CHEM-BIO AGENTS TODAY

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SUMMARY

The number of biological and chemical agents that may be used for terrorism is potentially huge. Of these, some are more destructive than others. Biological agents have been categorized by the Centre for Disease Control (CDC) in the United States into Category A, B and C. Those in category A are high priority agents that are easily disseminated or transmitted person-to-person, cause high mortality, are likely to cause public panic and social disruption, and which require special action for national preparedness. The agents in this category are smallpox, anthrax, plague, botulism, tularaemia, the filoviruses and the arenaviruses. Chemical agents that may be used by terrorists range from warfare agents to toxic chemicals commonly used in industry. There are no less than twelve categories of chemical agents that are potential terrorist weapons. A strategic plan for preparedness and response to such biological and chemical attacks has been developed by the CDC. This plan has five focus areas namely, preparedness and prevention, detection and surveillance, diagnosis and characterization of biological and chemical agents, response, and communication. Attention to each of these areas is of importance in the development of an effective strategic plan to deal with biological and chemical terrorist acts.

INTRODUCTION

"Unfortunately, as long as there are unstable countries and individuals in the world who are willing to use chemical and biological weapons, health professionals will need to be familiar with the effects of these agents and the treatment of associated casualties."

– Jim Carson, 1997

This quotation from a US Commander, US Navy Duke University Medical Centre gives the rationale of the need to be in touch with the subject of biological and chemical weapons used to inflict casualties.

The deliberate use of micro-organisms and toxins has been attempted throughout history. Biological warfare has evolved from the crude use of cadavers to contaminate water supplies to the development of specialized munitions for battlefield and covert use (Christopher et al, 1997)[1]. The latest episode was the anthrax outbreak which started with an inhalational case in Palm Beach County in Florida in October 2001. Additional cases were reported from Florida and New York City. A total of 22 cases were eventually confirmed to have met the CDC case definition; 10 were confirmed inhalational anthrax, and 12 (seven confirmed and 5 suspected) were cutaneous anthrax (Malecki et al, 2001)[2].

POTENTIAL BIOLOGICAL AND CHEMICAL AGENTS

Common characteristics

A broad range of potential biological warfare agents, including bacteria, viruses, and toxins (of microbial, plant, or animal origin) exists. Common characteristics of this diverse group of agents are:

- the ability to disperse them in aerosols of 1–5 micron particle size, which can penetrate the distal bronchioles

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- the ability of these aerosols to be delivered by simple technology, and the feasibility of these agents, if delivered from a line source (such as an airplane) upwind from the target, to infect large numbers of the population
- additional routes of exposure include oral (intentional contamination of food/water supply) and possibly percutaneous, although these routes are considered much less likely.

DIFFERENT IMPACTS

Bombings and chemicals

Bombings and chemical terrorism acts draw our attention to the scene of action. The effects of chemical agents absorbed through inhalation or by absorption through the skin or mucous membranes are usually immediate and obvious. Such attacks consequently elicit almost immediate response from police, fire brigade, and emergency personnel.

Biological agents

Attacks with biological agents are potentially more dangerous. Dissemination of a biological agent in a public place will not have an immediate impact because of the incubation period between exposure and onset of illness. The first casualties are likely to be identified by physicians or other primary health-care providers.

For example, the covert release of the contagious smallpox virus will be manifested by patients appearing in doctors' offices, clinics, and emergency rooms during the first or second week, complaining of fever, back pain, headache, nausea, and other symptoms of what initially might appear to be an ordinary viral infection.

As the disease progresses, these persons will develop the papular rash characteristic of early-stage smallpox, a rash that physicians might not recognize immediately. By the time the rash becomes pustular and patients begin to die, the disease will be disseminated through the population by person-to-person contact.

Only a short window of opportunity exists between the time the first cases are identified and a second wave of the population becomes ill. During that brief period, public health officials will need to confirm that an attack has occurred, identify the organism, and prevent more casualties through prevention strategies such as mass vaccination or prophylactic treatment.

As person-to-person contact continues, successive waves of transmission could carry infection to other worldwide localities. These issues might also be relevant for other person-to-person transmissible etiologic agents such as plague or certain viral hemorrhagic fevers (Khan et al, 2000)[3].

Contamination of food and water with chemical agents may also be covert and hard to detect for a while. There is the need to make prompt diagnoses of such attacks by noting unusual or suspicious health problems in animals as well as humans.

CLASSIFICATION OF BIOLOGICAL AGENTS

Critical biological agents have been categorized by the Center for Disease Control into Category A, B & C (Khan et al, 2000)[3].

Category A

These are high-priority agents include organisms that pose a risk to national security because they

can be easily disseminated or transmitted person-to-person; cause high mortality, with potential for major public health impact; might cause public panic and social disruption; and require special action for public health preparedness epidemiological capacity. Such capacity includes the ability to detect and respond to biological attacks, supply diagnostic agents, stockpile appropriate vaccines and drugs, and encourage research on antiviral drugs and vaccines.

Category A agents include: variola major (smallpox); Bacillus anthracis (anthrax); Yersinia pestis (plague); Clostridium botulinum toxin (botulism); Francisella tularensis (tularaemia); filoviruses (Ebola hemorrhagic fever, Marburg hemorrhagic fever); and arenaviruses (Lassa (Lassa fever), Junin (Argentine hemorrhagic fever) and related viruses). The two agents that lead the pack are anthrax and smallpox.

Category B

These are of second highest priority agents include those that are moderately easy to disseminate; cause moderate morbidity and low mortality; and require specific enhancements of diagnostic capacity and enhanced disease surveillance of local providers.

Category B agents include: Coxiella burnetti (Q fever); Brucella species (brucellosis); Burkholderia mallei (glanders); alphaviruses (Venezuelan encephalomyelitis, eastern and western equine encephalomyelitis); ricin toxin from Ricinus communis (castor beans); epsilon toxin of Clostridium perfringens; and Staphylococcus enterotoxin B.

A subset of List B agents includes pathogens that are food or waterborne. These pathogens include but are not limited to Salmonella species, Shigella dysenteriae, Escherichia coli O157:H7, Vibrio cholerae, and Cryptosporidium parvum.

Category C

Category C agents are emerging pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination; as well as the potential for high morbidity and mortality, and major health impact.

Category C agents include Nipah virus, hantaviruses, tickborne hemorrhagic fever viruses, tickborne encephalitis viruses, yellow fever, and multidrug-resistant tuberculosis.

Preparedness for List C agents requires ongoing research to improve disease detection, diagnosis, treatment, and prevention. Knowing in advance which newly emergent pathogens might be employed by terrorists is not possible; therefore, linking bioterrorism preparedness efforts with ongoing disease surveillance and outbreak response activities as defined in CDC's emerging infectious disease strategy is imperative (CDC, 1998)[4].

CLASSIFICATION OF CHEMICAL AGENTS

Chemical agents that might be used by terrorists range from warfare agents to toxic chemicals commonly used in industry. Criteria for determining priority chemical agents include chemical agents already known to be used as weaponry; availability of chemical agents to potential terrorists; chemical agents likely to cause major morbidity or mortality; potential of agents for causing public panic and social disruption; and agents that require special action

for public health preparedness including the capacity to detect and respond to these attacks, ability to stockpile chemical antidotes.

Hundreds of new chemicals are introduced internationally each month. What is the best way to deal with these agents? Treating exposed persons by clinical syndrome rather than by specific agent is more useful for public health planning and emergency medical response purposes.

Public health agencies and first responders might render the most aggressive, timely, and clinically relevant treatment possible by using treatment modalities based on syndromic categories (e.g., burns and trauma, cardiorespiratory failure, neurologic damage, and shock). These activities must be linked with authorities responsible for environmental sampling and decontamination.

Categories of chemical agents include:

- nerve agents – tabun (ethyl N,N-dimethylphosphoramidocyanidate); sarin (isopropyl methylphosphanofluoridate); soman (pinacolyl methyl phosphonofluoridate); GF (cyclohexylmethylphosphonofluoridate); and VX (o-ethyl-[S]-[2-diisopropylaminoethyl]-methylphosphonothiolate);
- blood agents – hydrogen cyanide, cyanogen chloride;
- blister agents – lewisite (an aliphatic arsenic compound, 2-chlorovinyldichloroarsine); nitrogen and sulfur mustards; and phosgene oxime;
- heavy metals – arsenic, lead, and mercury;
- Volatile toxins – benzene, chloroform, trihalomethanes; pulmonary agents (phosgene, chlorine, and vinyl chloride);
- incapacitating agents – BZ (3-quinuclidinyl benzilate);
- pesticides, persistent and nonpersistent;
- dioxins, furans, and polychlorinated biphenyls (PCBs);
- explosive nitro compounds and oxidizers – ammonium nitrate combined with fuel oil;
- flammable industrial gases and liquids – gasoline and propane;
- poison industrial gases, liquids, and solids – cyanides and nitriles; and
- corrosive industrial acids and bases – nitric acid and sulphuric acid.

Steps in preparing public health agencies for chemical attacks are:

- Enhance epidemiological capacity for detecting and responding to chemical attacks
- Enhance awareness of chemical terrorism among emergency medical service personnel, police officers, firefighters, physicians, and nurses
- Stockpile chemical antidotes
- Develop and provide bioassays for detection and diagnosis of chemical injuries
- Prepare educational materials to inform the public during and after a chemical attack.

STRATEGIC PLAN FOR PREPAREDNESS AND RESPONSE

CDC in the United States has identified five focus areas in a strategic plan for preparedness and response to biological and chemical terrorism. These areas and the elements in each of these five areas as described by CDC (Khan et al, 2000)[3] are reproduced below.

Preparedness and Prevention

- Maintain a public health preparedness and response cooperative agreement that provides support to state health agencies that are working with local agencies in developing coordinated bioterrorism plans and protocols
- Establish a national public health distance-learning system that provides biological and chemical terrorism preparedness training to health-care workers and to state and local public health workers
- Disseminate public health guidelines and performance standards on biological and chemical terrorism preparedness planning for use by state and local health agencies.

Detection and Surveillance

- Strengthen state and local surveillance systems for illness and injury resulting from pathogens and chemical substances that are on the critical agents list
- Develop new algorithms and statistical methods for searching medical databases on a real-time basis for evidence of suspicious events
- Establish criteria for investigating and evaluating suspicious clusters of human or animal disease or injury and triggers for notifying law enforcement of suspected acts of biological or chemical terrorism.

Diagnosis and Characterization of Biological and Chemical Agents

- Establish a multilevel laboratory response network for bioterrorism that links public health agencies to advanced capacity facilities for the identification and reporting of critical biological agents
- Establish regional chemical terrorism laboratories that will provide diagnostic capacity during terrorist attacks involving chemical agents
- Establish a rapid-response and advanced technology laboratory to provide around-the-clock diagnostic support to bioterrorism response teams and expedite molecular characterization of critical biological agents.

Response

- Assist state and local health agencies in organizing response capacities to rapidly deploy in the event of an overt attack or a suspicious outbreak that might be the result of a covert attack
- Ensure that procedures are in place for rapid mobilization of terrorism response teams that will provide on-site assistance to local health workers, security agents, and law enforcement officers
- Establish a national pharmaceutical stockpile to provide medical supplies in the event of a terrorist attack that involves biological or chemical agents.

Communication

- Establish a national electronic infrastructure to improve exchange of emergency health information among local, state, and federal health agencies
- Implement an emergency communication plan that ensures rapid dissemination of health information to the public during actual, threatened, or suspected acts of biological or chemical terrorism
- Create a website that disseminates bioterrorism preparedness and training information, as well

as other bioterrorism-related emergency information, to public health and health-care workers and the public.

The strategic plan described here needs to be related to the document Bioterrorism Readiness Plan: A template for Health Care Facilities, which was developed jointly by the APIC (Association for Professionals in Infection Control and Epidemiology) Bioterrorism Task Force and the CDC Hospital Infections Program Bioterrorist Working Group in 1999. This document can be downloaded from the CDC website. The URL of the file is http://www.cdc.gov/ncidod/hip/Bio/13apr99APIC-CDCBioterrorism.PDF (English & Malone, 1999)[5]. It deals with the response to bioterrorism and communication tasks in the practice setting and broadly corresponds to the areas of response and communication in the CDC strategic plan of five focus areas issued in 2000.

TAKE HOME MESSAGES

- The number of potential biological agents for intentional harm are many.
- Biological agents can be classified into three categories depending on the agent's destructiveness and the ease of dissemination.
- Chemical agents are best classified by the effects that they create syndromically.
- CDC's strategic plan of five focus areas released in 2000, covering the areas of preparedness and prevention; detection and surveillance; diagnosis and characterization of biological and chemical agents; response; and communication, provides a framework for dealing with chem.-biological agents that may be intentionally released
- The Bioterrorism Readiness Plan: A template for healthcare facilities released in 1999 deals with the areas of response and communication in the CDC strategic plan of 2000.

REFERENCES

1. Christopher GW et al. Biological Warfare: A Historical Perspective. JAMA 1997 Aug 6; 278: 412-7.
2. Malecki J et al. Investigation of bioterrorism-related anthrax, 2001. MMWR.2001; 50: 1008-10.
3. Khan et al. Biological and chemical terrorism: Strategic plan for Preparedness and Response. Recommendations of the CDC Strategic Planning Workgroup. MMWR April 21 2000; 49: RR-4; 1-14.
4. CDC. Preventing emerging infectious diseases: a strategy for the 21st century. Atlanta, Goergia: US Department of Health and Human Services, 1998.
5. APIC Bioterrorism Task Force, CDC Hospital Infections Program Bioterrorism Working Group Bioterrorism Readiness Plan: A Template for Healthcare Facilities, 1999 http://www.cdc.gov/ncidod/hip/Bio/13apr99APIC-CDCBioterrorism.PDF