Structural Bioterrorism at the Beginning of the 21st Century

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Abstract: The aim of this paper is to raise awareness of the danger represented by structural bioterrorism. There are presented as examples, three of the biological agents belonging to the three classes (A, B, C). As structural bioterrorism is a new concept, it has been tried to define it and what role it plays in the bioterrorism equation + state actions = Security.

Keywords: bioterrorism; security; biological weapons; violence; behavior; biological agents

1. Introduction

For the "phenomenon of terrorism" there is no unanimously accepted definition in the literature or legal regulations covering all dimensions of this scourge. The definitions in the specialty literature include the following concepts (Alex Schmid et. al., 1984):

- ✓ Violence and force (83,5%);
- ✓ Political motivations (65%);
- ✓ Fear, emphasis on terror (51%);
- ✓ Threat (47%);
- ✓ Psychological effects and anticipated reactions (41,5%);
- ✓ Discrepancy between targets and victims (37,5%);
- ✓ Intentional, planned, organized and systematic actions (32%);
- ✓ Fighting method, strategy and tactics (30,5%).

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If it were, however, to give a definition of the concept of terrorism, we can find it in the work (Gheorghe Văduva, 2002) whereby terrorism is defined as "an extremely complex social phenomenon consisting of the spectacular manifestation of violence, with the purpose of attracting attention, to frighten, to torment and to impose a certain type of behavior, sometimes through a very diversified range of border actions, in which the man is both a weapon and a victim, a rogue and a convict".

In the specialized literature, bioterrorism has been defined as the "Trojan horse" (Adrian Mircea Baciu, 2012) of international terrorism, being a global challenge not only at the world level but also at the political and social level, focusing on the exclusive inviolability and intangibility of fundamental rights and freedoms human rights, such as the right to life, health and safety.

Considering the above, although bioterrorism has many definitions, the one provided by the FBI is one of the most complete (Bogdan, 2013, pp. 47 - 48) and represents "*the illegal use of viruses, bacteria, fungi, toxins or pathogenic materials against another government, civilian population, animals, cultures or any segment of the state to promote political, social and / or economic objectives* ".

2. Biological Weapon and Biological Agents

Biological weapon is defined as a means of producing the dissemination of a biological agent or vector of the biological agent with harmful or even lethal effects to humans, animals or agricultural crops (Moran, Taban, Abrahamian, 2008, pp. 145 -187, Măciucă, Toma, 2004).

Biological agents are "*living organisms, of any kind, or infected materials, derived from them, which are used for hostile purposes and intentionally to generate morbidity and mortality, effects that depend on their ability to multiply*" (Robert C. Spencer, Mark H. Wilcox, 1993).

Biological agents have the following characteristics:

- They are relatively cheap and easy to buy;
- They are easy to mask;
- They have dual use (Civil and military).

In the specialized literature, biological agents are classified as follows (Păun, 2003):

- Category A - germs and / or toxins with high risk (primary) of human transmission or which can be easily spread in the population: *Bacillus anthracis* (anthrax), *Clostridium botulinum* (botulism), *Yersinia pestis* (plague), *Variola major* (smallpox), *Francisella tularensis* (tularemia), Ebola hemorrhagic fever virus, Marburg hemorrhagic fever virus, Lassa virus, Machupo virus.

- Category B - germs with medium (secondary) transmission risk: *Brucella sp.* (brucellosis), *Epsilon toxin* from Clostridium perfringens, threats to food security (Salmonella sp., Escherichia coli O157: H7, Shigella sp.), *Burkholderia mallei*, *Burkholderia pseudomallei*, *Chlamydia psittaci*, *Coxiella burnetti*, *Toxin Ricin* common *Ricin toxin* from *Staphylococcus sp.*, *Rickettsia prowazekii*, *Equine encephalitis virus* from Venezuela, *East / West equine encephalitis virus*, threats to water security (Vibrio cholera, Cryptosporidium parvum).

- Category C - low-risk (tertiary) germs can be any other pathogenic microbes (bacteria, virus, fungus, parasite, etc.), Nipah virus, Hantavirus etc.

The main characteristics of a biological agent are the following (Thavaselvam, Vijayaraghavan, 2010):

· *Infectivity* - the ability of a biological agent to invade the body;

· *Virulence* - the degree of severity of the disease induced by the microorganism; different strains of the same bacterial species can cause the disease to varying degrees of severity;

· *Toxicity* - the ability of a microbial agent to produce toxins and release into the body and / or the severity of the toxicity produced by the biological toxin;

· *Pathogenicity* - expresses the ability of a biological agent (microorganism or toxin) to cause disease of the organism;

· *Incubation* - the time elapsed from exposure (penetration into the body) to the biological agent until the first signs of disease appear; is a characteristic of each biological agent, depending on the contaminant dose, virulence, pathogenicity, gateway to the body, etc.;

· *Transmissibility* - the possibility of a biological agent being transmissible from person to person (human transmission), from animal to human (zoonosis) or via a vector, usually an arthropod and / or hematophagous insect (vector transmission);

· *Lethality* - it expresses the mortality rate that a microbial agent causes in the infected and sick population;

· *Viability (stability)* - the ability of a microbial agent to survive in an external environment; it depends on the weather, chemical and biological pollution.

3. Bacillus Anthracis

Anthrax is a category A of biological agents being an infectious disease caused by the bacteria Bacillus anthracis (H. Smith, J. Keppie, 1954). This bacterium infects the human and animal body, attacking the respiratory system, the skin or the digestive tract. Depending on the route of entry into the body, the anthrax may or may not be fatal, as the skin is rarely fatal, while the inhaled anthrax, a potential bioterrorism weapon, is very dangerous and fatal to both the human and animal body. (Hanna, 1998). After anthrax spores are inhaled, they adhere to the alveolar macrophages where they germinate. Then bacteria migrate to the lymph nodes where they multiply very rapidly (Hanna, Acosta, Collier, 1993) and secrete an exotoxin consisting of three proteins.

The three exotoxin constitutive proteins secreted by Bacillus anthracis are: protective antigen (PA, 83 kDa), lethal factor (LF, Zn^{2+} - metaloprotein, 90 kDa), edemic factor (EF, 89 kDa) (Hanna, Acosta, Collier, 1993; Stubbs, 2002; Mock, Fouet, 2001).

PA is a 4-domain protein (C. Petosa, R. J. Collier, K. R. Klimpel, S. H. Leppla, R. C. Liddington, 1997) that binds to the surface of the receptor cell through the terminal carboxyl groups. After proteolytic activation by furin-protease, PA releases an N-terminal fragment (PA20, 20 kDa) and a C-terminal fragment (PA63, 63 kDa) domains (C. Petosa, RJ Collier, KR Klimpel, SH Leppla, RC Liddington, 1997). PA63 heptamerizes and is able to bind both LF and EF. Following endocytosis (membrane transport) of the resulting complex, the LF and EF molecules are released and exert their toxic action (Scobie, Rainey, Bradley, Young, 2003).

In the literature it has been shown that LF is an essential target for therapeutic agents that can inhibit its catalytic activity or block the association with PA (Forino, Johnson, et. alli, 2005; Johnson, Jung, et. alli., 2006). In this sense, our research will be directed only to this component (LF) of *Bacillus anthracis*.

3.1 Lethal Factor (LF)

As shown, lethal factor (LF) is a metalloprotease capable of binding six members of the MAPKK family (the only known cellular substrate of LF) via the N-terminal (Vitale, et.alli., 2010). The LF action signals the MAPKK protein signal to other immune cells to fight infection (Duesbury, et. alli., 1998).

LF consists of four structural domains. Domain I is represented by the head of the LF linking with the PA. Domain II resembles the toxin-VIP2 enzyme secreted by Bacillus cereus although it does not exhibit catalytic activity. Domain III is inserted in domain II and appeared as a result of the duplication of structural elements of domain II. Domain IV, which resembles domain I, represents the catalytic center of LF (Pannifer, et alli., 2001). Domains II, III and IV together form a 40 'groove' in which a peptide consisting of 16 amino acids represents the N-terminus of its natural MAPKK-2 substrate.

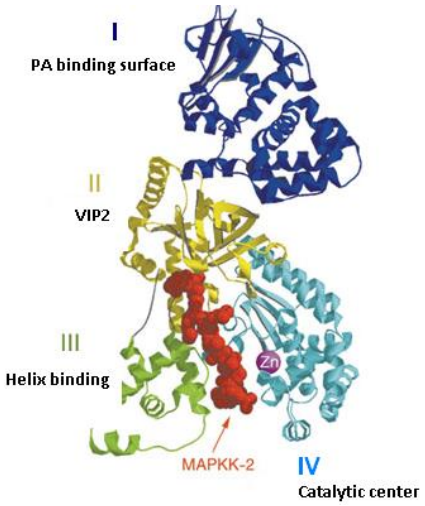

Figure 1. Structural domains of LF (A.D. Pannifer, T.Y. Wong, R. Schwarzenbacher, M. Renatus, C. Petosa, J. Bienkowska, D. B. Lacy, R.J. Collier, S. Park, S.H. Leppla, P. Hanna, R.C. Liddington, 2001) (PDB code 1J7N)

Source: (Protein Data Bank, http://www.pdb.org/pdb/home/home.do)

4. Salmonella Infections

Salmonella is part of the B category of biological agents that contaminate humans through ingestion of food or infected water. The main foods that transmit Salmonella are: chicken meat, dairy products, eggs (Su, Chiu, 2007). Another way of infecting humans is through contact with pets and especially reptiles such as lizards, turtles or snakes.

Symptoms of Salmonella infection begin after 12-72 hours after ingestion of contaminated food, but there have been cases when symptoms do not appear after 1 year, as people are carriers that can quickly infect other people.

There are forms of Salmonella such as Salmonella enterica that have much more severe manifestations such as typhoid fever (Faruk van Doleweerd, 2018).

The vast majority of Salmonella infections are cured without treatment, but the use of antibiotics is especially important in typhoid fever. The bacterial destruction occurs only by thermal process.

5 Biological Agents of C Category

They can be carried out in the laboratory with a high potential to cause morbidity or mortality (examples: nipa virus and drug resistant tuberculosis). Agents can be transmitted in several ways, of which only two are likely to reach a large number of people: by digestive tract and by air (Păun, 2003).

5.1 Brucellosis

Brucellosis (I. Lopez-Goni, D. O'Callaghan, 2012) is an infectious disease produced by Brucella sp., which is transmitted from animals to humans (zooanthroponosis), most often through unpasteurized milk, cheese and other dairy products. The bacterium can spread by air or by direct contact with the infected animals or with the secretions derived from them, under the conditions of a tegmental continuity solution (plagues).

Human brucellosis-producing organisms are Brucella abortus (from cattle), Brucella melitensis (from pigs), Brucella canis (from dogs) have caused sporadic infections. The most important sources of infection are farm animals and raw dairy products. Brucella infections have also occurred in deer, bison, horses, mice, caribou, rabbits, hens and desert rats.

Brucellosis results from direct contact with the secretions and excretions of infected animals and by indigestion of raw milk or dairy products containing viable organisms. It is rarely transmitted from human to human. With a higher prevalence in rural areas, Brucellosis is an occupational disease of those who pack meat, veterinarians, sellers and producers of cattle.

6. Why Structural Bioterrorism?

The probability of a terrorist attack with weapons of mass destruction - chemical, biological, radiological or nuclear, is very high. In recent years, the threat of unconventional terror has increased, becoming the most serious aspect of the proliferation of unconventional weapons. In particular, the possibility (inevitable, some analysts consider) that terrorists use biological weapons, which have the potential to produce mass casualties exceeded only of atomic weapons, requires rethinking strategies for monitoring the programs for the production of weapons of mass destruction.

Bioterrorism can be directed to certain state structures, to certain categories of population for producing terror, which is why the concept of structural bioterrorism appeared.

7. Security Level and Combating of Bioterrorism

The United Nations Convention on Toxic and Biological Weapons (BTWC) opened for signature simultaneously in Moscow, Washington and London on April 10, 1972 and entered into force on March 26, 1975, is at present the main instrument against biological warfare. In December 2000, 153 states had ratified or acceded to the convention, and another 16 had signed but not ratified, and in 2008, 159 states had ratified or acceded to the convention. It is becoming increasingly clear that security and the concept of security can no longer be limited to "military security". Security involves several levels, such as personal security, economic security (for companies, states, etc.), society security (including health and safety issues of water and food), political security (survival of regimes), and environmental security.

It can be concluded from the ones presented that the threat of bioterrorism remains a real danger. The prevention of biological contamination has been and is a challenge for all structures, military or civilian. Preventing an epidemic or pandemic is easier

than trying to limit / eliminate its effects, due to the extreme characteristics of biological agents / toxins.

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