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BRUCELLOSIS: NEW DEMANDS IN A CHANGING WORLD

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A b s t r a c t: *Aim:* To provide an up-to-date overview on the role of *Brucella* as a possible biological (B-) agent to be used in biological warfare, biological crimes and biological terrorism (with special respect to agroterrorism) scenarios.

Methods: An analysis of current literature and of Internet-based sources was made.

Results: Brucella spp. have always been in the focus of military decision. The main reason for military research on *Brucella* was driven by the finding that the organism can easily be transmitted via aerosols. Confronted with the new challenge of global terrorism in the last decades of the 20th century, experts tried to evaluate the risk that *Brucella* spp. are used against the civilian population. Based on criteria concerning public health demands brucellosis was rated to have only a lower medical and public impact. Nevertheless, small-scale outbreaks in humans will pose problems in all those countries where first responders are usually not aware of the clinical syndrome. Countries which have eradicated brucellosis from their livestock successfully may face another severe threat: agroterrorism. *Brucella* spp. might be introduced intentionally into livestock (cattle, small ruminants, pigs). Undeterminable losses for a state's economy may be the result of such an attack.

Conclusions: The world has become safer in the last decades due to the intensive efforts of the global community to effectively ban the use of weapons of mass destruction. However, bio- and agroterrorism especially an attack against the agricultural infrastructure is considered to be a permanent danger.

Key words: Brucellosis, zoonoses, prevention and control, population surveillance, bioterrorism, agroterrorism.

Introduction

The idea to use pathogenic agents, toxins of biological origin or pests against humans, livestock or crops has a long history. However, the revolution of knowledge in biology, medicine, biotechnology but also in military engineering stimulated the efforts to weaponize biological agents (bacteria, viruses, fungi, pests and toxins) for their use in weapons (i.e. a biological agent and its means of delivery) of mass destructions in the 20th century. The 'Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or other Gases and of Bacteriological Methods of War' of 1925 and the 'Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction' of 1972 banned biological weapons and offensive research. Hence, various countries including Japan, Great Britain, USA and USSR developed and stockpiled biological weapons during and especially after WWII [1–3]. The James Martin Center for Nonproliferative Studies, Monterey, USA, a nongovernmental institution, lists 8 states which had offensive programmes in the past but also accounts 14 others states with possible offensive B-agent programmes [4]. In those programs *Brucella* was often included. Besides the fact that B-weapons can be used by states' armies, the fear that they are used against civilian targets is increasing. The UN expressed their consideration by the following statement: '…modern technology is making it increasingly likely they (addendum by the author: biological weapons) could be acquired by private organizations, groups of people or even individuals. The use of these weapons by such non-state actors is known as bioterrorism. Biological weapons have been used in politically-motivated or criminal acts on a number of occasions during the 20th century' [5].

A careful risk assessment for the possible use of *Brucella* in weapons of mass destruction (military use) and in weapons of mass disruption (use against civilian targets) will be made.

Methods

An analysis of current literature and of Internet-based sources was made with special regard to 'Brucellosis'.

Results and Discussion

Brucella and its use as a biological agent in weapons of mass destruction.

The Holy Bible describes the occurrence of brucellosis and anthrax as diseases in animals forcing the Egyptian pharaon finally to free the Jewish people (Book of Exodus). But *Brucella* has been also considered to be a suitable biological agent to be used in weapons of mass destruction in modern wars by military decision-makers. Brucellosis belongs to the 'dirty dozen', the diseases most likely to be used against humans. These agents have the following characteristics: availability and ease of production, a high degree of incapacitation or lethality, a suitable particle size in aerosols, stability and ease of dissemination, susceptibility vs non-susceptibility in population and man–to-man transmission which is, however, not true of *Brucella* [1–3]. *Brucella* bacteria seemed to be of prominent interest as they can easily be transmitted via aerosols to humans. The organism is believed to have a low inffective dose in humans of only 10 bacteria and 50 to 80% of exposed persons will develop clinical disease [6]. A WHO expert committee believed that 50 kg of *Brucella melitensis* would cause 5,000 fatal casualties and 125,000 diseased persons and a loss of 477.7 millions of US $ per 100,000 of inhabitants if deployed in an aerosol upstream of a city with 500,000 inhabitants [6]. The enormous amount of biological material calculated with highlights important requirements for a biological warfare programme: considerable amounts of funding for personnel, equipment, research and development, for biological and military engineering, and – most important – a preserving political willingness to run an offensive programme violating international conventions. The United States of America e.g. started an offensive programme on *Brucella suis* not until 1942 being in fear of the assumed capabilities of the enemy, weaponized the agent and made field trials on animals. The offensive programme was finally terminated in 1967 [1–3]. *Brucella*-containing weapons were also intended to be used against animals [7]. Many states nowadays run defensive programmes including research on *Brucella* under the rules set up by the Biological Weapons Convention and prepare yearly declarations of their activities which are in part also available to the public [8].

Brucella and Bioterrorism

Confronted with the new challenge of bioterrorism in the last decade of the 20th century, army and public health experts now tried to evaluate the risk that *Brucella* could be used as a possible B-agent against the civilian population. They put special emphasis on the influence of a disease outbreak on public health and medical infrastructure on a large scale [9]. Based on the criteria of public health impact, the delivery potential to large populations, public perception, i.e. public fear and civil disruption, and special public health preparedness needs, brucellosis was ranked in the category B having a lower medical and public impact [9]. It has to be stressed that this ranking was done for a scenario

based in the US and that the conclusions drawn cannot and should not be transferred to any other country without careful reflection on the local conditions. Thus, an assessment has to be done by local experts considering endemicity, awareness of a disease by first responders, public health systems, preparedness, etc. Brucellosis is a food-borne disease and even small-scale outbreaks will pose problems in all those countries where brucellosis has been successfully eradicated because the first responders, e.g. the family physicians, are usually not aware of the clinical syndrome. A long-term German study on brucellosis showed that the diagnostic delay in patients was up to six months in more than 50% of the cases, resulting in above-average mortality [10]. In a multi-author review Pappas *et al*. stated that the use of *Brucella* in a biological weapon delivered through the food chain is feasible although the contamination of the food has to be done after the pasteurisation process [11]. In addition only a few expert laboratories experienced in dealing with serological diagnosis, cultivation or even agent identification exist in either developed or less developed countries. Thus, a worldwide need for the improvement of public health, i.e. medical awareness, surveillance and laboratory diagnostic capabilities, is obvious.

Brucella and agroterrorism – biocrime

'Agroterrorism is the deliberate tampering with and/or contamination of the food supply with the intent of adversely affecting the social, economic, physical, and psychological well-being of society' [12]. Agroterrorism is believed to be more attractive to terrorists because it carries less risk to the terrorist, could be carried out more covertly, does not need the sophisticated skills of weaponization and a prolonged incubation time will make tracking of the terrorist difficult [13]. Vulnerable targets include farm animals (cattle, swine, sheep, horses, poultry and fish), field crops, processed food and storage facilities [14]. Key vulnerabilities are the intensive and concentrated production practices, monitoring of diseases only at the herd level, increased disease susceptibility due to naïve populations, rapid and fast movement of animals and their products over long distances, insufficient farm – and food-related security and surveillance, inefficient disease-reporting systems, lack of experience of exotic diseases on the part of the first responding veterinarian, and lack of awareness of the sector of agricultural production on the part of the consumer [15]. 'Food' is nowadays associated with retail shops but not with farms anymore. Its availability is taken for granted. Attacks are believed to cause immediate economic disruption of markets due to eradication procedures (mass culling!), considerable loss of jobs, difficulties in sustaining an adequate food supply, increased consumer costs, indirect multiplier effects (compensation for the animal owners) and last but not least international trade embargos [15]. In the case of an attack with a zoonotic

agent human casualties may occur and the sectors of bioterrorism and agro-terrorism overlap, challenging the cooperation of public health and veterinary public health. Countermeasures will also cause restrictions of civil liberties [13]. The reputation of the government and its administration could be severely damaged by the impression that they can-not protect the food supply effectively and in conclusion will also not be able to protect their citizens [15]. An example of a list with agents which could be used against animals is the former OIE category A list of agents. The transmissible diseases caused by these agents have a potential of serious and rapid spread, cause serious socio-economic or public health consequences and are of major importance for international trade in animals and products. Various plant pathogenic bacteria or fungi may also cause disastrous economic losses and their spores may easily be distributed via air or water [13]. The good news is that for most transboundary plant and animal pathogens appropriate countermeasures have been set up by states and international organisations to protect international trade. These measures are in force and are regularly challenged by natural outbreaks of diseases, e.g. Bluetongue or Foot and Mouth Disease in ruminants. Biological crimes of single persons or groups will not be a topic of this review although most of the recent critical incidents can be attributed to this sector, e.g. the release of viral rabbit haemorrhagic disease virus in New Zealand in 1997 [13].

Brucellosis is a disease listed on the former OIE category B list of agents. Those agents cause transmissible diseases that are considered to be of socio-economic and/or public health importance within countries and that are significant in the international trade in animals and animal products [16]. Thus, countries which have eradicated brucellosis from their livestock successfully may face a severe threat when brucellosis is deliberately introduced into their livestock (cattle, small ruminants, pigs). A natural outbreak of *Brucella suis* on a well-maintained holding can run up to six month before being detected [17]. The agent will spread along the (global) supply chains and within the pig-producing industry. Brucellosis outbreaks will then involve control measures by the local authorities resulting in losses for the individual animal owner. A notification to the OIE, the world organisation of animal health, will also attract international trade restrictions for living animals and their products. Undeterminable losses for a state's economy may be the result of such an attack. In the course of an outbreak of brucellosis in animals human infection is very likely to occur if *Brucella melitensis*, *B. abortus* and *B. suis* biovar 1 and 3 are used.

Conclusions

It is particularly noteworthy that the use of biological weapons in recent wars has (to my knowledge) never been reported, although various states had

the technical skills and the weaponry to do so. A consolidated view of available information indicates that the use of biological weapons by states has become unlikely due to the manifold control efforts made by the global community in recent years.

However, bio- and agroterrorism, especially an attack against the agricultural infrastructure, is considered to be a permanent danger [15]. Consequently the EU has started various activities to combat this challenge. One of these activities was to set up the 'Chemical, Biological, Radiological and Nuclear Task Force (CBRN TF) which was working on the issue how to enhance biosecurity in Europe. This group launched the EU CBRN Action Plan with special recommendations for prevention, detection and preparedness, and response [18]. A further activity is an EU-funded ring trail and training programme called 'Establishment of Quality Assurances for Detection of Highly Pathogenic Bacteria of Potential Bioterrorism Risk' [19] in which 23 laboratories in 21 European countries work together. Several European states have also set up their own programmes to strengthen civilian public security. Germany has developed a 'National Strategy for Critical Infrastructure Protection' [20]. Various research projects have already been funded [21] and in some of those projects *Brucella* plays an important role. It can only be hoped that national and international multi-state efforts will also make the use of biological agents and weapons or their military use as unlikely as is believed to be the case.

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Резиме

БРУЦЕЛОЗА: НОВИ ПОТРЕБИ ВО СВЕТОТ ШТО СЕ МЕНУВА

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Цел: Да се овозможи обновен преглед на улогата на *Brucella* како можен биолошки (Б-) агенс кој би се користел за биолошка војна, биолошки криминал и биолошки тероризам (со особено внимание на агротероризмот).

Методи: Беше направена анализа на постојната литература и извори од Интернет.

Резултати: Brucella spp. секогаш била во фокусот на војните одлуки. Главната причина за воените истражувања за бруцелата потекнуваат од податокот дека организмот може лесно да биде пренесен преку аеросоли. Соочени со новиот предизвик на глобалниот тероризам во последните декади на XX век, експертите се обидоа да го евалуираат ризикот од користење на Brucella spp. против цивилното население. Базирано на критериумите кои се однесуваат на јавно-здравствените побарувања, бруцелозата беше оценета како заболување со пониско медицинско и јавно-здравствено влијание. И покрај тоа, епидемиите кај луѓето со мал размер ќе предизвикаат проблеми во сите оние земји каде што оние кои први треба да реагираат не се свесни за клиничкиот синдром. Земјите кои успешно ја ерадицираа бруцелозата кај нивниот добиток се соочија со друга сериозна закана: агротероризмот. Со *Brucella* spp. добитокот може да се зарази интернационално (говеда, ситен добиток, прасиња). Непроценливи губитоци за државната економија може да бидат резултат на таков напад.

Заклучок: Светот стана посигурен во последните декади како резултат на интензивни напори на глобалното општество за ефективна забрана за користење на оружје за масовно уништување. Но, био- и агротероризмот, особено напади против агрикултуралната инфраструктура, се смета за еден вид на перманентна опасност.

Клучни зборови: Бруцелоза, зооноза, превенција и контрола, набљудување на популацијата, биотероризам, агротероризам.

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