Policy

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# Biothreat & One Health: Current scenario & way forward

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**There is an increased connectedness among humans, animals, and the environment and the current pandemic has taught the interlinking of the health of humans, animals and the planet. This inter-connectedness and factors like population growth, migration, urbanization, and climate change contribute significantly to the enhanced probability of emergence of previously unknown wildlife source pathogens at any place, any time, and without warning. Lurking in the background is the massive potential for the deliberate use of biological agents as weapons by State or non-State entities. Biological weapons have been used in wars since antiquity, however, newer research and techniques have led to these being real threats with a vast potential of harm to humans, animals, and crops. Over a period, it has become increasingly difficult to differentiate between deliberate and natural biothreat incidents. The response to both types is alike to safeguard lives, livestock, crops and the environment and reduce the consequent socio-economic ramifications. Biothreat may be targeted towards humans, animals, or crops, or all these concurrently. Every country including India is at risk of biothreat. The concept of one health is thus essential for responding to emerging infectious diseases or biothreats. Comprehensive surveillance for early detection, reporting and early concerted action is needed for prevention and blunting the effect of biothreats, which require close coordination and collaboration among various stakeholders within each country as well as globally.**

**Key words** Bioterrorism - biothreat - One Health

Severe acute respiratory syndrome (SARS, 2003), the first novel pandemic of the current millennium, demonstrated the possibility of the emergence of previously unknown wildlife source pathogens at any place, any time, and without any warning[1]. Alas, the appropriate lessons were not learnt. The measures to prevent and control such occurrences in the future are inadequate, as exposed by the current pandemic of SARS-CoV-2, which has adversely affected society's social, economic, and cultural fabric around the globe. There have been ample warnings in the recent past like the spread of highly pathogenic pandemic H1N1 influenza in 2009, influenza H7N9 in 2013, Middle East respiratory syndrome coronavirus (MERS-CoV), Zika, and Ebola[2].

All three coronavirus epidemics have been epidemiologically linked with zoonosis[3], and two-thirds of all new and emerging infectious diseases are zoonotic[4]**.** In today's world, with close

interconnectedness amongst humans, animals, and the environment, factors like population growth, migration, urbanization, and climate change contribute significantly to the increased probability of biological threats (biothreats)[5]. Although the diseases affecting humans are of an immediate concern, the overall food security and socio-economic well-being are directly affected by plant and animal health. The current pandemic has demonstrated the linkages among health of humans, animals and the planet that sustains us. Thus, well planned, concerted actions taken to protect environmental, plant and animal health can prevent economic and public health disasters. Lurking in the background is the massive potential for deliberate use of biological agents as weapons by State or non-State entities which can affect health of humans, animals, damage crops and contaminate environment. This is the basic concept of One Health that there is an interlinkage of health of humans, animals and environment (Fig. 1) and the intensity of the linkages determines the emergence and circulation of microbes[6]. The concept of One Health can be extended for understanding and prevention of biorisks.

**Biorisks and biological agents**

Biorisks have a spectrum ranging from natural to biowarfare (Fig. 2)[7]. When deliberate, the key ingredient required for developing a bioweapon is widespread availability of pathogens/biological agents (BAs). BAs consist of microorganisms like viruses, bacteria, fungi, protozoa, prions, or other toxins produced by living organisms that may be produced and released deliberately for causing disease and death in humans, animals, or plants, with the potential of an epidemic or pandemic. Insects can also be used as agents for bioweapons. Biological weapons (BWs) are a subset of weapons of mass destruction, called chemical, biological, radiological, and nuclear weapons (CBRN), with a vast potential of misuse against all living organisms. Consequently, the challenges posed by proliferation of BWs and biothreats are daunting. Thus, all outbreaks of especially dangerous pathogens must be viewed as potential proliferation events, as these generate samples that could be used to design BWs; for example, approximately 300,000 samples of Ebola virus have been stored in facilities across various countries post 2014–2016 outbreak in West Africa[8]. The use of BAs is a serious and burgeoning problem with an enhanced risk of a bioterrorist attack[9,10].

The use of BWs is known since antiquity and these have often been used in conjunction with chemical and traditional weapons of warfare. The use of infected arrows and contamination of wells was resorted to by Persians, Greeks, and Romans[11,12]. During the second world war, plague-infested fleas were used by Japan in Manchuria, China[13]. Records of last 100 years show approximately 200 incidents involving toxic biological materials[14].

During the last few decades, the incidence, and the potential of biothreats have increased tremendously due to advances in biological warfare research and development. With the shifting geopolitical scenarios and enhanced global competition, despite being signatory to the Biological and Toxic Weapon Convention (BTWC, 1972), a few members have increased their activity in biotechnological, genetic

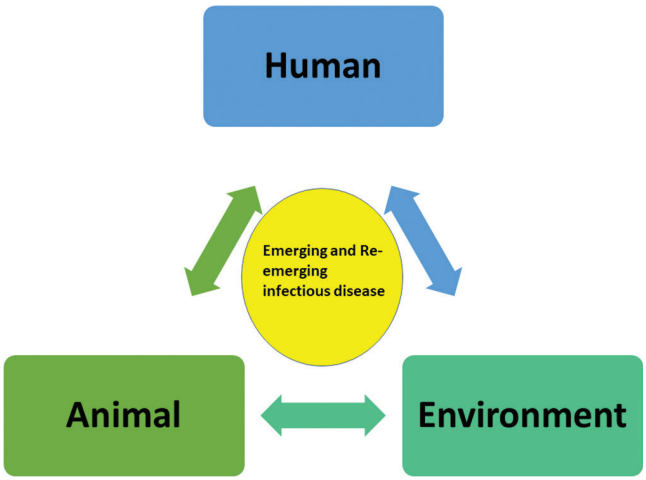


**Fig. 1.** One Health concept: Interlinkage between human health, animal health, and ecosystem.

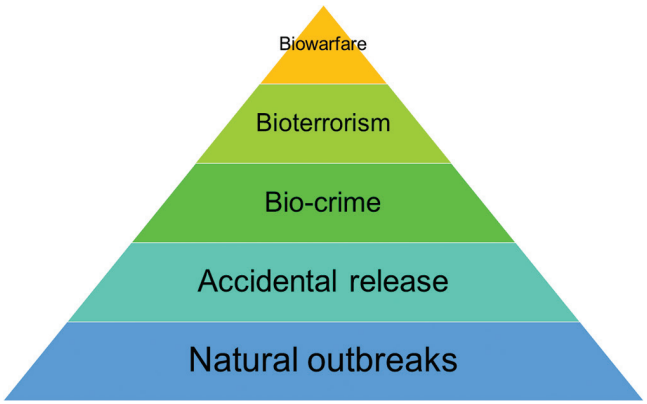


**Fig. 2.** Spectrum of biorisk.

engineering, and synthetic biology tools to develop highly potent and deadly chimeric biowarfare agents[15]. The US had a robust "germ warfare testing" programme from 1949 to 1969, involving 239 field tests and at least one publicly known trial on unsuspecting humans[16]. The testing of anthrax on Gruinard island by the UK in 1942 led to forced quarantining of the island for 48 long years[17]. Pathogens released in a Russian factory accident raised suspicion about its programme of weaponized biological agents[18].

BWs are appealing to all as these are easy to mass-produce, and existing stocks can be easily destroyed and/or restored. The easy availability, transportation and dispersal, low production costs, and non-detection by basic security systems of BAs provide them a strategic and tactical advantage. Still, most countries do not fully rely on this approach as BWs are slow-acting, unpredictable, difficult to deliver and control, and have the potential of misuse by non-State agencies, terrorist organizations, and other groups[19]. Despite this, non-war related use of BWs by the non-State agencies has been increasing in the last few decades[12]. Notable examples being use of *Salmonella* in Oregon, USA, by members of a cult, anthrax by Aum Shinrikyo in Japan, anthrax by mail to many US government officials, and the foiled attack using Ricin in June 2018 in Germany[12,20,21].

## Biothreat

Multiple factors favour the emergence of new pathogens naturally, including high human population density, wildlife and microbial diversity, and environmental factors like climate change, conflicts and natural catastrophes, which increase man-animal contact[20]. The animal spillover, cross-species jumping can lead to introduction of novel pathogens which can spread like a fire in a nascent population[22]. Based on the technology available, many hotspots have been identified for the emergence of new microbes with pandemic potential[23]. Newer techniques like Geographic Information System (GIS), remote sensing may be used to track real time changes in ecosystem and its effects on atmospheric condition[24].

Besides these known or unknown microbes with the potential of the pandemic, there is a real possibility of genetically engineered BAs and an enhanced use and misuse of newer pathogens in the future. The modernization and weaponization of genetically engineered BAs to develop extremely contagious, fast-acting, and lethal strains may overwhelm the human immune system and resistance to all known management modalities[12]. The research includes weaponizing resistant recombinant novel pathogen strains, chimeric viruses using newer technologies like Clustered regularly interspaced short palindromic repeats (CRISPR)[25]. The delivery methods/ formulations are undergoing modifications with potent aerosols or powder formulations, which would be easy to deliver through routine disinfection vehicles/ equipment or small bombs, as per requirement[26].

These novel strains or newer microorganisms may pose dangers to health and local, national, and international economic conditions, bringing misery to human, animal, and plant/crop health with its wider implications. Another important aspect of biothreat is that unless there is a clear evidence of linking or owning to it by some group or facility, it can be disguised as a natural phenomenon. The differentiation between natural outbreaks and deliberate induced outbreaks becomes blurred[27].

Several groups have suggested methods to identify the deliberate disease outbreak act or biothreat[27–29]. One such group used epidemiology of the event (clinical presentation, increased morbidity or mortality, time, place, and person distribution, *etc*.) for possible clues to the index of suspicion for an unnatural event[27]. Another group suggested assessment using non-conclusive and conclusive criteria, which were assessed qualitatively on a scale of 0-3 with a total range from 0-54[28]. Yet another method is based on the bioterrorism risk assessment model having qualitative and quantitative indicators and three categories of natural, probable deliberate, and highly probable deliberate[29]. However, these need to be tested in laboratories or by simulations as their validity and reliability are currently unknown.

## Challenges

One of the foremost challenges is early identification of deliberate or natural bioagent, which would help to control such events with minimal disruption. For early identification of such events a robust surveillance system is required. The concept of One Health is useful for extending the surveillance system to animal as well as crops. It entails knowledge of microbes circulating not only among humans but also in animals and plants. The identification of pathogens which can jump from one species to another

and further keeping close watch over them so as to prevent the outbreaks is key for early identification. A policy on microbial forensics is required which can collaborate, identify and characterize the data from human, animal and plants[14].

After identification, quick response to limit or contain the microbes is required. At the macro level it will require preparedness and coordination of various departments and ministries. The nodal ministry for counterterrorism is the Ministry of Home Affairs, whereas the epidemics among humans are dealt with by the Ministry of Health and Family Welfare. The Ministry of Agriculture deals with animals and crops. The Indian Council of Medical Research (ICMR) looks after various aspects of biomedical research and the National Centre for Disease Control (NCDC) is the nodal authority for all surveillance and outbreak response activities. The Defense Research and Development Organization (DRDO), with an extensive network of laboratories, is engaged in research on various aspects of CBRN and individual protective equipment. The other research and development entities dealing with biotechnology, drugs, and toxicology are the Council for Scientific and Industrial Research (CSIR) and the Department of Biotechnology (DBT). The agriculture and animal science domain is with the Indian Council of Agricultural Research (ICAR).

The National Disaster Management Authority (NDMA), mandated to plan, prepare and respond to natural and man-made disasters in the country, has prepared guidelines on all types of disasters[30]. It also has the National Disaster Response Force for a specialized response to natural and man-made disasters, with four of its battalions trained and equipped for CBRN emergencies. However, the focus of NDMA is on post-disaster management and not on prevention, research, and surveillance activities[30].

Development of diagnostics, treatment and vaccinations to mitigate the effects of microbes is an important area. These need to be developed at a rapid pace for newer BAs and we need adequate stockpiles for the older ones. The advent of newer techniques like molecular diagnostics, mRNA techniques, biosensors, biochips, *etc*., have increased the pace of development of diagnostics and vaccinations as is evident in the current SARS-CoV-2 pandemic. However, not all countries are equally equipped. Here comes the role of international collaborations, WHO, World Organisation for Animal Health (OIE) and UNICEF for equity and fair distribution. These newer techniques can be applied to human as well as animal health. The prevention of diseases in livestock will decrease the risk of transmission to humans and vice versa. However, the treatment has become difficult because of intensification of livestock activity and widespread misuse or improper use of antibiotics leading to antimicrobial resistance coupled with limited antivirals having limited efficacy and availability.

Monitoring of environment for microbes through the world is another major challenge. The hand-held sensors for identification of harmful pathogens have been developed, however, sensitivity and specificity of these sensors have been questioned[31]. The role of big data analytics for monitoring required facilities as well as trained manpower are lacking at present.

The concept of One Health is also at varied levels in different countries. Various specialities (trans-Disciplinary approach) have to work together, however, domain control, power equations, hesitancy, *etc*., play a role in slow progress towards achieving this. In the past decade, India has made policy which is in the direction of One Health, however it is in its nascent stage[32].

**The way forward**

Internationally, BTWC States Parties have tried to ensure the relevance and effectiveness of the Convention despite advances in science and technology, changing geopolitics, and security scenarios. Five yearly meetings have been held regularly to review the operation of the BTWC, with the ninth review due in November 2021[33]. Organizations like the WHO, Food and Agricultural Organization (FAO), and United Nations Office for Drugs and Crime (UNODC) are involved in assessing and helping the Member States in mitigation efforts. In response to this growing threat, UNODC delivered an online awareness-campaign titled *"*The International Legal Framework against Biological Terrorism" in September 2020 to make all Member States aware of the existing international legal instruments[34]. However, it would be naïve to assume that all Member States attend these meetings, update their current situations regularly and will abide by the legal framework. To combat biothreats at international, national and regional level, a commitment towards

funding and incentives for collaborative research across disciplines for One Health are essential.

Notwithstanding the intention, whether natural or man-made, biothreats pose the same consequences and consequently need a similar prevention and management approach. Early suspicion or detection remains the key. The need for a robust surveillance system including BAs, human diseases, diseases in animals, crop affliction, and environmental degradation does not require any further emphasis. A comprehensive surveillance strategy should alert the public health system in the early stages of biothreat or outbreaks. The preparation, flexibility, and resources would determine the response of the system. The newer techniques and advances primarily related to the genome sequence have helped to understand the molecular mechanisms of pathogenesis, designing drugs and vaccines which can be gainfully utilized to counter biothreats[35].

Digitalization of health and big data analytics, including artificial intelligence, would help in early detection and better response. There would be a requirement of trained epidemiologists to identify the specifics for prevention of natural and/or deliberate outbreaks. Multi- and trans-disciplinary teams are required at national, State, and district levels, along with enhanced capability and capacity to deal with biothreats to humans, animals, and plants/crops.

Appropriate lessons need to be learnt from the current pandemic. The actions taken by India need to be upscaled to further strengthen the trained human resources, newer surveillance and research techniques, and public health laboratory network; employment and availability of trained multi-disciplinary teams at all levels; capacity of public health facilities to manage cases with the availability of drugs, equipment, and ancillary facilities; availability of protective equipment; and continued investment in the health system. At the country level, planning, coordination, and activities acquiring global best practices adopting new tools and approaches towards prevention, control, and mitigation of the biothreat, whether natural or man-made (bioterrorism), will also pay dividends in improving the overall health of the community. A legal framework and a National level institution for One Health will go a long way to give impetus to One Health.

The concept of One Health is essential for responding to any emerging infectious diseases or biothreat. However, except for during the current pandemic, there has been little progress in India till date to bring key stakeholders, including infectious disease specialists, public health specialists, veterinarians, agriculturists, environmentalists, and other related disciplines at the common platform and formal mechanisms need to be in place for such efforts[32,36,37].

At the international level, organizations like the WHO, FAO, and UNODC need to be proactive, transparent and meaningfully engage with all stakeholders in a spirit of equality for early warnings and steps for prevention and control biothreats and also for collaborative research. The long-term policies which can reduce frequency or intensity of human-animal contact and maintain balance of ecosystem can help in decreasing animal spillover or cross-species jumping.

## Conclusion

The possibility of biothreat whether natural or deliberate is real. The newer molecular techniques and scientific developments can act as both opportunities and obstacles. Early detection, mitigation of effect, and the response would be enhanced by the One Health approach, which recognizes the link between human, animal, and plant health and the effect of disease on food supplies and the economy. A One Health approach with enhanced coordination, trans-disciplinary and multisectoral actions for designing and implementing policies, programmes, and legislation based on basic and applied research coupled with effective surveillance systems, early detection, and actions to contain outbreaks of local / national / international concern along with rapid and transparent information sharing with enhanced global cooperation and participation would be effective to tackle the biothreats effectively.

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## References

1. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int J Antimicrob Agents* 2020; *55* : 105924.
2. World Health Organization. Emergencies, preparedness, response: Disease outbreaks by year. Available from: *http://www.who.int/csr/don/archive/year/en/*, accessed on February 20, 2021.
3. Schmiege D, Perez Arredondo AM, Ntajal J, Minetto Gellert Paris J, Savi MK, Patel K, *et al.* One Health in the context of coronavirus outbreaks: A systematic literature review. *One Health* 2020; *10* : 100170.

4. Centers for Disease Control and Prevention. *Emerging and zoonotic infectious diseases*. Available from: *https://www.cdc.gov/ncezid/pdf/infectious-diseases-brochure-2017.pdf*, accessed on February 19, 2021.
5. Behravesh CB. One Health: People, Animals, and the Environment. *Emerg Infect Dis* 2016; *22* : 766–7.
6. Ellwanger JH, Veiga ABG da, Kaminski V de L, Valverde-Villegas JM, Freitas AWQ de, Chies JAB, *et al*. Control and prevention of infectious diseases from a One Health perspective. *Genet Mol Biol* 2021; *44* (1 Suppl 1) : e20200256.
7. National Research Council. *Science Needs for Microbial Forensics: Developing Initial International Research Priorities*. Washington, DC: The National Academies Press; 2014.
8. Osterhaus ADME, Vanlangendonck C, Barbeschi M, Bruschke CJM, Christensen R, Daszak P, *et al*. Make science evolve into a One Health approach to improve health and security: a white paper. One Health Outlook 2020; *2* : 6.
9. World Health Organization. *Biological weapons*. Available from: *https://www.who.int/westernpacific/health-topics/biological-weapons*, accessed on February 19, 2021.
10. Chaudhry FN, Malik MF, Hussain M, Asif N. Insects as Biological Weapons. *J Bioterror Biodef* 2017; *9*: 156.
11. eMedicineHealth. *What is biological warfare? Agents use*. Available from: *https://www.emedicinehealth.com/biological_warfare/article_em.htm*, accessed on February 19, 2021.
12. Carus WS. The history of biological weapons use: what we know and what we don't. *Health Secur* Mary Ann Liebert, Inc., publishers; 2015; *13* : 219-55.
13. The Vintage News. *During World War II Japan "bombed" China with fleas infected with Bubonic plague*. Available from: *https://www.thevintagenews.com/2016/10/15/during-world-war-ii-japan-bombed-china-with-fleas-infected-with-bubonic-plague/*, accessed on February 20, 2021.
14. The National Academies Press. *Science and technology to Counter Terrorism: Proceedings of an Indo-U.S. Workshop 2007*. Available from: *https://www.nap.edu/read/11848/chapter/15*, accessed on February 20, 2021.
15. India Foundation. *Science of biological warfare and biopreparedness*. Available from: *https://indiafoundation.in/articles-and-commentaries/science-of-biological-warfare-and-biopreparedness/*, accessed on February 1, 2021.
16. Business Insider. *Over and over again, the military has conducted dangerous experiments on Americans*. Available from: *https://www.iflscience.com/health-and-medicine/the-military-has-conducted-dangerous-biowarfare-experiments-on-americans/*, accessed on February 20, 2021.
17. BBC News. *Britain's "Anthrax Island"*. Available from: *http://news.bbc.co.uk/2/hi/uk_news/scotland/1457035.stm*, accessed on February 20, 2021.
18. The Sverdlovsk Incident Was One of the World's Worst Bio Weapons Mishaps. Available from: *https://warisboring.com/the-sverdlovsk-incident-was-one-of-the-worlds-worst-chemical-weapons-mishaps/*, accessed on February 20, 2021.
19. CBW Magazine. *Biological Weapons: The impact of new technologies*. *Available from: https://idsa.in/cbwmagazine/Biological-weapons-snaik*, accessed on February 20, 2021.
20. Barras V, Greub G. History of biological warfare and bioterrorism. *Clin Microbiol Infect* 2014; *20* : 497-502.
21. Stimson. Ataxia: The chemical and biological terrorism threat and the US response. Available from: *https://www.stimson.org/2000/ataxia-chemical-and-biological-terrorism-threat-and-us-response/*, accessed on February 20, 2021.
22. Ahmed AK. Spillover: Animal infections and the next human pandemic. *Yale J Biol Med* 2013; *86* : 107-12.
23. Morse SS, Mazet JA, Woolhouse M, Parrish CR, Carroll D, Karesh WB, *et al*. Prediction and prevention of the next pandemic zoonosis. *Lancet Lond Engl* 2012; *380* : 1956-65.
24. Thakur JK, Singh SK, Ekanthalu VS. Integrating remote sensing, geographic information systems and global positioning system techniques with hydrological modeling. *Appl Water Sci* 2017; *7* : 1595-608.
25. DiEuliis D, Giordano J. Gene editing using CRISPR/Cas9: implications for dual-use and biosecurity. *Protein Cell* 2018; *9* : 239-40.
26. World Health Organization. Public health response to biological and chemical weapons: WHO guidance (2004). Available from: *https://www.who.int/csr/delibepidemics/biochemguide/en/*, accessed on February 2, 2021.
27. Dembek ZF, Kortepeter MG, Pavlin JA. Discernment between deliberate and natural infectious disease outbreaks. *Epidemiol Infect* 2007; *135* : 353-71.
28. Grunow R, Finke E-J. A procedure for differentiating between the intentional release of biological warfare agents and natural outbreaks of disease: its use in analyzing the tularemia outbreak in Kosovo in 1999 and 2000. *Clin Microbiol Infect* 2002; *8* : 510-21.
29. Radosavljevic V, Belojevic G. Unusual epidemic events: a new method of early orientation and differentiation between natural and deliberate epidemics. *Public Health* 2012; *126* : 77-81.
30. National Disaster Management Authority, Government of India. Available from: *https://ndma.gov.in/*, accessed on February 20, 2021.
31. Sapsford KE, Bradburne C, Delehanty JB, Medintz IL. Sensors for detecting biological agents. *Mater Today* 2008; *11* : 38-49.
32. Aggarwal D, Ramachandran A. One Health Approach to Address Zoonotic Diseases. *Indian J Community Med Off Publ Indian Assoc Prev Soc Med* 2020; *45* : S6-8.
33. United Nations Office of Disarmament. *Meetings under the biological weapons convention*. Available from: *https://www.un.org/disarmament/biological-weapons/about/meetings/*, accessed on March 2, 2021.
34. United Nations Office on Drugs and Crime. *UNODC upscales efforts to promote the international legal framework against biological terrorism*. Available from: *https://www.unodc.org/unodc/en/terrorism/latest-news/2020_international-legal-*

*framework-against-biological-terrorism.html*, accessed on March 2, 2021.

35. National Research Council. *Making the nation safer: The role of science and technology in countering terrorism*. Washington, DC: The National Academies Press; 2002.
36. Bhatia R. Implementation framework for One Health approach. *Indian J Med Res* 2019; *149* : 329-31.
37. Yasobant S, Bruchhausen W, Saxena D, Falkenberg T. One Health collaboration for a resilient health system in India: Learnings from global initiatives. *One Health* 2019; *8* : 100096.

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