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Review Article

Biowarfare: Where do we stand?

Kalpita S. Shringarpure[1], Keyur Brahme[2]*

[1]Department of Preventive Medicine, [2]Department of Medicine, Medical College, Baroda, Gujarat, India

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***Correspondence:**
Dr. Keyur Brahme,
E-mail: keyurbrahme@gmail.com

ABSTRACT

Use of biological weapons has dated since times immemorial and the fear of such weapons in sync with the ever growing technology looms large on every part of the world. Biological warfare dates long back, when Hannibal first used the 'serpents' in earthen pots to be hurled against the enemy to sophisticated Biowarfare weapons such as *Bacillus anthracis* and *Pseudomonas pseudomallei*. To prohibit the use of such biological weapons, international treaties were prepared in 1925 and 1972; but to no avail. Many nations have stocked biological warfare agents, and there is possibility that terrorists may acquire the expertise to use these destructive agents. Advantages of Biowarfare agents are that they are produced rapidly, are cost-effective, can disseminate and affect a large area leading to high morbidity and mortality. With the upsurge in chances of biological warfare being used for defense or terrorism, there is a need for a robust surveillance system involving the health care sector along with integration of public health personnel, security, intelligence, diplomats and law enforcement agencies. Thus for the world, the time has come to establish a mindset to wage a war against this Biowarfare, try to discover newer antibiotics and personal protective equipment, acquire '*state-of-the-art*' detectors and focus on the available intelligence. Awareness among the public, clinicians and public health experts, stock piling of drugs and vaccines, allocation of funds and Biowarfare preparedness is the need of the day.

Keywords: Bioterrorism, Warfare, Biowarfare preparedness

INTRODUCTION

Well, this is '*the Fact'* in the context of bioterrorism or Biowarfare and not a mere nursery rhyme! The effectiveness of biological weapons is beyond question and the extent of their destruction unfathomable.[1,2] Use of biological weapons has dated since times immemorial and the fear of such weapons in sync with the ever growing technology looms large on every part of the world.[2,3] So much so, the depiction of biological attacks in fiction movies as well as books is well know.[4] This gives ground to the theory that biological pathogens can be used for increasing terrorism and warfare.[1,2]

***"Bacteriological warfare is science stood on its head…a gross perversion."*[5]**

Biological warfare dates long back, when Hannibal first used the 'serpents' in earthen pots to be hurled against the enemy in a naval battle. Disease organisms, poor sanitation, excreta, corpses of humans and animals being thrown in wells to pollute water etc. were the indigenous methods of Biowarfare used in ancient times (14th and 15th centuries). Small pox laden clothing and blankets were used/gifted during the French-Indian and revolutionary wars.[6]

Sophisticated Biowarfare weapons such as *Bacillus anthracis* (causative organism for anthrax) and *Pseudomonas pseudomallei* (causing glanders in animals) were used in the 1900s. Attempts to spread cholera and plague were also rampant during the World War I era.

Contaminated rice and fleas being used to spread bubonic plague were also used by the Japanese against the Soviet Union and Mongolia during the World War II era. Prisoners of war were used as 'guinea pigs' for experiments with agents leading to anthrax, botulism, brucellosis, cholera, dysentry, gas gangrene, meningococcal infection, and plague.[1-3,6]

In order to prohibit the use of such biological weapons, international treaties were prepared in 1925 and 1972. Initially viruses were not differentiated from other bacteria, hence were not specifically mentioned, which was later taken up as an addendum. The Geneva Protocol of 1925 was signed by 108 nations. In 1972 Convention on the Prohibition of the Development, Production, and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, i.e. the Biological Weapons Convention was convened and signed by 103 nations. However, the functionality of these weapon control agreements is still doubtful, with several countries being involved in suspicious Biowarfare research and experimentation.[1] The Ricin toxin incident in 1978 and the mysterious anthrax explosion in 1979 are proof of this.[1,7-9]

Iraq, in 1991 admitted to conducting research into the offensive use of *Bacillus anthracis*, botulinum toxins, and *Clostridium perfringens.*[10] Letters containing anthrax bacilli were sent in the wake of the September 2001 terrorist attacks on the United States. Sex terrorist suspects were arrested in December 2002 in England (Manchester) as they had a stock of ricin in their laboratory. Arrests were made in January 2003 by the British police for a possible Chechen plan to attack the Russian embassy. In February 2004 ricin toxin was found in a mailroom that serves Senate Majority Leader's office.

Based on the history of biological warfare, it can be concluded that any microorganism (such as bacteria, viruses, or fungi) or toxin (poisonous compounds produced by microorganisms) found in nature can be used as a biological agent to cause biowarfare. These could be used as a hoax most of the times, but are often seen to be put in actual use. Many nations have a store or aspire to have biological warfare agents that may be acquired by terrorists and put to use for mass destruction. The long term adverse effects of these agents also act as a plausible threat.[11]

Since there are several emerging infectious diseases over the world, all the developed as well as developing countries like India need to ensure that these bioterrorist attacks do not get masked as natural disease outbreaks or outbreaks of unknown origin, or classified as an emerging infectious disease.[12]

There are more than 12,000 agents that could be used for Biowarfare, of which relatively lesser numbers possess the ideal characteristics of incapacitating or killing people in large numbers.[11] Using these agents is easy due to open information available on how to develop and use them. Biological warfare weapons against humans should thus have characteristics of high infectivity, high virulence, non-availability of vaccines and availability of an effective and efficient delivery system. They are required in small amounts for effect and their small size would help make their concealment and transportation easier. The agent should also be able to retain the infectivity and virulence for a long duration. There should be a possibility to control the spread of the agent.[11]

Modern day Biowarfare or germwarfare can be categorized as offensive, anti-personal, anti-agriculture, anti-crop, anti-vegetation or anti-fisheries, anti-livestock, entomological biowarfare and defensive. The biological weapons may backfire and harm the offensive groups, such as small pox and other airborne viruses may affect the home country also.[11] These agents could also incapacitate or harm the person who has it in his charge or can harm agriculture, crops, vegetation, livestock and the target against whom the agent is prepared. Entomological warfare; using insects to harm the enemy viz. plague, bees, wasps etc has been in use since antiquity till the modern times.[1,6]

Advantages of Biowarfare agents are that they are produced rapidly, are cost-effective, can disseminate and affect a large area leading to high morbidity and mortality; with easy person-person transmission. The additional psychological havoc and panic is also an asset. One can cite the hoax call of bioweapons being horded by Iraq which lead to its destruction by the US, solely because of the panic it caused in such a huge powerful nation!

The centers for disease control and prevention (CDC) developed a ranking system for potential biological agents based on the level of morbidity and mortality associated with a disease, delivery potential of the disease, public perception (certain diseases generate greater fear and civil disruption) and public health preparedness needs, such as needs for vaccine or mass chemoprophylaxis (preventive treatment).

With the upsurge in chances of biological warfare being used for defense or terrorism, it is necessary to prepare the countries for the surveillance of such attacks. Most of the classical as well as modern weapons and pathogens can be derived from plants or animals who in turn are naturally infected.[13]

There is a need for a robust surveillance system involving the health care sector especially the clinicians, public health experts and veterinarians. They could help early identification of the attack of bio-weapons and help differentiate it from outbreaks and epidemics.[14] Thus, it could help provide prophylaxis to the exposed people and prevent serious illness in them. In case of anthrax, those small percentage of people who are exposed to large

toxic dose of organisms or are prone to illness due to immune-compromised status may be identified early through virtually unique x-ray findings, and other people may be averted from getting the disease by prophylactic antibiotic treatment.

It is necessary to be aware of common epidemiological clues that may herald a biological attack.[15] These include the following features to be kept in mind; such as

1. There may be a single cause of a certain disease caused by an uncommon agent. There may not be a plausible epidemiological explanation to this.
2. Genetically engineered agent.
3. High morbidity and mortality rates with the same or similar symptoms.
4. Unusual or abnormal disease presentation or geographic or seasonal distribution.
5. Disease, though endemic, but increasing in relevance.
6. Rare transmission (aerosols, food, water).
7. Common ventilation system being a cause of disease spread; co-existence of various diseases in the same patient.
8. Rare illness affecting large population or certain age-group; with unusual trends of mortality or morbidity.
9. Clustering of cases for treatment, genetically similar agents being identified.

Thus, any Biowarfare or potential outbreak can be diagnosed clinically, epidemiologically or through laboratory investigations.

Along with this, strengthening biodefense to improve and integrate the efforts of health care providers and public health personnel along with security, intelligence, diplomats and law enforcement agencies is the need of the day. With this, efforts could be made to develop newer tools to address current and future destructive, deliberate biological weapons. To this day, there are tools to perform on the spot analysis and identification of encountered suspect materials, such as *'sandwich immunoassay'* wherein the fluorescent dye-labeled antibodies are attached to silver and gold nanowires, that help to identify pathogens.[16] The Netherlands has designed Bioaerosol Single Particle Recognition eQuipment (BiosparQ), which will be implemented into the national bioweapons response plan.[17] A lab-in-a-pen device called as the BioPen can detect biological agents in 20 minutes, which is a fiber optics ELISA.[18] Thus, the world has the capability to fight against the newer biological agents which could be biologically synthesized.

However, there is a possibility of newer novel Biowarfare agents which could play with the genetic makeup (Genetic Biowarfare) and have the capacity to render a vaccine ineffective; confer resistance to therapeutically useful antibiotics or antiviral agents; enhance the virulence of a pathogen or render a non-pathogen virulent; increase transmissibility of a pathogen; alter the host range of a pathogen; enable the evasion of diagnostic/detection tools and enable the weaponization of a biological agent or toxin.[19-21]

Thus, there are those who say that

'*The first world war was chemical, the Second nuclear and the Third, God forbid, will be……..biological'*[22]

We could have a 'sword-for-a sword' technology, wherein novel biotechnology measures

could be taken in future**.** This *'black biology'* would focus on DNA synthesis and risk of producing genetic lethal material from viruses.[22-24] However, there is a CRISPR/Cas system which speeds up time to weeks in order to edit gene sequences, which is considered to be the most important innovation in synthetic biology.[13]

Early detection of biological agents helps early diagnosis and prompt action along with specific treatment. It gives a lead time to treat those who are exposed but not yet having any signs or symptoms. Important role of doctors is to identify early symptoms, victims and a possible biological warfare based on the unusual symptoms and patterns. These should be promptly reported to public health officials for rapid response and mitigation.[11]

Thus for the world the time has come to establish a mindset to wage a war against this Biowarfare, identify personnel, try to discover newer antibiotics and personal protective equipment, try to acquire '*state-of-the-art*' detectors. It is necessary to focus on the available intelligence and strengthen co-ordination among different forces in league with the Center for Disease Control (CDC) and the United Nations (UN). A task force should be kept ready to identify control and handle the Biowarfare, if it ever occurs. Along with this, awareness among the public and clinicians and public health experts, stock piling of drugs and vaccines, allocation of funds for the same and Biowarfare preparedness is the need of the day.[25,26]

"...the intentional release of an infectious particle, be it a virus or bacterium, from the confines of a laboratory or medical practice must be formally condemned as an irresponsible threat against the whole human community."[27]

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