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An Overview on Biological Weapons and Bioterrorism

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Abstract Bioterrorism is the deliberate or threatened use of biological agents; viruses, bacteria, toxins or other agents to cause illness or death in people, animals, or plants. Since most priority bioterrorism agents are zoonotic in origin, there is a heightened awareness and concern about the possibility of bioterrorism involving animals. Veterinarians and livestock owners may be the first to diagnose the early cases of a bioterrorist act, as livestock can be sentinels of such an exposure. List of the most likely biological agents to be used in an act of bioterrorism had been prioritized and these agents are classified into A, B and C categories. Category A agents and disease are easily transmitted from animals to human, (except for smallpox, which has no animal reservoir) person to person, having high mortality rates and potential for a major public health impact. Category B agents and disease are moderately easy to disseminate and result in moderate morbidity rates and low mortality rates. Category C agents and diseases include emerging pathogens that could be engineered for mass dissemination. Although society has limited ability to prevent bioterrorist attacks, there still is a need to take preventative steps to reduce potential risks for such attacks. Increased laboratory scrutiny for disease agents, greater controls for investigations involving these pathogens and other security measures implemented, are necessary to restrict access to dangerous biological agents. Detection of disease in animals may be essential in predicting a bioterrorism event since most threat agents of bioterrorism are microbes causing zoonotic diseases. Veterinarians and veterinary diagnostic laboratories should become a part of nationwide active surveillance for category A, B, and C agents and diseases, as well as for new and emerging bioterrorism agents.

Keywords: bioterrorism, biological weapons, biowarfare, zoonoses, public health

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1. Introduction

Bioterrorism is the use of microorganisms (bacteria, viruses and fungi) or toxins by terrorist or extremists' groups to produce weapons which cause death and disease among humans, animals and plants. Terrorism is the unlawful use of force or violence against person, animals or property to intimidate or coerce a government or civilian population to gain political or social objectives [15]. The use of biological agents (Bio-weapons) to cause harm or death is not a new concept; countries have been engaging in bioterrorism for hundreds of years. Bioterrorism dates to the 14th century, when cadavers were dropped into enemy wells to poison the drinking water. Similarly, bioterrorism occurred during the French and Indian wars, when native Americans were given smallpox-laden blankets. This action is believed to have initiated smallpox in this previously unexposed population and resulted in a 40% mortality rate. More recently, bioterrorism events have been noted, one is the intentional contamination of salad bars in the Dalles, Oregon, using *Salmonella* and

the other, the 2001 attack using anthrax-laden letters mailed to media organizations and politicians [26].

The potential impact of bioterrorism depends on the agent used, the amount being disseminated, the dispersal method, the weather/release conditions, the pre-existing immunity of the exposed population, and how quickly the attack was identified. There are a broad range of potential bioterrorism agents, including bacteria, viruses, and toxins (of microbial, plant, or animal origin). Common characteristics of this diverse group of agents include: the ability to be dispersed in aerosols of 1 to 5 mm particles, which can penetrate the distal bronchioles, the ability to deliver these aerosols with simple technology, the feasibility of these agents, if delivered from a line source (airplane) upwind from the target, to infect large numbers of the population; and the ability to spread infection, disease, panic, and fear [15]. Bioterrorism has the potential to result in high morbidity and mortality, because aerosolized biological agents can infect or kill many people in a short period of time. Even non-aerosolized attacks, such as the anthrax attack can result in morbidity and mortality [53]. These weapons are difficult to detect (tasteless and odorless) and can be disseminated via air. A

high index of suspicion should be present when many people develop similar symptoms. Enclosed spaces provide ideal targets, particularly those that draw large crowds such as sporting events, recreation grounds, and probably all those places where people gather in huge numbers. The number of terrorist acts worldwide has decreased over the last few years, but what is of great concern is the increase in their lethality [3].

Before the 20th century, the use of biological agents took three major forms, deliberate contamination of food and water with poisonous or contagious material using microbes, biological toxins, animals, or plants (living or dead) in a weapon system, and using biologically inoculated fabrics and persons. Now a days, sophisticated bacteriological and virological techniques allowed the production of significant stockpiles of weaponized bio-agents able to spread and cause diseases such as; *Anthrax*, *Brucellosis*, *Tularemia*, *Smallpox*, *Viral hemorrhagic fevers*, and *Botulinum*, and *Ricin poisoning* [38]. The most likely route of dissemination is an aerosolized release of 1-5 mm particles. Other methods of dissemination include oral, intentional contamination of food/water supply, per-cutaneous, infected animal vector e.g., release of infected fleas. Human-to-human spread, where an individual infected with communicable disease walks among a crowd of healthy people has also been noted. As evidenced from the anthrax attacks of 2001, it has been confirmed that even physical objects, such as letters, can be used to help spread biological agents [38].

Recently, with advancements in technology, bio-weapon diseases have been known to spread faster and prove much more difficult to control and eradicate than the historical ones. However, bioterrorism preparedness helps mitigate potential negative outcomes, and is required by healthcare and public health regulating agencies as part of a comprehensive emergency management program. Formulating a significant healthcare, public health, and emergency management response is the need of the hour [8]. The main objective of this paper is to review the historical perspectives, potential exposures due to various microbes and their metabolites, which may induce significant risk upon health care due to bioterrorism and to highlight what needs to be done to prevent and reduce morbidity and mortality arising from bioterrorist actions.

2. Historical Background

Rudimentary forms of biological warfare have been practiced since antiquity or in the former ages [41]. During the 6th century BC, the Assyrians poisoned enemy wells with a fungus that would render the enemy delirious. The advent of the germ theory of disease and advances in microbiological techniques brought a new level of sophistication to the theoretical use of bio-agents in war. Biological sabotage in the form of anthrax and glanders were undertaken on behalf of the Imperial German government during World War I (1914–1918), with indifferent results [17].

The use of biological agents as war weapons is not a modern era novelty, as evidenced by the fact that in pre-Christian era, around 300 B.C., the Greeks used animal cadavers to contaminate water wells of enemies.

This strategy was also used the by the Romans and Persians [59]. In a later period, during the battle of Tortona, Italy, 1155 bodies of dead soldiers and animals were used to contaminate water wells by Emperor Barbarossa's troops [18]. In the 14th century, during the siege of Kaffa by the Tartars among the Tartar army, an epidemic of plague was spread. The besiegers thought to catapult the cadavers of their dead comrades within the walls of the city of Kaffa, resulting in a turning point in the war; the Genoese fled from Kaffa, carrying with them their sickness. On the return trip to Genoa, they halted at several ports in the Mediterranean Sea. While some sources believe a possible correlation between the epidemic of plague in Kaffa and the pandemic that decimated most of the population of Europe in the following decades (Black Death), most authors believed that the two events were in fact independent [61].

In 1422, during the siege of Carolstein, Lithuanian soldiers catapulted cadavers of dead soldiers and excrements into the city, frightening the population, and spreading lethal fevers in many places [44]. The next documented use of biological agents as a war weapon occurred more than three centuries later. During the French-Indian War (1754-1767), the British commander ordered the distribution of blankets infected with smallpox to counter the population of Indian tribes hostile to the British. The distribution of infected blankets occurred in the summer of 1763, and the resurgence of the virus among the indigenous population lasted for more than 200 years [6].

2.1. Bio-Weapons, Their Status Post World War I (WW I)

It is frequently reported that the Germans inoculated cattle with *Bacillus anthracis* and *Pseudomonas mallei*, responsible to cause severe diseases such as anthrax and glanders disease, before sending them into enemy states [52]. As WW I saw the large-scale use of non-conventional chemical weapons, it was expected that WW II would see more extensive use of biological weapons. During this war, many countries conducted research programmes to develop bio-weapons; the Japanese programme to produce a bio-weapon, was considered as the most ambitious (1892-1959). The research in this direction started in 1928; when Lieutenant general (Lt. Gen.) Ishii visited many European and American countries to learn useful techniques and information about the possible uses of biological weapons. Upon returning to his homeland, he was provided a substantial grant to constitute some massive bio-weapons research center, known as the Unit 731, located at Beiyinghe in Manchuria. The research centre staffed over 3,000 scientists, mainly microbiologists. The experiments were conducted on prisoners of war, principally Koreans, Chinese and Russian soldiers. The prisoners were used to test numerous bioweapons, including *Yersinia pestis*, *Vibrio cholerae*, *Neisseria meningitidis* and *Bacillus anthracis* [39]. During this research, several thousand prisoners died because of the experiments conducted on them. However, the mortality rate around the area of Unit 731 remained very high for several years as high as 200,000 deaths due to the activities carried out by Lt. Gen. Ishii [29]. In 1942,

the poor control of an infection spread resulted in the death of 1,700 Japanese soldiers [57].

Many other nations carried out experiments on potential biological agents. The experiments conducted in 1942 by the British army on the Island of Gruinard, off the Scotland coast, where anthrax bombs were tested, were considered as dirty [40].

2.2. Bio-Weapons, Their Status Post World War II (WW II)

Until WWII, the U.S. remained considerably behind other nations with regards to research on bio-weapon (BW). The golden age for both development and testing of BW in the U.S. has started immediately after the conclusion of WWII, when it received the results of the experiments performed by the Japanese Unit 731. The U.S. also worked directly with Lt. Gen. Ishii, the former director of Unit 731 [17].

It was noted that during September 1950, the U.S. navy conducted an experiment on civilians to assess the vulnerability of a large American coastal town to a biological attack; in the San Francisco Bay. A cloud of *Serratia marcescens* (a low pathogenic bacterium mainly responsible for infections of skin and respiratory tract) was spread using a boat, initiating infection and spread, as confirmed by subsequent checks, which involved almost the entire population (1 million people). Even though the bacterium was almost harmless, several individuals developed respiratory diseases and some of them even succumbed to death [17]. Another report revealed that during the years between 1956 and 1958, in Georgia and Florida, swarms of mosquitoes, probably carriers of yellow fever were released to verify vulnerability to an air attack. Even though the documents are kept in top secret, several sources reported that some individuals died from the bites of insects and the resultant yellow fever. A large-scale experiment which was documented in the United States, involved the dissemination of *Bacillus subtilis* in the New York subway in the summer of 1966. The experiment resulted in the infections, although without consequences, among more than one million people. It demonstrated that the spread of a pathogen in the whole subway network from a single station, due to the displacement of air in the tunnels, was possible [9,63].

In the 1970's, the Union of Soviet Socialist Republics (USSR) conducted an ambitious research programme on BW's, but unlike the U.S. programmes, whose secrecy has been partially revealed, an aura of mystery about Russian research programmes remains. According to Davis [22], the USSR, between 1973 and 1974, formed an organization called the Chief Directorate for Biological Preparation (Biopreparat), with the purpose of developing a BW's. Although there was no unambiguous data about the number of individuals employed by Biopreparat, it is believed that more than 50,000 people were working in the whole system connected to the programme, including scientists and technicians, who were placed in 52 research and production factories. In these facilities, high amounts of etiologic agents of plague, tularemia, anthrax, glanders, smallpox, and *Venezuelan equine encephalomyelitis* were studied and produced. In addition to biological agents from natural sources, the Soviets also studied and applied

technologies of genetic engineering to increase the aggressiveness of biological agents through biotechnology. The aim of this work was to develop a new, more dangerous, more easily spread, and more difficult to identify, combat generation of BW's. Among the countries which run massive programmes on BW's research in the post-World Wars era, included Iraq. It started its research and development programmes in the field of biological warfare in 1974, contextualizing it in an organization called the State Organization for Trade and Industry [22]. The programme consisted of the study and production of botulinum toxin, anthrax, aflatoxin, and ricin, as well as antiplants and viral agents, such as rotavirus, infectious hemorrhagic conjunctivitis, and camel pox. Iraqi programmes involved about 300 scientists, who completed their training in Western European countries [9,39].

2.3. Categories of Agents Used as Biological Weapons

Bioterrorism is defined as the deliberate release of viruses, bacteria or other germs (agents) used to cause illness or death in people, animals, or plants (CDC, 2013). These biological agents are classified into three categories. Category A: Agents that can be easily disseminated or transmitted from person to person. They result in high mortality rates and have the potential for major public health impact. They might cause public panic and social disruption, and require special action for public health preparedness. Category B: Agents those are moderately easy to disseminate. They result in moderate morbidity rates and low mortality, and require specific enhanced diagnostic capacity and disease surveillance. Category C: Emerging agents that could be engineered for mass dissemination in the future because of their availability. They are easy to produce and disseminate. They were potentially linked to high morbidity and mortality rates, and major health impact [15].

BWs are relatively easy and inexpensive to produce, cause death or disabling disease, and can be aerosolized and distributed over large geographic areas. There is a long list of potential pathogens for use by terrorists; however, only a few are easy to prepare and disperse as shown in Table 1. Zoonoses of offensive biological warfare (biowarfare) programs have included the causative organisms of anthrax, plague, tularemia, glanders, Q fever [45,47].

2.3.1. Anthrax

The disease anthrax is a zoonotic disease caused by the gram-positive, non-motile *Bacillus anthracis* [47]. Anthrax has been a scourge of cattle and other herbivores for centuries. During the industrial revolution, the inhalation form was first recognized as an occupational pulmonary disease in workers in the wool industries of Europe [10]. Anthrax makes an ideal biological weapon. The inhalation form of disease is highly lethal, easy of production and dissemination, the bacteria are easy to cultivate and spore production is readily induced. Moreover, the spores are highly resistant to sunlight, heat and disinfectant, anthrax spores may be easily dispersed over large population through missile, bombs and air flying from flying air craft and the spores can maintain

virulence for decades and they can be milled to the ideal particle size for optimum infection of the human respiratory tract, this makes anthrax most selective for biological weapons [20].

Inhalation is most commonly used for Bio-terrorism and must be aerosolized; this is difficult because the spores must be ground into a fine powder by certain technological processes. Once in proper form the delivery is simple through the use of commercial aerosol products. Most recent outbreak was spread through the postal services by letters containing the anthrax powder. Anthrax spores were weaponized by the United States in the 1950's and 1960's before the old U.S. offensive program were terminated. Other countries have weaponized this agent or are suspected of doing so. Iraq admitted to a United Nations inspection team in August of 1991 that it had performed research on the offensive use of *B. anthracis* prior to the Persian Gulf War, and in 1995 Iraq admitted to weaponizing anthrax. A recent defector from the former Soviet Union's biological weapons program revealed that the Soviets had produced anthrax in ton quantities for use as a weapon. This agent could be produced in either a wet or dried form, stabilized for weaponization by an adversary and delivered as an aerosol cloud either from a line source such as an aircraft flying upwind of friendly positions, or as a point source from a spray device. Coverage of a large ground area could also be theoretically facilitated by multiple spray bomblets disseminated from a missile war head at a predetermined height above the ground (CDC, 2001).

Nevertheless, the recent Anthrax attack in 2001 through letters caused worldwide concerns regarding the threats of bioterrorism. Beginning in mid-September 2001, the USA experienced unprecedented biological attacks involving the intentional distribution of *B anthracis* spores through the postal system. In 2001, in the fall of letters containing

anthrax spores were mailed to many prominent people in the U.S. Tom Brokaw, Senator Tom Daschle, and the offices of the *New York Post* were among those who were targeted (CDC, 2001). The full impact of this bio-terrorist activity has not been assessed, but already the toll is large. Hundreds of people were affected. In the 20th century series of cases, the mortality rate of occupationally acquired inhalational anthrax was 89%, but majority of these cases occurred before the development of critical care units and in most cases before the advent antibiotics [54].

2.3.2. Q fever

Q fever is a zoonotic disease caused by the rickettsia, *C.burnetii*. Its natural reservoirs are sheep, cattle, goats, dogs, cats and birds [47]. The organism grows to especially high concentrations in placental tissues. The infected animals do not develop the disease, but do shed large numbers of the organisms in placental tissues and body fluids including milk, urine, and faces [5]. When considering microbes as weapons they can simplistically be divided into lethal agents and incapacitating agents. Lethal agents, such as *Yersinia pestis*, induce an acute disease with a high associated mortality rate. Incapacitating agents make people ill enough that they cannot carry on with normal life for a period, but ultimately most people will recover. Q fever belongs primarily to the incapacitating agents. It is considered that a biological attack will affect the largest number of people if disseminated as an aerosol. Q fever has been shown to travel over large distances on the wind during natural outbreaks, and is a relatively resistant organism in the environment. In addition, as described above, the infectious dose for man is extremely low. For this reason, the pathogen attracted attention in offensive programmes of the last century. However, a significant impediment to use of *C burnetii* is the difficulty in culturing the pathogen [4].

Table 1. Major Categories of biological agents with probability to be used as bio-weapons [15]

Groups	Diseases	Agents
A	Anthrax	<i>Bacillus anthracis</i>
	Botulism	<i>Clostridium botulinum</i> toxin
	Plague	<i>Yersinia pestis</i>
	Smallpox	<i>Variola major</i>
	Tularemia	<i>Francisella tularensis</i>
	Viral hemorrhagic fevers	<i>Filoviruses and Arenaviruses</i>
B	Brucellosis	<i>Brucella spp.</i>
	Epsilon toxin	<i>Clostridium perfringens</i>
	Food safety threats	<i>Salmonella spp., E.coliO157:H7, shigella</i>
	Glanders	<i>Burkholderia mallei</i>
	Melioidosis	<i>Burkholderia pseudomallei</i>
	Psittacosis	<i>Chlamydia psittaci</i>
	Q fever	<i>Coxiella burnetii</i>
	Ricin toxin	<i>Ricinus communis</i>
	Staphylococcal enterotoxin B	<i>Staphylococcus spp.</i>
	Typhus fever	<i>Rickettsia prowazekii</i>
	Viral encephalitis	<i>Alphaviruses</i>
	Water safety threats	<i>Vibrio cholerae, Cryptosporidium parvum</i>
C	Emerging infectious diseases	<i>Nipah virus and Hantavirus</i>

2.3.3. Tularemia

F. tularensis, the causative agent of tularemia, is a small, aerobic nonmotile, gram negative coccobacillus. Tularemia also known as rabbit fever and deer fly fever is a zoonotic disease that humans typically acquire after skin or mucous membrane contact with tissues or body fluids of infected animals, or from bites of infected ticks [47]. Tularemia was recognized in Japan in the early 1800's and in Russia in 1926. Tularemia as a biological weapon is the difficulty in culturing and growing these bacteria, however, it can be isolated from infected organisms. In addition, it has been weaponized by the United States and Soviet Union in the past and can be easily disseminated through aerosol release [1]. Tularemia could be used as a biological weapon in several scenarios, causing varying degrees of casualties. The most dangerous scenario involves an aerosol release with large numbers of persons exposed. Additional complications would result if an antibiotic-resistant strain, as is claimed to have been developed in the former Soviet Union, were used [1].

Researchers have estimated that a large-scale aerosol release of 50 kg over a large metropolitan area could cause 250,000 incapacitating casualties. Most of those affected could present with a nonspecific febrile illness 3 to 5 days after exposure depending on the inoculum of exposure and would subsequently develop pulmonary symptoms consistent with pneumonic tularemia [24]. However, because of the difficulties in tularemia diagnosis and the nonspecific clinical presentation, the determination of tularemia as the causative agent may be delayed. The initial presentation of cases may be difficult to distinguish from a natural influenza outbreak or other respiratory pathogens [24]. Tularemia may also be confused with another biological weapon. Epidemiological clues to distinguish tularemia from plague or anthrax is the clinical course slower with tularemia, case fatality rate, higher with plague [33] and possibly the pattern of pulmonary manifestations observed on chest radiograph, such as the large pleural effusions and mediastinal widening characteristic of inhalational anthrax. Pulmonary tularemia may be difficult to distinguish from Q fever, another potential biological weapon agent [34].

2.3.4. Plague

The plague, which is caused by *Yersinia pestis*, a gram-negative rod-shaped, non-motile, non-sporulating bacterium has a great historical significance. Plague is a zoonotic disease transmitted to humans by rodents (e.g., rats, mice, ground squirrels). Fleas that live on the rodents can transmit the bacteria to humans, who then suffer from the bubonic form of plague. The bubonic form may progress to the septicemic and pneumonic forms. Pneumonic plague would be the predominant form having potential to be used as a BW, due to its ease of aerosol dissemination [30].

This is the only weapon besides smallpox, which can cause devastation beyond those persons who are initially infected. With modern air travel, containing an outbreak of plague could be challenging. The lethality and contagiousness of plague makes the plague a life threatening biological agent. Although its capability is limited by the presence of effective antibiotic treatment

and the difficulties in its weaponization, plague remains to be an advantage for BW's development [49].

Early in the history plague was called as a black death, which remained to be a form of bubonic-flea-borne variety of plague. Now we see the evolution of far more contagious pneumonic variety as a cause of human epidemics. Direct human exposure to aerosolized plague bacilli was the most effective way to cause human illness and death as reported previously. The biological weapons programs of the USA and the former Soviet Union have pursued aerosol transmission capabilities for plague [28]. Although Soviets had intercontinental ballistic missile warheads containing plague bacilli available for launch before 1985, yet, virtually insurmountable problems arose in the production and aerosol dispersal of substantial quantities of plague organisms by modern weapon systems [22]. Despite these difficulties, plague is viewed as a high-risk disease for bio-weapons production [31].

2.3.5. Botulism (*Clostridium botulinum*)

C botulinum is a spore forming and obligate anaerobe, etiological agent of botulism, which can be isolated from the soil, its natural habitat. Four species of *C botulinum* are known, characterized by different genomes and their common botulinum toxin. In addition, seven distinct antigenic types of botulinum toxin (A-G) are defined by the absence of cross-neutralization. The toxin is responsible for the disease and is a di-chain polypeptide: a heavy chain of 100 KDa is joined by a single disulfide bond to a 50 KDa light chain, which is zinc containing endopeptidase that blocks acetylcholine-containing vesicles from fusing with the terminal membrane of the motor neuron, resulting in flaccid muscle paralysis [2].

Botulinum toxin is the most lethal toxin known and all seven types act in similar ways. Death often occurs as a result of paralysis of pharyngeal and diaphragmatic muscles, followed by respiratory arrest [6]. Botulinum toxin poses a major bio-weapon threat because of its extreme potency and lethality; its ease of production, transport, and misuse; and the need for prolonged intensive care among affected persons [7]. An outbreak of botulism constitutes a medical emergency that requires prompt provision of botulinum antitoxin and, often, mechanical ventilation, and it constitutes public health emergency that requires immediate intervention to prevent additional cases. Timely recognition of a botulism outbreak begins with an astute clinician who quickly notifies public health officials. Botulinum toxin is the most poisonous substance known [43].

3. The Properties of an Ideal Biological Weapon

A biological weapon can be more effective, pound for pound, than the hydrogen Bomb. This analysis of biological weapons illustrates the impact that a potent agent could have. Biological attacks are designed to devastate a population, either by inducing illness or more commonly, killing large numbers of people through mass destruction. The following desired characteristics are

listed in order of relative importance: Extremely toxic, highly infectious, preferably communicable among humans, stable, both in storage and dispersal, creates difficulty in medical response, easy to grow and produce manipulable effects [42]. While there are numerous pathogens (bacteria, viruses and toxins) that cause diseases in humans, animals and plants, only very few possess the characteristics to be a BW. Eitzen [27] described the characteristics that make a biological agent a potential BW. Ideally, a BW should be easy to find or produce. To develop a biological attack towards sensitive targets or the population, large amounts of biological agents are in fact required; it must be considered that it is necessary to have quite many biological agents (or a certain amount of toxin) to generate a disease in a target. The ideal BW also must have a high capacity to incapacitate the affected or, alternatively, be highly lethal. It is appropriate to choose an agent with an incubation period depending on whether immediate or delayed effects are required. Other important characteristics for a biological weapon are the route of transmission, and hence, the ease of dissemination with an appropriate method of delivery. Finally, the stability of the agent must be assessed, especially when large quantities must be stored for indefinite periods [36].

Generally, biological agents or BW can be further classified according to certain characteristics that define the hazard to health : Infectivity: The aptitude of an agent to penetrate and multiply in the host; Pathogenicity: The ability of the agent to cause a disease after penetrating into the body; Transmissibility: The ability of the agent to be transmitted from an infected individual to a healthy one; Ability to neutralize: Its means to have preventive tools and or therapeutic purposes [46].

4. Mode of Delivery and Method of Dissemination of Biological Weapons

Biological agents may be delivered in either wet or dry form. Dry powders composed of very small particles tend to have better dissemination characteristics, and have advantages in storage. Dried agents require an increased level of technological sophistication to produce, although freeze drying or spray dries technology has been available in industry for several years. Most commonly, delivery methods used are aerosolized agent. The agent can be dispersed by attaching a spray device to a moving conveyance. An industrial insecticide sprayer designed to be mounted on an aircraft is an example. A line of release would then occur while the sprayer is operating. This is known as a line source and is sprayed perpendicular to the direction of the wind, upwind of the intended target area. Up to a certain range, anyone downwind of such a line source would theoretically be at risk [15].

The range that the infectious or toxic agent would reach depends on many factors, including wind speed and direction, atmospheric stability, and the presence of inversion conditions; and on characteristics of the agent itself. Biological agents can be dispersed by spraying them into the air, by infecting animals that carry the disease to humans and by contaminating food and water. Potentially, hundreds of human pathogens could be used as weapons;

however, public health authorities have identified only a few as having the potential to cause mass casualties leading to civil disruptions. There are number of causes why biological weapons are potentially more powerful agents to mass casualties leading to civil disruptions. An ideal biological warfare agent would be easily disseminated in the open air by using off-the shelf devices such as industrial sprayers or other types of aerosol-producing devices. Aerosols biological agents are dispersed into the air, forming a fine mist [65].

Biological warfare agents are most effectively delivered as an aerosol. Aerosol delivery systems aim to generate invisible clouds with particles or droplets between 0.5 and 10 micrometers in diameter, which can remain suspended for long periods. The aerosol release of respirable particles in that size range results in a predominantly inhalation hazard since the particles can settle deep in the lungs. Biological warfare agents may be used to contaminate food or water systems or supplies. Heat destroys most pathogens and toxins; thus, to be effective most agents would have to be used on food that will be served raw or added after the food is prepared and presented for serving. Standard water purification methods (chlorination and filtration) may well inactivate many pathogens and some toxins. However, chlorination will not inactivate many spores and commercial filtration will be largely ineffective against spores, cysts, viruses, and many bacteria. Filtration will be all but useless against toxins unless something like activated charcoal is used. Biological warfare agents have been delivered by covert injection. Some agents (for example, ricin) are lethal when injected. The possible modes of BW attack in any operational environment will vary significantly with location, depending on the nature of the delivery system employed, the time of day, the weather conditions, and the local geography [50].

5. Routes of Exposure of Biological Weapons

Biological agents can be transmitted through one or more ways. The transmission modes are: parenteral; agents that are transmitted through body fluids or blood, airway (by droplets); agents that are emitted by infected individuals, which can then be inhaled by surrounding people. Contact; through which the agents present on the surface of the infected organism can infect another organism. Oral-fecal route: through objects, foods or other items contaminated with the feces of infected patients, or through sexual contact [37].

5.1. Respiratory System

Inhalation most dangerous, inhaled, resembles flu symptoms but progresses to fluid in lungs and respiratory failure. The body is most vulnerable to this route of exposure because of the large surface area and gas exchanging function of the lungs; because of the susceptibility of mucous membranes to infection; and because of the presence of phagocyte cells that, if unsuccessful in destroying a pathogenic microorganism, may instead carry it to the lymph system where it may proliferate and cause most biological agents affect the

lungs, Unlike vapors, aerosol particles of a certain size are accumulated over time in the respiratory system [58].

5.2. Skin and Mucous Membranes

Cutaneous, skin, least harmful, enters through abrasion or cuts, causes lesion with black scab. The presence of injuries, sores or skin rashes might change this significantly and allow even biological agents to enter the body by this route. As a rule, the thinner, more vascular, and moister the skin, the more prone it is to penetration. High relative humidity promotes skin penetration. Liquid spills and aerosols cause a hazard for skin penetration that can be several deliveries. In case of makeshift devices, a larger fraction of agent will be in the spills and a smaller part will usually order of magnitude higher than from vapors. Spills will occur mainly around the point of be aerosolized [51].

5.3. Digestive System

Gastrointestinal, ingesting infected meat or water, nausea, abdominal pain and bleeding, fever, vomiting, can be treated with antibiotics early on. Biological weapons can enter the digestive system in contaminated food or drinking water, by hand-mouth contact after touching contaminated surfaces, or by swallowing of respiratory mucus after an accumulation of larger aerosol particles in the nose/throat and upper airways. Of all exposure routes this is the easiest to control, provided that the contaminated sources are known [51].

6. Animals as Sentinels of Biological Agents

Most of the bioterrorism agents (80%) are zoonotic in origin and can be used as biological weapons [48]. As a result, an attack on human populations with a bioterrorism agent would likely pose a health risk to animal populations in the target area; therefore, integrating veterinary and human public health surveillance efforts is essential. It is recommended that prompt diagnosis of unusual or suspicious health problems in animals, as well as establishing criteria for investigating and evaluating suspicious clusters of human and animal disease or injury and triggers for notifying law enforcement of suspected acts of biological or chemical terrorism (CDC, 2000).

Similarly, an indicator of a biological terrorism attack would be increased numbers of sick or dead animals, often of different species. Some BW agents can infect/intoxicate a wide range of hosts [19]. In part because of such recommendations, calls have been made for enhanced veterinary surveillance for outbreaks of animal disease caused by bioterrorism agents and better communication between animal health and human health professionals. For such efforts to succeed, the relevance to human health of disease events in animals must be established. The potential use of animals as sentinels of a human bioterrorism attack can be differentiated from the possibility of a direct attack on animals of agricultural importance (agroterrorism) [15]. First, animals could

provide an early warning to humans if clinical signs could be detected before human illness emerged or soon enough to allow preventive measures to be initiated. This early detection could occur because an animal species had increased susceptibility to a agent, because the disease caused by the agent had a shorter incubation period, or because animals were exposed sooner (or at more intense and continuous levels) than the human population (CDC, 2000) [19].

The simultaneous appearance of disease signs and symptoms in animals may contribute to the more rapid identification of a biological warfare agent that was producing nonspecific effects in nearby persons. Second, if a released biological agent persists in the environment (such as soil, water, or air), active surveillance for sporadic illness in animals could help detect ongoing exposure risks. Additionally, the geographic pattern of sick or dead animals could indicate the persistence of a biological threat [19].

Finally, animal populations such as wild birds, commercially shipped livestock, and animals involved in the local or international pet trade, could play a role in the maintenance and spread of an epidemic attributable to an intentional release of a biological agent. Detecting the agent in such mobile populations could therefore signal the ongoing spread of the agent and provide an opportunity for interventions to prevent further spread (CDC, 2000).

7. Impacts of Bioterrorism on Animals and Humans

Even a small-scale biological attack with a weapon grade agent on an urban center could cause massive morbidity and mortality, rapidly overwhelming the local medical capabilities. For example, an aerosolized release of little as 100kg of anthrax spores upwind of a metro city of a size of Washington DC has been estimated to have the potential to cause up to three million deaths. And it causes massive morbidity and mortality in animals and economic loss as shown in Figure 1 [10].



Figure 1. Animal bioterrorism [10]

Many of the disadvantages of biological weapons use relate to difficulties in executing an attack. For example, it is difficult to protect workers during the processes of production, transportation, and delivery, while immunization may be ineffective or simply irrelevant. The danger that biological agents can also affect the health of the aggressor forces, the dependence on prevailing winds and other weather conditions on effective dispersion, the effects of temperature, sunlight, and desiccation on the survivability of some infectious organisms. Also, the environmental persistence of some agents, such as spore-forming anthrax bacteria, which can make an area uninhabitable for long periods, the possibility that secondary aerosols of the agent will be generated as the aggressor moves through an area already attacked, The unpredictability of morbidity secondary to a biological attack [65].

8. General Measures for Protection and Prevention against a Biological Weapon

The general population should be educated and made aware of the threats and risks associated with biological agents. Only cooked food and boiled/chlorinated/filtered water should be consumed, insects and rodents control measures must be initiated immediately, clinical isolation of suspected and confirmed cases is essential. An early accurate diagnosis is the key to manage casualties of biological warfare. Therefore, a network of specialized laboratories should be established for a confirmatory laboratory diagnosis. Existing disease surveillance system as well as vector control measures and mass immunization programme in the suspected area should be pursued more rigorously. Enhancing the knowledge and skills of clinicians plays a vital role in controlling the adverse impact of the attack. As bioterrorism, and related infections will remain rare events, creative ongoing strategies will be required to sustain attention to potential new cases [15].

The effects of many BW threat agents are preventable or can be mitigated with proper precautions. Immunizations, pre-exposure and post-exposure prophylaxes, therapeutics, and protective clothing are available to provide protection. Personnel must have all required immunizations administered prior to entering an area of operations where BW agent employment is a threat. If an attack is felt to be imminent, or is known to have occurred, command-directed chemoprophylaxis would be appropriate for all personnel in the area. However, it is impractical and wasteful to place everyone located in a potential target area on prolonged, routine antimicrobial prophylaxis in the absence of such a threat condition [10]. All immunizations should be administered in sufficient time to provide the initial protection to take effect before troops are deployed to the area of operations; when administration prior to deployment is impossible, troops must receive the immunizations as soon as the mission permits operations. Some immunizations are used in conjunction with pre-exposure chemoprophylaxis or post-exposure chemoprophylaxis to provide protection. Specific immunizations, therapeutics, and chemoprophylaxis are

required for the area of operations. For those BW agents for whom a specific immunization is not available, the use of protective equipment combined with chemoprophylaxis may be employed to provide protection [55].

Vaccination is an important practical means of providing continuous protection against BW threats prior to, as well as during, hostile actions. Vaccines against a few potential BW agents are available. Many of these vaccines were developed for the protection of laboratory workers or individuals working where the target diseases are endemic [15].

9. Trend of Biological Weapons in Ethiopia and East Africa

The Great African Rinderpest, an epizootic of a century ago could be considered as a suitable model for predicting the potential effects of the proliferation of a highly virulent and contagious BW disease, which might pose a risk to wildlife and livestock species. Rinderpest virus was introduced into Africa in 1887 through cattle imported to Ethiopia from India. The subsequent epidemic outbreak of rinderpest that began in 1889 swept from the Horn of Africa to the southern cape, in less than a decade. This spread had exhibited an effective average dispersal rate of approximately 3 km per day during an era pre-dating automobiles and aircraft. The rinderpest epizootic proliferated rapidly among native African cattle breeds and susceptible wild ungulate species, killing an estimated 90% to 95% of the cattle, African buffalo (*Syncerus caffer*), and wildebeest (*Connochaete taurinus*) in East Africa less than 3 years from its first appearance in the region [21].

Use of BW's decreased cattle populations and African buffalos were noted to be extirpated from most of their range in southern and eastern Africa. The African buffalo's, formerly the most characteristic and abundant ungulate of the African plains, were reduced to a few small, scattered relict herds [56]. Despite intensive control measures taken over the past century, rinderpest is still enzootic with in East Africa, with periodic outbreaks occurring among livestock and wildlife populations in the region [25]. The importance of buffalo as a food resource for African hunter-gatherer societies was surpassed by giving immense significance to domesticated cattle by pastoral and agricultural societies of eastern and southern Africa. Cattle have served for centuries and in some instances perhaps millennia, as the principal source of food, wealth, and motion energy for the Nilotic and Bantu peoples of Eastern and Southern Africa. The rinderpest epidemic effectively dispossessed indigenous African people off food resources, traditional livelihood, and wealth and prosperity in ways that were potentially more disruptive to traditional cultural milieus than the physical displacement from traditional territories and the political and economic subjugation of African peoples by European colonial administrations. Milk and meat from cattle which provide critically important sources of essential dietary protein in African pastoral and agrarian societies, were now in danger owing to diseases, both natural and by threat of BW's [32].

10. Role of Veterinarians in Combating a Bioterrorist Attack

Because the fields of veterinary and human medicine overlap in many areas, it makes sense that veterinary medical first responders have the same tools as human medical first responders to combat the same threats and that open communication between the two disciplines flows freely [60]. Animals and veterinarians play important roles in the surveillance for diseases of public health significance, and the input of veterinary medical professionals into the public health system is crucial to the health of humans and animals alike. Obviously, the susceptibilities of different animal species to the Category A, B, and C agents vary. Clinical signs of disease observed in animals will differ depending on multiple factors such as route of exposure, dose, species susceptibility, age, overall health status, and immune status. Clinical signs of disease that develop after a bioterrorist attack will not necessarily be identical to those of naturally acquired disease (CDC, 2001).

Occasionally, veterinarians may encounter naturally occurring cases of disease caused by some of the category A and B agents, but many of these diseases are rarely (and some never) seen by a typical practitioner. Awareness among veterinarians that certain types of clinical signs in animals are associated with infection with organisms that are potential bioterrorism agents may aid in the early recognition of a bioterrorist attack. Moreover, practitioners would need to assess whether the animals presented to them were ill because of natural versus intentional exposure. Veterinarians must be alert for indications that a bioterrorism event has occurred. With the intentional release of a biological agent, just as with a naturally occurring outbreak, there is a delay from time of exposure until onset of clinical signs. This incubation period is an advantage for terrorists who will have time to escape the area after the covert release of a bioterrorism agent. Veterinarians already need to maintain a reasonable but high degree of suspicion when examining animals with a potential infectious disease to rule out a zoonosis that threatens public health or a foreign animal disease that threatens agriculture [15,35].

It is a natural extension to carry this suspicion over to include potential zoonotic bioterrorism agents. Veterinarians may see an ill animal and an ill owner at the same time; although the disease may not have the same clinical signs in humans as it does in an animal species, the early suspicion and investigation of such a connection could mean the difference between stopping the spread of a highly contagious pathogen and not detecting it altogether. Early detection a Veterinarians must take an active approach to bioterrorism and become involved in preparedness and response and in public health overall [23].

As stated by Noah and others [45], veterinarians are vital components in combating bioterrorism. There is a need for immediate reporting for better bioterrorism preparedness. Veterinarians play a significant role in surveillance for bioterrorism agents, controlling disease, and even in the treatment of the ill. They are a key to an effective, robust surveillance and early warning system for

bioterrorism that usually targets humans and indirectly animals. If the war against bioterrorism and emerging diseases is expected to be remotely winnable, integration of practitioners and veterinary diagnostic laboratories into public health and disease-reporting systems and establishment of means for rapid communication and dissemination of information to these stakeholders is necessary. Terrorists will always have the advantage; terrorism cannot be stopped. However, through planning, education, communication, and awareness, the impact of the attacks that are carried out can be lessened and perhaps prevented from occurring altogether. Veterinarians are at the front line for education regarding zoonotic diseases and are the experts on zoonotic Category A, B, and C agents. To prevent a national crisis, vigilance is essential, and so too are veterinarian [23].

11. Conclusion and Recommendations

Biological weapons have not been frequently used throughout human history, and their efficacy to be used as a war weapon has not been completely confirmed. Because natural infections pose a great risk for human health, as in case of infection with *Influenza* virus, where there is an involvement of large population, mostly owing to easy spread, a threat of its use as a BW cannot be underestimated. There has been a continual fascination with biological weapons by nations in the last century, an addiction that continues even today. Particularly where regional hegemony (or resisting it) may require unconventional weapons, BW's remain a major threat. With zoonoses as the most likely infectious diseases to be used by bioterrorists to develop BW's, human and veterinary medicine can benefit from cross-collaboration. As barriers between animal species collapse, it expands the knowledge base of human and veterinary medicine. Integrating veterinary and human public health surveillance efforts is essential in dealing with bioterrorism. This effort will require improved communication and collaboration. A coordinated and cohesive effort by scientists, health-care providers, veterinarians, and epidemiologists is needed to control the global impact of bioterrorism.

Therefore, we recommend that there should be an improvement of mass public awareness before, during and after such an attack (presumably). The people should be educated regarding potential exposure of a biological weapon, and various steps that are required to be taken to check our bio-defense capabilities and ensure sufficient protection from emerging threats. The federal government should provide emergency health insurance coverage during a bioterrorist attack.

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