www.ijarp.com ISSN 2456-9992 Page: 01-18

International Journal Advanced Research Publications

Research Article

Volume: 02
Issue: 04

BIOTERRORISM THROUGH THE AGES: HISTORICAL EVOLUTION OF BIOLOGICAL AGENTS

Movva Navya[1], Pradnya deolekar*[1], Kavitha Dongerkery[1], Akash sinha[1], Atharva Dahibhate[1], Prateek DT[1], Sankeerth Chanamolu[1], Srirambabu V[1], Prathmesh Deolekar[2], Kawshik Movva[3], Reshma Pothugunta[4].

1. Department of Pharmacology, D Y Patil Medical College, Navi Mumbai.
2. Resident, General Medicine, Meenakshi Medical College, Enathur, Kancheepuram.
3. Resident, General surgery, Siddhartha Medical College, Tumkur.
4. Resident, Radiation Onchology, Viswabharti Medical college, Kurnool.

Article Received: 18 March 2026, Article Revised: 08 April 2026, Published on: 28 April 2026

***Corresponding Author: Pradnya deolekar**
Resident, General Medicine, Meenakshi Medical College, Enathur, Kancheepuram.
DOI: https://doi-doi.org/101555/ijarp.5472

INTRODUCTION

Bioterrorism refers to the deliberate use of biological agents to cause disease, disability, or death in humans, animals, or plants, with the intent to instill fear, disrupt societies, or achieve political objectives. These agents include a wide range of microorganisms such as bacteria, viruses, and fungi, as well as biologically derived toxins. Among the various modes of dissemination, aerosol release is the most common and effective method, as it enables widespread exposure through inhalation. Additionally, contamination of food and water supplies can result in large-scale outbreaks. The use of mechanical devices or advanced delivery systems further enhances covert dissemination, making bioterrorism a major public health and global security concern (1).

History of Bioterrorism

The history of bioterrorism dates back to ancient times and has evolved alongside advances in warfare and microbiology. As early as the 6th century BCE, Assyrian forces reportedly contaminated enemy water sources with ergot fungus, causing illness and hallucinations.

During the 1346 Siege of Caffa, plague-infected corpses were catapulted into the city, representing one of the earliest documented uses of biological warfare. In 1763, during

Pontiac's Rebellion, smallpox-contaminated blankets were allegedly distributed to Native Americans.

The 20th century marked a transition to organized biological warfare programs, particularly during the 1930s–1940s, when Japan's Unit 731 conducted large-scale human experimentation and released pathogens such as plague, anthrax, and cholera. Growing global concern led to the establishment of the Biological Weapons Convention, which prohibited the development and stockpiling of biological weapons. However, modern incidents such as the 2001 anthrax attacks demonstrate that the threat persists in contemporary times (2).

These historical events highlight a clear evolution from crude biological methods to sophisticated, scientifically driven strategies, emphasizing the increasing relevance of bioterrorism in modern public health preparedness.

Classification of Bioterrorism Agents

Bioterrorism agents are classified based on their ease of dissemination, mortality, and public health impact:

Category	Criteria	Examples
Category A	High mortality, easily disseminated, requires special public health action	*Bacillus anthracis*, *Yersinia pestis*, *Variola major*, *Francisella tularensis*, Filoviruses, Arenaviruses [1,2]
Category B	Moderately easy to disseminate, moderate morbidity	*Brucella* spp., *Salmonella* spp., *Escherichia coli* O157:H7, *Vibrio cholerae*, Alphaviruses [1,2]
Category C	Easily produced, potential for high morbidity and mortality	*Mycobacterium tuberculosis*, Nipah virus, Hantavirus [1,3]

This classification aids in prioritizing surveillance, preparedness, and response strategies in biodefense systems.

BACILLUS ANTHRACIS

The history of *Bacillus anthracis* as a bioterrorism agent began with its identification by Robert Koch in 1876, which established its role in infectious disease causation and laid the foundation for modern microbiology (3). During World War I, anthrax was explored as a biological weapon, particularly by targeting livestock to disrupt enemy food supplies and economies (3). This interest expanded during World War II, when organized biological warfare programs, including those conducted by Japan's Unit 731, investigated

its large-scale use (3). A major accidental release occurred in 1979 in Sverdlovsk (former Soviet Union), where airborne anthrax spores led to multiple fatalities, highlighting the risks associated with weaponization (4). The threat of anthrax in modern bioterrorism became evident during the 2001 anthrax attacks, where spores were deliberately disseminated through postal mail, resulting in infections, deaths, and widespread public fear (5).

Implication:

Due to its spore-forming ability, long-term environmental stability, ease of aerosolization, and high lethality in inhalational anthrax, *Bacillus anthracis* remains a critical Category A bioterrorism agent, necessitating rapid detection systems, vaccination strategies, and preparedness for aerosol-based exposure scenarios.

YERSINIA PESTIS

Yersinia pestis, the causative agent of Plague, is historically associated with the Black Death, one of the deadliest pandemics in human history, causing massive mortality and profound socio-economic disruption (3). The disease spread rapidly through the rat–flea–human transmission cycle, wherein infected fleas transmitted the organism from rodents to humans, leading primarily to bubonic plague. In some cases, progression to pneumonic plague enabled direct person-to-person transmission via respiratory droplets, further accelerating outbreaks (3).

The potential use of *Yersinia pestis* in biological warfare dates back to the Siege of Caffa, where infected corpses were reportedly used to spread disease among besieged populations. In the 20th century, this was followed by experiments conducted by Japan's Unit 731, including the release of plague-infected fleas over civilian areas (6). During the Cold War, several countries explored its potential as an aerosolized agent, particularly due to the high lethality of pneumonic plague (3).

The identification of *Yersinia pestis* and the understanding of its transmission dynamics significantly advanced control measures such as vector control and quarantine.

Implication:

Its high infectivity, rapid disease progression, and ability for person-to-person transmission in pneumonic form make it a critical Category A bioterrorism agent,

necessitating early detection, strict surveillance, and prompt public health response.

FRANCISELLA TULARENSIS

Francisella tularensis, the causative agent of tularemia, was first identified in 1911 in Tulare County, California, from which it derives its name (3). It was later associated with "rabbit
fever" due to its occurrence in wild animals such as rabbits and rodents, and transmission through ticks and direct contact (3). The organism attracted significant attention because of its extremely high infectivity and very low infectious dose, making even minimal exposure sufficient to cause disease.

During the mid-20th century, particularly in World War II and the Cold War era, *Francisella tularensis* was investigated as a potential biological weapon (7). Its ability to be aerosolized and cause pneumonic tularemia made it especially concerning. Reports suggest that both the United States and the former Soviet Union explored its large-scale production, with the latter believed to have stockpiled the organism. Unlike highly lethal agents, tularemia was considered strategically useful due to its capacity to cause prolonged debilitating illness, potentially overwhelming healthcare systems and reducing workforce efficiency.

Implication:

The combination of high infectivity, ease of aerosol spread, and capacity to incapacitate large populations makes *Francisella tularensis* a significant Category A bioterrorism agent, highlighting the need for early detection, surveillance, and preparedness for aerosol exposure scenarios.

VARIOLA MAJOR

Variola major, the causative agent of smallpox, has one of the most devastating histories among infectious diseases, affecting human populations for thousands of years (3). Evidence of smallpox-like lesions has been identified in ancient Egyptian mummies, indicating its long-standing presence in human civilization (3). Over centuries, smallpox caused repeated epidemics across Asia, Europe, and the Americas, with high mortality and disfiguring complications among survivors.

One of the earliest documented instances of its use as a biological weapon occurred in 1763 during Pontiac's Rebellion, when British forces reportedly distributed blankets contaminated with smallpox virus to Native American populations, leading to outbreaks and significant mortality (8). This event is often cited as a classic example of deliberate biological warfare.

The turning point in the history of smallpox came in 1796, when Edward Jenner developed the first successful vaccine, introducing the concept of immunization. This discovery ultimately led to a global eradication campaign led by the World Health Organization, culminating in the declaration of smallpox eradication in 1980, making it the first human disease to be completely eliminated (8).

Despite eradication, concerns remain due to its past use in warfare, high transmissibility, and the fact that most of the current global population is unvaccinated.

Implication:

The historical use of infected materials, high mortality, and efficient person-to-person transmission make *Variola major* a critical Category A bioterrorism agent, emphasizing the importance of vaccine stockpiling, strict biosecurity, and rapid outbreak preparedness.

FILOVIRUSES (Ebola and Marburg Viruses)

Filoviruses, including Ebola and Marburg viruses, are among the most severe viral pathogens known, causing hemorrhagic fever with high case fatality rates (3). The first recognized outbreak occurred in 1967, when the Marburg virus caused infections among laboratory workers in Germany and Yugoslavia, linked to imported African green monkeys (9). This event marked the identification of a new group of highly dangerous viruses.

In 1976, Ebola virus was identified during two simultaneous outbreaks in Sudan and the Democratic Republic of the Congo, near the Ebola River, which gave the virus its name (9). These outbreaks were characterized by rapid transmission, severe bleeding manifestations, and high mortality, drawing global attention. Since then, multiple outbreaks have occurred, particularly in Africa, with the 2014–2016 West African Ebola outbreak being the largest, resulting in widespread mortality and international concern

(10).

Although primarily naturally occurring, filoviruses have raised concerns in the context of bioterrorism due to their high lethality, rapid disease progression, and potential to create widespread panic. Their transmission through direct contact with infected body fluids and the need for high-level biosafety containment (BSL-4) further complicate outbreak control.

Implication:

Their high mortality, epidemic potential, and requirement for specialized containment facilities justify their classification as Category A agents, emphasizing the importance of biosafety infrastructure, rapid diagnostics, and effective outbreak response systems.

ARENAVIRUSES (Lassa, Junin, Machupo Viruses)

Arenaviruses, including Lassa virus, Junin virus, and Machupo virus, are important zoonotic pathogens responsible for viral haemorrhagic fevers with significant morbidity and mortality (3). These viruses are primarily transmitted from rodent reservoirs to humans, highlighting their zoonotic nature.

Lassa virus was first identified in 1969 in Lassa during an outbreak among healthcare workers and has since become endemic in parts of West Africa (11). Junin virus was identified in the 1950s in Argentina, primarily affecting agricultural workers exposed to infected rodents (11). Similarly, Machupo virus was discovered in the 1960s in Bolivia during outbreaks of haemorrhagic fever (11).

Historically, these viruses have caused localized outbreaks with high case fatality rates, particularly in rural areas where human–rodent contact is common (11). During the Cold War era, arenaviruses attracted attention as potential biological warfare agents due to their severity, potential for aerosol transmission, and limited treatment options at that time (7).

Although there is no confirmed large-scale use as bioweapons, they are classified as Category A bioterrorism agents due to their potential to cause serious public health emergencies (3).

Implication:

Their high case fatality, zoonotic transmission, and potential for aerosol spread justify

their classification as Category A agents, emphasizing the need for surveillance, early diagnosis, and preparedness for outbreak control.

BRUCELLA SPECIES

Brucella species, the causative agents of brucellosis, have a long history as zoonotic pathogens and were first recognized in the 19th century among British soldiers stationed in Malta, where the disease was termed "Malta fever" or "Mediterranean fever" due to its chronic, relapsing nature (3). In 1887, Sir David Bruce identified the causative organism, later named *Brucella melitensis* (12). Over time, additional species such as *Brucella abortus*, *Brucella suis*, and *Brucella canis* were identified, establishing the disease as one closely linked to livestock and transmission through direct contact or consumption of contaminated animal products (3).

During the 20th century, particularly in World War II and the Cold War period, *Brucella* species attracted attention as potential biological warfare agents. Their ability to be aerosolized and cause prolonged, debilitating illness made them suitable for incapacitating populations rather than causing high mortality (7). Several countries reportedly explored their use, especially *B. suis*, in biological weapons programs (7).

Implication:

Due to their moderate ease of dissemination, chronic disease pattern, and impact on both human health and livestock, *Brucella* species are classified as Category B agents, highlighting the need for surveillance, occupational safety, and control of zoonotic transmission (3).

SALMONELLA SPECIES

Salmonella species, including both typhoidal and non-typhoidal strains, have long been recognized as important human pathogens. The genus was identified in the late 19th century and named after Daniel Elmer Salmon, although it was first isolated by Theobald Smith (3).

Salmonella enterica serovar Typhi is the causative agent of typhoid fever, a systemic illness historically associated with poor sanitation and contaminated water, leading to major outbreaks worldwide (3). Non-typhoidal strains such as *S. Typhimurium* and *S. Enteritidis* are commonly responsible for foodborne gastroenteritis and have been linked to numerous outbreaks (3).

A landmark event in the history of bioterrorism occurred in 1984 in The Dalles, Oregon, where a cult deliberately contaminated salad bars with *Salmonella Typhimurium*, resulting in more than 700 cases of food poisoning (13). This incident demonstrated the feasibility of using common foodborne pathogens for deliberate outbreaks.

Implication:

Because of their ease of cultivation, stability in food and water, and ability to cause large outbreaks, *Salmonella* species are classified as Category B agents, emphasizing the importance of food safety, surveillance, and outbreak control measures (3).

ESCHERICHIA COLI O157:H7

Escherichia coli O157:H7, a pathogenic strain of enterohemorrhagic E. coli (EHEC), was first identified as a significant human pathogen in 1982 following outbreaks of hemorrhagic colitis linked to contaminated food (14). Unlike commensal strains, this organism produces Shiga toxins, which can cause severe disease, including bloody diarrhoea and complications such as haemolytic uremic syndrome (HUS), particularly in children and elderly individuals (3).

Subsequent outbreaks, including the well-known 1993 outbreak in the United States associated with contaminated hamburgers, highlighted the organism's public health impact and led to major improvements in food safety regulations (14). Its low infectious dose and ability to spread through contaminated food and water have raised concerns regarding its potential misuse.

Implication:

Due to its high infectivity, foodborne transmission, and potential to cause severe complications, *E. coli* O157:H7 is classified as a Category B agent, underscoring the importance of strict food hygiene, surveillance, and rapid outbreak response systems (3).

VIBRIO CHOLERAE

Vibrio cholerae, the causative agent of cholera, has a long and significant history as a global public health threat. The disease has been recognized for centuries, particularly in the Ganges Delta region, and the first pandemic began in 1817, spreading across Asia, Europe, and Africa (15). Over the next two centuries, multiple pandemics occurred, causing widespread mortality and highlighting the role of contaminated water and poor

sanitation (15).

Major scientific breakthroughs in the 19th century improved understanding of cholera. In 1854, John Snow demonstrated its waterborne transmission, and later, Robert Koch identified *Vibrio cholerae* as the causative organism (15). Despite advances in sanitation, outbreaks continue to occur in resource-limited settings.

Implication:

Due to its ability to spread rapidly through contaminated water and cause large-scale outbreaks, *Vibrio cholerae* is classified as a Category B agent, emphasizing the importance of water sanitation, public health infrastructure, and rapid response systems (3).

ALPHAVIRUSES (Venezuelan Equine Encephalitis Virus and Related Viruses)

Alphaviruses, including Venezuelan equine encephalitis virus (VEEV), Eastern equine encephalitis virus (EEEV), and Western equine encephalitis virus (WEEV), are mosquito-borne RNA viruses known to cause febrile illness and, in some cases, severe neurological disease such as encephalitis (3). These viruses primarily affect both animals (especially horses) and humans, highlighting their zoonotic significance.

Venezuelan equine encephalitis virus (VEEV) was first recognized in the early 20th century during outbreaks among equine populations in Venezuela and Colombia and was isolated in 1938 (16). Human infections were later documented, presenting mainly as acute febrile illness, with a small proportion progressing to encephalitis, particularly in children (16).

Large-scale epidemics occurred periodically, notably during the 1960s and 1970s, affecting tens of thousands of humans and causing extensive mortality in equine populations. These outbreaks resulted in significant economic losses and public health burden due to their rapid spread and vector-borne nature (16).

During the mid-20th century, particularly in the context of World War II and the Cold War, alphaviruses such as VEEV gained attention as potential biological warfare agents. Their high infectivity, low infectious dose, and ability to be transmitted via aerosol made them suitable as incapacitating agents rather than highly lethal ones (16). As a result, they were studied in several military research programs.

Although the Biological Weapons Convention of 1972 prohibited the development and stockpiling of such agents, alphaviruses remain classified as Category B bioterrorism agents. This is due to their moderate ease of dissemination, potential to cause outbreaks, and impact on both human and animal health (3).

Implication:

Their ability to cause large outbreaks of febrile illness with occasional neurological complications, combined with aerosol infectivity and zoonotic transmission, justifies their classification as Category B agents, emphasizing the need for vector control, surveillance systems, and preparedness for outbreak management.

MYCOBACTERIUM TUBERCULOSIS

Mycobacterium tuberculosis is the causative agent of Tuberculosis (TB), one of the oldest and most widespread infectious diseases affecting humans. Evidence of tuberculosis dates back thousands of years, with characteristic lesions identified in ancient Egyptian mummies and early human remains (3). Historically referred to as "consumption" due to its progressive wasting, TB was a leading cause of death in Europe and other parts of the world during the 18th and 19th centuries (3).

A major breakthrough occurred in 1882 when Robert Koch identified *Mycobacterium tuberculosis* as the etiological agent, establishing a scientific basis for diagnosis and control (17). In the early 20th century, advancements such as the BCG vaccine and the discovery of Streptomycin significantly improved disease management and reduced mortality (3). However, tuberculosis continues to be a major global health challenge, especially with the emergence of drug-resistant forms such as Multidrug-resistant tuberculosis and Extensively drug-resistant tuberculosis (3).

Although primarily a naturally occurring airborne disease, *Mycobacterium tuberculosis* has been considered a potential bioterrorism agent due to its transmission via respiratory droplets, ability to cause chronic illness, and capacity for latent infection (7). Its aerosol spread and difficulty in treating resistant strains contribute to biodefense concerns (7). It is classified as a Category C agent, reflecting pathogens that pose a future threat due to their global prevalence and adaptability (3).

Implication:

Its airborne transmission, persistence in latent form, and increasing drug resistance justify its classification as a Category C agent, emphasizing the need for early detection, effective treatment strategies, and strengthened public health control programs.

NIPAH VIRUS

Nipah virus is a highly pathogenic zoonotic virus that has emerged as a significant public health concern and a potential bioterrorism agent due to its high mortality and ability for human-to-human transmission (3). It was first identified during an outbreak in 1998–1999 in Malaysia and Singapore, where it caused severe encephalitis among pig farmers and individuals in close contact with infected animals (18).

The outbreak was linked to fruit bats of the genus Pteropus, which act as natural reservoirs, with pigs serving as intermediate hosts (18). Subsequent outbreaks have been reported in Bangladesh and India, often associated with consumption of raw date palm sap contaminated by bat secretions or through direct human-to-human transmission (18). These outbreaks are characterized by high case fatality rates, neurological manifestations, and occasional respiratory involvement, facilitating rapid spread (18).

Although there is no confirmed use of Nipah virus as a biological weapon, its high lethality, absence of widely available specific treatment, and outbreak potential have raised concerns regarding possible misuse (3). It is therefore classified as a Category C bioterrorism agent, representing emerging pathogens that could be engineered for mass dissemination (3).

Implication:

Its high fatality rate, zoonotic transmission, and potential for person-to-person spread justify its classification as a Category C agent, highlighting the importance of surveillance, zoonotic control measures, and preparedness for emerging infectious diseases.

HANTAVIRUSES (Hantaan Virus, Sin Nombre Virus)

Hantaviruses are a group of zoonotic viruses known to cause severe human diseases such as haemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS)

(3). The history of hantavirus infection dates back to the early 20th century but was first clearly recognized during the Korean War, when thousands of United Nations troops developed a severe febrile illness later termed HFRS (19).

The causative agent, Hantaan virus, was identified in the 1970s in South Korea, with rodents established as the primary reservoir (19). In 1993, a major outbreak in the United States led to the identification of Sin Nombre virus, responsible for hantavirus pulmonary syndrome (HPS), a severe respiratory illness with high fatality (19). Since then, multiple hantavirus species have been identified worldwide, each associated with specific rodent hosts and geographic regions (19).

Transmission to humans typically occurs through inhalation of aerosolized viral particles from rodent urine, droppings, or saliva (3). Although hantaviruses have not been widely used as biological weapons, their high mortality, environmental aerosol transmission, and lack of widely available specific antiviral therapy raise biodefense concerns (7). They are classified as Category C bioterrorism agents (3).

Implication:

Their zoonotic nature, aerosol transmission from environmental sources, and high mortality justify their classification as Category C agents, emphasizing the need for rodent control, environmental hygiene, and surveillance systems.

NERVE AGENTS TABUN (GA)

Tabun is one of the earliest discovered nerve agents. It was first synthesized in 1936 by Gerhard Schrader during research on organophosphate pesticides (20). Its potent inhibition of acetylcholinesterase leads to accumulation of acetylcholine and severe disruption of nerve transmission (20).

Recognizing its military potential, Nazi Germany initiated large-scale production during World War II, making it the first nerve agent to be weaponized, although it was never used in combat (20). Post-war, knowledge of Tabun contributed to the development of more advanced agents such as sarin and soman (20).

Today, Tabun is regulated under the Chemical Weapons Convention as a Schedule 1 chemical, indicating high toxicity and no legitimate civilian use (21).

Implication:

Its historical role as the first weaponized nerve agent and potent acetylcholinesterase inhibition highlight the importance of strict international regulation and preparedness for chemical exposure management.

SARIN

Sarin is a highly toxic nerve agent synthesized in 1938 in Nazi Germany by a team led by Gerhard Schrader (20). It acts rapidly by inhibiting acetylcholinesterase, leading to cholinergic crisis and death (20).

Although produced during World War II, it was not used in combat. During the Cold War, Sarin became a major focus of chemical weapons programs due to its high volatility and effectiveness as an inhalational agent (20). It gained global notoriety in the Tokyo subway attack by the Aum Shinrikyo cult and has also been used in the Syrian conflict (22).

Sarin is classified as a Schedule 1 chemical under the Chemical Weapons Convention (21).

Implication:

Its rapid action, high volatility, and documented use in terrorist attacks emphasize the need for emergency preparedness, rapid detection, and antidote availability (e.g., atropine, pralidoxime).

SOMAN

Soman is a highly toxic nerve agent synthesized in 1944 by Richard Kuhn (20). It is characterized by rapid and irreversible inhibition of acetylcholinesterase, with “aging” of the enzyme complex occurring quickly, making treatment difficult (20).

Although not used in World War II, Soman was later stockpiled during the Cold War due to its high toxicity and persistence (20). Its ability to act through both inhalation and skin absorption increased its military relevance (20).

It is classified as a Schedule 1 chemical under the Chemical Weapons Convention (21).

Implication:

Its rapid aging property and high toxicity make it particularly dangerous, underscoring the

need for immediate medical intervention and global prohibition measures.

GF (CYCLOSARIN) AND VX

Cyclosarin and VX represent later developments in nerve agents with enhanced persistence and lethality (20).

Cyclosarin (GF) is structurally related to sarin but is more persistent and lipid-soluble, allowing greater skin penetration and longer environmental survival (20). It was developed during or shortly after World War II and became part of Cold War chemical weapons research (20).

VX, developed in the 1950s by Ranajit Ghosh, is one of the most potent nerve agents known (23). It is less volatile but highly persistent, remaining in the environment for prolonged periods and posing a significant risk through dermal exposure (23). VX gained notoriety in the Assassination of Kim Jong-nam (24).

Both are classified as Schedule 1 chemicals under the Chemical Weapons Convention (21).

Implication:

Their extreme toxicity, environmental persistence, and potential for dermal exposure highlight the need for strict global regulation, rapid decontamination protocols, and preparedness against chemical threats.

BURKHOLDERIA MALLEI (Glanders)

Burkholderia mallei is the causative agent of Glanders, a zoonotic infection primarily affecting horses, mules, and donkeys, with occasional transmission to humans through direct contact with infected animals or contaminated materials (3). The disease has been recognized since ancient times, particularly among cavalry animals, where it caused significant morbidity and mortality, thereby affecting military transport and logistics (25).

The deliberate use of *Burkholderia mallei* as a biological weapon dates back to World War I, when German agents reportedly used it to infect horses and livestock of Allied forces (25).

During World War II, both Germany and Japan further explored its potential, with Unit

731 conducting experiments involving glanders (7).

The organism's ability to infect via inhalation, ingestion, or skin contact, along with its high infectivity and potential severity, made it a candidate for biological warfare programs (3).
During the Cold War, it continued to be studied and stockpiled by some nations (7). However, the Biological Weapons Convention prohibited such activities (3).

Today, *Burkholderia mallei* is classified as a Category B bioterrorism agent due to its moderate ease of dissemination and ability to cause serious disease in both humans and animals (3).

Implication:
Its zoonotic transmission, multiple routes of infection, and historical use in warfare justify its classification as a Category B agent, highlighting the need for veterinary surveillance, laboratory safety, and outbreak preparedness.

STAPHYLOCOCCAL ENTEROTOXIN B (SEB)
Staphylococcal Enterotoxin B is a potent toxin produced by Staphylococcus aureus and acts as a superantigen, causing massive immune activation and systemic toxicity (3). It was initially recognized as a cause of food poisoning but later gained attention for its potential in biological warfare (26).

During the Cold War, several countries, including the United States, investigated SEB for its incapacitating effects rather than lethality (26). Inhalational exposure can lead to fever, respiratory distress, and intense immune responses. Due to its stability and high potency at low doses, SEB was studied for aerosol dissemination in military programs during the 1950s and 1960s (26).

Although later prohibited under the Biological Weapons Convention, SEB remains a concern due to its ease of production and ability to cause widespread incapacitation (3). It is classified as a Category B bioterrorism agent.

Implication:
Its superantigen activity, aerosol potential, and incapacitating effects justify its classification as a Category B agent, emphasizing preparedness for mass exposure and

supportive management strategies.

BOTULINUM TOXIN

Botulinum toxin, produced by Clostridium botulinum, is one of the most potent toxins known (3). It was first identified in the late 19th century in association with foodborne illness linked to improperly preserved foods (27).

The toxin causes flaccid paralysis by inhibiting acetylcholine release at the neuromuscular junction, leading to respiratory failure in severe cases (27). Its extreme potency attracted military interest during World War II, when the United States conducted research on its potential use as a biological weapon, including food and aerosol dissemination strategies (27).

During the Cold War, further research and stockpiling occurred in several countries due to its high lethality and potential for mass casualties (27). Despite prohibition under the Biological Weapons Convention, concerns about its misuse persist (3).

Botulinum toxin is classified as a Category A bioterrorism agent due to its extreme toxicity and high mortality risk (3). Despite this, it also has important therapeutic uses in controlled medical settings.

Implication:

Its extreme potency, high lethality, and potential for mass exposure justify its classification as a Category A agent, emphasizing the need for rapid diagnosis, antitoxin availability, and strict regulatory control.

CONCLUSION

Bioterrorism is an evolving threat that connects infectious diseases, toxicology, and global security. From ancient methods like contaminating water to modern use of highly potent biological and chemical agents, it has become more advanced and scientifically driven over time. Various agents—bacteria, viruses, and toxins—are classified based on their impact, with Category A agents posing the highest risk due to high mortality and easy spread.

The rise of zoonotic diseases, antimicrobial resistance, and advances in biotechnology further increase the risk of bioterrorism. Many of these agents have dual uses, making it

challenging to balance scientific progress with safety. Despite global efforts like the Biological Weapons Convention and Chemical Weapons Convention, the threat still exists.

Effective preparedness requires early detection, strong surveillance, rapid diagnosis, and good public health systems. Healthcare professionals play an important role in identifying unusual outbreaks early. Overall, better preparedness and strict regulations are essential to protect public health from bioterrorism threats.

REFERENCES

1. Centers for Disease Control and Prevention. Bioterrorism agents/diseases classification. Atlanta: CDC; 2024. Available from: https://www.cdc.gov/bioterrorism/agents.html
2. Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Philadelphia: Elsevier; 2020.
3. Murray PR, Rosenthal KS, Pfaller MA. Medical Microbiology. 9th ed. Philadelphia: Elsevier; 2020.
4. Meselson M, Guillemin J, Hugh-Jones M, Langmuir A, Popova I, Shelokov A, et al. The Sverdlovsk anthrax outbreak of 1979. Science. 1994;266(5188):1202–8.
5. Jernigan DB, Raghunathan PL, Bell BP, Brechner R, Bresnitz EA, Butler JC, et al. Investigation of bioterrorism-related anthrax, United States, 2001. N Engl J Med. 2002;346(20):160–7.
6. Wheelis M. Biological warfare at the 1346 siege of Caffa. *Emerg Infect Dis*. 2002;8(9):971–5.
7. Dennis DT, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, et al. Tularemia as a biological weapon: medical and public health management. *JAMA*. 2001;285(21):2763–73
8. Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. *Smallpox and its eradication*. Geneva: World Health Organization; 1988.
9. Kortepeter MG, Bausch DG, Bray M. Basic clinical and laboratory features of filoviral hemorrhagic fever. J Infect Dis. 2011;204(Suppl 3):S810–6.
10. World Health Organization. Ebola virus disease outbreak 2014–2016: situation reports. Geneva: WHO; 2016.
11. McCormick JB, Fisher-Hoch SP. Lassa fever. *Curr Top Microbiol Immunol*. 2002;262:75–109
12. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. *Lancet Infect Dis*. 2006;6(2):91–9.
13. Török TJ, Tauxe RV, Wise RP, Livengood JR, Sokolow R, Mauvais S, et al. A large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. *JAMA*. 1997;278(5):389–95.
14. Riley LW, Remis RS, Helgerson SD, McGee HB, Wells JG, Davis BR, et al. Hemorrhagic colitis

associated with a rare *Escherichia coli* serotype. *N Engl J Med*. 1983;308(12):681–5.

15. Harris JB, LaRocque RC, Qadri F, Ryan ET, Calderwood SB. Cholera. *Lancet*. 2012;379(9835):2466–76.
16. Forrester NL, Weaver SC. Evolution and spread of Venezuelan equine encephalitis complex alphavirus. *Emerg Infect Dis*. 2017;23(6):e161135.
17. Daniel TM. The history of tuberculosis. *Respir Med*. 2006;100(11):1862–70.
18. Chua KB, Goh KJ, Wong KT, Kamarulzaman A, Tan PSK, Ksiazek TG, et al. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. *Lancet*. 2000;354(9186):1257–9.
19. Jonsson CB, Figueiredo LTM, Vapalahti O. A global perspective on hantavirus ecology, epidemiology, and disease. *Clin Microbiol Rev*. 2010;23(2):412–41.
20. Sidell FR, Takafuji ET, Franz DR. Medical aspects of chemical and biological warfare. Washington, DC: Borden Institute; 1997.
21. Organisation for the Prohibition of Chemical Weapons (OPCW). Chemical Weapons Convention and schedules of chemicals. The Hague: OPCW; 2019.
22. Okumura T, Suzuki K, Fukuda A, Kohama A, Takasu N, Ishimatsu S, et al. The Tokyo subway sarin attack: disaster management, Part 1. *Acad Emerg Med*. 1998;5(6):613–7.
23. Ellison DH. Handbook of chemical and biological warfare agents. 2nd ed. Boca Raton: CRC Press; 2007.
24. Organisation for the Prohibition of Chemical Weapons (OPCW). OPCW statement on the use of VX in Malaysia, 2017. The Hague: OPCW; 2017.
25. Whitlock GC, Estes DM, Torres AG. Glanders: off to the races with *Burkholderia mallei*. *FEMS Microbiol Lett*. 2007;277(2):115–22.
26. Ulrich RG, Sidell FR, Taylor TJ, Wilhelmsen CL, Franz DR. Staphylococcal enterotoxin B and related toxins. In: Sidreviell FR, Takafuji ET, Franz DR, editors. *Medical aspects of chemical and biological warfare*. Washington, DC: Borden Institute; 1997. p. 621–30.
27. Arnon SS, Schechter R, Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, et al. Botulinum toxin as a biological weapon: medical and public health management. *JAMA*. 2001;285(8):1059–70.