Biological weapons and bioterrorism preparedness: importance of public-health awareness and international cooperation

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Biological weapons and biological terrorism have recently come into focus due to the deliberate release of Bacillus anthracis via mail delivered in the USA. Since the 1930s, biological weapons have been developed in a number of countries. In 1975, the Biological and Toxin Weapons Convention entered into force; this prohibits the use of these weapons and has been signed by a large majority of countries (144). Unfortunately, several countries failed to respect this treaty. The Soviet Union continued and expanded its biological weapons program, and after the Gulf War it was revealed that Iraq also had an extensive biological weapons program. Large-scale deliberate release of, Bacillus anthracis, for example, or an epidemic following a release of smallpox virus, would have a devastating effect. This has motivated the world community to strengthen the Biological and Toxin Weapons Convention with a control mechanism which has, as yet, not been successful. Sweden, like other countries, is enhancing its preparedness with regard to stocks of antibiotics and vaccines, related to these improving the diagnostics these and similar agents, and is setting up an epidemiologic task force that can be used in infectious disease emergencies such as the deliberate release of biological warfare agents. International cooperation in this area has to be enhanced, not least in the European Union.

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BIOLGICAL WARFARE

Biological weapons are microorganisms, in particular bacteria, virus and fungi, but also other organisms, that can be deliberately dispersed to incapacitate or cause disease and death to humans, animals or plants. Biological warfare agents can be natural or genetically modified. Genetic modification of microorganisms is common and is worrisome if the technique is misused, as the progress in cell and molecular biology technology has opened new and dangerous possibilities. Here, we define bioterrorism as either the threat of use or deliberate use of biological agents to cause harm or disease by criminals, including terrorists, individuals or groups with political, economic, religious, ecological or other ideological motivations.

Microorganisms, and also toxins, have been used for such purposes for a long time. This misuse has its background in the fact that many of these pathogens are inexpensive and relatively easy to produce if one has basic microbiological training. Only small quantities are required to cause large and terrifying effects. Another important factor is that the effects of these types of biological warfare agents are not immediate; as there is an incubation period, there will be a short or long time delay, which makes it simple to carry out a covert attack. There could also be dangerous secondary effects, due to the dramatic overburdening of the healthcare system, demands on other community services, and the risk of further epidemic spread of the disease.
The idea of using microorganisms as warfare agents has a very long history. An early example of this was the contamination of water wells with dead corpses of humans or animals to prevent the enemy from obtaining fresh drinking water. It is believed that the plague (the black death) in the Middle Ages started in Europe when that affliction spread among the Mongolian tartars besieging the Genoese city of Caffa on the Crimea in 1346. When the city could not be taken, the attackers catapulted corpses of their soldiers who had died of plague over the city walls. In this way, an epidemic was initiated which then spread via those with devastating effects those who fled by ship from the Crimea to the Mediterranean region and further up throughout Europe. Another important example is the fact that British military forces in eastern North America gave hostile Native Americans blankets previously used by people who had died of smallpox as presents, in order to spread the disease. This resulted in an epidemic among the Native Americans, who had no protection against the disease [1].

Microbiological science made big advances in the first half of the 20th century. In some circles, ideas were being developed concerning how these scientific developments could be used for military purposes. It was during the 1930s and 1940s that this resulted in the expansion and development of biological weapons programs. Such programs were initiated in Canada, France, the UK, Poland, the Soviet Union, the USA, and several other countries [1]. The Japanese also developed biological weapons during this period; they tested them on large numbers of prisoners of war, and used them against civilians in China. The Allies developed biological weapons because intelligence information had indicated that Germany and Japan already had such weapons. During World War II, the USA, the UK and Canada worked primarily with Bacillus anthracis as a biological warfare agent. The US program on offensive biological weapons continued until it was finally terminated during the Nixon administration in 1969, in order to make possible an international agreement to ban biological weapons. A treaty prohibiting the acquisition, development, storage and production of biological and toxin weapons was completed in 1972; however, all references to control procedures had been deleted from the text, as they were not be accepted by the Soviet Union. Most countries, numbering 144 at present, have signed and ratified the Biological and Toxin Weapons Convention (BTWC), which entered into force in 1975. Countries that have not yet done so include some in the Middle East. Many countries believed, when the Convention was signed, that biological weapons no longer constituted a problem, and several states drastically cut down on their biological defense research. In retrospect, it has been shown that the Soviet Union, in spite of its ratification of the Convention, initiated a dramatic expansion of its biological weapons program [1,2].

Biological weapons have not so far been used on a large scale during warfare between states. One reason for this is that the military authorities have no experience of their use, and have found it difficult to calculate the effects in advance of use. Furthermore, they have believed that reprisals from the enemy would be too severe. Today’s rogue states or terrorist organizations do not, perhaps, see the same limitations.

**BIOLOGICAL WARFARE AGENTS**

Many pathogens or toxins could be used for warfare or terrorism. Examples of pathogens are the smallpox, Venezuelan equine encephalitis, yellow fever, Ebola and Marburg viruses, and the bacteria *B. anthracis*, *Yersinia pestis*, and *Francisella tularensis*. Biological warfare agents would ideally be spread as an aerosol to maximize the effects. Other ways could be via food or water. Biological warfare agents could be spread using equipment for producing aerosols, such as spray devices, or via bombs or missiles. They could also be dispersed from aeroplanes, ships, or vehicles, or, as we have recently seen, via letters. In producing this type of agent, it is important that it is stable enough to survive environmental stress during dissemination. The particle size is also important, and should be 1–10 μm to allow good penetration into the lungs of humans [2].

In the Soviet Union, there were more than 60,000 people involved in research on, and development and production of, biological weapons in several organizations, including the Ministry of Defense, the Ministry of Agriculture, and the so-called Biopreparat [3]. Large amounts of microorganisms were tested and produced for use weapons, such as *B. anthracis*, *Y. pestis*, *F. tularensis*, and smallpox (variola), Venezuelan equine encephalitis and hemorrhagic fever viruses [4].
Especially worrisome is that large amounts of smallpox virus, many thousands of kilos, were produced for use weapons, use as because this virus and disease had been eradicated during the 1970s, and vaccinations are no longer done [5]. There is also an international agreement through the WHO that the remaining virus stocks should be stored in only two official laboratories, one in the USA and one in Russia. Discussions are in progress at the WHO, to the effect that the remaining stocks should be destroyed after a certain period, during which essential research could be performed under WHO control. Another problem is that there are suspicions that more countries or groups could still have small quantities of smallpox virus.

It is well known that Iraq, since the 1970s, has had a well developed biological weapons program, including bombs and SCUD missiles filled with anthrax bacteria, botulinum toxin and aflatoxin [6]. This was of major concern during and after the Gulf War. Following the war, the United Nations Special Commission (UNSCOM), under its chairman, the Swedish ambassador Rolf Ekéus, made great efforts worked hard to identify and destroy facilities used for producing biological weapons. Iraq refused further UN inspections in 1998 as a result of US and UK bombing of Baghdad. The new United Nations Commission (UNMOVIC), under its chairman Hans Blix, has so far been unable to resume inspections. Of the Iraqi biological weapons program consisted/consists. As far as is known, based on Iraqi declarations, of agents such as B. anthracis, botulinum toxin, ricin and aflatoxin. The extent of the program is still not today. There are indications that as many as ten countries, as well as Russia and Iraq, are trying to acquire or have a program for research and development of biological weapons.

The proliferation of knowledge or technology that can be misused to develop biological weapons is today a serious problem. Internationally, work is therefore in progress to strengthen the BTWC a control regime, and by including to strengthen the existing export control arrangement, according to the Australia Group, which excludes microorganisms or equipment that can be misused. It is important to limit the proliferation of knowledge from the former Soviet biological weapons program: Western economic support to Soviet scientists may prevent them from making their knowledge available to rogue states that are trying to acquire biological weapons. In Sweden, the questions connected with biological weapons have recently been highlighted in the latest Defense Bills and by the Parliamentary Defense Commission's reports.

BIOTERRORISM

The list of possible biological warfare agents that could be used by potential terrorists or disturbed individuals is long, and the threat of use is still very real and serious [3,7–13]. In 1984, a religious sect in Oregon in the western USA spread Salmonella typhimurium bacteria in a number of salad bars in order to cause disease; it is theorized that this was done so that members of the sect might win a local election. This deliberate release resulted in 751 cases of disease [13,14]. Another organization with religious/political motives, the Japanese Aum Shinrikyo, which dispersed the chemical nerve gas sarin in Tokyo's underground railway in 1995, causing 12 deaths and hundreds of injured individuals, also had a biological weapons program. Anthrax bacteria were spread from a building in Tokyo, but without success, as it was shown later that the bacterial strain used was not virulent [14]. The sect also tried to acquire of Ebola virus during the epidemic in Kikwit, Zaire in 1995, but this was not accomplished.

Since September and October 2001, when letters containing B. anthracis were sent within the USA, the situation has changed. In total, 22 persons have been diagnosed with B. anthracis infection, either cutaneous or pulmonary, So far, five of 11 patients with confirmed pulmonary anthrax infection have died [15]. Anthrax bacteria have been further spread via the postal distribution system in the Washington area, and this has resulted in contamination in a number of localities, for example, the US State Department, the Pentagon, and news media such as ABC, NBC and the New York Times. At the same time, a large number of letters, approximately 12,000, with suspected contents were discovered and had to be analyzed. Most of these contained some type of powder, but no anthrax. The situation in the Washington area became very difficult when large quantities of mail and a number of facilities had been contaminated. The same situation, with large numbers of suspect letters, has occurred in many countries, including Sweden, where more than 400 suspect letters have been identified and analyzed.
The recent events in the USA prove that there are people or organizations prepared to use virulent microorganisms to cause disease and death. Before these events, this was a possible scenario, but the situation is now an actuality [3]. Although the US anthrax incident has caused five deaths and accounts for a great economic loss, the direct effects are limited. This can be compared to the mass destruction that *B. anthracis* would cause if dispersed on a large scale as an aerosol in a city, in the ventilation system of a large building, or in a metro system. The casualties would then amount to thousands or even more. The hospital system would be overwhelmed, and large stocks of antibiotics would be necessary to limit the consequences. These consequences would be even worse if smallpox virus was used. It should be noted that the technical problems when producing smallpox virus are greater than those when producing bacteria such as *B. anthracis* or *Y. pestis*. On the other hand, very small quantities of smallpox virus could initiate an epidemic in today’s world, where the population at large is not vaccinated and limited amounts of vaccines are available [5].

**SWEDISH PREPAREDNESS**

Swedish preparedness is based on the same principals as those applicable when combating natural epidemics [3]. It is probable that the first signs of a bioterrorist attack will appear in the same way as when new or changed patterns of infectious disease are identified. General practitioners and/or infectious disease physicians in hospitals will probably be the first to notice a new pattern of disease. These doctors will have noticed unusual cases or an unusual number of cases with the same symptoms. They will notify the County Medical Officer in charge of infectious disease control, who will investigate these cases, not least by a detailed epidemiologic analysis. Meanwhile, this information will also be forwarded to the Swedish Institute of Infectious Disease Control. If the information gained does not fit the usual pattern, further investigations will be done by national and county authorities. Necessary countermeasures will primarily be the responsibility of the County Medical Officer, with assistance from the national authorities when necessary. Today, with these new threats, it is even more important for the emergency ward staff and general practitioners to quickly respond to unusual incidences or increased numbers of unusual cases and rapidly report them to the County Medical Officer, in order to enable a further investigation when needed.

The recent management in Sweden of a large number of suspect letters containing some kind of powder, suspected to be anthrax, has shown that Sweden has a fairly good capacity to handle this kind of biological threat. It has also been a good opportunity to evaluate our preparedness, both its strong and weak points. The new maximum containment laboratory at the Swedish Institute for Infectious Disease Control was used during this time, and proved to be an important resource. A review of the organization and capacity of the regional clinical laboratories in Sweden with respect to their preparedness for a larger bioterrorist incident is now needed.

In Sweden, every county (population approximately 400 000) has an infectious disease clinic with containment facilities. In order to treat patients with highly contagious serious infectious diseases, Sweden has a special containment unit at the university hospitals in Linköping and Stockholm. Sweden also has a special field epidemiologic group that can be called upon to investigate outbreaks of disease of different types, on both a national and an international level. In Sweden, the storage of antibiotics and vaccines has recently been reviewed and upgraded, and there is a well developed network linking all organizations involved in handling a biological threat.

The Swedish Defence Research Agency Division of NBC Defense analyzes the international developments and threats concerning biological weapons and bioterrorism. The research is, among other things, focused on the development of methods and technology for detection/identification of and protection against biological warfare agents. The Swedish Defence Research Agency cooperates with the Swedish Institute for Infectious Disease Control with regard to identification of specific biological warfare agents.

**INTERNATIONAL MEASURES**

In order to counter threats of biological warfare or bioterrorism, there is a need for more intensive international cooperation for threat assessment and planning, and also to enhance society’s awareness. It is also important to limit the proliferation of this type of knowledge to organizations/states.
that have an interest in acquiring an arsenal of biological warfare agents and weapons.

In this context, it is important to bear in mind the Soviet program for biological weapons, with about 10 000 highly qualified scientists. After the fall of the Soviet Union, the economic resources for this type of research in Russia were dramatically cut, leaving many scientists unable to support, and many have, in one way or another, found their way to countries outside Russia. There is a themselves, temptation for these scientists to immigrate to countries that want to acquire biological weapons. In order to meet this threat, several initiatives have been taken by the world community. An example of this the Department of Defense Cooperative Threat Reduction Program (DOD CTR) in the USA, as well as other US agencies. Economic support is also given through the International Science and Technology Center (ISTC) in Moscow and the Science and Technology Center Ukraine (STCU) in Kiev, which are financed by the USA, the European Union (EU), Japan, and others. In June 1999, the EU agreed on a common strategy for Russia, which includes measures to limit the proliferation of weapons of mass destruction and promote disarmament, support weapons control, implement international treaties, and support export controls. In Sweden, the Ministry for Foreign Affairs has supported research cooperation between the Swedish Defense Research Agency (FOI), the Swedish Institute for Disease Control (SMI) and the Scientific Research Institute Vector in Novosibirsk, Russia in the areas of biosafety and diagnostics.

Since the BTWC entered into force in 1975, work, not least by Sweden, has been carried out in order to strengthen the Convention with a control regime. In 1994, it was agreed to start negotiations on such a control system, and during the spring of 2001 the chairman presented a compromise final text which should be the basis for termination of the negotiations. This proposal consisted of, among other things, an obligation to submit annual declarations of specific biotechnology activities, and the carrying out of 50–100 random visits to such facilities in order to verify their declarations. Another possibility was to carry out challenge inspections in cases of suspicions of a breach of the Convention [16]. All states except the USA agreed to continue work on the chairman’s text. At the final session of the negotiations in July 2001, the USA would not agree on a final report of the negotiations to be forwarded to the 5th Review Conference of the BTWC, to be held in Geneva in November 2001. This meant that the negotiations collapsed. At the Review Conference, the USA stated that it could not continue work on a control regime based on the chairman’s text and that the approach of the negotiations since 1994 had been wrong. The USA presented new proposals, which gained limited support. There was no agreement at the conference after three weeks of negotiations, and the conference had to be postponed until November 2002. At present, it is not possible to say when or if agreement on a control mechanism for biological weapons will be possible. This is most unsatisfactory, as the threat from biological weapons is more real than ever, and the USA has been at the forefront in raising awareness of this threat.

Many countries have initiated plans for handling a bioterrorism attack. In the USA, more than 120 major cities now have special teams that, 24 h per day, can react to a suspected biological attack. Stores of antibiotics and vaccines have been built up, and recently the USA decided to acquire smallpox vaccine for its entire population. In a recent bill to Congress, three billion dollars were requested to improve preparedness against bioterrorism. In the EU, work has now been initiated, and discussions are underway concerning the need to better coordinate preparedness against bioterrorism [3]. At the EU Gent Summit of heads of state in October 2001, a program was proposed to improve preparedness against biological terrorism, which is now being developed, and includes initiatives on research and public-health measures.

**DISCUSSION**

Comparing Europe with other parts of the world, it can be argued that the Middle East or the USA are more likely to be targets for terrorism. Our preparedness in Sweden and the rest of Europe should be based on a realistic threat assessment that will result in balanced countermeasures. Strengthening the public-health and infectious disease infrastructure is probably one of the most effective steps towards averting the suffering that could be wrought by terrorist use of biological agents. International cooperation, not least in the EU, must be enhanced. Effective disease surveillance is an essential first step and is important in helping infectious disease control personnel and
law enforcement officials to react swiftly. In Europe, there is a need to improve the surveillance system as well as improve the central coordination [17]. Adequate epidemiologic and laboratory capacity nationwide are prerequisites for effective surveillance systems. Preparations must also include plans for the rapid identification and characterization of the agents involved. There is also a need to further improve the network of qualified laboratories on a European level, as no single laboratory or country can have specialists on all of the exotic diseases that can possibly be used as biological warfare agents. The presence of a number of maximum biosafety (P4) laboratories in different countries is important in the battle against bioterrorism, since rapid diagnosis/identification of all possible microorganisms is necessary. Examples of recently opened European facilities are the Laboratoire P4 Jean Meureix in Lyon, France, and the Containment laboratories at the Swedish Institute of Infectious Disease Control in Stockholm, Sweden. Bioterrorism poses a formidable new challenge to the clinical microbiology laboratory. Many of these do not possess the capacity or expertise to detect and accurately identify those biological agents classified as high priority, like those causing anthrax, tularemia, botulism, plague or smallpox [18]. Planning is also required for emergency distribution of medical supplies, especially antibiotics and vaccines. For example, in the case of smallpox, it is essential to rapidly identify those who might have been infected and to vaccinate them as well as all who might have come into contact with them. At present, the stocks of vaccine in many countries are very limited.

Coordination and communication also need to be strengthened, to minimize response times. If a bioterrorist event is suspected, established communication must be among hospital personnel, local and central healthcare departments, specialized laboratories, central and regional authorities for disease surveillance, and police and rescue services. A biological attack will also require of preservation evidence (at the scene of a crime), a unified command system, and the need to protect emergency responders against possible secondary devices intentionally placed to maim or injure them [19,20].

The management of the disease might not follow normal procedures, since diagnostic laboratory confirmation might take too long. Instead, it will be necessary to initiate a response based on the recognition of high-risk syndromes. Epidemiologic principles must be used to assess whether a patient’s presentation is typical of an endemic disease or is an unusual event that should raise concern [21]. There should also be specialist teams on standby that can rapidly analyze any potential threat and give recommendations to responsible authorities. After an incident, there might be a need for decontamination of the affected area, depending on the type of agent and the quantity released; this is also an area for international cooperation, as expertise is not always available in the country under attack. From a European perspective, it can be questioned whether each country can afford or be motivated to set up qualified rapid response teams that could, at short notice, be deployed to the scene of a bioterrorist attack. Perhaps this could be one area for cooperation between countries. What could be a realistic goal for such teams in a European context? In the area of research and development, to enhance our knowledge of agents of concern and to develop rapid methods for identification and detection of agents, international cooperation is vital, given today’s scarce economic resources. Another area for cooperation across borders is the training of personnel in handling situations involving the threat or use of biological warfare agents.

Legislation has a central role in countermeasures, such as national legislation in line with the BTWC. All countries that have not yet passed domestic legislation making the treaty prohibitions binding on their citizens and businesses should be strongly pressured to do so as soon as possible. It is also essential to break the recent deadlock in the negotiations to strengthen the BTWC with a control mechanism, and here the scientific community has a responsibility to put pressure on governments to create legislation concerning control and further proliferation as well as storage, handling, transfers of highly pathogenic microorganisms. There is a proposal to instate legislation that could impose liability on anyone who publishes recipes for producing chemical or biological agents [22]. There has also been a proposal to make the possession of biological weapons a crime under international law, which could facilitate the prosecution of those who possess biological warfare agents and the means to deliver them [23]. Steps could be taken in order to curb terrorism activities by agreeing to initiate negotia-
tions on a multilateral convention banning biological and chemical terrorism.

REFERENCES


