapons Convention*. Washington, DC: Center for Strategic and International Studies; 1994.

6. Friedman T. Molecular medicine. In: Davis BD. *The Genetic Revolution*. Baltimore, Md: The Johns Hopkins University Press; 1991.

7. Lee TF. *Gene Future: The Promise and Perils of the New Biology*. New York, NY: Plenum Press; 1993.

8. Weiss R. Gene therapy at a crossroads. *Washington Post*. 18 Oct 1994;Health:12.

9. Drlica KA. *Double-Edged Sword: The Promises and Risks of the Genetic Revolution*. Reeding, Mass: Addison-Wesley; 1994.

10. Dubuis B. *Recombinant DNA and Biological Warfare*. Zurich, Switzerland: Institut für Militarishe Sicherheitstechnik; October 1994.

11. Rabinovich NR, McInnes P, Klein DL, Hall BF. Vaccine technologies: View to the future. *Science*. 1994;265:1401–1404.

12. Ellis RW, Douglas RG Jr. New vaccine technologies. *JAMA*. 1994;271:929–931.

RECOMMENDED READING

Roberts B, ed. *Biological Weapons: Weapons of the Future?* Washington, DC: The Center for Strategic and International Studies; 1993. This 101-page book is a collection of essays on various aspects of biological warfare and covers in depth some of the concepts presented briefly in this chapter.

Bailey KC, ed. *Director's Series on Proliferation*. University of California: Lawrence Livermore National Library; 1994. This 112-page book is a collection of essays compiled under a US Department of Energy contract (UCRL-LR-11470-4) on various aspects of the biological warfare threat and proliferation. The document is available from the National Technical Information Service, US Department of Commerce, 5285 Port Royal Road, Springfield, Virginia 22161.