

Bioterrorism: an overview

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Introduction

Nuclear war was the main threat during the period of the Cold War, with exchange apparently imminent on several occasions. The reality of such a conflict played on the consciousness of many during the 1970s and '80s, and had an impact on art, literature and music. Although bioterrorism was also a threat, it failed to reach the forefront of the public's imagination.¹ The threat has always been real but the end of the Cold War relieved some of the tension associated with bioterrorism. Recent events, however, pose new threats and have increased tension.²

The use of biological agents almost became a reality during the Gulf War, as Iraq could not compete militarily with the forces range against it and dependence on biological or chemical agents seemed its only means of achieving success. Although not used against Western troops, the existence of biological weapons in the region has raised fears for potential future conflicts.¹

Increased tension in the region has raised the spectre of biological warfare again; however, the real threat lies with terrorist organisations that have links with countries that possess biological weapons.

The assault on American society on 11 September 2001 has raised the stakes and the response by Western countries, particularly the USA and UK, continues in an attempt to quash further threats.

Biological terrorism

All weapons, be they traditional, nuclear, biological or chemical, are evaluated on effectiveness, method of delivery, cost and availability. Biological weapons score highly on all these criteria, although it is extremely difficult to produce a perfect biological weapon. Even so, due to the lack of countermeasures, their effect is amplified compared to that of other weapons. Therefore, terrorists or developing nations can pose a real threat to those that are powerful in

ABSTRACT

Bioterrorism has reached the forefront of the public imagination following recent events across the world. The disaster of 11 September 2001, followed by anthrax letters sent via the US postal system and now renewed tension over Iraq have all brought the possibility of bioterrorism closer. A number of biological agents could be used in a terrorist attack, including anthrax, plague, smallpox and botulinum toxin. The serious diseases that these agents produce have been brought under control in the developed world; however, a lack of protective immunity against such diseases could cause considerable morbidity and mortality if used in a terrorist attack. This essay provides a background to bioterrorism, discusses many of the current points of interest and gives an update to the economic consequences of such an attack.

KEY WORDS: Anthrax. Biological warfare. Smallpox.

traditional methods of warfare.

There is a long history of chemical and biological warfare but it remained limited until the start of the 20th century and the growth in the chemical industry.³ During the 20th century, a bipolar (East versus West) power base predominated, which resulted in the two World Wars and the Cold War. With the new century has come a multipolar power base, with increased power in the Middle East and Far East. More countries now have a nuclear capability and the threat of terrorism has increased due to the power and finance behind terrorist organisations.

Sadly, one has learned to 'accept' terrorism in its basic form in the modern world, although such acts do not normally affect thousands or millions of people. Bioterrorism, however, is a real threat to modern society as the availability of certain bacteria or viruses to those who would wish to use them poses a real and ongoing threat to mankind.

Seven agents are thought most likely to be involved in a bioterrorist campaign (Table 1),^{4,5} of which four are bacteria (or their toxins) and two are viruses. Other bacteria and viruses could be used but the diseases produced are less pronounced and more easily treated, thus the agents are less suitable for use in bioterrorism.

Many of the diseases involved are very serious and, although under control in developed countries for many years, have left an imprint on the history of mankind. Smallpox is a good example. Most nations abandoned smallpox vaccination programmes before the final case of smallpox in 1980, and this has led to the development of immunologically naive populations worldwide.

Although a number of Western nations have stockpiled smallpox vaccines, it is unlikely that the public will receive

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Table 1. Potential agents of bioterrorism

Agent	Disease
<i>Bacillus anthracis</i>	Anthrax
<i>Francisella tularensis</i>	Tularaemia
<i>Yersinia pestis</i>	Plague
Variola virus	Smallpox
Haemorrhagic viruses	Viral haemorrhagic fever
Botulinum toxin	Botulism
<i>Brucella</i> spp.	Brucellosis
<i>Vibrio cholerae</i>	Cholera
<i>Burkholderia pseudomallei</i>	Glanders
<i>Coxiella burnetii</i>	Q fever

immunisation at present;^{6,7} a decision based mainly on the level of the perceived threat. Also, mass immunisation is not without its own problems, as it is estimated that up to 1000 deaths could occur as a result of vaccine-related complications – particularly among those with human immunodeficiency virus (HIV) infection – if smallpox immunisation were given to the whole US population.⁸ In the event of a smallpox outbreak, teams of first responders and medical personnel – a group that could total 20,000 individuals in the USA – would be vaccinated rapidly.⁹ Ring vaccination would then take place to keep the outbreak under control.

The long-term effects of bioterrorism are also important. If a bioterrorist act, however small, were to take place, there is the potential for long-term contamination issues. For example, anthrax spores can survive in the environment for many decades and it would be virtually impossible to decontaminate an area targeted in this way, making it inhospitable.

Economic effects of bioterrorism

Bioterrorism is often politically or religiously motivated and can have profound political, religious, economic and societal effects. Of course, it does not have to be directed against human beings to have an effect on world economies or human health. Although the most deadly and likely agents to be used in bioterrorism are anthrax, plague, smallpox and botulinum toxin, use of other biological agents could have major economic consequences.

The four most deadly agents require specialist knowledge and expertise for delivery as agents of war and do not, therefore, provide the most obvious channel for terrorists with limited resources. In addition, the aim of terrorists is to cause disruption rather than death. Although 1000s of deaths occurred on 11 September in the attack on, and subsequent collapse of, the World Trade Center, the 'cost' in economic terms is much greater. Economies have remained in a poor state for a number of reasons, one of which is the downturn in trading in areas that rely on international tourism and travel.

Animals or crops, which represent a high percentage of domestic product, can be targeted.¹⁰⁻¹² Outbreaks such as the

recent foot-and-mouth epidemic in the UK could be started as an act of bioterrorism, and cost billions of pounds in terms of animal loss, decreased revenues from tourism and large compensation costs.

War against bioterrorism

Over a number of decades, large amounts of money have been spent by Western nations on the development of biological weapons and, more recently, on the development of countermeasures. Since the terrorist attacks of 11 September and the subsequent deliberate release of anthrax via the US mail system (Figure 1), funding has increased considerably because bioterrorism has risen to the top of the political and scientific agenda.^{13,14} In the US, the National Institute of Allergy and Infectious Diseases (NIAID) has received a budget increase of \$1.5 billion for 2003, in addition to its existing \$270 million budget.

The overall US biodefence budget has been increased by over 300% for 2003, one of the aims being to establish up to 10 centres of excellence in US universities and institutes, leading to a boost in the research undertaken by microbiologists, cell biologists, virologists and biochemists. The work performed in these centres will not only cover agents of bioterrorism but also diagnostics, therapeutics and the development of vaccines. Bacterial genomic data will form integral components of this research.

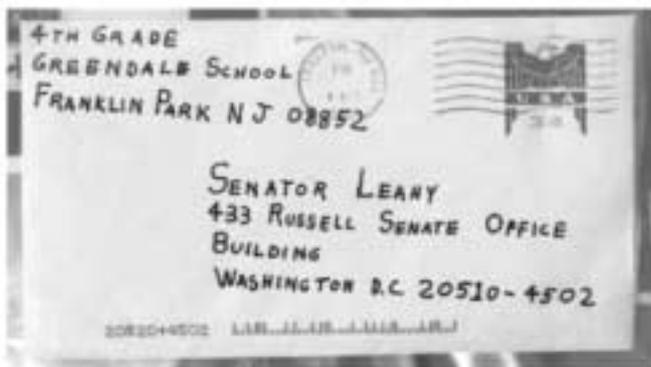
Already, there is ongoing discussion about the establishment of a European Centre for Infectious Diseases, which would coordinate and advise all activities relating to infectious disease throughout Europe. It would collect data, analyse trends and detect the spread of pathogens in Europe. Although not set up specifically to counter bioterrorism, it would certainly aid in the detection and handling of a bioterrorist attack. However, the Eurosurveillance Project (www.eurosurveillance.org) already exists and has demonstrated the importance and usefulness of a central European information source.

Should we go further? The UK government intends to reform all public health agencies to create the Health Protection Agency, which will combine some of the functions of the Public Health Laboratory Service with those of the National Radiological Protection Board, the Centre for Applied Microbiology and Research, and the National Focus for Chemical Incidents. Although not instigated in response to the threat of bioterrorism, it may help in such an event. However, further resources will be required in the UK and other countries to develop adequate detection and countermeasure programmes.

The clinical microbiologist

As in many other areas of public health microbiology, the clinical microbiologist often has only an indirect role in incident management. However, the clinical microbiologist has an essential part to play in detecting, identifying and characterising agents of bioterrorism.^{5,15} In the UK and other countries, specialised laboratories exist for handling Category 4 pathogens. Other agents of bioterrorism in lower pathogen categories can be handled in most public health and diagnostic laboratories.

Fig. 1. One of the anthrax letters received in the US in 2001



The network of laboratories, expertise and modern technologies enable bioterrorism agents to be identified in a minimum of time. Fingerprinting techniques, such as pulsed-field gel electrophoresis (PFGE), multilocus enzyme electrophoresis (MLEE) and multilocus sequence typing (MLST), enable high-level characterisation of bacteria, while polymerase chain reaction (PCR) and RNA sequencing enable the characterisation of viruses.^{16,17}

In summary

Biological warfare, and bioterrorism in particular, is the new superpower. Like the nuclear threat of the 1970s and '80s, bioterrorism is now a potential reality. Instability of the modern world in a more Westernised era has led to the increased potential for rebellion against Western ideas and globalisation. Political and religious agendas have changed, while some nations feel that they should not. In response to the threat of bioterrorism, the West has taken huge steps in an attempt to counteract such activities, believing it is important to crush terrorist organisations before they can reach the level of activity where bioterrorism is possible. Hopefully the events of last September and October in the US will not be repeated, but we should all remain vigilant. □

References

- 1 Kortepeter MG, Cieslak TJ, Eitzen EM. Bioterrorism. *J Environ Health* 2001; **63** (6): 21-4.
- 2 Hamburg MA. Bioterrorism: responding to an emerging threat. *Trends Biotechnol* 2002; **20**: 296-8.
- 3 Noah DL, Huebner KD, Darling RG, Waeckerle JF. The history and threat of biological warfare and terrorism. *Emerg Med Clin North Am* 2002; **20**: 255-71.
- 4 Leggiadro RJ. The threat of biological terrorism: a public health and infection control reality. *Infect Control Hosp Epidemiol* 2000; **21**: 53-6.
- 5 Klietmann WF, Ruoff KL. Bioterrorism: implications for the clinical microbiologist. *Clin Microbiol Rev* 2001; **14**: 364-81.
- 6 Meltzer MI, Damon I, LeDuc JW, Millar JD. Modeling potential responses to smallpox as a bioterrorist weapon. *Emerg Infect Dis* 2001; **7**: 959-69.
- 7 Koplan J. CDC's strategic plan for bioterrorism preparedness and response. *Public Health Rep* 2001; **116** (Suppl 2): 9-16.
- 8 Kemper AR, Davis MM, Freed GL. Expected adverse events in a mass smallpox vaccination campaign. *Eff Clin Pract* 2002; **5**: 84-90.
- 9 Osterholm MT. How to vaccinate 30,000 people in three days: realities of outbreak management. *Public Health Rep* 2001; **116** (Suppl 2): 74-8.
- 10 Owens SR. Waging war on the economy. The possible threat of a bioterrorist attack against agriculture. *EMBO Rep* 2002; **3**: 111-3.
- 11 Williams JL, Sheesley D. Response to bio-terrorism directed against animals. *Ann N Y Acad Sci* 2000; **916**: 117-20.
- 12 Wilson TM, Gregg DA, King DJ et al. Agroterrorism, biological crimes, and biowarfare targeting animal agriculture. The clinical, pathologic, diagnostic, and epidemiologic features of some important animal diseases. *Clin Lab Med* 2001; **21**: 549-91.
- 13 Malakoff D. US budget. Spending triples on terrorism R&D. *Science* 2002; **295** (5553): 254.
- 14 Malakoff D. U.S. budget. Biomedicine gets record raise as Congress sets 2002 spending. *Science* 2002; **295** (5552): 24-5.
- 15 Robinson-Dunn B. The microbiology laboratory's role in response to bioterrorism. *Arch Pathol Lab Med* 2002; **126**: 291-4.
- 16 Olive DM, Bean P. Principles and applications of methods for DNA-based typing of microbial organisms. *J Clin Microbiol* 1999; **37**: 1661-9.
- 17 Clarke SC. Nucleotide sequence-based typing of bacteria and the impact of automation. *Bioessays* 2002; **24**: 858-62.