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Toxicology

Biological weapons—uncertainty, frustrations, worries

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Summary:

This paper describes putative tactic and aims of bioterrorism. Examples of proper reactions to acts of bioterrorism are demonstrated, based on hypothetical threats. Characteristics of signs useful in biological attack identification, as well as practical preventive measures, including the need of establishing new vaccine production technologies, are also presented. Apart from preventive measures, the importance of technically difficult damage reparation endeavours was discussed. Finally, main risks of bioterrorism are assessed, including factors potentially used as weapons, especially smallpox and anthrax. In conclusions, the need of effective prevention of terrorist attacks is emphasized. One of the priorities is improving the capabilities of intelligence agencies in predicting and preventing acts of terrorism, which nowadays are considered as a threat as serious as nuclear weapons were in the past.

Key words: bioterrorism, frustrations, ignorance, worries, prognoses, prevention, reparation, tasks.

Introduction

The nature of modern civilization contributed to broadening of the concept of war as a small group of people may destroy any living force with great effectiveness. Naturally, it applies to terrorism which nowadays assumed a global level and became the most important problem of the modern world and humanity. [1]

Global community knows little on the nature of biological terrorism. For today, there are virtually no records of a significant event related to this type of terrorism, terrorist groups, their tactic, particular motives and aims of their activity. All those data are necessary for the analyses which may then be used as a base for establishing strategies of combating that threat [1]. Some agents have been used sporadically in acts of individual terrorism during military conflicts [2] and in the only specific, yet limited in range, act performed after the World Trade Center attacks in the USA in 2001, when several letters containing pulverized anthrax spores were sent by post [3]. However, terrorist groups in the future will be more interested

in mass killing using such weapons. The most probable tactic of bioterrorists will be releasing pathogenic agents in the form of aerosol, i.e. air suspension of droplets or microscopic particles shaped as a stable cloud. Thus dispersed agents will be invisible and odourless, and nobody will be aware, that an act of bioterrorism has been committed. As there is no system for a quick detection of aerosols containing biological weapons, terrorists will be able to use them in their attacks against any target.

Limited possibilities in reacting to bioterrorism

The most important task during the preparation of preventive measures is conducting studies of possible methods of reaction to terrorist attacks, particularly major ones. The results of analyses performed to date are far from being encouraging. The lack of preparation is a result of several factors [4]:

1) Difficulties in preventing events which have never occurred before.
2) In the case of biological terrorism, the size of human loss may be shockingly vast and many officials keep the blind faith that such acts may somehow be prevented by the combined efforts of the police, security services and intelligence agencies. It is therefore required to improve training methods and coordinate actions taken by different services responsible for appropriate reactions to terrorist threat.

As for the reactions to biological terrorism, there is a need of, for example, equipping hospitals with appropriate devices, as well as antibiotic and anatoxin reserve. It is also necessary to improve the competences of medical personnel in the identification of various symptoms characteristic of diseases caused by biological weapons, so that the victims may quickly receive appropriate therapy. Most physicians in their practice have never seen, for example, clinical cases of anthrax, not to mention smallpox or haemorrhagic fevers [5].

An important aspect of the reaction to biological terrorism will also be controlling the psychological reactions of people employed in damage reparation services [2,6]. Particular emotional problems may be generated by handling bodies of the victims of mass destruction attacks [2].

Hypothetical examples of bioterrorism threats

Even in the 1950s, American scientists alerted that the USA is not protected strategically or tactically against biological weapons. An example of a hypothetical threat was an enemy submarine attack from several miles off the coast, involving the dispersion of the Q fever microbes in the area spanning from Norfolk to Portland and covering 700 nautical miles. Constant winds occur there which blow several miles into the land before they are dispersed by land air masses. It is one of the most populated areas with approx. 80 million inhabitants. It has been estimated that approx. 30% population may become infected and approx. 30 million may become disabled for 7–10 days even if properly treated with antibiotics. Another example of hypothetical strategic attack is an air strike on Washington, involving the dissemination of tularaemia bacteria of anthrax spores. Putatively, within 4–7 days the attack would cause morbidity in hundreds of thousands of people and 20% of cases would result in death without an appropriate antibiotic therapy [5,6].

Aspects of epidemiological identification of a bioterrorist attack

A bioterrorist attack will be identifiable based on the following signs:

1) Presence of a main epidemic focus with a large number of affected and dead patients over a short period of time, e.g. within 12–46 hours.
2) Very high effectiveness of the attack, e.g. 60–80% morbidity in the attacked population.
3) Frequent incidence of pulmonary complications indicating aerosol as the carrier of the pathogens causing such diseases as plague, tularaemia, anthrax, or Q fever.
4) Unprecedented territorial range of the epidemic, e.g. Crimean–Congo haemorrhagic fever occurring in Alaska or New York, or Venezuelan equine encephalitis in England.
5) High mortality rate due to much higher exposure to microorganisms than in the case of natural epidemics.

6) Localization of the sites of incidence. Outbreak occurrence following wind direction from the site where the attack was conducted.
7) Infections (even single ones) caused by microorganisms never reported in a given area.
8) High mortality of many animal species.
9) Effective protection against infection in people staying in places in which the air is filtered or even in closed rooms.
10) Almost simultaneous occurrence of similar outbreaks in different places.
11) Finding direct evidence of an attack, e.g. pieces of contaminated ammunition; supposition that biological weapons have been used by the enemy forces or terrorists; confirmation of an attack; information from intelligence agencies stating that biological weapons have been used by enemy's agents orcollaborating parties.

As it has already been emphasized, currently there is no detection system which would indicate approaching biological threats. Within the next few years, unusual cases of disease and death in humans and animals will be the only threat identification methods [5].

Civilian population is not immunized against most diseases caused by biological weapons or equipped with appropriate protective means, such as filtered ventilators and efficient gas masks.

The most effective defence method against biological agents is immunoprophylaxis. Yet, vaccine production involves certain difficulties [7,8]. Most of all, in the case of a biological attack, most of the pathogens are exotic. This creates some technological difficulties in undertaking preventive endeavours. The difficulties stem from poor knowledge of microorganisms and the need of having well-equipped laboratories along with sets of bacterial and viral strains necessary for vaccine production. A good command of production technology is of great importance as well.

Another problem is the effectiveness of vaccines in the case of atypical route of infection. The most probable method of attack is aerosol dispersion. People and animals, even if vaccinated parenterally, may not be sufficiently protected against infections originating in system [8].

Another issue is the availability of vaccines. Nowadays vaccines are produced in small quantities sufficient only to prophylactically immunize laboratory personnel and other selected groups within medical services or military medical personnel serving in locations endemic for particular diseases. On a rapid increase in the demand for those vaccines low production rates would be encountered along with the inability to conduct clinical studies of vaccines and their safety. Logistic aspects also play an important role in this regard. Even the widely available vaccines might not be administrable on a fully mass scale. Alternatively, conventional vaccine administration using needles should be substituted with jet injectors using high pressure and capable of performing 600-1000 immunizations per hour [8].

The US government is still interested in vaccine distribution through aerosol. This route, similarly to vaccination employing drinking water, would be very useful for mass vaccinations. However, the aerosol method has three key disadvantages:
1) Requires much larger quantities of vaccines than conventional methods.
2) Extremely complicates individual dosage control.
3) Requires mass transport of the immunized population to immunization facilities, where appropriate stationary vaccination equipment is based.

Another commodity in performing mass immunizations may be the use of polyvalent vaccines, which reduce the number of required injections. Likewise, adjuvants and other vaccine enhancers are successfully used. Passive immunoprophylaxis might be effective as well, however, it would be of limited significance in mass operations due to large quantities of immune sera required for immunizations [8].

Damage repair endeavours

When numerous cases of an unidentified disease occur it may be assumed a priori that a bioterrorist attack using bacteria or Rickettsiae is involved and that prophylactic antibiotic administration will "moderate" the infective process until a proper determination of the infective factor and its susceptibility is conducted [5].

If more cases of infection occur, 4–5 groups for test treatment may be created without waiting for pathogen isolation and determination of its drug resistance profile. By using only one antibiotic per group, therapeutic effect of each of them may be assessed [2,5].

Immunization undertaken immediately after the occurrence of bioterrorist attack is inefficient as most diseases may have short incubation period. Specific therapy employing monoclonal antibodies is still not refined enough to become the method of choice within the next few years [4,5].

One of efficient methods of biological agent deactivation is disinfection. However, practical execution of mass-scale disinfection operations would exceed the technical capabilities of any attacked population. When used to a limited extent, successful disinfection methods are those employing formaldehyde or ethylene oxide, although they are toxic for the operative personnel and may damage precision instrumentation and other equipment [4,6].

In the light of a multitude of potentially used biological agents, the simplest means of disinfection are soap and water for body hygiene and boiling or soaking in chlorine solution for garments.

Other endeavours involving environment-related actions include the protection against insects as vectors of many infective diseases, which requires creating appropriate insecticide reserve. In extreme situations, like the aforementioned hypothetical aerosol-based attack using tularaemia bacteria or anthrax spores, it may be expected that appropriate medical aid may not be provided to the entire group of victims of such an event, exactly as in the case of other weapons of mass destruction. Medicine reserve would rapidly deplete, hospital would quickly become overcrowded and other public (school, churches) and private buildings would have to be adopted for medical purposes. Coordination of all medical endeavours would be extremely difficult if, thinking optimistically, medical services were still sufficiently operative to be able to fulfil their duties. Mass-media would be flooded with telephone calls which might lead to service suspension. The lack of one main information centre or its complete block would add to a potentially rising public disorder.

After a mass-scale attack, additional problem potentially constituting another source of infection would be mass gathering of unburied human and animal bodies. What appears to be a secondary problem, may actually force public services to undertake unconventional actions [3,5,6].

Assessment of main risks related to bioterrorism

Until 1980s in the USA, not to mention other countries, there was a general feeling of self-confidence about the immunity to bioterrorism, the funds for defensive measures were reduced, most of the serious research programmes were closed, and the participating research groups were disbanded. This self-confidence was ruined by the Soviet dissidents' reports on the size of the Russian offensive biological weapons programme [9] and by the fact that at least 10 states have biological weapons currently at their disposal. The signing of the Biological Weapons Convention in 1972 was an opportunity for the Soviet Union to gain advantage over Western countries. For example, the considered eradication of smallpox along with the cease in immunizations in 1980 was regarded as such an opportunity. Large-scale production of the smallpox virus as a biological weapon was initiated. In 1989 a total annual productivity of 12 metric tons was reached.

By 1992, the Soviet and then Russian research and application programme of biological weapons development was taken over and continued by at least two different organizations: "Biopreparat" subordinated to the Ministry of Medical and Microbiological Industry and a special, unidentified enterprise subordinated to the Ministry of Defence. Well-known is a still operative part of the multi-laboratory "Biopreparat" complex composed of 9 facilities and formerly employing 60,000 people. One of those facilities is the State Research Center of Virology and Biotechnology located in Koltsovo, Novosibirsk Oblast. It has been licensed by WHO to store the smallpox virus (another deposit is located in the CDC headquarters

in Atlanta, USA). The Koltsovo centre has a Biohazard Level 4 (BL-4) laboratory permitting studies of the most virulent pathogens, such as smallpox and haemorrhagic fevers. Currently, like other laboratories in Russia, the institution is experiencing financial problems. A substantial number of researchers have left their positions and their current employment is not known. What is dangerous, countries such as Iran, Syria, and North Korea keenly enrol such specialists. A mix of rogue states and generously financed religious cults with researchers desperately seeking fund sources creates an unclear and dangerous political situation which may potentially evoke serious consequences [3].

Factors potentially used in bioterrorism

Although many biological agents capable of inducing infection may be considered as potential biological weapons, only few of them may actually constitute a serious threat. Few of them may be cultured and dispersed efficiently to cause morbidity and deaths in quantities which might put the functioning of the attacked population at risk. The characteristics which qualify pathogens as potential biological weapons are: specificity, potential to transmit from human to human, environmental stability, the size of infective dose and the availability of preventive and therapeutic measures.

The regulations by the Centers for Disease Control and Prevention (CDC) introduced in 1997 list 24 microorganisms and 12 toxins, whose possession requires registration and special permission for transfers.

The WHO guide (1) lists the following pathogen-related diseases: anthrax, brucellosis, glanders, melioidosis, plague, Q fever, typhus, coccidioidomycosis, Venezuelan equine encephalitis, smallpox.

The listed toxins are: botulinum toxin, staphylococcal enterotoxins, aflatoxins and other fungal, algal, and plant toxins. The smallpox and anthrax pathogens are characterized by high infectivity when dispersed in the form of aerosol and have mortality rates of 30 and 80%, respectively. These two pathogens have other advantages as potential biological weapons. They may be easily cultured in large quantities and are resistant to environmental factors. Therefore they are suitable for disseminating by aerosol dispersion over large areas and populations. The plague bacterium and botulinum toxin are less likely to be used. The results of the former US offensive biological weapons programme indicate that the production and dispersion of large quantities of the plague bacteria and botulinum toxin poses problems impossible to solve. Thus the microorganisms exposed at the top of the list are the smallpox [1,7] and anthrax [1,3] pathogens.

Smallpox and anthrax constitute the greatest threat also due to their different clinical and epidemiological properties. The outbreaks of smallpox in Yugoslavia (1972) and anthrax in the Soviet Union (1979) permit us to imagine the size and nature of the problem.

Analysis of risks related to smallpox

Smallpox constitutes an extremely serious threat due to a significant susceptibility to the virus in humans and the cease in mass immunizations ordered many years ago as a consequence of virus eradication. Since the immunity among the population diminishes, many people are probably not immune to smallpox anymore. Among the nonimmune, mortality rate after smallpox contraction might reach 30% and there is no effective therapy. Virus dispersed in the form of aerosol might retain its virulence for over 24 hours and remain highly infective even in small doses. A disease outburst in which only 100 people contract the disease might already pose a serious challenge for healthcare services. Due to the risk of large-scale spreading of the virus in aerosol, the patients would have to be kept in negative pressure isolation rooms, whose air ducts would have to be equipped with special filters. Even in the USA few hospitals have such rooms. A protective immunization programme would also have to be introduced among the people who were in direct contact with the patients. A vaccine administered after 3–4 days of exposure might protect most of them from developing an infection. However, it is unlikely that smallpox would be diagnosed early enough and the vaccination programme

would be introduced rapidly enough to prevent infections in people exposed to the pathogens on the occurrence of first cases. Few physicians have ever seen the signs of smallpox and even fewer, if any, have been trained in diagnosing this disease. A second wave of smallpox cases would be almost inevitable.

The initial vaccinations would be necessary for medical personnel in contact with the patients. With the increasing number of cases, contacts and involved areas, mass immunization would quickly become the only practically applicable way of combating the epidemic. Nonetheless, mass immunization would also be impossible, as current vaccine reserve is limited to 5–7 million doses. In comparison, 6 million New York residents were vaccinated in 1947 after the occurrence of just 8 cases of smallpox. Moreover, smallpox vaccine is currently not in production. Reliable assessments indicate that major supplies might be provided no earlier than 36 months after the first outburst of the disease [7].

Analysis of risks related to anthrax

A scenario of inhalational anthrax epidemic is by no means a lesser problem [10]. Anthrax aerosol might be liberated stealthily and drift in the environment, as it happened in 2001 [1]. After 2–3 days patients with various aspecific symptoms, such as fever, cough, or headache, would appear in emergency departments and doctors' offices. Within 1–2 days those patients would become critically ill and after further -3 days deaths would occur. It is dubious that antibiotic therapy might be helpful once the symptoms of the disease have developed.

As has been mentioned before, the mortality rate would reach 80%. Even though anthrax is not transmitted from human to human, it has other properties which pose threat. People exposed to anthrax pathogens may become ill even after 8 weeks of the first exposure [8]. In this type of cases preventive measures in the form of antibiotics may be employed, but such therapy should be continued for at least 60 days [4].

The above period may be shortened by a proper vaccine administration. Experimental studies indicate that 2 vaccine doses administered separately during 15 days may immunize the subject after 30 days of the first dose administration. Yet, the vaccine is currently not available to the civilian population [3]. Even in the USA, magazines holding antibiotic reserve are still only planned and no city has a plan of antibiotic distribution allowing their administration for more than 60 days.

The history of studies of the anthrax pathogens as biological weapons has alarming and so far unexplained holes which increase the worries related to potential terrorist attacks. These are: 1. The undefined content of the anthrax aerosol from Sverdlovsk [11]. The possibility of obtaining anthrax strains with confusing characteristics leading to misidentification and incorrect treatment [12]. Varying condition of pulverized spores in the anthrax-containing letters from 2001 [13] and the results of the unexposed investigation aimed at determining the perpetrators [14].

Conclusions

Biologists, mainly in the field of medicine and public health, present as critical views on confronting the problems posed by biological weapons as physicists and chemists do on the nuclear and chemical threats, respectively.

There is a need of training physicians in the early recognition of most of dangerous diseases. Likewise, laboratory and public health employees along with epidemiologists need to be trained in combating dangerous infective diseases.

The inability to develop endeavours considered as solutions in the case of a bioterrorist attack might lead to a biological disaster with unimaginable consequences.

In the 20th century, the humanity experienced the results of chemical and thermonuclear warfare but, fortunately, managed to avoid disasters expected to occur after a biological attack. Lessons from remote past seems to teach us very well in this regard. Considering the world population and the death-to-case ratio, it may be assumed that the greatest human loss in our history was caused in Europe by the plague pandemic ("black death") in the 14th century. The estimated number of deaths was 23,840,000 which constituted one fourth of the entire European population at that time.

Despite the passing of 6 centuries, this lesson is a terrifying illustration to a horror story which nowadays may be represented by a large-scale use of biological weapons. Currently the threat is emphasized by the means allowing a large-scale production of toxins and pathogens with genetically enhanced infective properties.

We need a new and broad perspective on the real threat of biological weapons, and a system to prevent the use of such weapons, as well as the most effective procedures for eliminating the consequences of their use. The emergency services and health services should have well-developed and tested procedures of action in circumstances of a threat. Moreover, what is also necessary, is the rapid recognition and accurate identification of risk factors, as well as developed and tested procedures to eliminate the consequences of the use of biological weapons. These actions are related to individual and collective inactivation, and inactivation of the environment, organization of first aid to victims, organization of the system of segregation and transport of patients. It is necessary to keep ready a certain number of beds in well-equipped departments of infectious diseases, which would enable hospitalization of patients with especially dangerousinfectious diseases. [16]

Problems related to biological disaster management are so complex that they are impossible to solve by people of one profession. They require combined knowledge from many different disciplines at different administration levels. As much support as possible is necessary for any actions leading to increasing the importance of the Biological Weapons Convention. One of the priorities is improving the capabilities of intelligence agencies in predicting and preventing acts of terrorism. Inspiring international research programmes in that field encourages openness and constructive dialogue.

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