**Bioterrorism: what is the threat?**

**Introduction**

The usefulness of an agent for bioterrorism depends on a number of factors including the mode of transmission, the infectivity of the agent, its stability and the environmental conditions. If the agent is readily transmissible as an aerosol, then its potential as a bioterrorist agent is greatly enhanced. However, the infectivity of different agents can vary from as low as 0.2 virus infectious units for measles, to 10 for Q fever and tularemia, 180 for *Shigella flexneri*, at least 1300 for anthrax, 10 for typhoid, 10 for cholera and 10 for shigellosis.

If the agent is stable, such as *Bacillus anthracis* spores, it can survive in the environment for long periods, sometimes exceeding 100 years. However, if it is of relatively low stability, it might not survive for an hour. The environmental conditions greatly affect the survival and ability of agents to be transmitted. For example, the dark and cold conditions in the United Kingdom in 1967-68 facilitated extensive wind-borne spread of foot-and-mouth disease virus. In contrast, in the tropics, where there is bright sunlight and moderately high temperatures, the virus is transmitted mainly by contact and can be readily controlled by restricting animal movements.

**Transmission**

**Aerosols**

The most common route of transmission of microorganisms is in aerosols. Organisms do not travel as single organisms but in water droplets or particles containing many organisms; the size of these droplets or particles determines their ultimate fate. The larger the particle, the less likely it is to cause infection, with the majority of particles falling to the ground or being retained on surfaces. For the particles to reach the alveoli and initiate infection, it is necessary for the size range to be from 1-5μm with an optimal size of 3μm. If the agent is released into the environment, air movements can considerably affect transmission, with strong winds rapidly dispersing and diluting the agent, resulting in little infection. Relatively still conditions, or those that allow agents to move in a single concentrated plume, result in high levels of transmission.

**Ingestion (food and water)**

There is considerable concern that organisms and toxins could enter the food-supply chain. The Center for Disease Control and Prevention (CDC) in Atlanta considers food- and water-borne threats as being of particular concern since many of these agents are readily obtainable and relatively easy for potential terrorists to administer without detection – these are listed as Category B agents in Table 1. The results can range from severe diarrhoea to death.

For this reason, there are extensive guidelines to protect foods against attack and in Australia there are plans to protect the water supply systems. However, it is possible for these systems to be breached.

---

**Table 1. CDC list of critical agents**

<table>
<thead>
<tr>
<th>Agent category</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td></td>
</tr>
<tr>
<td>Variola major (smallpox)</td>
<td></td>
</tr>
<tr>
<td><em>Bacillus anthracis</em> (anthrax)</td>
<td></td>
</tr>
<tr>
<td><em>Yersinia pestis</em> (plague)</td>
<td></td>
</tr>
<tr>
<td><em>Clostridium botulinum</em> toxin (botulism)</td>
<td></td>
</tr>
<tr>
<td><em>Francisella tularensis</em> (tularemia)</td>
<td></td>
</tr>
<tr>
<td>Haemorrhagic fevers (Ebola, Marburg, Lassa viruses etc)</td>
<td></td>
</tr>
</tbody>
</table>

| **B** |
| *Coxiella burnetii* (Q fever) |
| *Brucella species* (brucellosis) |
| *Burkholderia mallei* (glanders) |
| Alphaviruses (Venezuelan encephalitis, eastern and western encephalomyelitis) |
| Ricin toxin from *Ricinus communis* (castor beans) |
| Epsilon toxin of *Clostridium perfringens* |
| *Staphylococcus* enterotoxin B |

| **B: Food- or water-borne** |
| *Salmonella species* |
| *Shigella species* |
| *Escherichia coli* O157:H7 |
| *Vibrio cholerae* |
| Cryptosporidium *parvum* |

| **C** |
| Nipah virus |
| Hantaviruses |
| Tick-borne haemorrhagic fever viruses |
| Tick-borne encephalitis viruses |
| Yellow fever virus |
| Multidrug-resistant *Mycobacterium tuberculosis* |
and unexpected outbreaks of food poisoning and gastroenteritis need to be investigated and monitored.

In Focus

Inoculation

Inoculation is a very effective means of infecting a person but, because of the high probability of detection and the limited scope for spread of the infection, it is unlikely to be utilised, except for very specific purposes. A well-known example where it was used was for the assassination of the Bulgarian defector, Georgi Markov, in September 1978.

Other means of transmission

The use of insects, fleas and ticks to transmit infectious agents, particularly plague and some of the plant and animal pathogens is an area of concern. The Japanese used plague-infected fleas to spread the disease in China and Manchuria during the second World War. The USA carried out research at Fort Detrick into the production of mosquitoes infected with yellow fever virus.

Organisms: risk classifications

There is a wide range of agents that could be considered to have potential for use by bioterrorists. Table 1 shows a listing prepared by CDC, in which the agents in Category A would be restricted and the others less so. The exceptions would be those in biosafety level 4, some of the high risk level 3 and exotic animal or plant pathogens.

CDC maintains the USA Select Agent List of human agents and the US Department of Agriculture maintains a list of animal and plant pathogens. The Australia Group also maintains a list that contains many more agents and toxins. It is of great concern how these lists are maintained and also how authorities use them to regulate the use and research on microorganisms. It affects how these organisms are transported, what is published on them and the level of physical security required for holding them.

High priority

The CDC Category A agents (Table 1) include organisms that pose a risk to national security because they can be easily disseminated or transmitted person-to-person; cause high mortality; with potential for major public health impact; might cause public panic and social disruption; and require special action for public health preparedness.

Anthrax

*Bacillus anthracis* has been used a number of times as a bioterrorist agent. Its use in World War I on cattle and the accident at the USSR anthrax plant at Sverdlovsk were evidence of the potential of anthrax. Bacillus anthracis is easy to grow and to produce spores. The final phase of drying the organism and producing a fine powder with a particle size around 3 µm is more difficult and hazardous, but can be achieved without great complexity. The Aum Shinrikyo attempted unsuccessfully to use anthrax as a biological weapon in Tokyo.

Anthrax is a common disease of grazing animals. In Australia, the stock route of the late 1800s from Southern Queensland to Northern Victoria has been a source of anthrax spores with regularly scattered outbreaks. The last large outbreak occurred in the Stanhope and Tatura area of central northern Victoria in January 1997. Over 100 cattle died and there was one human infection, a cutaneous anthrax infection that was readily treatable with antibiotics.

Chest X-ray of pulmonary anthrax.

Smallpox

Smallpox was used as a biological weapon against the native populations in the Americas. The studies at Vector that the USSR carried out on the development of an aerosol smallpox weapon have already been mentioned. As vaccination ceased when the virus was declared eradicated in 1980, most of the world’s population is susceptible to smallpox. At present there are no effective anti-viral agents and protection will rely on movement controls and vaccination.

Tularemia

Francisella tularensis, the cause of tularemia, is one of the most infectious bacteria, requiring as few as 10 organisms to initiate an infection in humans. The disease is found in much of North America, Europe and Asia. It is usually found in rural environments and is a natural disease of voles, mice, water rats, rabbits and hares. The disease is transmitted by biting insects such as ticks, mosquitoes and flies, or by exposure to a contaminated environment.

Japan researched the use of *F. tularensis* during World War II and may have used it in China. Both the USA and USSR developed aerosolised tularemia weapons and Alibek claimed that the USSR engineered strains of *F. tularensis* with antibiotic resistance. It is obviously an agent with a high potential for use as an aerosol or water delivered weapon.

Plague

It was reported that the Japanese dropped *Yersinia pestis* (plague) infected fleas in China during World War II and that this caused outbreaks of plague. The problem of using fleas as a vector for transmission of plague was overcome by both the USA and USSR who developed techniques for transmitting it as an aerosol.

Plague is transmitted by fleas living on rats and other small animals. Human plague usually occurs when infected fleas bite people, causing bubonic plague. A small number of people with bubonic or septicaemic plague can go on to develop...
pneumonic plague. The bacteria are then spread in aerosolised droplets to cause primary pneumonic plague in contacts. The disease occurs worldwide in all continents except Australia and Antarctica. Enzootic foci are not only associated with rats but also with ground squirrels, prairie dogs and other rodents.\textsuperscript{4, 5}

**Clostridium botulinum toxin**

*Clostridium botulinum* toxin is the most deadly substance known. A single gram of crystalline toxin could kill 1 million people – obviously delivery of this would be difficult. Terrorists have already tried to use the toxin, such as the abortive attempts by the Aum Shinrikyo in spraying it at a number of sites in Japan.\textsuperscript{6} After the Gulf War of 1991, Iraq admitted to United Nations inspectors that it had produced 19,000 litres of concentrated toxin, of which 10,000 litres was loaded into warheads.\textsuperscript{7, 8, 9}

**Medium priority**

The CDC Category B agents (Table 1) include those that are moderately easy to disseminate; cause moderate morbidity and low mortality; and require specific enhancement of diagnostic capacity and disease surveillance.\textsuperscript{1}

One of the highest concerns is the use of agents to contaminate the food and water supplies.\textsuperscript{5, 6, 7} A real-time monitoring system, such as QZFoodNet and the National Enteric Pathogen Surveillance System, need to be enhanced and funded in order to ensure that there is a robust surveillance system that can recognise outbreaks and patterns of enteric disease in a timely manner.

A range of other viruses have been developed into biological weapons and they could pose a significant threat.\textsuperscript{2, 10, 11} These include Eastern, Western and Venezuelan equine encephalitis viruses, yellow fever virus (together with the mosquito vector) and Marburg virus. There have also been studies on Lassa and Ebola viruses. Peters\textsuperscript{12} adds a range of other South American Arenaviruses, the Phlebovirus Rift Valley fever, the Nairovirus Crimean Congo haemorrhagic fever, Hantaviruses and the tick-borne Flaviruses to the list of primary agents of concern. He also lists a number of other viruses of concern: smallpox, monkeypox, viral encephalitides, ‘eradicated’ poliovirus, influenza A 1918 strain and influenza A Hong Kong H5N1 strain.

**Brucella suis** was one of the first biological agents weaponised by the USA.\textsuperscript{1} *Brucella* sp. are very effectively transmitted to humans by aerosol. There have been over 1300 reported laboratory infections with *Brucella* sp.\textsuperscript{1} Similarly, the agents of Q fever (*Coxiella burnetii*), typhus (*Rickettsia prowazekii*) and psittacosis (*Chlamydia psittaci*) are readily transmitted by aerosol. *Burkholderia mallei* (glanders) was effectively utilised as a biological warfare agent during World War I and there are records of laboratory infections, both aerosol and mucocutaneous.\textsuperscript{1}

**Agricultural bioterrorism**

In many cases the most disruptive form of bioterrorism is against the agricultural system in the country. It can totally disrupt the economy of a country, such as occurred with the outbreak of foot-and-mouth disease in the United Kingdom in 2001, that was estimated to have cost in excess of $8 billion. It not only disrupted the livestock industry, but tourism and local town communities and businesses.\textsuperscript{10}

In 2002 the Productivity Commission estimated that an outbreak of foot-and-mouth disease in Australia would result in cumulative losses in export earnings and decline in revenue from domestic sales that would be between $2 billion and $3 billion in Gross Domestic Product for a short outbreak, rising to between $8 billion and $13 billion for a 12 month outbreak.\textsuperscript{11}

Bioterrorism against animals and plants is a major threat to the Australian economy and could be readily carried out by terrorists with a low risk of detection. As a result there is a need to carry out simulations, such as the 2002 Operation Minotaur that tested Australia’s foot-and-mouth disease preparedness and to ensure that the States and Commonwealth are well prepared to recognise and handle any disease incursions.

### Challenges in the response to incidents

#### Recognition of incident

The first people to become aware of someone with exposure to a biological agent might be the local general practitioner or staff at the local hospital, and they may well treat the initial non-specific clinical signs as a cold or the flu. There is a need to ensure that there is sufficient reporting of clinical syndromes in order to recognise any emerging pattern.

#### Identification of organisms

Samples from the emergency response team or diagnostic specimens from the medical system are sent to the diagnostic laboratory. When there has been an overt incident, such as a ‘white powder’ incident, then the sample will be processed in a PHELN laboratory, usually at physical containment level 3 (PC3). For the preliminary assessment of the specimen a wet preparation is usually examined under phase contrast and an assessment made of whether spores are present (about 100 are needed). This is usually accomplished in the first hour. Growth and full characterisation of isolates takes 18-48 hours.
A set of diagnostic case definitions has been developed by the PHLN for the CDC Category A agents and many of the Category B agents. Polymerase chain reaction (PCR) amplification of selected genes plays a critical role in definitive identification of agents.

It would be useful to have a test that can be performed at the site and give an almost instantaneous and specific result. Immunodiagnostic slides exist for a range of agents and portable PCR machines can be taken to the site. However, there were significant problems with the specificity and sensitivity of such tests in the USA and in Australia it was recommended that such devices not be used. There is a continuing need to develop more rapid and sensitive tests with a high level of specificity. Hopefully studies in the CRCs for Diagnostic Technology and Australian Biosecurity will help this international effort.

Access to the appropriate reagents and protocols has been an issue, particularly as it is becoming increasingly difficult to access listed organisms and reagents. The Commonwealth Department of Health and Aged Services has negotiated with CDC for some of the PHLN laboratories to become members of the Laboratory Response Network in the USA. Membership has been agreed, but access to reagents still remains an issue as the USA continues to tighten access controls for listed agents.

**Decontamination and disinfection**

Decontamination of a large area affected with a biological agent poses many problems. This was well demonstrated in the attempts to decontaminate the Hart Senate Building in Washington using chlorine dioxide. It was also evident in the decontamination of the Brentwood Mail Exchange in Washington and the newspaper office in Florida (see US Postal Service website). There are no really safe and effective ways of decontaminating large building spaces, and the use of formaldehyde and chlorine dioxide poses many significant safety and environment issues. It is an area that needs major attention.

In any contaminated area it is important to shut down the air handling system as soon as possible and not to enter the space until a time has elapsed that allows particles to settle. Appropriate personal protective equipment (PPE) should be worn, which is usually a coverall (such as Tyvek), gloves, a respirator with P3 filter (or a combined filter if chemicals are present), and protective footwear. Liquid disinfectants capable of inactivating spores include bleaching and oxidising agents such as sodium and calcium hypochlorite, chlorine dioxide, peroxides and phenol based agents. If there is extensive contamination of the space and air handling systems, then fumigation needs to be considered.

Most microorganisms can be readily inactivated by sodium hypochlorite solution. This is used at various concentrations depending on the nature of the biological material and the area to be decontaminated. The use of chlorine bleach is one of the most effective means of inactivation, provided that the surface is readily accessible, there are not high concentrations of organic materials present (which absorb and neutralise the hypochlorite) and there is no equipment and plant that contains metals that could be corroded by the chlorine. Also certain materials are affected by hypochlorite such as some PPE, so care in the selection of appropriate PPE needs to be taken.

Large-scale fumigation of a room, building or other facility represents many major problems. If the fumigant, usually formaldehyde, is capable of inactivating spores, then it is likely to be extremely hazardous and toxic. Formaldehyde vapour, usually generated from paraformaldehyde crystals by heating, is one of the most effective inactivants. Before decontamination, the surfaces are cleaned down with water and detergent to remove any organic material. Carpets and porous material may need to be destroyed.

Formaldehyde has become less popular for fumigation in recent years as its been classified as an IARC Group 2A carcinogen and there are strict environmental regulations on its use. It is critical to seal the area being fumigated and to either neutralise the formaldehyde after a suitable retention period or chemically scrub the air outlet to remove any formaldehyde. Humidity and temperature conditions need to be accurately controlled, and spore strips used to verify the effectiveness of the fumigation.

Following the October 2001 anthrax incidents in the USA, chlorine dioxide was used to decontaminate the facilities. Again there are environmental restrictions on the use of chlorine dioxide; it is very hazardous and conditions need to be well controlled. However, it is not a carcinogen and there are not the problems of off-gassing experienced with formaldehyde.

**Handling the information**

**Internal data communication**

Communications between all the agencies involved in a bioterrorist response is crucial to a successful outcome. At present there are many barriers to good sharing of information between the relevant authorities. In particular, incompatible laboratory information systems, an unwillingness to release data
from the States to the wider Australian authorities in a timely manner, differences in data collected by different States, particularly regarding notifiable diseases, and a range of other issues make timely information dissemination difficult.

Standardisation of laboratory information systems, reporting formats and sharing information is at present being worked on by veterinary authorities, but we are yet to see significant progress in the medical area. In addition, the field data collection is disjointed and does not link directly into the laboratory systems or into the control systems. There is considerable productive work that could be done in this high priority area.

**External communication**

Handling the press and the community is important in order to give reassurance and to prevent panic. In the USA following the October 2001 white powder incidents, there was an excess and unwarranted demand for Ciprofloxacin, despite the fact that all the USA cases were treatable with penicillin 25. In Australia, during the first three weeks of October 2001, it was observed that peaks in the ‘white powder’ incidents followed extensive press coverage of anthrax or white powder incidents, particularly on television. Because of actions by health authorities there was no shortage of Ciprofloxacin in Australia (see Australia’s biosecurity health response website).

The handling of liaison and information provision to the press needs to ensure that they are fully aware of the situation and that they have adequate information to present a balanced story.

**Conclusions**

Except for large international events, such as the Olympics and Commonwealth Games, Australia is unlikely to be the target of a major bioterrorist attack. However, targeted attacks on key individuals and institutions are probable. The October 2001 ‘white powder’ incidents could prove to be a reality in the future and we need to guard against their eventuality.

In the case of major events, which have an international audience, such as the Olympics, CHOGM or similar events, these could well prove to be the target of international terrorists and they may well choose to utilise aerosolised agents or contaminate food or water supplies. The main aim is to create terror and uncertainty; today’s terrorist does not care about human life.

Whether Australia is fully prepared to meet such incidents is of great concern, as the resources necessary to respond at the local level do not seem to have flowed from Canberra. Certainly reviews of research and development needs such as those published in the USA by the Institute of Medicine might help in ensuring that limited funds are directed to those areas of highest priority 26.

**References**