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REVIEW ARTICLE

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Review on Major Microorganisms that are Mostly in Use as Biological Weapons

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ABSTRACT

Since years ago, humans started to use toxic substances to poison their enemies. Later, biological agents or microbes and/or their products have been used by different countries for purposes of experiments and wars; and then became the target of terrorists. The review was gird with the objectives: to present a compiled data regards to microorganisms that are most frequently used as biological weapons and to raise awareness of the rationale of using microorganisms as biological weapons. Bioterrorism is the deliberate release of microbes and/or their products to cause illness or death in living creatures. We are now with an increased global trade, expanding agricultural systems, deforestation and urbanization which are predisposing factors to the emergence of many biological agents. Biological agents/microorganisms like: Bacillus anthracis, Variola virus, Francisella tularensis, Ebola and Marburg viruses; and emerging viral diseases like Influenza and Severe acute respiratory syndrome are some of the most feared, as biological weapons, in the current world because of their transmission, availability, dissemination and weaponisation characteristics.

Currently, the world is in desperate need of proven strategies to control possible bioterrorism attacks, associated with the use of biological agents. Therefore, there is a need to set and/or develop newly/advanced prevention and control methods, vaccines, antimicrobials, and creative control strategies in the near future to prevent and control the terrorist risks that these biological agents will pose on living creatures.
Key words: Microorganisms, Biological Weapons, Bacillus anthracis, Variola virus, Francisella tularensis, Ebola and Marburg viruses.

INTRODUCTION

Terrorism can be defined as politically motivated violence or the threat of such violence, especially against civilians, with the intent to instill fear, harm or both. The main objective is to create psychological terror, which in turn can cause chaos and panic (TURK, 2002). A bioterrorism is a terrorism involving the deliberate release or dissemination of biological agents like viruses, bacteria, or other germs or the poisonous compounds that can be produced by some microbes; in order to cause illness or death in people, animals, or plants. Those agents may be spread through air, water, or in food and some can be spread from person to person (CDC, 2016 and Barras and Greub, 2014). Bioterrorism is considered, by bioterrorists, as an attractive weapon because the toxicants are relatively easy and inexpensive to obtain, can be easily disseminated, and can cause widespread fear and panic beyond the actual physical damage (Nikoleli *et al.* 2016).

Terrorists may use biological agents because they can be extremely difficult to detect and do not cause illness for several hours to several days. While a biological agent may injure or kill people, animals, or plants, the goal for the terrorist is to further their social and political goals by making their civilian targets feel as if their government cannot protect them. Many biological agents are found in nature; however, they can be modified by the terrorist, to make the agents and their products more dangerous. The reason for these agents being of concern is based on their availability to terrorists and the ease by which these agents can be disseminated (Edmond, 2016).

With ever-increasing travel and expanding populations, it can confidently be predicted that so-called emerging infections will steadily increase in number and that bioterrorist attacks will be major problems due to growing number of more sophisticated laboratories, more extensive biological training, and more information on the Internet (Henderson, 2014).

Hospitals and clinicians have the first opportunity to recognize and initiate a response to a bioterrorism attack. Individual healthcare providers will be the first to recognize and respond to a bioterrorist event. In the case of a suspected terrorist event, communication must include local, zonal and regional/state health departments of a country. The diseases/conditions having potential bioterrorist implications that healthcare providers must report immediately to local health departments are suspected or confirmed cases of: Anthrax, Botulism, Brucellosis, Plague, Smallpox, Tularemia, Varicella deaths, viral hemorrhagic fevers, Occurrence of any unusual disease, and Outbreaks of any disease (Fielding *et al*., 2012). The review was gird with the objectives: (i) to present a compiled data regards to microorganisms that are most frequently used as biological weapons and (ii) to raise awareness of the rationale of using microorganisms as biological weapons.

History of bioterrorism

Poisons have been used for assassinations for as long as humans can remember but it is unclear when they were first used intentionally for the purpose of warfare. However, it is believed that poisons were administered to enemy water supplies as early as the sixth

century BC (Frischknecht, 2003 and Sassoon, 2016) In the 1340s, Europeans catapulted dead bodies into besieged cities and castles in the hope of causing unlivable conditions and spreading infections such as plague. By the 1420s, they had added animal manure to increase infections caused by the rotting cadavers. British commander, Lord Geoffrey Amherst, in 1763 ordered that small pox contaminated blankets be distributed among American-Indian tribes to cause an epidemic (David and India, 2004 and Stefan, 2004).

Table 1. Summary of selected possible events of biological warfare.

Year	Event	Disease agents and outcomes
< 1000 BC. (Trojan War)	Legend of Scythian archers using poison arrows.	Clostridium (?) causing gangrene and tetanus.
<500 BC.	Assyrians poisoned enemy wells.	Rye ergot fungus causing hallucinations.
590 BC.	Greeks poison water supply of Kirrha during the first Sacred War.	Hellebore root causing diarrhea. Kirrha falls and the population slaughtered.
184 BC.	Bithynians catapult jars filled with snakes towards enemy ships.	Snakes causing panic. Sea battle is won.
1155	Emperor Barbarossa poisons water wells.	Decomposing human bodies.
1346	Europeans throw rotting and plague-infected cadavers over city and castle walls.	*Yersinia pestis* (?) causing plague. City is abandoned.
1495	Spanish sell wine mixed with blood from leprosy patients to enemy.	
1763	British distribute blankets from smallpox patients to native Americans,	*Variola virus* causing smallpox. Epidemic develops.
1797	Napoleon floods fields around Mantua to enhance malaria.	
1915 – 1918	Germans attempt to infect allied livestock	Anthrax and Glanders.
1932 – 1945	Japanese conduct large - scale human experiments and biological warfare in China.	Many different pathogens killing tens of thousands.
1980- 1990s	Iraq use biological weapons to attack Iran	Anthrax and mycotoxins`
1993- 1995	AumShinrikyo fails in attempts to release anthrax and botulinum toxin in Tokyo.	Anthrax and botulinum toxin
2001	Five die, eleven infected by anthrax attacks carried out through the United States mail.	Anthrax spore
2016	Three people 'who plotted biological attack in Kenya' are arrested	Bacillus anthraces: Anthrax

By World War I, the Germans tried to inject livestock with anthrax and glanders (a disease that mostly affects horses but, like anthrax, has also been developed as a biological weapon against humans). By World War II, Japan's Unit 731, the most infamous and experienced army unit, used agents such as anthrax, cholera and plague on the Chinese people by using different methods such as contaminating food and drinking water and dropping bags of plague infected fleas over cities from airplanes. Since the Japanese attacks in World War II, the best known cases were the reported use of biological weapons in the 1980s and 1990s by Iraq in attacks against Iran, where intelligence reports indicated evidence of both anthrax and mycotoxins (toxic chemicals produced by fungi) (Edmond, 2016 and Hoyle, 2016).

In December 2002, six terrorist suspects were arrested in Manchester, England; Their apartment was serving as a "ricin laboratory."Later, on Jan. 5, 2003, British police raided two residences around London and found traces of ricin, which led to an investigation of a possible Chechen separatist plan to attack the Russian embassy with the toxin. On Feb. 3, 2004, three US Senate office buildings were closed after the toxin ricin was found in a mailroom that serves Senate Majority Leader Bill Frist's office. Finally, a series of anthrax attacks occurred in the USA starting from September 2001 to December 2001 in which letters containing anthrax spores were mailed to several news media offices and two Democratic Party senators, killing five people and infecting 17 others (Hoyle, 2016).

Bioterrorism Agents Category

Bioterrorism agents can be separated into three categories, depending on easiness of dissemination or transmission, and the extent/severity of morbidity and mortality they impose. Criteria for categorization include the following; as described in (http://www.azdhs.gov/preparedness/emergency-preparedness/bioterrorism/#zebra-manual and https://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/cata.aspx):

1. Public health impact based on illness and death;
2. Delivery potential to large populations based on stability of the agent, ability to mass produce and distribute a virulent agent, and potential for person-to-person transmission of the agent;
3. Public perception as related to public fear and potential civil disruption; and
4. Special public health preparedness needs based on stockpile requirements, enhanced surveillance, or diagnostic needs.

Category A: These high priority agents include organisms or toxins that pose the highest risk to the public and national security because:

- ✓ They can be easily spread or transmitted from person to person.
- ✓ They result in high death rates and have the potential for major public health impact
- ✓ They might cause public panic and social disruption
- ✓ They require special action for public health preparedness. Possible biological agents in this group are Anthrax (Bacillus anthracis), Botulism (*Clostridium botulinum* toxin), Plague (*Yersinia pestis*), Smallpox (*variola major*), Tularemia (*Francisella tularensis*), Viral hemorrhagic fevers [*filoviruses* (e.g., *Ebola*, *Marburg*)] and *arena viruses* (e.g., *Lassa*, *Machupo*).

Category B: These agents are the second highest priority because:

- ✓ They are moderately easy to spread;
- ✓ They result in moderate illness rates and low death rates;
- ✓ They require specific enhancements of CDC's laboratory capacity and enhanced disease monitoring. Possible biological agents in this group are Brucellosis (*Brucella* species), Epsilon toxin of *Clostridium perfringens*, Food safety threats (e.g., *Salmonella* species,

Escherichia coli O157:H7, *Shigella*), Glanders (*Burkholderia mallei*), Melioidosis (*Burkholderia pseudomallei*), Psittacosis (*Chlamydia psittaci*), Q fever (*Coxiella burnetii*), Staphylococcal enterotoxin B, Typhus fever (*Rickettsia prowazekii*), Viral encephalitis (*alpha viruses* [e.g., *Venezuelan equine encephalitis*, *eastern equine encephalitis*, *western equine encephalities*, and Water safety threats (e.g., *Vibrio cholerae*, *Cryptosporidium parvum*).

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

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

Possible agents in this group are *Nipah virus*, *Hanta virus, SARS, H1N1* strain of influenza (flu), HIV/AIDS ((Nikoleli *et al.* 2016)).

Dissemination methods of biological agents

Ideal biological agents are relatively easy to acquire, process, and use. Only small amounts (on the order of pounds and often less) would be needed to kill or incapacitate hundreds of thousands of people in a metropolitan area. Biological warfare agents are easy to hide and difficult to detect or protect against. They are invisible, odourless, tasteless, and can be spread silently. The following are possible dissemination methods of biological agents that could be used by terrorists;

- ✓ Aerosol Dissemination: the likeliest route for dispersing most of the biological agents and the agent has to be refined;
- ✓ Used in explosives: artillery, missiles, and detonated bombs); not that much effective method because agents tend to be destroyed by the blast; 5% of them will be effective.
- ✓ Human Carrier: the agent need not be highly refined because the terrorists need to infect only one individual directly and relatively inexpensive and requires no difficult equipment to disseminate the agent;
- ✓ Oral Ingestion: involves deliberate contamination of food or water supplies (https://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/cata.aspx and http://www.emedicinehealth.com/biological_warfare/page3_em.htm#how_biological_agents_are_delivered_and_detected).

Selected Possible Biological Agents as Weapons

Bacillus anthracis

Anthrax is primarily a disease of herbivores and the etiological agent is *B. anthracis* which is a gram-positive, aerobic, spore-forming, and rod shaped bacterium. *Bacillus anthracis* infects humans through the respiratory system, the skin or the digestive system. Anthrax is widely available. The bacterium occurs naturally in domestic livestock and certain wildlife. Humans are secondarily infected by contact with infected animals and contaminated animal products or directly expose to B. anthracis spores (David and India, 2004 and Mehmet, 2016).

The spores are highly resistant to heat, pressure, ultraviolet and ionizing radiation, chemical agents and disinfectants. For these reasons, *B. anthracis* spores are an attractive choice as biological agents for the use of bio weapon and/or bioterrorism (Mehmet, 2016). The ease of delivery and the physiology of the bacterium that can live as a "vegetative cell," growing and dividing in a rapid and cyclical fashion are also some of the features that have made the bacterium an attractive weapon for terrorists (Hoyle, 2016).

Anthrax is very lethal but not easy to disseminate so it needs to be refined (weaponized) and is one of the most likely agents to be used in cases of bioterrorism attack because:

✓ Anthrax spores are easily found in nature, can be produced in a lab, and can last for a long time in the environment and can travel as far as four kilometres away from the release site.

✓ Anthrax makes a good weapon because it can be released quietly and without anyone knowing. The microscopic spores could be put into powders, sprays, food, and water. Because they are so small, you may not be able to see, smell, or taste them.

✓ Anthrax has been used as a weapon before (http://www.cdc.gov/anthrax/bioterrorism/threat.html).

An anthrax attack could take many forms. For example, it could be placed in letters and mailed or it could be put into food or water. Anthrax also could be released into the air from a truck, building, or plane. This type of attack would mean the anthrax spores could easily be blown around by the wind or carried on people's clothes, shoes, and other objects. It only takes a small amount of anthrax to infect a large number of people (Sassoon, 2016 and http://www.emedicinehealth.com/biological_warfare/page3_em.htm#how_biological_agents_are_delivered_and_detected).

Inhalational/pulmonary anthrax, which affects the respiratory system, is the most lethal form of the disease and is therefore currently believed to be the form most likely used in terrorist attacks. Only about 5,000 to 8,000 spores are sufficient to cause the lung infection when they are inhaled. From the lungs, the infection spreads to the lymph nodes in the chest, and within hours or days, the bacteria begins producing large amounts of deadly toxin. Coetaneous anthrax infections occur when open wounds or cuts come in contact with the anthrax bacterium. Naturally occurring gastrointestinal anthrax results from ingestion of meat contaminated with anthrax bacteria. Untreated gastrointestinal anthrax may kill about 50 percent of patients, but antibiotic treatment can greatly reduce this fatality rate (Edmond, 2016 and Sassoon, 2016).

Antibiotic treatment is available, but most successful if begun before the toxin is released. An anthrax vaccine also exists, but it is not a treatment option; it is effective only if the first of six inoculations is given at least four weeks before exposure. The vaccine is mostly given only to those considered to be at a heightened risk of exposure, including laboratory workers and certain members of the armed forces (Nikoleli *et al.* 2016, Edmond, 2016, Henderson, 2014 and Fielding *et al*., 2012).

2. *Francisella tularensis*

Francisella tularensis, a highly infectious Gram negative coccobacillus that causes a potentially serious illness called Tularemia. It is one of the biological agents (found in animals specially rodents, rabbits and hares) that could be used to terrorize peoples. Tick borne transmission of *F. tularensis* was recognized in 1923 and since then ticks have been indicated as a possible reservoir. People may get Tularemia in many different ways: (i.e. being bitten by an infected tick, deerfly or other insect, handling infected animal carcasses, eating or drinking contaminated food or water, and breathing in the bacteria, *F. Tularensis*). Tularemia is not known to be spread from person to person (Manfredini, 2015). *Francisella tularensis* is very infectious. A small number (10-50 or so organisms) can cause disease. If *F. tularensis* were used as a weapon, the bacteria would likely be made airborne for exposure by inhalation. People who inhale an infectious aerosol would generally experience severe respiratory illness, including life-threatening pneumonia and systemic infection, if they are

not treated. The bacteria that cause Tularemia occur widely in nature and could be isolated and grown in quantity in a laboratory and this results in easy production and use of the bacteria as a biological weapon (http://emergency.cdc.gov/agent/tularemia/facts.asp). No vaccine is currently available. A few antibiotics are active against *F. tularensis*, but strains resistant to these antibiotics could be used in the context of bioterrorism (Max, 2016).

3. *Clostridium botulinum*

The cells are Gram-positive, motile with peritrichous flagella, obligate anaerobe, straight or slightly curved rods (2–10 mm long), and form central or sub terminal oval spores (AMS, 2013). It is essentially a soil saprophyte and widely available. Botulinum toxin which is produced by the bacterium *Clostridium botulinum* is the most poisonous substance known to man, with a lethal dose for an adult human in the order of 8-10 gm. Botulinum toxins are neurotoxins; unlike enterotoxins, which act locally in the gut, they affect primarily the cholinergic nerves of the peripheral nervous system. Symptoms of botulism toxin exposure include double vision, drooping eyelids, dry mouth and difficulty swallowing and talking. The toxin produces a descending paralysis known as botulism. Botulinum toxin could be employed as a bioweapon via aerosol dissemination or the intentional contamination of food or drinks. Botulism is not contagious, so cannot be spread from person to person; only those who ingest or inhale the toxin will become ill. About 60 percent of those with untreated and less than 5% with treated ingestional botulism will die (Sasoon, 2016, Hoyle, 2016, http://www.cdc.gov/nczved/divisions/dfbmd/diseases/botulism/, AMS, 2013).

Botulism can occur in humans in two additional forms not relevant to bioterror. Infantile botulism occurs when children less than one year old ingest large amounts of the spore form of the Clostridium botulinum (not harmful to older children and adults). Wound-type botulism is extremely rare and occurs when an open wound comes into contact with Clostridium botulinum (CDC, 2012).

Botulinum toxin is unstable in the environment, and also a high degree of technical expertise would be necessary to render it suitable for aerosol release. The high toxicity of botulinum toxin, its wide availability and the probable need for long-term medical care for infected persons make it an effective bioweapon. Treatment is the same for inhalation (aerosolized) exposure as for ingestion (food borne). Care is supportive. Long term mechanical ventilation may be needed for several weeks to months and currently, there is no commercially available vaccine (Sasoon, 2016 and Hoyle, 2016).

4. *Yersinia pestis*

Yersinia pestis is a rod-shaped gram negative bacterium which causes the disease Plague. Plague is naturally transmitted to humans either by inhalation (person to person) or by the bite of a flea that has previously bitten a rodent infected with the bacterium. Infection of *Yersinia pestis* in humans can result in three forms of Plaque: pneumonic, bubonic and septicemic. Pneumonic plague has a lethality rate of almost 100 percent if left untreated and approximately 50 percent if treated. *Yersinia pestis* is not extremely stable; it degrades in sunlight or heat but can remain viable for up to a year in the soil. Its lethality, contagiousness and infectivity (infectivity dose 10-500 organisms) make it one of the most deadly and potentially effective bioweapons (Sasoon, 2016 and Hoyle, 2016). In the case of a bioterror attack, the bacterium might be released in an aerosolized form into the air. Pneumonic plague is thought to pose the greatest risk for a bioterror attack because it infects people more easily than the other forms and also is the only form that is contagious.

Refining the bacteria to an effective, airborne form that can cause pneumonic plague requires a high degree of technical expertise (David and India, 2004).

5. *Drug-Resistant TB (tuberculosis)*

Globally in 2014, an estimated 480,000 people developed multidrug-resistant TB (MDR-TB) and there were an estimated 190,000 deaths from MDR-TB. Globally, data show an average cure rate of only 50% for treated MDR-TB patients. Extensively drug-resistant TB (XDR-TB) was reported by 105 countries in the year 2015. An estimated 9.7% of people with MDR-TB have XDR-TB. Because of its ease of aerosol transmission and resistance of available drugs, this agent could be the choice to be used as a biological weapon (WHO, 2015).

6. *Variola virus*

Smallpox is a disfiguring and potentially deadly infectious disease caused by the Variola major virus (the deadly disease), one of the Orthopox viruses. Smallpox is highly contagious. In most cases, people get smallpox by inhaling droplets of saliva, which are full of viruses, during face to face contact with an infected (often after symptom developed) person. Variola represents a significant threat as a biological warfare agent. Variola is highly infectious and is associated with a high death rate and secondary spread. *Variola virus* is highly infectious when released into the air. It is environmentally stable and can retain its ability to infect people for long periods. There are two types of recognized smallpox; viz: (i) Variola major, the most severe form, may cause death in up to 30% of unvaccinated people who developed it (3% of vaccinated people may also develop variola major); and (ii) Variola minor, a milder form of smallpox, produces death in 1% of unvaccinated people. The failure to recognize mild cases of smallpox in people with partial immunity permits rapid person to person transmission. Exposed people may shed virus through coughing without ever showing the signs and symptoms of the disease (http://www.emedicinehealth.com/biological_warfare/page11_em.htm#smallpox).

There is no proven treatment for smallpox. However, medical experts believe the vaccine may lessen the severity of, or even prevent, illness in unvaccinated people if given within 4 days of exposure to the virus but may leave the patient with disfiguring scars. To prevent the spread of smallpox, healthcare providers must isolate infected people and vaccinate people which might be in close contact with infected people. The currently licensed smallpox vaccine, which consists of a laboratory strain of vaccinia virus, is highly effective in preventing infection (https://www.niaid.nih.gov/topics/smallpox/Pages/default.aspx). The only way to truly reduce the threat of a smallpox bioterrorist attack is to be prepared. Anti-epidemic and therapeutic measures such as effective detection systems, quarantine and isolation procedures, vaccine prophylaxis, and appropriate therapies for early and late stage infections must be developed (Alibek, 2004).

7. Viral haemorrhagic fevers

Viral haemorrhagic fevers (VHFs) include four distinct families of viruses: Filoviruses (e.g., Ebola and Marburg), Arenaviruses (e.g., Lassa), Bunyaviruses (e.g., Rift Valley Fever), and Flaviviruses (e.g., yellow fever and dengue). All may cause haemorrhagic syndromes characterized by severe internal and external bleeding. Some VHFs such as Ebola, Marburg and Lassa are contagious. These viruses are generally unstable in the environment and do not fare well as aerosols; a high degree of technical sophistication would be necessary to make such viruses viable as biological weapon. Due to the high fatality rate and infectivity of

these agents, they are generally studied in high-security laboratories (David and India, 2004).

7.1. *Ebola virus*

Ebola virus causes an acute serious illness, Ebola virus disease (EVD), which is often fatal if untreated. Ebola virus disease(EVD), a Filovirus haemorrhagic fever, is often a devastating disease in humans as it involves the body's vascular system resulting in significant internal bleeding and multi organ system involvement. Ebola virus is highly contagious and because of its potential aerosol and droplet transmissibility, it is included in the 'category A' of bio terrorism agents. Till date, no effective prophylaxis, anti-viral treatment, or vaccination is available for this fatal disease and as a result it could be one of the biological agents that can attract the terrorists interest (Passi *et al*., 2015).

Ebola virus is introduced into the human population through close contact with almost any body fluids and organs from infected animals. It spreads through human to human transmission via direct contact with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials contaminated with these fluids (Alibek, 2004 and WHO, 2016). Ebola virus disease (EVD) was first reported in 1976, with 2 simultaneous outbreaks; one in what is now, Nzara, South Sudan, and the other in Yambuku, Democratic Republic of Congo. The latter occurred in a village near the Ebola River, from which the disease takes its name. The current outbreak in West Africa, (first cases notified in March 2014), is the largest and most complex Ebola outbreak since the *Ebola virus* was first discovered in 1976 (WHO, 2016).

The disease process is characterised by rapid immune suppression and multisystem involvement, leading to the impairment and eventual collapse of various organs and systems, and resulting in hypovolemic shock and death (Matua *et al*., 2015). EVD represents one of the most serious viral diseases known, characterized by a fatality rate around 40–50% (that achieves 90% in some virus strains). Although obtaining, handling and weaponizing *Ebola virus* presents obstacles for bioterrorists, the extent makes natural outbreaks a threat due to its accessibility (Cenciarelli *et al.*, 2015). Having very easy and broad transmission cycle within the human population and no available effective vaccination and treatment, could initiate terrorists to target *Ebola virus* as a potential biological weapon (Alibek, 2004 and WHO, 2016).

7.2. *Marburg virus*

Marburg virus is a genetically unique zoonotic RNA virus of the Filovirus family and it causes the disease Marburg hemorrhagic fever (Marburg HF), a rare but severe hemorrhagic fever which affects both humans and non-human primates. *Marburg virus* was first recognized in 1967 in laboratories in Marburg and other countries. The reservoir host of *Marburg virus* is the African fruit bat, *Rousettus aegyptiacus*. Fruit bats infected with *Marburg virus* do not show obvious signs of illness. Transmission occurs through unprotected contact with infected bat faces or aerosols, person-to-person contact in several ways: direct contact to droplets of body fluids from infected persons, or contact with equipment and other objects contaminated with infected blood or tissues and handling of infected non-human primates or come in direct contact with their fluids. The case fatality rate for Marburg hemorrhagic fever is between 23-90%. Clinical diagnosis of the disease is difficult because the sign and

symptoms overlap with Malaria and Typhoid fever (CDC, 2016 or http://www.cdc.gov/vhf/marburg/).

7.3. *Lassa virus*

The virus, a member of the virus family Arenaviridae, is a single-stranded RNA virus and is zoonotic. Lassa fever is an acute viral illness that occurs in West Africa. The number of *Lassa virus* infections per year in West Africa is estimated to be 100,000 to 300,000, with approximately 5,000 deaths. *Lassa virus* transmits from infected rodent ("multimammate rat" (*Mastomys natalensis*)) waste products to humans through ingestion or inhalation. Once infected, this rodent is able to excrete the virus in urine for an extended time period, may be for the rest of its life and these rodents also breed frequently and produce large numbers of offspring. In addition, Mastomys readily colonizes human homes and areas where food is stored (CDC, 2016).

8. *Brucella* species

Brucellosis is a bacterial disease caused by various Brucella species, which mainly infect cattle, swine, goats, sheep and dogs. Brucella species are facultative intracellular gram-negative cocco-bacilli, non-spore-forming, non-capsulated and non-motile (Seleem, 2010). Brucella organisms can localize in the reproductive organs of host animals, causing abortions and sterility. Humans generally acquire the disease through direct contact with infected animals, by eating or drinking contaminated animal products, or by inhaling airborne agents. The toxin of Brucella is quite potent; it takes fewer than 100 of the Brucella bacteria to produce infection. Its lethality rate is low (fewer than 5 percent of infected individuals will die), but it is very stable in the environment. There is no vaccine (David and India, 2004)

9. Enterohaemorrhagic *Escherichia coli* (EHEC)

Escherichia coli is a bacterium that is commonly found in the gut of humans and warm blooded animals. EHEC can cause severe food borne disease. It is transmitted to humans primarily through consumption of contaminated foods, such as raw or undercooked ground meat products, raw milk and contaminated raw vegetables and sprouts. *E. coli* O157:H7 is the most important EHEC serotype in relation to public health that causes Shiga-like toxin. The infection can cause haemolyticuraemic syndrome (HUS), characterized by acute renal failure, haemolytic anaemia and thrombocytopenia. It is estimated that up to 10% of patients with EHEC infection may develop HUS, with a case fatality rate ranging from 3 to 5% (WHO, 2011).

E. coli O157 bacteria are commonly found in the gut of cattle and other farm animals. One may become infected by: eating infected food (mainly meat), unpasteurised milk and cheese, contact with infected animals (such as at farms or animal sanctuaries), contact with other people who have the illness, through inadequate hand washing after using the toilet and/or before food-handling (particularly in households, nurseries and infant schools), eating unwashed vegetables (which may have been infected by manure from infected cattle), and drinking or swimming in infected water (such as river water, stream water or water from drinking wells)
(https://www.rnoh.nhs.uk/sites/default/files/e_coli_1194947360190.pdf).

CONCLUSION AND RECOMMENDATIONS

A biological attack is an undercover sabotage mission, means the destructive blow is not immediately apparent like other terrorist attacks and the attack's nature and extent will be revealed only with time. Biological agents are used to terrorize the human population because they can be easily accessible (available) for the terrorist group, often they have unnoticed infection in the targeted group for at least a while, most of them are highly contagious and can be easily, due to the modern technology, weaponized (refined) and disseminated.

Currently, new respiratory epidemics such as severe acute respiratory syndrome, Middle East respiratory syndrome, and pandemic influenza which recur frequently and Ebola outbreaks are the most concerns of the world. Therefore, there is a need to set and/or develop new and better control methods, vaccines, antimicrobials, and creative control strategies in the near future to prevent and control the terrorist risks that these biological agents will pose on living creatures.

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