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# **Healthcare Issues**





Review Article

# A Review of Viruses as Biological Warfare Agents with Medical Aspect

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## Abstract

Since ancient times, various types of weapons have been used to eliminate the enemy, whether at the level of soldiers, farms, livestock, or property. Among those weapons was the use of biological agents such as microbes to achieve these goals, and this is what is known as biological warfare (BW). Dangerous aspects in use of biological agents as BW represented by the ability to be produced by relatively simple facilities and cost. Besides BW can be easily loaded on weapon and dispersed widely though air, water and food to infect people. Also, BW the harmful effect cannot be detected immediately after used but it can take days to weeks to be appeared. Treatment of these biological agent may be not available or hard to performed. All these parameters can make general panic and significant fear among population or troops; therefore, theses trend can attract bioterrorist to use these advantages to perform their dangerous purposes. Good preparedness is required o overcoming potential of biological attack on civilian or military facilities.

# Introduction

The employment of microorganism like bacteria, viruses, and fungi intentionally with the purpose of spreading illness, causing death, or harming the environment is referred to as biological warfare. Utilizing transmission modes such as food, drink, aerosols, or insect vectors. In general, their mode of action involves either infection or intoxication [1]. These microbial agents selected to be extremely contagious, quickly spread, incredibly damaging, slow-acting, and challenging to prevent and treat [2].

Bioweapons, which have been in use since before the birth of Christ, have decimated entire communities and altered the geopolitics of numerous locations during different period of history [3].

The Geneva Convention was signed in 1925 for the purpose of preventing the production, stockpiling and use of such weapons and considering them internationally prohibited due to the losses they cause in lives, property, facilities and the environment. However, some countries were not committed to this pledge, which prompted the rest of the countries to violate this treaty [4].

Many properties like the ease of spread, the intensity of sickness and mortality ratio, and the likelihood of usage were used by the Centers for Disease Control and Prevention (CDC) to classifying pathogens into categories A, B, and C [5]. The CDC has identified several viral viruses as potential biological terrorism agents or weapons of mass destruction. Because they are extremely contagious and very simple to generate, agents like viral hemorrhagic fever viruses, smallpox, encephalitis viruses, and others are a cause for concern [6]. As mentioned in Table 1

Concerning the technical limitations and challenges, the probability of biological strike will be successful is limited. Even if the number of mortalities is probably restricted, a biological assault might still have a significant impact [7].

The ideal agent for biological attack would be able to cause illness in a significant portion of those exposed must contain many criteria such as be easily spread to affect large numbers of people (for example, through aerosol), A pathogen's low infective dose, capacity to be

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aerosolized, remain stable and transmissible despite exposure to the hard environment, and be readily producible by facilities in sufficient quantities. Fortunately, these qualities are rare among agents. Threats to water and food safety are another issue to be concerned about [8, 9].

Table 1: Classification of biological warfare agent according to CDC

Category A	Category B	Category C
High priority agents include organisms that	Second highest priority agents include	Third highest priority agents include
pose a risk to national security because they	those that are:	emerging pathogens:
are:		0.01
	Moderately easy to disseminate	That could be engineered for mass
Easily disseminated	<ul> <li>Cause moderate morbidity</li> </ul>	dissemination in the future
<ul> <li>Cause high mortality</li> </ul>	<ul> <li>Require enhanced disease</li> </ul>	<ul> <li>Have potential for high morbidity,</li> </ul>
<ul> <li>Cause public panic and social disruption</li> </ul>	surveillance and public health	mortality and major health impact
· Require special action for public health	diagnostic capacity	
preparedness.	,	
proparedness		
Bacillus anthracis (anthrax)	Alpha viruses	Hanta viruses
Clostridium botulinum toxin (botulism)	Eastern and western equine encephalomyelitis	
Francisella tularensis (tularemia)	WEE)	tuberculosis
Variola major (smallpox)	Venezuelan equine encephalomyelitis virus (Vi	EE) • Nipah virus
Yersinia pestis (plague)	Brucella species (brucellosis)	Tickborne encephalitis viruses
Filo viruses	Burkholderia mallei (glanders)	Tickborne haemorrhagic fever
<ul> <li>Ebola virus (Ebola hemorrhagic fever)</li> </ul>	Coxiella burnetii (Q fever)	viruses
<ul> <li>Marburg virus (Marburg haemorrhagic fever)</li> </ul>	· Epsilon toxin of Clostridium perfringens	<ul> <li>Yellow fever</li> </ul>
Arena viruses	· Ricin toxin from Ricinus communis	
<ul> <li>Junin virus (Argentinian haemorrhagic fever) and</li> </ul>	Staphylococcal enterotoxin B	
related viruses	A subset of Category B agents includes pathoge	ens that are
Lassa virus (Lassa fever)	food or waterborne.	
	These pathogens include but are not limited to:	
	Cryptosporidium parvum	
	Escherichia coli O157: H7	
	Salmonella species	
	Shigella dysenteriae	
	<ul> <li>Vibrio cholerae</li> </ul>	

There are many types of viruses that could be used as biological weapon agents due to they contain some or all previous criteria and can be used as potential biological agent such as:

# Small pox

A contagious illness that only affects people, etiologic agent called Variola virus (VARV). Only known host of VARV is a human. The virus variation Variola major, which has a fatality rate of 30%, is one of the deadliest diseases and is said to have killed between (300-500) million people in the  $20^{th}$  century. The consequences of this sickness are lifelong, yet survivors are guaranteed immunity. In 1980, the WHO announced smallpox extinct [10, 11].

Variola virus belongs to the genus Orthopoxvirus and family Poxviridae. Regarded as a large brick-shaped and complex virus with diameter around (200 nm), double-stranded with DNA virus that replicates, transcripts in the cytoplasm of host cells [12, 13].

Respiratory droplet nuclei are the primary method of smallpox transmission, while contaminated clothing or bedding have the potential to spread the illness [14]. This infections appear as a non-specific febrile symptoms marked by a elevated fever, nausea, chills, headache backache, and stomach pain. The lesions of skin begin on the face or forearms and disperse to the rest of the body after 1-3 days [15].

Smallpox lesions are concentrated in the centrifugal (peripheral) regions of the centripetal distribution. The most frequent diagnostic conundrum in the differential diagnosis is chickenpox, which can be quite serious in elderly people and individuals with impaired immune systems [16].

There are numerous ways to verify the diagnosis of smallpox infection such as electron microscopy, specimens can be directly checked for the presence of virions, and immunohistochemistry tests can be used to identify viral antigen. Variola virus can be recognized using a polymerase chain reaction assay.29-32 viral isolation in live-cell cultures. Serologic test results do not distinguish between orthopoxvirus species [17].

The majority of those who were born before 1971 received one smallpox vaccination. The general public is not now advised to receive a smallpox vaccination, and there is no known cure for the disease. The treatment of smallpox with Tecovirimat has recently confer approval use from the Food and Drug Administration [18].

# Venezuelan equine encephalitis

The Venezuelan equine encephalitis (VEE) complex alphaviruses are significant re-emerged arboviruses that can cause human infections as well as fatal sickness in equids. Venezuelan equine encephalitis virus (VEEV) continues to be a highly developed biological weapon as well as a naturally occurring disease danger [19, 20].

Equine viral encephalitis is caused by multiple virus families, the majority of this groups are zoonotic arthropod-borne viruses (arboviruses), family Togaviridae member, which also includes Alphavirus genous. They make up a group of arboviruses that cause illness epidemics in humans and animals all over the world. These viruses regarded as A (+ ss RNA) genome of about 11,400 base pairs is present in VEEVs [21–23].

VEE is mostly spread by mosquitoes to humans and horses, although it is also known to spread by other biting flies or through laboratory accidents involving viral inhalation. Numerous hosts, including mammals, birds, reptiles, amphibians, and arthropods, are capable of supporting their replication [24].

Human sickness would be the main outcome of the virus's aerosolization and spread. A large number of sick people and horses in a specific area would probably be the basis of an outbreak because disease symptoms in humans are similar to the flu and are difficult to distinguish. A major factor in why VEE is regarded as a militarily useful biowarfare agent is that the infective dose for humans is thought to be 10-100 virus. Regardless high intensity of infected mosquito or aerosol concentration of viral particle, VEE transmission during bio warfare attack will be high effective [25].

The symptoms of VEE infections can range from mild flu-like symptoms to severe ones, which can affect 4–14% of human patients. Encephalitis, disorientation, coma, photophobia, and seizures are among the severe symptoms. Depending on the patient's age and the outbreak, VEE-related deaths are uncommon but happen in about 1% of cases [26].

The primary methods for diagnosing VEEV infection at the moment are direct detection, such as genome or viral isolating from blood or cerebrospinal fluid (CSF), or serology tests, as the isolation of VEEV- IgM in the CSF by specific types of ELISA [27]. Recently, no approved medications or vaccinations for treatment of VEEV infection [28].

# Viral hemorrhagic fevers

Viral hemorrhagic fevers (VHF) are a collection of medically similar illnesses that can be caused by infection with enveloped RNA viruses basically from the families of Flaviviridae, Arenaviridae, Filoviridae, and Hantaviridae. These viruses are enveloped with single stranded RNA genome, the secondary structure of RNA viruses is important for many viral functions, from capsid formation to budding from the cell and host defense mechanism. Viruses such the Hantavirus, Ebola, Yellow and Dengue fever are members of the serious and frequent VHF [29, 30].

Humans can acquire VHF viruses from arthropod vectors by being bitten. Some viruses, such as Lassa fever, Marburg, and Ebola viruses, can spread through intimate contact between people or through contact with bodily fluids (blood, urine, feces, or saliva) of an infected person or coming into contact with infected objects [31–34].

The severity of the illness brought on by these agents varies greatly; whilst yellow fever and dengue virus infections are primarily asymptomatic diseases, Ebola and Marburg hemorrhagic fevers have extraordinarily high fatality rates [35].

VHF cause contagious disorders that frequently result in serious symptoms such as damages the vascular system significantly, causing coagulation abnormalities that lead to bleeding and increased vascular permeability that can cause a drop-in blood pressure, shock, and death [36].

The agents that cause VHF are frequently categorized as biosafety level 4 (BSL-4) pathogens, necessitating specialized lab settings with the highest level of safety precautions [37].

The ability to diagnose VHF quickly is crucial to initiatives that will stop outbreaks. The most accurate test for identifying known VHF in symptomatic individuals is molecular detection by RT-PCR in blood. The lack of specificity in the early symptoms, the scarcity of effective treatments, the severity of the disease, the stringent criteria for infection control, and the tendency to spread epidemics with secondary cases in healthcare personnel make diagnosis and management difficult [37, 38].

Key elements should be considered when treating VHF that include specialized antiviral therapy and life support to prevent multiorgan failure [39]. The management of VHF generally follows the septic shock management protocol is supportive. A few VHFs have shown promise when treated with convalescent plasma and the antiviral medication ribavirin [40].

CDC classifies VHF viruses as category A bioweapon agents because they are thought to be potential biological weapons due to their properties [36].

#### Hantavirus

Hantavirus (HTV)is a negative-sense RNA virus that belongs to the Bunyaviridae family. This virus is emerging zoonotic disease which able causes a variety of illness syndromes that range in severity [41, 42]. Transmission modes of this virus varies widely such as aerosols contaminated with the feces, urine, or saliva of infected rodents which can be inhaled by humans, who then acquire the virus through their respiratory system. Rarely, humans also contract the virus through direct contact with the faces or urine of infected rats, or very rarely, through rodent bites [43].

HTV infections in people can result in one of two clinical syndromes: hantavirus cardiopulmonary syndrome (HCPS) that appear in North America and South America and hemorrhagic fever with renal syndrome (HFRS) that appear in Europe and Asia, both of which are brought on by old- world hantaviruses [44].

Even though HTVs are categorized only as category C agents on the CDC's table of bio-agents, there is concern about their possible use as biological weapons due to their widespread existence and primary mode of transmission by aerosols. The actuality that immunity in specific populations is typically quite poor, there are several strains lacking cross-protection, and there are no vaccinations available all raise their potential threat. The public organization is highly interested in new infections like hantaviruses due to generating infections in people, with a 35% case mortality ratio [45, 46].

From the first day after the onset of disease, polymerase chain reaction (PCR) can be used to quickly identify the hantavirus genome in clinical samples like blood, serum, or organ fragments. There have been reports of viral genomes being found in patients before the first day of manifestations [47].

Different types of indirect Elisa recommended to be used rather than direct one as serological test. indirect immunofluorescence tests often employed for diagnosis even show less specify [48]. There are currently no antiviral medications that have been approved by FDA for treat HFRS or HPS infections. As a result, only supportive care used in the dealing of serious cases that involve maintaining fluid and electrolyte balance is crucial without specific antiviral drug that can work effectively [49, 50].

## Nipah virus

Nipah virus (NiV), regarded a paramyxovirus belongs to Henipahvirus genus member of Paramyxoviridae family, is the etiologic infection known as NiV illnesses. This virus contain18.2 kb of (-ss encapsulated RNA) that ranges in size from 40 to 1900 nm [51].

Fruit bats of the genus Pteropus have been identified as the NiV's natural reservoir. The virus was spread from pigs to dogs, cats, and horses, among other animals. Both of humans and other animals, like as pigs, can contract this disease, and there are two ways in which it spreads: from human to human and from animal to human through infected bats and pigs. This extremely contagious virus grew quickly among pigs and was easily communicated to people who came into touch with diseased animals [52].

It is widespread in south-east Asia and the western Pacific, with outbreaks also occurring in Bangladesh, India, Malaysia, Singapore, and the Philippines [53].

The NiV virus can incubate for 4 to 21 days and then appear as extremely lethal virus that primarily causes acute encephalitis and respiratory illnesses. However, A small portion of infected individuals shows no symptoms. Fatality rates are 6% or higher. They categorized as Biosafety Level 4 virus due to their high mortality rate after human infection and the absence of curative vaccinations or treatments [54].

Serious cases of NiV infection involve encephalitis with accompanying fatigue and loss of orientation, which can quickly develop to convulsions and then coma within 48 hours. NiV infection also produces severe febrile encephalitic disease and/or respiratory disease. Depending on the intensity, patients may also have vertigo, nausea, vomiting, malaise, headache, myalgia, fever, and headaches [55].

Acute NiV infections can be diagnosed primarily by isolating the viral agent directly using real-time RT-PCR, immunohistochemistry, or other molecular techniques [56]. There are currently no treatments or vaccinations that have been licensed for use in humans despite the serious pathogenicity of these viruses and their potential for pandemics. For the treatment of serious respiratory and neurologic symptoms, critical supportive care is recommended [57–59]

## Conclusion

The use of biological weapons is an increasing danger, especially after we know that it is possible to obtain them with relatively simple techniques and capabilities. Therefore, it is possible that some terrorist groups or individuals, as well as armies, may exploit these features and work on manufacturing and developing such weapons in order to achieve their goals and objectives in an easy way. We recommended some criteria to be ready to avoid BW risks such as increasing of public awareness about BW risks, training of medical staff, civilian defense and security forces to be well prepared to overcome potential using of biological attack either that could targets public or army facilities as soon as possible in order to reduce the heavy losses caused by such weapons.

#### **Article Information**

**Disclaimer** (**Artificial Intelligence**): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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