Selected agents of biological warfare

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Summary:

The article, describing the characteristics of the means of biological warfare based on the CDC classification of bioterrorism agents, presents the most significant pathogens which may potentially be used as biological weapons of mass destruction. Selected infectious diseases, routes of infection and ways of transmission are characterized, along with short descriptions of the most severe symptoms accompanying those diseases

Key words: biological warfare, identification, detection

1. Introduction

The events of 2001, such as the biological terrorism acts using anthrax, demonstrated the need of a profound turnover in perceiving biological agents by global society, and the protection against biological agents of mass destruction gained in significance [1]. Successful protection against biological attacks requires the creation of efficient early detection systems [2], management procedures and crisis simulations. Yet, it has to be taken into account, that acts of biological terrorism do not involve infrastructural damage, but rather mass infections with high mortality rate along with a psychological effect leading to mass panic [3]. This article presents the characteristics of biological warfare, classification of bioterrorism agents according to the Centers for Disease Control (CDC) and selected infectious diseases which may potentially be used as biological weapons of mass destruction.

Definition of biological weapons
Biological weapons may include such organisms as bacteria, viruses, protozoans and fungi along with their chemical products, but also some higher organisms, as insects and rodents constituting vectors for diseases [4].

2. Characteristics of biological weapons

Among the characteristics of biological agents decisive for their use as biological weapons, the following features may be listed:

- low infectious dose;
- high mortality rate (e.g. approx. 80% for anthrax);
- ease in obtaining and mass production;
- low molecular weight facilitating aerosol dispersion;
- long-lasting postproduction virulence;
- no efficient therapy available;
- low cost allowing the use as a warfare agent [1,4,5].

The form, in which a biological weapon of mass destruction may be used depends mostly on the technical capabilities of the terrorist [4,6]. Infection with a biological agent occurs mainly via respiratory ways, digestive tract and open wounds.

The aerosol variant, i.e. air contamination, constitutes the most realistic and the most dangerous method of biological agent dispersion by terrorists. Skin is another potential locus of infection.

3. Bioterrorism agents according to *The Centers for Disease Control*

According to CDC (Centers for Disease Control and Prevention, Atlanta, USA), hazardous biological agents considered as potential biological weapons are divided into three categories: A, B and C (Table 1).

Table 1: Classification of bioterrorism agents according to the CENTERS FOR DISEASE CONTROL.

Category	Agents
A • easily spread or transmitted from person to person, • resulting in high death rates and having the potential for major public health impact, • potentially causing public panic, • requiring special preparedness from public services (mainly public healthcare).	Variola vera Bacillus anthracis Yersinia pestis Clostridium botulinum toxin Francisella tularensis Filioviridae: Ebola, Marburg virus Arenaviridae: Lassa, Junin virus
B • moderately easy to spread, • resulting in moderate illness rates and low death rates, • requiring enhancements in diagnostic capacity and enhanced disease monitoring.	Coxiella burnetti Brucella spp Burkholderia mallei Alphavirus Ricin Clostridium perfringens epsilon toxin Staphylococcus aureus enterotoxin B Salmonella spp Shigella dysenteriae Escherichia coli O157:H7 Vibrio cholerae Cryptosporidium parvum
C • easily available, • easily spread.	Nipahvirus Hantavirus Arboviridae Flavivirus Mycobacterium tuberculosis Filioviridae: Ebola, Marburg and other haemorrhagic fever viruses

Category A comprises pathogens with the highest priority due to their high virulence and mortality rate, as well as their ease of transmission and required preventive measures. Category B encompasses pathogens with the second highest priority due to their ease of transmission and high virulence, but low mortality rate. Analogically, Category C groups pathogens with the third highest priority, characterized by the ease in obtaining and production, high virulence and mortality rate [4].

4. Selected infectious diseases

Among the pathogenic agents inducing infectious diseases, four groups may be distinguished: bacteria, viruses, Rickettsiae and toxins of bacterial and fungal origin (Table 2) [1,4].

Table 2: Selected infective agents of biological weapons of mass destruction.

Bacteria	Viruses	Rickettsiae	Toxins
Anthrax	Smallpox	Q Fever	Botulinum toxin
Plague	Viral haemorrhagic fevers	Typhus	Ricin
Tularaemia	Venezuelan equine encephalitis		
Cholera			

Anthrax is an acute zoonosis caused by the bacterium *Bacillus anthracis*, which forms spores endowed with very high resistance to environmental conditions [7]. The disease occurs mainly in sheep, goats, cattle and horses. Humans may contract the disease by direct contact with infected animals or their meat, whereas the locus of infection may be the respiratory ways, digestive tract and skin lesions [8,9]. In human population, the disease may occur as three different syndromes: inhalational, cutaneous or gastrointestinal. In the case of inhalational anthrax, flu-like symptoms develop over 1-6 days, with a short, transitory improvement lasting a few days. At this stage, it is difficult to differentiate anthrax from influenza due to the aspecificity of the symptoms, however, typical symptoms for anthrax may be shortness of breath and gastrointestinal problems of increased severity. Introduction of therapy at this stage often saves the patient's life. Within three days of the occurrence of the initial symptoms, signs

of respiratory failure (cyanosis, dyspnea, stridor) occur, followed by circulatory failure with lung oedema, as well as pleural and pericardial exudate. Lack of inflammatory infiltrate within the pulmonary parenchyma is characteristic for this syndrome.

Consumption of restricted animal products is the most common cause of gastrointestinal anthrax. The symptoms include nausea, vomiting, fever and lack of appetite, followed by severe abdominal pain with haemorrhagic diarrhoea and vomit. Typically, characteristic clinical signs of this syndrome are mouth and throat ulcerations (black pustules) along with fever and neck oedema [10]. Gram-positive bacteria are usually detected in blood cultures after 2-3 days of infection, similarly to the inhalational syndrome. Cutaneous anthrax occurs most commonly on the head, forearms and hands. In the initial phase, intense itching may be noticed at the infection site, which then forms a nodule resembling an insect bite within two days. Subsequently, the lesion forms a blister filled with fluid, which turns into a painless, hollow ulcer covered with a necrotic eschar [9,11].

Plague is caused by the Gram-negative bacterium *Yersinia pestis*. Wild rodents are the reservoir of the disease, which is then transferred to humans by rat fleas. The bacterium is resistant to heat and disinfectants [10]. Plague may occur in two principal clinical forms: pneumonic, contracted via respiratory ways, and bubonic, developing in humans infected by fleas preying on animals. The pneumonic form is considered as one of the most severe human diseases, as it may advance into haemorrhagic bronchogenic pneumonia [13]. Frequently occurring respiratory and circulatory problems with concurrent lung oedema are the most common mortality factor. The bubonic form demonstrates such symptoms as high fever, headache and vertigo, disorders of consciousness, vomiting. Incubation period of the pneumonic form ranges from 1 to 5 days, whereas in the bubonic form incubation period lasts up to 7 days [12,13].

Tularaemia, similarly to plague, constitutes a highly infectious zoonosis. It is caused by the bacterium *Francisella tularensis*. Two forms of the disease may be distinguished: Eurasian, less virulent in humans, and American, endowed with higher virulence [14]. Infection usually occurs by direct contact with infected animals. The disease may also be transmitted by ticks previously preying on infected animals. Clinical image includes acute headaches, chills and high fever. In some cases, cutaneous eruptions may be observed [4]. Considering the clinical image of the patient, seven forms of the disease may be identified: glandular, pneumonic, oropharyngeal, oculoglandular, ulceroglandular, gastrointestinal and its subtype, typhoidal. Diagnosing tularaemia based on clinical signs is very difficult, therefore the identification is conducted in laboratory tests. Incubation period averages 3 to 5 days.

Cholera is an infectious disease induced by the bacterium *Vibrio cholerae*. The disease is characterized by one of the most severe courses and may be contracted by direct contact with an infected person or via food and water. The symptoms include acute vomiting and abundant, pinkish diarrhoea resulting in quick, severe dehydration of the patient [4]. In the case of dry cholera (cholera sicca), diarrhoea does not occur due to intestinal motility impairment with fluid accumulation in the bowels and death occurs short time after contraction. Incubation period is approx. 2-3 days.

Smallpox is one of the diseases with strict quarantine requirements. The epidemiological factor of smallpox is a virus of the *Orthopoxvirus* genus [15]. Infected patients themselves are the reservoir of the virus. The disease is characterized by purulent blisterous eruptions. Initially, flu-like symptoms appear, such as: acute headache, vomiting, sore throat, sacrum and limb pain. Typical incubation period is 10 to 12 days [16]. Thanks to prophylactic vaccinations, immunity to the disease has covered almost 100% of global population [15].

Viral haemorrhagic fevers are a large group of viral diseases, whose main common element is the occurrence of haemorrhagic diathesis [17]. Examples of those diseases include Ebola haemorrhagic fever and Lassa fever. In the former case, the aetiological factor is a virus of the Filoviridae family, whereas the main reservoir are monkeys. Incubation period ranges from 2 to 21 days. Clinical signs occur suddenly and include acute headache and muscle pain, sore throat, cough and vomiting. Mucosal eruptions

and cutaneous rash also appear. After approx. 7 days of infection, signs of haemorrhagic diathesis occur, such as bleeding from the gastrointestinal tract, nose, respiratory ways and, in women, vagina. The above reactions lead to multiple organ dysfunction. Positive diagnosis for those clinical signs confirms the disease, however, Ebola haemorrhagic fever has to be distinguished from malaria, yellow fever, typhoid fever or Lassa fever, the latter mentioned above as an example of viral haemorrhagic fever. Ebola virus disease is caused by a virus of the Arenoviridae family, whose reservoir are rodents (especially rats) with complete carrier state. Humans may contract the disease via respiratory ways or by direct contact with the faeces of infected animals. Occasionally, cases of infection through bites by an infected animal are reported. Characteristic symptoms include high fever, muscle pain, mouth ulceration and haemorrhagic cutaneous eruptions. Incubation period is 6 to 14 days [4,17].

Venezuelan equine encephalitis (VEE) is caused by Alphaviruses belonging to the Togaviridae family. The vectors transmitting VEE are blood-sucking arthropods, whereas the reservoir species comprise wild mammals, birds and arthropods [4]. Humans contract the disease by mosquito or tick bites. The most common clinical signs are headache, vomiting, pareses and tremors. In almost 100% of cases, symptoms of encephalitis occur. Incubation period ranges from 2 to 6 days.

Q fever is a zoonosis caused by *Rickettsia burneti* [4]. The disease is characterized by a particularly high infectivity, while the course of the disease exhibits such symptoms as pneumonia with high fever, often accompanied by headache and weakness. Incubation period spans 2 to 4 weeks. Sources of infection include the blood, meat, milk and its products, as well as the faeces of infected animals.

Typhus, also known as rickettsiosis, is induced by the *Rickettsia prowazekii* species. Both the reservoir and the source of infection is an infected person [18]. Two forms of typhus may be distinguished: "classical" epidemic typhus and delayed relapsing typhus, also known as Brill-Zinsser disease. In the first case, the vector transmitting the disease is the body louse, whereas in the latter case, endogenous infection occurs. Characteristic patches of haemorrhagic rash are a typical symptom of the disease.

Botulinum toxin or "sausage poison" is produced by the anaerobic bacterium *Clostridium botulinum*. Currently, several phenotypic groups of this microorganism are known, but those causing infections in humans are the A, B, E and F types [19]. The reservoir of the bacteria are the superficial layers of soil, as well as silt deposited at the bottom of water bodies. Poisoning with botulinum toxin, botulism, is a particular form of food poisoning [20]. The occurrence of the symptoms of botulism may vary in time, according to the gravity of poisoning, from several hours to several days. Clinical signs include vomiting, diarrhoea, weakness, vision disorders and neurological problems: swallowing difficulties, dilation and uneven size of the pupils or strabismus [19,21]. In the later phase, the above symptoms may be accompanied by limb weakness, loss of facial expression, paralysis of thoracic muscles and the diaphragm.

Ricin is a neurotoxic protein obtained from the plant *Ricinus communis*. The substance interferes with protein synthesis. Clinical signs of poisoning are bad disposition and weakness [22]. Large doses may induce septic shock and eventual death of the patient. The symptoms appear after 5-12 hours of the contact with poisonous aerosol.

5. Conclusions

Many reports of the use of biological weapons of mass destruction may be found in the literature, occurring from the ancient times until present. Technical advances resulted in eradication of some diseases, but this does not preclude the fact, that infectious biological agents may be stored in secret laboratories. During the Geneva conference in 1925, General Sosnkowski warned, that "biological weapons may be easily, cheaply and secretly produced." The above characteristics mentioned by Sosnkowski are encourage various terrorist groups to use that kind of agents. Protection against infectious diseases should be based on the systems of early case detection, efficient treatment methods and isolation of patients to prevent the occurrence of epidemics.

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