Contemproary Issue

Bioterrorism : A Public Health Perspective

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Abstract

The intentional release or threat of release of biologic agents (i.e. viruses, bacteria, fungi or their toxins) in order to cause disease or death among human population or food crops and livestock to terrorize a civilian population or manipulate the government in the present scenario of increased terrorist activity has become a real possibility. The most important step in the event of a bioterrorist attack is the identification of the event. This can be achieved by generating awareness, having high degree of suspicion and having a good surveillance system to assist quick detection.

Bioterrorist attacks could be covert or announced and caused by virtually any pathogenic microorganism. Bioterrorist agents of major concern have been categorized as A, B and C based on the priority of the agents to pose a risk to the national security and the ease with which they can be disseminated. The five phases of activities in dealing with a bioterrorist attack are preparedness phase, early warning phase, notification phase, response phase and recovery phase.

A bioterrorism attack in a public place is a public health emergency. Early detection and rapid investigation is the key to contain such attacks. The role of public health epidemiologist is critical not only in determining the scope and magnitude of the attack but also in effective implementation of interventions.

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Key Words : Bioterrorism; Anthrax; Botulism; Plague; Smallpox; Public health emergency; Category A, B and C agents

Introduction

The threat of biological warfare seems remote to most industrialized and developing nations. However, the threat of bioterrorism, in which biological agents are used by extremists as weapons against civilian populations, is a matter of concern. Nations and dissident groups exist that have both the motivation and access to skills to selectively cultivate some of the most dangerous pathogens and to deploy them as agents in acts of terrorism. Although a bioterrorist attack is difficult to predict, the consequences of a successful attack could be devastating and cannot be ignored.

Bioterrorism and its effects can impose heavy demands on the public health care system which will be called upon to handle the consequences. An effective public health care system with strong disease surveillance, rapid epidemiological and laboratory investigation, efficient medical management, information, education and communication (IEC) will be required to counter any act of covert or overt bioterrorist attack.

In India there has been no documented case of bioterrorism so far. For this very reason we need to know and learn about this form of terror before it becomes a formidable challenge to our public health system and the society [1].

Historical Perspective: The use of biological weapons has been reported as early as the sixth century B.C. when contamination of water supply with the fungus *Claviceps purpurea* (rye ergot) by the Assyrians had been reported. The hurling of the dead bodies of plague victims over the walls of the city of Kaffa by the Tartar army in 1346 and the spreading of smallpox via contaminated blankets by the British to the Native American population loyal to the French in 1767 are the most frequently cited episodes of poisoning [2]. In the recent past, mycotoxins (fungal toxins) were reported to have been used in Afghanistan in the form of what is popularly known as 'yellow rain'. The growth of religious cults and extremist political groups also increases the threat of bioterrorism today. The most significant biological attack in the United States (US) was the intentional contamination of restaurant salad bars with Salmonella by a religious cult in Oregon in 1984 [2].

In September 2001, the American public was exposed to anthrax spores as a bioweapon delivered through the US postal system. The centre for disease control and prevention (CDC) identified 22 confirmed or suspected cases of anthrax during this attack. These included 11

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patients with inhalational anthrax, of whom five died and 11 patients with cutaneous anthrax (seven confirmed), all of whom survived [2].

What is bioterrorism? Bioterrorism is the intentional release or threat of release of biologic agents (i.e. viruses, bacteria, fungi or their toxins) in order to cause disease or death among human population or food crops and livestock to terrorize a civilian population or manipulate the government [3].

Is bioterrorism a legitimate threat? Epidemics of plague in India, avian (H5N1) influenza in Hong Kong, ebola haemorrhagic fever in central Africa and Nipah virus (NiV) infection in Malaysia and Singapore required national and international response. During the plague and ebola investigations, concerns regarding possibility of bioterrorism were raised, though not supported by subsequent findings [4]. Investigations into these outbreaks has taught us a number of important lessons. The challenges posed by biological weapons are availability of multiple agents and delivery means, variable incubation periods, high mortality rates and potential for geographic dispersion of the agent (due to travel) during the incubation period. At times prompt identification or distinction between a bioterrorist attack and natural disease outbreak may be difficult. Many of the important prophylactic drugs/vaccines may not be available during a bioterrorist attack or have limited shelf lives and cannot be stockpiled. Even today, at least 17 countries are known to have a biological weapons program. Consequent to the collapse of the erstwhile Soviet Union, microbe stocks and technology appear to have passed into terrorist hands [5].

Bioterrorist attacks could be caused by virtually any pathogenic microorganism. However micro organisms (like virus, bacteria, fungi or toxins) to be effective as a bioterrorist agent should consistently produce a given effect, death or disease, at low concentrations. The agent should be highly contagious, have a short and predictable incubation period. The target population should have little or no immunity against the organism. The agent should be amenable to economic mass production, difficult to identify in the target population and little or no prophylaxis or treatment should be available with the native population.

The bioterrorist agents with highest priority are the causes of anthrax (*Bacillus anthracis)*, botulism (*Clostridium botulinum),* plague *(Yersinia pestis),* smallpox (variola major), tularaemia *(Francisella tularensis)* and viral haemorrhagic fevers (filoviruses and arena viruses). There are many other common foods or water-borne agents that could potentially be used in a bioterrorist attack [6]. The biological weapons as per the CDC classification are classified into three categories, Category A, B and C, as given in Table 1, based on the priority of the agents to pose a risk to the national security and the ease with which they can be disseminated [7]. The microbiological agents are listed in Table 2. Common signs, symptoms and clinical syndromes caused by bioterrorism agents are given in Table 3.

The routes of entry of biological weapons into the human body are mainly inhalation, contact (skin / mucous membrane) and the gastrointestinal tract. Methods of delivery could be through bomblets delivered by aircrafts or use of spray tanks mounted on aircrafts/ tall buildings. The agents of anthrax, plague, brucellosis, smallpox, viral encephalitides and viral haemorrhagic fevers can be aerosolized and distributed over large geographic areas. Other methods include delivery by post or by deliberate infiltration of infected animals, vectors and pests through the international border. In preparation against biological weapons attacks, newer methods for early detection/warning have been devised by certain countries e.g. the BioWatch program in the US, which uses a series of pathogen detectors colocated with air quality monitors. These detectors collect airborne particles onto filters which are later manually collected at regular intervals and analyzed for potential biological weapon pathogens using polymerase chain reaction (PCR) techniques. It is expected that this system will provide early warning of a pathogen release, alerting authorities before victims begin to show symptoms and providing the opportunity to deliver treatment earlier. However the deployment of such bioterrorism detection system may not be viewed as an appropriate response to the current threat [8]. In the

Table 1

Classification of agents of bioterrorism

Category A	Category B	Category C
High priority agents include organisms that pose a risk to national security because they are: • Easily disseminated • Cause high mortality • Cause public panic and social disruption • Require special action for public health preparedness.	Second highest priority agents include those that are: • Moderately easy to disseminate • Cause moderate morbidity • Require enhanced disease surveillance and public health diagnostic capacity	Third highest priority agents include emerging pathogens: • That could be engineered for mass dissemination in the future • Have potential for high morbidity, mortality and major health impact

Table 2

Agents of Bioterrorism

Category A agents	Category B agents	Category C agents
• Bacillus anthracis (anthrax) • Clostridium botulinum toxin (botulism) • Francisella tularensis (tularemia) • Variola major (smallpox) • Yersinia pestis (plague) • Filo viruses • Ebola virus (Ebola hemorrhagic fever) • Marburg virus (Marburg haemorrhagic fever) • Arena viruses • Junin virus (Argentinian haemorrhagic fever) and related viruses • Lassa virus (Lassa fever)	• Alpha viruses • Eastern and western equine encephalomyelitis viruses (EEE, WEE) • Venezuelan equine encephalomyelitis virus (VEE) • Brucella species (brucellosis) • Burkholderia mallei (glanders) • Coxiella burnetii (Q fever) • Epsilon toxin of Clostridium perfringens • Ricin toxin from Ricinus communis • Staphylococcal enterotoxin B A subset of Category B agents includes pathogens that are food or waterborne. These pathogens include but are not limited to: • Cryptosporidium parvum • Escherichia coli O157:H7 • Salmonella species • Shigella dysenteriae • Vibrio cholerae	• Hanta viruses • Multidrug-resistant tuberculosis • Nipah virus • Tickborne encephalitis viruses • Tickborne haemorrhagic fever viruses • Yellow fever

event of a bioterrorist attack the most important step is the identification of the event. The cause of a disease or even the occurrence of something unusual may be very difficult to determine, especially if the initial cases are few. Any small or large outbreak of disease should be evaluated as a potential bioterrorist attack. Doctors in hospital out patient departments (OPDs), private practioners and family physicians could play a vital role in the initial recognition of a potential bioterrorism attack. Familiarity with the infectious agents of highest priority can expedite diagnosis and initial management leading to a successful public health response to such an attack. The first to notice could be a hospital laboratory seeing unusual strains of organisms, an epidemiologist keeping track of hospital admissions or even pharmacists distributing more antibiotics than usual. A bioterrorist attack may be difficult to distinguish from a naturally occurring infectious disease outbreak. A single diagnosed or strongly suspected case of smallpox, inhalational anthrax, cutaneous anthrax (with no known risk factors compatible with naturally-occurring disease), viral haemorrhagic fever (in a patient with no international travel history) or more than one case of pneumonic plague, pneumonic tularaemia (with at least one laboratory confirmed case, no known compatible risk factors and occurring in a brief time period) or a higher than expected number of unexplained morbidity and mortality in a brief time period within a defined geographic region should point towards possibility of a bioterrorist attack [9].

Public health emergency preparedness and response to bioterrorist attack : The responsibilities of public health agencies are surveillance of infectious diseases, detection and investigation of outbreaks, identification of etiologic agents and their modes of transmission and the development of prevention and control strategies. The measures needed to prevent and control emerging infections are strikingly similar to those needed to check the threat of bioterrorism. Maintaining effective disease surveillance and communication systems are fundamental components of an adequate public health infrastructure. Ensuring adequate epidemiologic and laboratory capacity are prerequisites to effective surveillance systems. One approach to early detection is "syndrome surveillance", in which electronic symptom data are captured early in the course of illness and analyzed for signals that might indicate an outbreak requiring public health investigation and response. Syndrome surveillance has been used for early detection of outbreaks to follow the size, spread and tempo of outbreaks, to monitor disease trends and to provide reassurance that an outbreak has not occurred. Syndrome surveillance systems seek to use existing health data in real time to provide immediate analysis and feedback to those charged with investigation and follow-up of potential outbreaks. The model of large scale exposure to the agents of bioterrorism (by use of vaccines and antibiotics) has dramatic potential for saving lives and expense [10-12]. The public health approach to bioterrorism must begin with the development of local

Table 3

Clinical syndromes caused by bioterrorism agents [2,7,9]

Acute respiratory distress with fever	Acute rash with fever	Neurologic syndromes	Influenza like illness
i. Inhalational Anthrax. Abrupt fever, respiratory distress, chest pain. Widened mediastinum Gram +ve bacilli in sputum. Treatment is with Ciproflox 500 mg 12 hourly or Doxycycline 100 mg 12 hourly or Clindamycin 900 mg thrice daily for 60 days Prophylaxis post exposure: Ciproflox 500 mg 12 hourly or Doxycycline 100mg 12 hourly for 60 days. Anthrax vaccine	i. Small Pox Fever with papular rash that begins on the face and extremities and uniformly progresses to vesicles and pustules; Clinical with laboratory confirmation; Treatment: Supportive. Prophylaxis: Vaccinia immunization	i. Botulism Acute bilateral descending flaccid paralysis beginning with cranial nerve palsies. Electromyography (EMG): augmented muscle action potential toxin assays of serum, faeces or gastric aspirate can be done. Treatment: Supportive, Equine antitoxin. Prophylaxis: Administration of antitoxin.	i. Brucellosis Irregular fever, chills, malaise, headache and pleuritic chest pain. Gram-ve coccobacilli in blood / bone marrow culture. Serologic testing and culture available. Treatment: Intramuscular Streptomycin 750 mg to 1 g daily for 14 to 21 days with Doxycycline 100 mg 12 hourly for 6 weeks. Prophylaxis: Vaccines based on live attenuated *B. abortus* strain are of uncertain value.
ii. Pneumonic Plague: Severe Pneumonia, shock, hemoptysis, cyanosis, gastrointestinal symptoms Gram –ve bacilli/coccobacilli in sputum, other confirmatory tests. Treatment: Streptomycin intramuscular or intravenous 1.0 gm thrice daily or Doxycycline 100mg twice daily or Chloramphenicol 500 mg 12 hourly. Prophylaxis: Doxycycline 100mg 12 hourly. Formalin Fixed Vaccine.	ii. Viral Haemorrhagic Fevers Fever with mucous membrane bleeding, petechiae, thrombocytopenia and hypotension. Definitive testing available. Treatment: Supportive Ribavirin in recommended doses. Prophylaxis:Vaccine for yellow fever.	ii. Encephalitis (Venezuelan, Eastern, Western) Encephalopathy with fever and seizures and/or focal neurological deficits. Serologic testing available. Treatment: Supportive Prophylaxis: Attenuated cell-culture propagated live vaccine. TC-83 only partially effective.	ii. Tularaemia (Typhoidal, Pneumonic) Fever, chills, rigors, headache, myalgias, sore throat; Substernal discomfort, dry cough. Gram-ve bacillus in smears / cultures. Chest radiograph shows infiltrate/effusion. Definitive testing available, Treatment: Streptomycin 1 g 12 hourly for 14 days Prophylaxis: Doxycycline 100 mg 12 hourly for 14 days
iii. Ricin Aerosolized Fever, chest pain and cough progressing to respiratory distress and hypoxemia not improving with antibiotics. Chest radiograph shows Pulmonary Oedema, ELISA test on sputum or immunohistoichemical techniques for direct tissue analysis to confirm diagnosis. Treatment: Supportive. No antitoxin yet available. No Prophylaxis available.			iii. T2 Mycotoxin Abrupt mucocutaneous and airway irritation including skin (pain and blistering), eye (pain and tearing), gastrointestinal (bleeding, vomiting, and diarrhea) and airway (dyspnea and cough) Treatment: Supportive. No antitoxin yet available. Prophylaxis: No Prophylaxis available presently.
iv. Staphylococcal entrotoxin B Acute onset of fever, chills, headache, non-productive cough and myalgia with a normal chest radiograph. Profuse watery diarrhoea, if ingested. Enterotoxins may be detected in environmental samples using a variety of antibody-based tests. Treatment: Supportive therapy. No Prophylaxis available.			

and state-level plans. Close collaboration between the clinical and public health communities is also critical. To effectively respond to an emergency or disaster, health departments must engage in preparedness activities. Completion of the following five phases of activities prior to an incident are essential for successful response to a bioterrorist attack [13]:

(a) Preparedness phase: This phase includes

actions to be taken by different agencies to ensure required state of preparedness. These include evaluation of the laboratory facilities and upgrading the same, evaluating the hospital preparedness in emergency response and case management in case of an imminent attack, conduct training of health professionals, rapid response team (RRT) and quick response medical team (QRMT) who would be the first responders, work out the legal provision and their implications, ensure that requirement of safe drinking water is met, ensure availability of adequate stocks of medicines and vaccines, coordinate with security organization, organize mock drills for health professionals, government departments, animal husbandry, security, law enforcing and other agencies so as to assess their preparedness levels to act in case of an attack, prepare contact details so that communications is unhampered during an attack. Public should be kept aware about imminent attacks so that voluntary reporting is encouraged. It is important to carry out review of situation based on current information of threat perception.

(b) Early Warning Phase: The early warning in the surveillance system includes activities like case definitions, notification, compilation and interpretation of epidemiological data. Early detection and rapid investigation by public health epidemiologist is critical in determining the scope and magnitude of the attack and to implement effective interventions.

(c) Notification Phase: It is mandatory to report any unusual syndrome or usual syndromes in unusual numbers to appropriate authorities. The activities in this phase include rapid epidemiological investigations, quick laboratory support for confirmation of diagnosis, quarantine, isolation, keeping health care facilities geared for impending casualty management and evolving public health facilities for control.

(d) Response Phase: In this phase the activities include rapid epidemiological investigation, quick laboratory support, mass casualty management and initiation of preventive, curative and specific control measures for containing the further spread of the disease (Table 4). In order to achieve them, following steps can be followed:

(i) Assess the situation: Initiate the response by assessing the situation in terms of time, place and person distribution of those affected, routes of transmission, its impact on critical infrastructure and health facilities, the agencies and organizations involved in responding to the event, communicate to the public health responders, local, state and national level emergency operation centres for event management etc.

(ii) Contact key health personnel: Contact and coordinate with personnel within the health department that have emergency response roles and responsibilities. Record all contacts and follow-up actions.

(iii) Develop action plan: Develop initial health response objectives that are specific, measurable and achievable. Establish an action plan based on the assessment of the situation. Assign responsibilities and record all actions.

(iv) Implementation of the action plan: The RRTs/ QRMTs investigate the outbreak /increase in the disease incidence, collect samples and send it to the

Table 4

Epidemiologic response to suspected/confirmed bioterrorism events

The epidemiologic preparedness and investigation checklists may be useful in the epidemiologic response planning process:		
(a)	Confirmation	Specimens to be forwarded to a reference laboratory for laboratory confirmation
(b)	Notification	If disease scenario meets the definition for bioterrorism, local, state and central bioterrorism response partners will be notified, the RRTs/QRMTs will be activated and serve as the core epidemiologic rapid response team
(c)	Coordination	Several types of personnel may be required for the epidemiological investigation like interviewers, environmental health inspectors, disease control investigators, epidemiologists, data entry operators and data managers
(d)	Communication	Information from the outbreak investigation is communicated to other bioterrorism response partners
(e)	Epidemiological Investigation	1. Hypothesis generating interviews with the initial cases 2. Case definition based on initial hypothesis-generating interviews 3. Case finding by local and state public health officials through alerts to multiple potential reporting sources 4. Case interviews using a uniform questionnaire 5. Data analysis for epidemiologic investigation and contact tracing activities in a coordinated manner
(f)	Contact tracing	For diseases transmissible from person-to-person, all possible contacts are identified and interviewed All clinical and epidemiologic information is entered into a database All contacts are referred for vaccination, prophylaxis, isolation and/or quarantine as appropriate and kept under active surveillance
(g)	Laboratories	Questions regarding specimen collection, packaging, storage and shipment should be clear
(h)	Expanded surveillance	If the disease outbreak is thought to involve animals, public health officials from the vector borne / veterinary health will be informed
(j)	Overt or announced bioterrorism threat	This is guided by the intelligence and law enforcement agency which coordinates the epidemiologic investigation All information e.g. time, place, mode and/or contents of the release made available to public health personnel

identified state/national laboratory for testing. Hospitals are alerted for receiving the patients and their treatment. If necessary tented hospitals are set up. Methods to control the disease and quarantine measures are instituted. Once the disease is identified, treatment protocols are sent to all concerned by the fastest possible means. Standard operating procedures (SOP) for laboratory testing is made by the identified laboratory and the same is sent to all the hospital laboratories and district hospitals for implementation. Laboratory reagents are distributed to the concerned laboratories. Public is taken into confidence to prevent any panic. The list of 'Do's and Don'ts' are circulated thorough the print and electronic media. Hospitals ensure appropriate isolation, quarantine, waste disposal and personal protective measures. All contaminated clothing and equipment are carefully disposed of by incineration. An impact assessment team assesses the impact of the attacks on humans, animals and plants.

(e) Recovery Phase: The setbacks suffered as a result of the bioterrorist attack are restored and lessons learnt in this phase are incorporated in the future preparedness plans. The damage done to the public health facilities and the essential items utilized during the response phase are replenished. Public advisories are issued regarding restoration of normalcy. The RRTs compile and analyze data to identify the deficiencies experienced in the implementation of the response measures. The necessary modifications are then incorporated in the contingency plan for future [11].

Conclusion

Bioterrorism remains a legitimate threat both from domestic and international terrorist groups. From a public health perspective, timely surveillance, awareness of syndromes resulting from bioterrorism, epidemiologic investigation capacity, laboratory diagnostic capacity and the ability to rapidly communicate critical information on a need to know basis to manage public communication through the media are vital. Ensuring adequate supply of drugs, laboratory reagents, antitoxins and vaccines is essential. Formulating and putting into practice SOPs/ drills at all levels of health care will go a long way in minimising mortality and morbidity in case of a bioterrorist attack.

Conflicts of Interest

None identified

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