# Challenges in Bio-Defense for India-A Plausible Approach

**Rakesh Bhargava**
Scientist, Defense R & D Establishment, Jhansi Road, Gwalior-474002, India

## Abstract

This review deals with aspects of bioterrorism with respect to bare minimum preparedness to tackle impending danger. The risk posed by various microorganisms as biological weapons or disease proliferating agent needs to be evaluated constantly and mode of their altered characteristics better understood. As these agents, may be present in a naturally occurring or as human-modified form when made to spread. Health care centers and public health officers are among the first lines of defense. The goal of biodefense should be to integrate the efforts of the national and state level medical services, public health, intelligence, and law enforcement communities of the country to provide layered defenses against any possible biological weapons attacks. A coordinated approach towards newer methods of early detection, faster diagnostics, newer drug discovery, and communication between biodefense agencies is required as counter measures.

## Introduction:

During the last 40 years or so, the progress made in biotechnology and genetic engineering has simplified the development of biological warfare agents and their weaponization. Development in technology allows even small groups to organize, and fund themselves. Coupled with desire to dominate and influence politically motivated objectives, sporadic use of biological agents by select groups acquires an ominous position. The threat of bioterrorism is real and significant in the present scenario. It can occur anywhere and at any point of time [1-4]. Despite a small number of incidents and casualties, bioterrorism has been identified as a major threat to public health and security [5]. Biological warfare is the use of microbial form of life to diminish the capabilities, disrupt the organization and terrorize (bioterrorism) the non-combatant population of an adversary [6,7]. A biological weapon has the potential to cause massive loss of human life, evoke fear and panic across any nation. Effects of bioweapon are extremely difficult to detect, as they are, surreptitiously used and could mimic naturally

-occurring diseases. As a result, these can be detected only after a considerable damage is noticed. It is understood, that biological warfare agents can be more potent than the conventional and chemical weapons in causing collateral damages, as humans are susceptible to microbial infections from many sources [6,8,9].

Bioterrorism is terrorism involving the intentional release or dissemination of bacteria, viruses, or toxins. These agents may be in a naturally occurring or a human-modified form [3,10,11]. This form of warfare has been used throughout history and has gained renewed interest with the current use of asymmetrical warfare. It is thus no surprise that, Governments across the world are preparing to counter a potential future thread in the

form of bioterrorist attack. The risk posed by various microorganisms as biological weapons needs to be evaluated and the historical development and mode of their usage better understood. It is said that Panic is unwarranted, but complacency would be imprudent. Advances in the biotech sector and shifting terrorist tactics that focus on disrupting India's social cohesion and economic prosperity oblige scientific community to look at the possibility of such attacks [12,13].

There are certain factors that make India susceptible to such threats. India is endowed with good rain fall as well as on an average 300 days of sunshine. These factors make the climate hot and humid and ideal condition for the growth of biological agents. The plethora of indigenous highly pathogenic and virulent agents naturally occurring in India due to large cattle, poultry population and water locked agriculture fields combined with poor-hygiene-habits make India a source of bioterrorism scourge if targeted. In addition, India's relatively weak public health system (on an average, a single Government doctor serves more than 12,000 people in India), coupled with high population density and their movement across the country means that a deliberate release of a disease-causing agent could go undetected and spread quickly for quite a while before authorities become aware [14,15].

Literature is replete with excellent reviews, reports and scientific studies on topics related to bioterrorism and Biodefense [1-3, 6-8, 16-18]. However, only a few articles have been devoted to India and India like scenario with respect to this man-made terror [12,13]. The present article deals with a common rationale that bioterrorism is inevitable and continuous vigil is needed. India should take advantage of its highly developed biotechnology field, research institutes and a chain of veterinary colleges in putting a continuous vigil against any such eventualities.

History of bio-warfare:

History has always been a good teacher for all those who really wanted to learn from the past. The history of use of biological weapons for terror is ancient and weird. A brief of events related to biological warfare is given below[6,16-18].

Assyrian politicians dumped fungus from rye into their opponents′ wells, giving them fatal ergot poisoning in 650 BC. ; Armies besieging a town relied on increased disease among the defending population and threw dead animals into water supplies, to spread it in Tortona, Italy. ; Tatars of the 14th century spread bubonic plague by catapulting diseased corpses into towns of Caffa and Crimean.; Spanish mixed wine with blood of leprosy patients to sell to their French foes in Naples in 1495.; Russian troops catapult human bodies of plague victims into Swedish cities around 1710.; In 1767 British distributed blankets from smallpox patents to native Americans loyal to French.; Napoleon flooded the plains around Mantua, Italy ,to enhance the spread of malaria.

Use of biological warfare became sophisticated during the 19th century. During 1863 confederates selled clothing from yellow fever and smallpox patients on to Union troops during the US civil war. The conception of Koch's postulates and the development of

microbiology during the 19th century made possible the isolation and production of stocks of specific pathogens. Substantial evidence suggests the existence of an ambitious covert biological warfare program in Germany during World War I. Biological agents like glanders and anthrax were used during World War I by German and French armies. It is alleged that Germans shipped horses and cattle inoculated with disease-producing bacteria, such as *Bacillus anthracis* (anthrax) and *Pseudomonas pseudomallei* (glanders), to the USA and other countries [16,17]. The same agents were used to infect Romanian sheep that were designated for export to Russia. Allegations of attempts by Germany to spread cholera in Italy and plague in St. Petersburg in Russia were reported. Germany, however denied all these accusation that biological bombs were dropped over British positions. During World War I, United States and Germany developed biological weapons to contaminate animal fodder.; In Cold War, United States and Soviet Union created arsenals of biological agents for use in battle and against civilian populations.; Dr. Anton Dilger worked with cultures of anthrax and glanders, between 1915 and 1916, with the intention of biological sabotage on behalf of the German Government.

During WW II, some of the countries involved in WW I(like Germany, UK, Japan Canada and Soviet Union), begun a rather ambitious biological warfare research program and employed hundreds of scientific workers on animal and crop disease, foot and mouth disease, Anthrax and like) [17-18]. Besides these recorded incidences, there were secret research programs that were underway in many countries.

Modern bioterrorist incidents include the followings,

In 1984, pseudo-Buddhist Rajneeshee cult distributed Salmonella in restaurants and grocery stores in Oregon to poison civic leaders and gain control of the local Government. In 1992, Russia had the ability to launch missiles containing weapons-grade small pox. A number of terrorist organizations, including Al-Qaeda, have explored the use of biological agents[19].

Psychological implications of biological weapons

Besides being lethal, psychological impact of bioweapons is equally damaging and long lasting. The impact has been categorized as Horror , Panic, Fear of invisible agents, Anger at terrorist, government or both, Attribution of arousal symptoms to infection, Paranoia, Social isolation , Demoralization and Loss of faith in social institution [20].

Defense against Bioterrorism:

Threat Awareness, Prevention and Protection, Surveillance and Detection, and Response and Recovery are perhaps the essential pillars of defense against any bioterrorism.

Threat Awareness:

Theoretically, speaking, biological agents are ideal agents to be used as weapons of mass destruction. However, all microbes cannot be used as weapons. Several characteristics are

required to make an organism an ideal candidate that can be used as a potential weapon of mass destruction or bioterrorism. These pertain to virulence, infectivity, lethality, ease of production, stability in environmental conditions, and post-dissemination retention of features, availability of a susceptible population and lack or inadequacy of tools to prevent or treat the disease. While many thousands of toxic chemicals and hundreds of pathogenic microorganisms have been investigated for their potential utility as military weapons, relatively few, around 40, have been found capable of meeting military requirements. Naturally occurring microorganisms or toxin products with the potential to be disseminated to cause mass casualties have been categorized by CDCP as follows.

Bioterrorism Agent Categories

Bioterrorism agents can be separated into three categories according to CDCP guidlines, depending on how easily they can be spread and the severity of illness or death they cause. Category A agents are considered the highest risk and Category C agents are those that are considered emerging threats for disease.

*Category A*

These high priority agents include organisms or toxins that pose the highest risk to the public and nationalsecurity because:

· They can be easily spread or transmitted from person to person
· They result in high death rates and have the potential for major public health impact
· They might cause public panic and social disruption
· They require special action for public health preparedness

(Small pox, Anthrex, Plague, Tularaemia, Botulinum, Haemorrhagic viruses.etc)

*Category B*

They require specific enhancements of CDC's laboratory capacity and enhanced disease monitoring.

· These agents are the second highest priority because:
· They are moderately easy to spread
· They result in moderate illness rates and low death rates

*(Coxiella burnetti*, *Brucella* species, *Burkholderia mallei*, Epsilon toxin (*Cl perfringens), Staphylococcus* enterotoxin B, Food or waterborne agents(*Salmonella, Shigella, etc)*

*Category C*

These third highest priority agents include emerging pathogens that could be engineered for mass spread in the future because:

· They are easily available
· They are easily produced and spread
· They have potential for high morbidity and mortality rates and major health impact.

**(**Nipah virus, Hanta viruses Tickborne hemorrhagic fever viruses, Tickborne encephalitis viruses, Yellow fever virus, Multidrug resistant M, tuberculosis

Enhanced Agents
These agents can be prepared by using traditional agents that have been modified or selected to enhance their ability to harm human populations or circumvent available countermeasures. They are, drug-resistant pathogens such as extensively drug-resistant (XDR) TB or multidrug-resistant (MDR) plague.

Emerging Agents
These are unrecognized pathogens that might be naturally occurring and present a serious risk to human populations. Diagnostic tools to detect these agents are needed. Example: Severe Acute Respiratory Syndrome (SARS) or avian influenza.

Advanced Agents
Novel pathogens or other biological materials that have been artificially engineered in the laboratory to bypass traditional countermeasures .

New highly fatal diseases have emerged or reappeared during the last 4 decades such as severe acute respiratory syndrome (SARS) [21], *Legionella* [22], hantavirus pulmonary syndrome (Sin Nombre virus)[23], Nipah virus encephalitis [24], avian influenza [25], West Nile encephalitis [26] and Rift Valley fever with adverse global or regional public health and economic impact [27]. Most emerging infectious diseases are the result of epizoonotic transmission from animals to man [28].

Indian Scenario

The goal of biodefense should be to integrate the corrodinated efforts of the national and state level medical services, public health, security, intelligence, and law enforcement communities to provide layered defenses against biological weapons attacks. Health care centers and public health officers are among the first lines of defense. Following are some of the basic points to be considered while dealing with biodefense strategies.

Over the years India has build a comprehensive three tier network of Sub-centres (SC), Primary Health Centre (PHC) and Community Health Centres (CHC) to take care of health of the population. These Health centers are the cornerstone of rural health services in India. SCs are the most peripheral and first contact point between the primary health care system and the community. One SC is to cover a population of 3000 in hilly/tribal region and 5000 in plains. PHC can take care of 20,000 to 30,000 population and CHS about 80,000 to 1,20,000 people. There are 23673 PHCs functioning in India as on March 2010 . The number of PHCs functioning on 24x7 bases is 9107. PHCs are the cornerstone of rural health services- a first port of call to a qualified doctor of the public sector in rural areas for the sick and those who directly report or referred from Sub-Centres for curative, preventive and promotive health care[14,15.] There are a number of excellent national research centres, state and university level microbiological laboratories in India which can act as sources of generalized as well as specific centres to monitor, collect and feedback the data related to any sign of disease out brake or bioterrorism related activities. The work domain of these microbiological centres can be expanded to work on genomic and proteomic data collection and analysis of microbes that can be used by

bioterrorist agents by sequencing the genomes of select organisms and strains. Some centres can be developed as central bioinformatic resources or for rapid use of genomic information. Cental universities can further expand basic research opportunities on microbial physiology, ecology, molecular pathogenesis, and animal model development for Category A, B, C, and D organisms. Early detection of microbes from environmental samples on continual basis is the need of the hour for any country including India.

A national communication network of above health and research centres may be created to work in a coordinated and tandem manner. Information regarding any disease outbreak within the country can be communicated via these centres. It is important to note that all of the classical and modern biological weapons organisms originate from animal diseases, the only exception being smallpox. Thus, in any use of biological weapons, it is highly likely that animals will become ill either simultaneously with, or perhaps earlier than humans [30 ]. A biological emergency may not be noticed until health care workers find a pattern of illness. Thus timely intra communications between these health centers are crucial and important in containing the spread of any outbreak. They can also serve as centers of surveillance. Subsequently, local or state officials will let know the masses, what symptoms to look for any diseases on the television, radio and Internet.

The preparedness against a bio-attack can be treated both as an opportunity as well as a threat. The impending danger of this type of attack makes one fully prepared by enhancing the existing public health activities. The spinoffs of the work on other diseases can be a substantial input towards the biodefence. Even if a bioterrorist incident never occurs, it is argued that such programs will boost public health by developing the infrastructure, human capital, and technological resources necessary for responding to naturally-occurring outbreaks of infectious disease and other public health problems. The surveillance system can be further improved by roping in the private medical and bio-medical institutions to the network. Basic and translational research into the biology and disease-causing mechanisms of pathogens is critical to any efforts to develop interventions against bioterrorism. Such research includes identifying and understanding the microbial components that define a pathogen's life cycle, transmission, virulence, and invasiveness. It is felt that with the current network of biological and medical institutions no new agencies may be required to tackle such threats immediately provided that the existing ones become proactive, prompt and professional in day to day surveillance activity.

Although India over the years, remained a major supplier of doctors and nurses to the developed countries the domestic scenario looks bleak. India ranks 67 among the developing countries in terms of doctor-population ratio. The total number of registered allopathic doctors in the country is 5.5 lakhs. The doctor-population ratio comes out to be 1:2000 (Approximately). There are around 3.72 lakhs nurses in the country and the nurses-population ratio approximately comes to 1:2950. Since majority of these doctors and nurses opt for Hospitals and clinics run by private organizations, there is a shortage of doctors who serve in rural population As a result on an average; a single Government doctor serves more than 12,000 people in India [14,15].

Indian climatic condition becomes suitable and congenial for bacterial growth in certain period of the year. Coupled with high population density, lack of proper sanitation and casual approach towards cleanliness makes the subcontinent a hot bed for the spread of diseases. This means that a deliberate release of a disease-causing agent could go undetected and spread quickly for quite a while before authorities could differentiate between the cause i.e. natural or man-made agents.

Development of novel agents previously unknown to the medical community would yield BW agents that are difficult to diagnose and treat. Unusual clinical presentation could allow a biological warfare attack to be misdetected as a natural outbreak and remain undetected. Advanced agents could be developed to circumvent vaccines or treatments designed to counter traditional agents. It is feared that agents could be tailored to target a specific population based on genetic or cultural traits. Sterilizing, oncogenic (cancer-causing), or debilitating agents could be created for use as a strategic bio-weapon against a target population for long-term effects (31-34].

Prevention of possible Bio-terror attack

The goal of biodefense has to integrate the sustained efforts of the national and state level medical facilities, public health, intelligence, and law enforcement communities. Health care providers and public health officers are among the first lines of defense. In some countries private, local, and state capabilities are being augmented by and coordinated with central assets, to provide layered defenses against biological weapons attacks. It is perceived that most likely attacks can be on high density population metros, where person to person contact on day to day basis cannot be avoided. Thus transmission becomes fast and widely spread. Therefore efforts should be directed to promote development of next-generation systems for environmental detection, medical diagnostics,prophylactics, and therapeutics. while we should continue to pursue avenues of prevention, including multilateral cooperation under the biochemical weapons conventions, we must develop stronger forensics that could track bioweapons back to their source. Most important, we must use technology to build the preparedness needed to protect civilian populations.

It is recommended to promoting scientific exchange and collaboration in the following areas. Developing and improving drugs and other prophylactics (vaccines, serums, bacteriophages, immunomodulators), new methods of diagnostics, drug discovery, detection, and decontamination. Developing aerosols especially as anatoxins and vaccines in emergency situations, e.g. to fight avian flu. Finding faster and standard methods of disinfection, against, anthrax and other dangerous infections [35,36]. Development of early and sensitive detection methods using multi-sensing reagentless biodetection systems is needed. Use of instrumental techniques like Raman, Mass spectroscopy, TIRF and other spectral methods for robust biodetection will enhance the preparation for detection of bioagents. Use of nanotechnology and other system to miniaturize the biosensors for the detection of bioagents is required. Easy-to-use devices for the detection of air, soil, water, and food-borne pathogens, without PCR is required. Rapid and sensitive detectors for bioagents at low resource conditions need to be developed. DRDO has patented a cell growth media that eliminates the use of FCS, a

costly and ethically questioned component of the cell media. This critical component of the cell culture media eliminates the requirement of ultra low temperature for the preservation of FCS. The alternative component is highly cost effective and addresses the ethical issues associated with FCS [37].

## Conclusion

Currently, bio-defense is challenged by the continuous bio-engineering of newer agents by many developed countries. Absence of real-time environmental detectors for biological agents is of concern to all. Detection systems currently under development focus largely on detecting hazardous bioaerosols by size, antigen recognition, or nucleic acid sequence. A number of technical considerations must be addressed regarding sensitivity, selectivity, specificity, and methodology for rapid and accurate detection of these bioagents. Developing a set of programs for training medical personnel, administrators and governmental bodies on regular basis on their roles in handeling such emergencies will go a long way for biodefense.

## Acknowledgements

The author sincerely thanks Director, Defence Research and Development Establishment (DRDE), Gwalior for encouragement and support. The author thanks Dr R.S. Chauhan, IDST Scientist, DRDO for motivation and inspiration to review the topic.

## References

1. Hust JA, Burgis NE (2013) Current trends in Bioterrorism and Biodefence. 53: 2156-2526.

2 Petro JB, Plasse TR, MsNully JA (2003) Biosecurity and Bioterrorism: Biodefense strategy practice and science. 1 (3) 161-168.

3 Gifhy I (2001) Bioterrorism by Biotechnology : Imprecations for clinical medicine: Encyclopedia of life support system {EOLS55)

4 Hugh-Jones ME, Rosenberg BN, Jacobsen S (2011) The 2001 attack of Anthrax. J. Bioterr. Biodef. 83.

5 Simon JD (2011) Why the Bioterrorism Skeptics are wrong. S2-001

6 Loike JD, Fiscibach RL (2013) Ethical challenges in Biodefense and Bioterrorism. Bioterrirism and Biodefense S12-002.

7 Powers JI, Ban Janathan (2002) Bioterrorism: Threat and preparedness. Engineering and household security. Springer USA.

8 Infectious disease (2010) Ed Jonathan Cohen, Steven M .pal and William G powderly, Elsevier USA.

9 Thursz M (2000) Genetic susceptibility in infectious diseases: Biotechnol Genet. Eng Rev. 17: 253-264.

10 Bioterrorism and infectiojus agents: A new dilemma for 21st century ed I W Fing, Kenneth Alibek Springer Science and Buoners media Inc NY 2005.

11 Bell P (2004) Synthetic biology: Starting from scratch. Nature. 431: 624-626

12 Bioterrorism: A public health perspective Medical Journal And Fores India 2010 r01-66 255-260 Das S kataria Vis

13 Plianbangchong S (2005) Strategies of preparedness against the threat of biological warfare and bioterrorism in South-East Asia. Asion Biotechnology &Development Review 8: 77-98.

14 Human Resourses for Health in India Tech Rept. 1: 2008.

15 Assocham Emerging Trends in health care- A journey from Bench to Bedside Feb. 2011 New Delhi

16 Eitzen EM Jr, Takafuji ET (1997) Historical overview of biological warfare. Medical aspects of clinical and biological warfare. (Eds) Sidell Fr, Takafuji ET Franz DR , Washington DC 415-423.

17 Christopher GW, Cieslak TJ Pavlin JA Eitzen EM (1997) Biological warfare A historical prespective. JAMA 278: 412-417.

18 Stefgan F (2004) Biological Warfare and Bioterrorism - A historical Review: Proc (Boys Univ Med Cent) 17 (4): 400-406.

19 David A Relman(2006) Bioterrorism – Preparing to fight the next war., N Engl J. Med, 354: 113-115.

20 Bhui KJ, Dinos S, James E (2012) Psychological process and pathways to radicalization. J Bioterror Biodef. S5: 003.

21. Drosten C, S Gunther, W Preiser, S van der Werf, HR Brodt, et al. (2003) I dentification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 348: 1967-1976.

22. McDade JE, CC Shepard, DW Fraser, TR Tsai, MA Redus, et al. (1977) Legionnaires' disease: isolation of a bacterium and demonstration of its role in other respiratory disease. N Engl J Med 297: 1197-1203.

23. Duchin JS, FT Koster, CJ Peters, GL Simpson, B Tempest, et al. (1994) Hantavirus pulmonary syndrome: a clinical description of 17 patients with a newly recognized disease. The Hantavirus Study Group. N Engl J Med 330: 949-955.

24. Flick R, P Walpita, M Czub (2005) Nipah and Hendra viral infections, in Tropical Infectious Diseases: Principles, Pathogens and Practice. Churchill Livingstone (Elsevier): Philadelphia: 586-589.

25. Beigel JH, J Farrar, AM Han, FG Hayden, R Hyer, et al. (2005) Avian influenza A (H5N1) infection in humans. N Engl J Med 353: 1374-1385.

26. Murray KO, E Mertens, P Despres (2010) West Nile virus and its emergence in the United States of America. Vet Res 41: 67.

27. Breiman RF, B Minjauw, SK Sharif, P Ithondeka, MK Njenga (2010) Rift Valley Fever: scientific pathways toward public health prevention and response. Am J Trop Med Hyg 83: 1-4.

28.Jones KE, NG Patel, MA Levy, A Storeygard, D Balk, et al. (2008) Global trends in emerging infectious diseases. Nature 451: 990-993.

29. Simon JD (1997) Biological terrorism: Preparty to meet the threat. JAMA 278: 428-430.

30. Roffey R, Lantoop K, Tegncll A, Elgh F (2002) Biological weapons and bioterrorism preparedness: Importance of public health awareness and international co-operation. 8: 522-528.

31Biodefense: Principles and pathogens Ed Michal S Bronze C Ronald A Geefield, 2005. ISBN 1-9094933-12-2

32. Kadlee RP, Zelicoff AF, Vrtis AM (1997) Biological weapon control. Prospects and implicationsfor the future. JAMA. 278: 351-352.

33. Bigalke H, Rummel A (2005) Medical aspects of toxin weapons. Toxicology. 214: 210-220.

34.Biodefense Research methodology and animal models. Ed by James R Snearengen. CRC Press Boca Rwton USA 2012.

35. Rose LJ, Rice EN, Jenson B, Muoga R, Peterson A, Darkan RM, Ardenno MJ (2005) Chlorine inactivation of bacterial bioterrorism agents. Appl. Envr. Microbiol.71L: 566-568.

36. Frowde JW, Stiles B, Pelat T, Thuliler P (2011) Antibodies for Biodefense. 3: 1-11.

37. Bhargava R, Chauhan R S, Shekhar K, Rahman Md,S (2012) A medium for cell culture. PCT /IB2007/003188.