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RESEARCH ARTICLE

A THREAT TO HUMAN RACE: BIOWARFARE & BIOTERRORISM

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ABSTRACT

This is the most advanced and seamlessly researched field of wars and terrorism. Due to ever increasing lust of power for all the countries have led to development in science and technology and subsequently emergence of some lethal and well-planned war strategies. Basically, when biological agents/infectious agents/toxins are used for dissolving the targeted country's funds or to take revenge of some previous disputes it is called GERM WAR. The use of these bioweapons against the civilians/common people is stated as bioterrorism while, use of bioweapons against the military/forces then it is stated as biowarfare. This review covers some vital points on this miserable turn of science and technology. The discussion revolves around the history, what characteristics make an organism fit to be a bioweapon, what are the organisms that are developed by countries for this purpose, how to minimize the effect on population of such mishaps and many other discussions.

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INTRODUCTION

The use of biological agents and their toxins against humans leading to mass morbidity and mortality have emerged in the new developed world. The bioweapons are also used against livestock and crops. The biowarfares are emerged due to some advantages viz. high number of mortalities, easily transmissible, no proof of who did it, wastage of country's funds, create fear among people. Bioweapons are been used from a very long time but, today's technology is overpowering this activity to a great extent.

HISTORY: The major events in history where the bioweapons were used was during the first and the second world wars but, even at times before the world wars, there was a use of these bioweapons. isn't that interesting? At that times the arrows, spears, swords, were poisoned with some plant toxins or were contaminated with faces. Along with this, people used to contaminate the food and water sources. if we still go back in time to around 184 BC The Carthaginian leader, named Hannibal used serpent's toxin in his naval battle. The distribution of infected fomites has been practiced in French Indian wars (1754 – 1767) in this case blankets infected with small pox virus were given to the native American by the British this was confirmed when the military leader wrote,

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"We gave them one handkerchief and two blankets from the Smallpox Hospital. I hope it will show the desired effect" World war 1: The germ theory proposed in 1860 by Robert Koch and louis Pasteur led to massive development in this field. This eventually gave rise to invention of immensely lethal bioweapons. The most remarkable first use of bioweapons was done by Germany where they did not pose any harm to the human life but infected livestock and animal feed. This action led to emergence of " the Geneva protocol" of 1925 which proclaimed complete prohibition of chemical and biological weapons use during war but, there was no prohibition on R&D and stock piling. But this protocol due to its weakness was not able to control this new emerging problem. Post WW1 many countries started developing their bioweapons and have been developing it till date. World war 2: Until this time that is till the year 1939 a lot of progress was made in the field of bioweapons. Plethora of funds were spent in research and development of bioweapons. The countries which were doing rigorous research were UK, US, Germany, Canada, japan and the USSR among which USA, USSR AND JAPAN were the most successful. As per records there was a use of anthrax, cholera, typhoid, plague for bioterrorism. Every biological attack was ranged to cause 1000 to 200000 deaths.

Ideal characteristics of a potent bioweapon:

- Ability to be produced in large quantities
- Stable for storage and transportation
- High mortality rate
- Highly infectious

- Person to person spread, contagious
- Ability to produce stable aerosol
- Genetically modified, to which no one has the immunity

Ideal qualities of an organisation to conduct bio war:

- Faultless organizational capacity
- Logistics
- Biotechnological advancement
- Ample finances
- Knowledge and skills

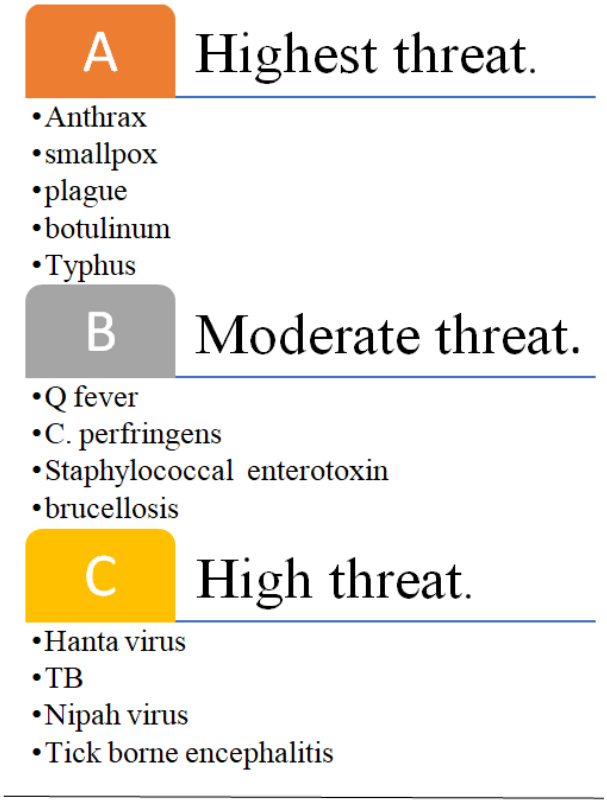

Figure 1. Classification of bioweapons based on level of threat to civilians

Due to the rising threat of bioweapons, recently the CDC of USA classified the organisms based on the level of threat they impose on the civilians in a state of biowarfare or bioterrorism. The classes were A, B and C, where the class A organisms showed high mortality, special action requirement, easy person to person transmission while B showed, moderate spread, moderate mortality and C showed high morbidity, mortality, easy production, high transmission. Shown in figure 1.

ANTHRAX: A disease caused by a gram-positivebacterium named bacillus anthracis, a zoonotic disease. Mainly seen in herbivores which include, cattle, sheep, swine, horse. Mode of transmission of this bacterium is cutaneous spread, ingestion and the respiratory spread, the latter being less common but highly lethal. The military is highly concerned about anthrax owing to characteristics like stable aerosol, easy transmission, very high mortality especially in the inhalational type. The largest epidemic of anthrax was witnessed in the year of 1979 in Sverdlovsk where, anthrax spores were released accidently by a military facility which led to spread of the infection in the surrounding area and further.

Figure 2: classification based on type of organism.

BACTERIA	VIRUS	TOXINS	ANTI-PLANT
Anthrax	Smallpox	Botulinum	Rye stem rust
Brucellosis	Yellow fever	Aflatoxin	Rice blast
Tularemia	Japanese encephalitis	Ricin	Wheat rust
Plague	Venezuelan equine encephalitis	Staphylococcal enterotoxin	
C. perfringens	Rotavirus	myotoxin	
Q fever	Camelpox		
Glanders	Enterovirus 70		

Viral haemorrhagic fever: lassa, Marburg, ebola, Bolivian fever.

Clinical signs and symptoms

- Cutaneous type: this is the most common mode of transmission, almost 95% of all causes of anthracis are spread by cutaneous route. The incubation period being 1 to 5 days from exposure. The primordial or the first finding is usually a small papule which grows to a vesicle within a couple of days, this vesicle contains serosanguineous fluid along with colonies of the organism within infiltrated with abundance of leukocytes. Vesicle size ranges from 1 to 2 cm leaves a necrotic ulcer, when ruptured. Common findings include ulceration, inflammation, coagulative necrosis, vasculitis etc. prodrome symptoms include fever, headache, malaise. Malignant Oedema a term when entire face or limb swells up is seen here. The peculiar finding is the BLACK ESCHAR formation which ruptures within 2 to 3 weeks of infection leaving a scar.
- Inhalational type: with an incubation period of 1 to 6 days, the disease is divided in two stages. The first stage begins with prodromal symptoms like malaise, fatigue, fever, myalgia, also topped with mild chest discomfort and non-productive cough. The second stage starts after a couple of days of these symptoms, which is seen with sudden onset of dyspnoea, cyanosis, stridor, sever respiratory distress and chest pain. Oedema seen in this type too. Not being persistent but pneumonia is seen in some cases. This disease may further progress to neurological symptoms. This mode of transmission is the most feared because it can lead to sepsis and death within 24 to 48 hours of infection.
- Ingestion type: incubation period of 2 to 5 days, gives symptoms like tonsillar ulcer, sore throat, toxicity, fever, oedema, nausea, vomiting, abdominal pain, dysphagia, mild respiratory distress. May lead to acute abdomen.

Protection

- Treatment with antibiotics
- Active immunization (biothrax)
- Passive immunization

PLAGUE: Again, a zoonotic disease caused by a gram-negative bacterium named yersinia pestis, this basically is a disease of rodents including, rattusnorvegicus (brown rat), deer mouse, squirrels, etc. the vector this the flea which bites the rodents and humans too spreading the disease. Can also be transmitted by direct entry into the blood i.e. By contact. The second route of transmission is by inhalation. Causing, bubonic or pneumonic plague respectively. The latter being more lethal and can cause death. Plague has caused a number

of pandemics in the early times of which the pandemics of 6th, 14th and 20th century were the greatest. The fear of plague is far decreased in todays world is only because of development of a very potent and successful vaccine which was used by the US soldiers during the Vietnam war.

First pandemic: Justinian plague (1346-1352)

Second pandemic: the black death (1327-1385)

Third pandemic: eastern to western countries (1894-1925)

The use of yersinia pestis as a bioweapon was very popular, it was used many a times for biowarfare viz. world war 2, Vietnam war,e Crimean port city of Caffa 1346-47, japan china war 1941.

Clinical signs and symptoms

- Bubonic plague: incubation period is of 2 to 8 days from the time of fleabite. The clinical presentation of this disease includes, malaise, prostrations, fever, rigor, chills, vomiting, headache among most of the cases while, some cases also showed mental disturbances, abdominal pain, cough and chest pain. Basically, buboes are lymph nodes which the bacteria have colonised and causing infection. The infection leads to inflammation and severe pain in the lymph nodes (inguinal and femoral most common sometimes axillary and cervical).
- Pneumonic plague: yersinia produces a stable aerosol, contributing to spread through inhalation. The symptoms include, bronchopneumonia, cough, dyspnoea, chest pain, productive cough, haemoptysis. Chest radiograph shows bilateral alveolar infiltrates. Pneumonic plague is highly discussed reason being its high mortality it can cause death within 2 to 6 days of infection.

Protection

- Isolation/ quarantine (48 hours)
- Treatment with antibiotics
- Use of insecticide
- Sanitation and health education
- Antibiotic prophylaxis to Close contact
- Vaccine named " pestis" (active immunization).

SMALLPOX

Small pox is caused by variola virus, the most feared bioweapon of all. Has caused around 500 million deaths in the 20th century. The virus now has been eradicated; the last appearance of the disease was in 1977. Characteristics which make this virus the most feared bioweapon:

- can be produced in large quantities
- high mortality
- stable storage and transportation
- produce stable aerosol
- highly infections
- most of the world has no immunity because of discontinuation of vaccine
- characteristics which led to eradication of this virus:
- slow disease
- effective and safe vaccine
- no carrier states
- no vectors
- infectious only with symptoms
- infection gives lifelong immunity
- cooperation of the world to eradicate the disease.

Officially 2 stocks of the virus: CDC and Russia

Infectious material: saliva, scabs, urine, vesicular fluids, blood.

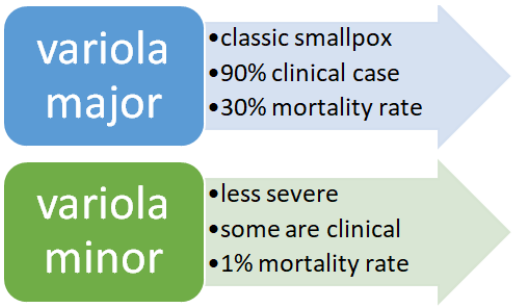

Figure 3. strains of variola virus.

Clinical signs and symptoms: Incubation period ranges from 7 to 17days, the virus implants on the oropharyngeal and respiratory mucosa. After the incubation period there is high fever onset with other prodromal symptoms like prostrations, malaise. Headache and backache also seen in infectious cases. The peculiar finding in this disease is the typical small pox rash. Rash develops after 1 to 2 days of incubation period, its first appears on mouth, tongue and oropharynx. It goes to the face and arms within 2 to 3 days of onset of rash and finally it appears on the legs and trunk. The most infectious period is from onset to 7 to 10 days of rash hence, highest care needs to be taken during this time. smallpox is feared because it can cause death in the 2nd week of illness due to toxaemia.
Rash pattern in smallpox infection:

- Maculopapular → vesicular → pustular→ scab → crust.
- Synchronous lesions (evolve at the same rate)
- Centrifugal distribution of rash
- Rash also seen on palms and sole
- Slow development
- They don't burst when probed.

On the day 3 or 4 the viral load in the lymph nodes increases causing risk of viremia. Following this the virus spreads to spleen and bone marrow till the day 8 which leads to secondary viremia and fever.

Protection:

- live vaccine DRYVAX
- vaccinia immune globulin
- isolation
- antiviral drugs (cidofovir)

Viral haemorrhagic fever: VHF is a severe infection leading to generalised bleeding in the body. Other symptoms include prostrations, malaise, increased vascular permeability, abnormal coagulation. All body fluids are infectious hence, highest level of care in needed.

VIRAL HEMORRHAGIC FEVERS OF HUMANS

Virus Family *Genus*	Virus	Disease	Natural Distribution	Source	Incubation (Days)
Arenaviridae					
Arenavirus	Lassa	Lassa fever	West Africa	Rodent	5–16
	Junin	Argentine HF	South America	Rodent	7–14
	Machupo	Bolivian HF	South America	Rodent	9–15
	Sabia	Brazilian HF	South America	Rodent	7–14
	Guanarito	Venezuelan HF	South America	Rodent	7–14
	Whitewater Arroyo	Unnamed HF	North America	Rodent	Unknown
Bunyaviridae					
Nairovirus	Crimean-Congo HF	Crimean-Congo HF	Africa, Central Asia, Eastern Europe, Middle East	Tick	3–12
Phlebovirus	Rift Valley fever	Rift Valley fever	Africa, Saudi Arabia, Yemen	Mosquito	2–6
Hantavirus	Agents of HFRS	HFRS	Asia, Balkans, Europe*	Rodent	9–35
Filoviridae					
Ebolavirus†	Ebola	Ebola HF	Africa	Unknown	2–21
Marburgvirus	Marburg	Marburg HF	Africa	Unknown	2–14
Flaviviridae					
Flavivirus	Dengue	Dengue HF	Asia, Africa, Pacific, Americas	Mosquito	Unknown
	Yellow fever	Yellow fever	Africa, tropical Americas	Mosquito	3–6
	Omsk HF	Omsk HF	Central Asia	Tick	2–9
	Kyasanur forest disease	Kyasanur forest disease	India	Tick	2–9

HF: hemorrhagic fever; HFRS: hemorrhagic fever with renal syndrome
*The agents of hantavirus pulmonary syndrome were isolated in North America.
†There are four species of Ebola: Zaire, Sudan, Reston, and Ivory Coast.
Reference: medical aspects of biological warfare, ZYGMUNT F. DEMBEK, PHD, MS, MPH Colonel, MSC, US Army Reserve US Army Medical Research Institute of Infectious Diseases

Majority events are due to dysfunction of innate immune system added upon this the virus replication in cells contribute to the clinical features too. The picture shows organisms causing HF with their characteristics.

A stepwise approach for management during such biowarfare situations: In situations of biowarfares one of the most important determinant of management is whether you have already identified the agent that is used as a bioweapon, in such cases the management follows a straightforward route. But if the agent is unknown the management becomes far more burdensome. It is very crucial to know whether the attack is really a biowarfare or is it just a heightened trend in the incidence of the disease. The following write up is a stepwise management program for such events.

Step1: suspect and wait for correct clinical feature

This step is most important for distinguishing a biological attack from chemical, nuclear or conventional attack. When a certain biological agent is used as a bioweapon, we always see the agent specific incubation period but a chemical or nuclear or a conventional attack do not posses such characteristics.

Step2: self-protection

The worst thing that could happen in this scenario is the saviours (health care workers) get themselves infected by the agent. This leads to lack of manpower and exponential increase of burden on other health care workers.

Step3: revive the patient

On complete self-protective measures undertaken, now the health care workers give their best to revive or save the patient.

Step4: decontamination

The decontamination process can be started once the patients are stabilised. This step is of least importance in biological attack because, of the specific incubation period.

Step5: diagnosis

For the best and effective treatment of the patient it is very essential to know the causal agent. The AMPLE diagnosis technique may help for diagnosis.

A: arthropod, allergies
M: medications
P: past illness
L: last meal
E: events that precede the incident.

Step6: treatment

After correct diagnosis of the agent a correct and effective treatment can be provided for the finest results. Some drug trials may be undertaken to find the most beneficial drug.

Step7: infection containment

The health care workers should prevent secondary infections among the patients. Highest threat is possessed by anthrax, tularemia, Q fever, glanders.

Conclusion

Biowarfare and bioterrorism, a concept which is evolving day by day, pose a great threat to humanity. This inhuman activity which started in 14th century has not stopped evolving ever since. The advances in science and technology and increasing conflicts among different nations pose a severe threat to the civilians.

One wrong step and the entire globe has to bear the consequences. It is undoubtably true what M.K. Gandhi once said, "An eye for an eye ends up making the whole world blind" so let's hope the world doesn't face such attacks in future. World peace is a project that we all have to do together.

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