Contemporary Issue

Bioterrorism : An Emerging Public Health Problem

Maj MP Cariappa*, Lt Col LS Vaz+, Dr Parul Sehgal#

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Introduction

Biological weapons have recently attracted the attention and the resources of the world. Discerning the nature of the threat of bioweapons as well as appropriate responses to them, requires greater attention to the biological characteristics of these instruments of war and terror. The dominant paradigm of a weapon as a device that explodes, leaves us ill-equipped conceptually and practically, to assess and thus to prevent the potentially devastating effects of bioterrorism. Strengthening the public health infrastructure, is an effective step toward averting the suffering that could be wrought by a terrorist's use of a biological agent [1].

Vulnerability to terrorist attack is the price that a free and democratic society has always had to pay. A terrorist is one, who aims to further his cause, by using tactics of intimidation and force, with the aim being to destabilize the existing government. Whilst prior preparation and planning are essential, more coherent, coordinated and centralised threat assessments are what is really required, to coordinate prevention and response strategies [2].

Biological Warfare

The development, production and use of biological and chemical weapons are prohibited by international treaties to which most states of the world have subscribed; the 1925 Geneva Protocol, the 1972 Biological and Toxin Weapons Convention, and the 1993 Chemical Weapons Convention. Not all nations have joined and valid concerns remain that some may yet resort to these weapons. Moreover, non-state entities may try to gain access to the weapons for terrorism.

Biological and chemical weapons have been described as the 'poor man's atom bomb". It is not enough that biological and chemical agents be highly infective or toxic, in order to be effective as a weapon, an agent needs also to be stable enough to resist degradation during handling and storage. In use, the agent must be spread in such a way that the necessary infective or effective dosage is delivered to the target population. The agent must be relatively easy to produce from available precursor compounds or from naturally occurring micro-organisms. Once produced, it must be weaponised and depending on the concept of deployment and use, stored without undue risk to its possessor. The WHO has defined biological-warfare agents as ones that depend for their effects on multiplication within the target organism and that are intended for use in war to cause disease or death in man, animals or plants [3].

The Spectre of Bioterrorism

The Sept 11, 2001 bombing of the World Trade Centre, New York, was an act of 'kamikaze' terrorism. The aftermath of the Afghan campaign by the US and its allies, in its 'Globe-Cop' role, has seen the emergence of a paradigm of terrorism which holds ominous portents for the future. 'Bioterrorism' is the usage of biological agents as a weapon of terror, by fundamentalists, and other such people who have adopted terrorism as a means of violent struggle.

An act of biological or chemical terrorism might range from dissemination of aerosolized anthrax spores to food contamination and predicting when and how such an attack might occur may not be feasible. However, the possibility of such attacks cannot be ignored, especially in light of events during the past decade (eg. the sarin gas attack in the Tokyo subway, the discovery of military bioweapons programs in Iraq and the former Soviet Union, the recent Anthrax scares). While it may not be possible to prevent or pre-empt bioterrorist attacks, the consequences of being unprepared could be devastating [4].

Terrorist incidents in the United States and elsewhere involving bacterial pathogens, have demonstrated that all nations are equally vulnerable to biological and chemical threats. Recipes for preparing "homemade" agents are readily available on the internet and reports of arsenals of military bioweapons raise the possibility that terrorists might have access to highly dangerous agents, which have been engineered for mass dissemination [5]. In contrast to conventional terrorist attacks using weapons and explosives, attacks

*Officer Commanding, Station Health Organisation, Ramgarh Cantt, +Reader, Department of Preventive & Social Medicine, Armed Forces Medical College, Pune - 411 040, #Consultant Physician, Ramgarh, Jharkhand.

with biological agents are more likely to be covert. They present different challenges and require an additional dimension of planning that involves the public health infrastructure.

Covert dissemination of a biological agent in a public place will not have an immediate impact because of the delay between exposure and onset of illness (the incubation period). The normal course of the disease may have a few dips after initial rise due to pockets of resistance, however, in attack there is a sharp rise due to susceptible population. Consequently, the first casualties of a covert attack probably will be identified by treating doctors in Medical Inspection (MI) Rooms etc.

Biological Agents

After the September 11 bombings, the CDC recommended heightened surveillance for any unusual disease occurrence or increased numbers of illnesses that might be associated with the terrorist attacks. Subsequent cases of anthrax in Florida and New York City have demonstrated the risks associated with intentional release of biologic agents [6]. CDC defines three categories of biologic agents with potential to be used as weapons, based on ease of dissemination or transmission, potential for major public health impact (eg. high mortality), potential for public panic and social disruption, and requirements for public health preparedness [4].

Agents of highest concern are *Bacillus anthracis, Yersinia pestis, Variola major, Clostridium botulinum* toxin, *Francisella tularensis, Filoviruses* (haemorrhagic fevers) and *Arenaviruses (Lassa, Junin)* [7]. Given below are brief descriptions of the commonly anticipated biological agent caused illnesses:

Botulism : Clinical features include symmetric cranial neuropathies (i.e. drooping eyelids, weakened jaw clench and difficulty in swallowing or speaking), blurred vision or diplopia, symmetric descending weakness in a proximal to distal pattern, and respiratory dysfunction from respiratory muscle paralysis or upper airway obstruction without sensory deficits. Inhalational botulism would have a similar clinical presentation as foodborne botulism, however, the gastrointestinal symptoms that accompany foodborne botulism may be absent [8].

Plague : Clinical features of pneumonic plague include fever, cough with muco-purulent sputum, haemoptysis and chest pain. A chest radiograph will show evidence of bronchopneumonia [9].

Smallpox : The acute clinical symptoms of smallpox resemble other acute viral illnesses, such as influenza, beginning with a 2-4 day nonspecific prodrome of fever and myalgias before rash onset. Several clinical features can help differentiate varicella from smallpox. In comparison to the rash of varicella, the vesicular/pustular rash of smallpox is typically most prominent on the face and extremities and lesions develop at the same time [10].

Anthrax : A nonspecific prodrome (fever, dyspnea, cough, and chest discomfort) follows inhalation of infectious spores. Approximately 2-4 days after initial

Table I
Critical biological agents

Category A
- *Variola major* (smallpox)
- *Bacillus anthracis* (anthrax)
- *Yersinia pestis* (plague)
- *Clostridium botulinum* toxin (botulism)
- *Francisella tularensis* (tularaemia)
- Filoviruses
  - ◊ *Ebola* hemorrhagic fever,
  - ◊ *Marburg* hemorrhagic fever
- Arena viruses
  - ◊ *Lassa* (Lassa fever)
  - ◊ *Junin* (Argentine hemorrhagic fever) and related viruses

Category B
- *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*
- *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 O 157:H7*
- *Vibrio cholerae*
- *Cryptosporidium parvum*

Category C
- Nipah virus
- Hantaviruses
- Tickborne hemorrhagic fever viruses
- Tickborne encephalitis viruses
- Yellow fever
- Multidrug-resistant tuberculosis

Note : Category A - High-priority agents that pose a risk to health 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;
Category B - Second highest priority agents are moderately easy to disseminate; cause moderate morbidity and low mortality and require specific enhancements of diagnostic capacity and enhanced disease surveillance;
Category C - These are emerging pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination and potential for high morbidity and mortality and major health impact

symptoms, sometimes after a brief period of improvement, respiratory failure and hemodynamic collapse ensue. Inhalational anthrax also might include thoracic edema and a widened mediastinum on chest radiograph. Cutaneous anthrax follows deposition of the organism onto the skin, occurring particularly on exposed areas of the hands, arms, or face. An area of local edema becomes a pruritic macule or papule, which enlarges and ulcerates after 1-2 days. Small, 1-3 mm vesicles may surround the ulcer. A painless, depressed, black eschar usually with surrounding local edema subsequently develops. The syndrome may include lymphangitis and painful lymphadenopathy [11].

Inhalational tularaemia : Inhalation of *F tularensis* causes an abrupt onset of an acute, nonspecific febrile illness beginning 3-5 days after exposure, with pleuropneumonitis developing in a substantial proportion of cases during subsequent days [12].

Haemorrhagic fever : (agent : *Ebola* or *Marburg* viruses). After an incubation period of usually 5-10 days (range : 2-19 days), illness is characterized by abrupt onset of fever, myalgia, and headache. Other signs and symptoms include nausea and vomiting, abdominal pain, diarrhoea, chest pain, cough and pharyngitis. A maculopapular rash, prominent on the trunk, develops in most patients approximately 5 days after onset of illness. Bleeding manifestations, such as petechiae, ecchymoses and haemorrhages, occur as the disease progresses [13].

Bioterrorism and the Role of Health-Care Providers

Medical officers need to be alert to illness patterns and diagnostic clues that might indicate an unusual infectious disease outbreak associated with intentional release of a biologic agent and should report any clusters or findings to the Preventive Medicine Specialist locally or at higher HQ. Suspicion can be based on detection of unusual disease at unusual location / time of year in an unusual population. The covert release of a biologic agent may not have an immediate impact because of the delay between exposure and illness onset, and outbreaks associated with intentional releases might closely resemble naturally occurring outbreaks. Indications of intentional release of a biologic agent include [7] :

(a) An unusual temporal or geographic clustering of illness or patients presenting with clinical signs and symptoms that suggest an infectious disease outbreak (e.g. $\geq$ 2 patients presenting with an unexplained febrile illness associated with sepsis, pneumonia, respiratory failure, or rash or a botulism like syndrome with flaccid muscle paralysis, especially if occurring in otherwise healthy persons).

(b) An unusual age distribution for common diseases (eg. an increase in what appears to be a chickenpox-like illness among adult patients, but which might be smallpox).

(c) A large number of cases of acute flaccid paralysis with prominent bulbar palsies, suggestive of a release of botulinum toxin.

Focusing on Preparedness Activities

Early detection of and response to biological or chemical terrorism is crucial. Without special preparation at various levels, a large-scale attack with a biological or chemical agent could overwhelm the health infrastructure. Large number of patients, including both infected persons and the "worried well", would seek medical attention, with a corresponding need for medical supplies, diagnostic tests and hospital beds. Medical personnel would be at a special risk and everyday life could be disrupted as a result of widespread fear [4].

Preparedness for terrorist-caused outbreaks and injuries should be an essential component of health surveillance and response system, which is designed to protect the Armed Forces against unusual health events. The epidemiologic skills, surveillance methods, diagnostic techniques and physical resources required to detect and investigate unusual or unknown diseases, as well as syndromes or injuries, are similar to those needed to identify and respond to an attack with a biological or chemical agent. Public Health specialists must prepare for the special features a terrorist attack probably would have (eg. mass casualties or the use of rare agents). Terrorists might use combinations of these agents, attack in more than one location simultaneously, use new agents, or use organisms that are not on the critical list (eg. common, drug-resistant, or genetically engineered pathogens).

Potential biological and chemical agents are numerous, however, the preparedness efforts must be focused on agents that might have the greatest impact on health and security, especially agents that are highly contagious or that can be engineered for widespread dissemination via small-particle aerosols. Preparing the Armed Forces to address these dangers is a major challenge facing us today. As with emerging infectious diseases, early detection and control of biological or chemical attacks depends on a strong and flexible public health system at the local, state and national levels. It has to be stressed that, primary health care practitioners, Regimental Medical Officers (RMOs), Authorised Medical Attendants (AMAs) in our settings must be vigilant because they will probably be the first to observe and report unusual illnesses or injuries.

The constitution of Quick Reaction Medical Teams (QRMT) might be considered, to form a strong decisive medical response to counter such attacks and provide a trained and dedicated resource to commanders.

Early detection requires increased biological and chemical terrorism awareness among front-line medical personnel especially RMOs because they are in the best position to report suspicious illnesses and injuries. Also, early detection will require improved communication systems between the medical officers at the periphery and Public Health specialists (DADH and the OC, SHO / FHO). In addition, diagnostic laboratories at the zonal level, must be equipped to identify biological and chemical agents that are rarely seen. Fundamental to these efforts is, comprehensive integrated training designed to ensure core competency in public health preparedness and the highest levels of scientific expertise among medical personnel [4]. Preparedness efforts by specialists and RMOs to detect and respond to biological and chemical terrorism will have the added benefit of strengthening the Armed Forces capacity for identifying and controlling injuries and emerging infectious diseases, as a collateral accruing benefit.

Strategies

Plans should be implemented for educating and reminding health-care providers about how to recognize unusual illnesses that might indicate intentional release of a biologic agent. Strategies for responding to potential bioterrorism could include [7]:

(a) Providing information to health-care providers and clinical laboratories about how to report events through the appropriate fastest channel.

(b) Implementing a sustained capacity to receive and act on any positive report of events that suggest intentional release of a biologic agent.

(c) Investigating immediately any report of a cluster of illnesses or other event that suggests an intentional release of a biologic agent and requesting assistance of a Preventive Medicine specialist when necessary.

(d) Implementing a plan, to collect and transport specimens and to store them appropriately before analysis at designated laboratories.

(e) Reporting immediately to higher HQ if the results of an investigation suggest release of a biologic agent.

Key Result Areas

Similar to the CDC's strategic plan [4], our endeavour in the Armed Forces should be based on the following focus areas, with each area integrating training and research.

1. Preparedness and Prevention

Detection, diagnosis, and mitigation of illness caused by biological and chemical terrorism is a complex process that involves numerous specialities, which must include Medical Microbiologists, Preventive Medicine specialists and experts in Public Health Chemistry if available. Meeting this challenge will require special emergency preparedness in all military stations.

2. Detection and Surveillance

Early detection is essential for ensuring a prompt response to a biological or chemical attack, including the provision of prophylactic medicines, antidotes, or vaccines. We need to integrate surveillance for illness and injury resulting from biological and chemical terrorism into the routine disease surveillance systems, while developing new mechanisms for detecting, evaluating, and reporting suspicious events that might represent covert terrorist acts. Close and ongoing liaison with RMOs in units would be needed to enhance detection and reporting of unexplained injuries and illnesses. Additionally, clinical laboratories in the Armed Forces should report any clusters or findings that could indicate intentional release of a biologic agent [9] to the higher HQ for necessary investigation on priority.

3. Diagnosis and Characterization of Biological and Chemical Agents

CDC has recommended creation of a multilevel Laboratory Response Network for Bioterrorism (LRNB). Pathology Departments at Command Hospital level would need to have close ongoing interaction with Public Health specialists at all levels and have facilities that can analyze biological agents. These laboratories must provide diagnostic, confirmatory and reference support for duly constituted terrorism response teams. There is a need for development of field kits for rapid detection, for utilization at the periphery by trained personnel.

4. Response

A comprehensive public health response to a biological or chemical terrorist event involves epidemiologic investigation, medical treatment and prophylaxis for affected persons, and the initiation of disease prevention or environmental decontamination measures. There is a need to develop protocols towards diagnosis and management of such suspected attacks that needs to be disseminated to all concerned in the medical echelon.

Irrespective of the availability of a Preventive

Medicine specialist in a station, expertise for investigating unusual events and unexplained illnesses, must be developed. In the event of a confirmed terrorist attack, the nearest available Biowarfare oriented specialists in Microbiology, Preventive Medicine and Public Health Chemistry must be deputed as a team (QRMT) to coordinate and investigate unexplained or suspicious illnesses or unusual etiologic agents and provide on-site consultation regarding medical management and disease control. Planners need to ensure the availability, procurement, and delivery of medical supplies, devices, and equipment that might be needed to respond to terrorist-caused illness or injury.

5. Communication Systems

Armed Forces preparedness to mitigate the public health consequences of biological and chemical terrorism depends on the coordinated activities of well trained health-care and public health personnel throughout the organisation who have access to updated information. Effective communication system that will support disease surveillance, rapid notification and information exchange regarding disease outbreaks that are possibly related to bioterrorism, dissemination of diagnostic results and emergency health information and coordination of emergency response activities.

Prioritization in Planning

Rosen (2000) commented that it has become apparent that the management of any biological attack must depend on systems already in place for managing new diseases or new epidemics of old diseases [14]. It may seem inappropriate to allocate resources to defend against a problem that has such a low incidence or threat potential. However, in 1999, the United States allocated $10 billion for anti-terrorism, with a substantial portion for bioterrorism [15]. Cohen et al (2000) aver that the proponents of anti-bioterrorism programmes have it backwards. Instead of pumping more resources into ill advised and risky anti-bioterrorism programmes, the stress should be to build national and international public health systems that can adequately reduce, detect and respond to natural disease outbreaks and industrial chemical accidents etc. Then, in the unlikely event of a bioterrorist attack, these systems will be available to manage the challenge [16]. Recent attention and interest have resulted in a commitment of substantial public resources, albeit an insufficient amount for definitive countermeasures. It is required to emphasize the similarity in appearance of naturally occurring infectious disease events and intentional bioterrorist acts, to highlight the dual-use nature of the outcome from current anti-bioterrorism research [17].

Medical Education

Currently, there is no standardized curriculum for training of undergraduate and postgraduate medical students about the health hazards related to weapons of mass destruction. The range of knowledge regarding even general disaster medical care is also variable among most medical professionals. Pesik et al (1999) had developed a survey to ascertain whether any formal training in biological weapons was conducted in emergency medicine programs, to determine the overall subjective ability or to recognize and clinically manage casualties of biological weapons agents and to identify which resources might be used by emergency physicians to identify and treat biological warfare casualties [18]. The existing lacunae necessitates the urgent introduction of specific syllabi aimed at inculcating knowledge in medical students about bioterrorism.

Recommendations

The WHO has recommended that institutions must work together to strengthen the public health infrastructure, including specialist laboratories. Investment in the public health system is the best possible defence against any outbreak of infectious disease, whether natural or deliberate [19]. The following practical recommendations [3] emerge thus :

(a) The Armed Forces have contingency plans prepared in case of a deliberate release of biological or chemical agents against civilian and military populations. The plans should be consistent or integral with existing plans that address outbreaks of disease, natural disasters, large scale industrial or transportation accidents, and terrorist incidents. These plans need to be disseminated down to the peripheral level.

(b) Standard principles of risk-management should allow preparedness against deliberate releases of biological or chemical agents, starting with an assessment of the relative priority that should be recorded to such releases in comparison with other dangers to public health.

(c) A major contribution to preparedness can be achieved by strengthening public health infrastructure, particularly for public-health surveillance.

(d) Managing the consequences of a deliberate release of biological or chemical agents may demand more resources than are available. International assistance could become essential, and such channels should be identified.

Conclusion

Underlying the concern about bioterrorism is the long history of the use of chemical and bilogical

weapons in war, which has been termed "public health in reverse". There have developed a number of initiatives, some of which, such as a worldwide surveillance program to detect the incidence and prevalence of infectious diseases, whether intentionally introduced, accidentally introduced, or naturally arising, would undoubtedly be useful in public health practice throughout the world. But other bioterrorism initiatives are more questionable. Before they are implemented by the public health community, such programs must be thoughtfully and scientifically examined in terms of their necessity, efficacy, safety, and cost. These initiatives may often divert resources from other, more urgently needed public health tasks. While working for adequate resources to prevent all infectious diseases, medical professionals must advocate solutions that "above all else, do no harm" [20].

In the final analysis, any comprehensive effort to recognize, characterize, manage, and prevent bioterrorism must involve interaction and cooperation between Clinicians, Pathologists, Microbiologists, and Public Health specialists [17]. They all play critical and complementary roles in recognizing and responding to illnesses caused by intentional release of biologic agents. Hence, the need of the present time, is a venture to combat the spectre of bioterrorism in an organized, comprehensive and sustainable manner, with all levels being kept informed of the same.

The statement by the World Health Assembly (1967) that "scientific achievements, and particularly in the field of biology and medicine - the most humane science - should be used only for mankind's benefit, but never to do it any harm" [21] remains as valid today as it was then. This stands out in stark contrast with the ideals of the perpetrators of bioterrorism and must remain as the guiding principle of the medical profession, in combating this newest affliction of humanity.

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