A Centre for Infectious Diseases and Microbiology - Public Health (CIDM-PH), and Sydney Emerging Infections and Biosecurity Institute (SEIB) publication

October 2011
Issue 25

The Broad Street Pump

Are we ready for the next biothreat?

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In August this year, CIDM-Public Health and the Sydney Institute for Emerging Infections and Biosecurity (SEIB) held a joint symposium and workshop on biosecurity. Its aim was to draw attention to the continuing threat of an unexpected, potentially devastating disease outbreak and to canvas ways in which health professionals and the community can prepare for such an event, despite its inherent unpredictability. The program and links to most of the presentations are available on the CIDM-Public Health website[1.]

Deliberate bioterrorism attacks or threats (often unsuccessful) have occurred throughout history. After the seige of Caffa (a trading post on the Black Sea), in 1346, the retreating Mongol army catapulted the bodies of their fellows, who had died from plague, over the city walls (Figure 1). As the Mongols intended, an outbreak of disease ensued and the Christian traders, who had been trapped for 3 years, fled to Italy, carrying infection with them[2]. It has been claimed, probably erroneously, that this was the origin of the devastating European plague, or Black Death (which, it now seems, may not have actually been caused by what we now recognise as the cause of plague, *Yersinia pestis*[3]). *Continued next page.....*

Inside this issue

** The articles in this issue are summaries of presentations at the recent CIDM-PH & SEIB 'Are we ready for the next bio-threat, natural, accidental or deliberate?" Symposium. Presentations can be found on the CIDM-PH website at www.cidmpublichealth.org*

News & Events

- SEIB 2011
  23-24 November 2011
- CIDM-PH Colloquium
  Date TBA
- Calls for Expression of Interest 'Workshop on Microbial Whole

Are we ready for the next biothreat?

Figure 1. Medieval trebuchets could sling about two projectiles per hour at enemy positions.
http://en.wikipedia.org/wiki/File:Trebuchet.jpg

It has been claimed that outbreaks of smallpox among Native Americans, in the 18th century, were caused by European settlers' giving them blankets, which had been deliberately contaminated, as an act of "goodwill". However, historians believe it more likely that disease was spread by Native Americans, themselves, infected by direct contact with Europeans.

There are many examples of attempted or actual biowarfare during the 20th century. The most egregious was in China, during the 1930s and 40s, when the infamous Japanese Unit 731 deliberately infected tens of thousands of prisoners and Chinese civilians with plague, typhoid and cholera (see Christian Enemark's article below). Thousands died from these diseases or were subsequently killed. More recently, the Aum Shinrikyo sect, unsuccessfully attempted to spread anthrax by aerosolising a liquid suspension of *Bacillus anthracis* from the roof of an eight-story building in Kameido, Japan. No-one was affected and subsequent investigations showed that: "The use of an attenuated *B. anthracis* strain, low spore concentrations, ineffective dispersal, a clogged spray device, and inactivation of the spores by sunlight are all likely contributing factors to the lack of human cases."[4]

The most recent deliberate act of bioterrorism that captured the world's attention was the "anthrax letters" incident in the weeks following 9/11, in the USA. Letters containing anthrax spores were sent to five media organisations in New York and, three weeks later, to two US Democrat Senators. As a result, 22 people were infected and five died from inhalational anthrax – a surprisingly small toll considering the widespread distribution of the spores[5]. Not unexpectedly, the repercussions were much greater than the direct effects. Hundreds of people were given prophylactic antibiotics, several mail exchanges and other government buildings were closed for months for decontamination (at an estimated cost of US$1 billion) and a massive FBI investigation, code-named Amerithrax, was initiated.

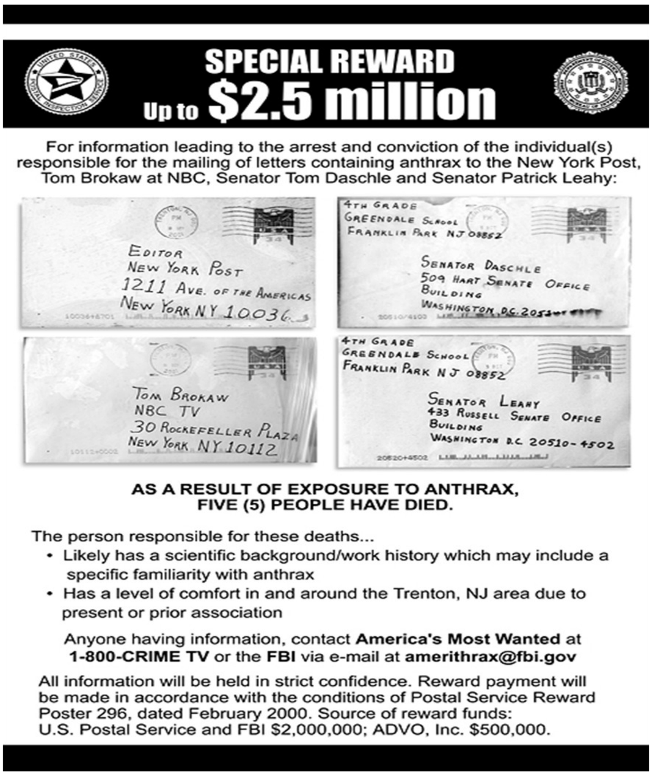

Figure 2. A reward for information totalling $2.5 million was being offered by the FBI and US Postal Service.
http://en.wikipedia.org/wiki/File:Anthraxreward.jpg

Are we ready for the next biothreat?

After seven years of investigation, the FBI announced, in August 2008, that they were about to bring charges against a former researcher from the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID), Fort Detrick, Maryland, which had already been identified as the origin of the spores. The suspect committed suicide before he could be brought to court, and the identity and motives of the perpetrator remain controversial. "Over the course of the investigation, the FBI and the Postal Inspection Service devoted 600,000 investigator work hours to the case……… The investigation spanned six continents; involved over 10,000 witness interviews, 80 searches, 26,000 e-mail reviews, and analyses of 4 million megabytes of computer memory … 29 government, university, and commercial laboratories assisted in … scientific analyses" [5].

Immediately after the incidents, laboratories around the world were inundated with thousands of suspicious "white powders" from letters sent by hoaxers or from objects submitted to police by anxious, well-meaning citizens (see Bates[1]). Australian public health laboratories, including CIDM, were not prepared for this, despite some early practice in screening for bioterrorism agents, during the 2000 Sydney Olympics. However, the Public Health Laboratory Network rapidly developed protocols for processing, handling and testing specimens and laboratory methods to identify anthrax spores. Nevertheless, it was obvious that laboratory facilities and staffing would be ill-equipped to cope with a major infectious diseases outbreak or a real bioattack and that major improvements were needed.

Australia's capacity to respond to deliberate, accidental or natural biothreats is now much better. All states have access to high security laboratory facilities with appropriately trained staff – including the PC3/4 "state-of-the-art" facility at CIDM. There are now laboratory biosafety and biosecurity standards, designed to protect laboratory workers and the public from potentially dangerous pathogens which, without these precautions, could be acquired by a potential terrorist.

Australia's list of security sensitive biological agents (SSBA) was determined on the basis of previous use as bioterrorism agents and the potential to cause mass casualties and/or economic effects. Laboratory handling of SSBAs is governed by the National Health Security Act (2007) and Regulations (2008) and the SSBA standard (2011). These regulations can impact on routine diagnostic microbiology laboratories, as some SSBAs are naturally-occurring pathogens. Disposal of them, after isolation from a clinical specimen, requires special precautions, which are quite cumbersome. However, there is now an appropriate administrative infrastructure, facilities and expertise for safe handling and definitive identification of these potentially lethal agents, in properly staffed and equipped laboratories (see James[1]).

Biothreats to food-producing animals and crops have the potential to threaten food security, worldwide. These threats have been the focus of the Office International des Epizooties (OIE), since it was established in the 1920s. Animal pathogens that have the potential to cause serious socio-economic or public health consequences or to impact on international trade of animals and animal products are included in the list of SSBAs (Ward[1]). Most emerging infectious diseases have their origins in animals, particularly wild animals such as bats or wild birds, and can spread to humans by direct contact, via arthropod vectors or via food-producing (chickens, pigs) or companion/sporting (e.g. horses) animals. This has been the basis for the worldwide "One Health" movement and an important motivating factor in the establishment of SEIB.

Other topics presented at the symposium included several emerging (or potentially emerging) zoonoses, including Hendra virus infection (see article by Gary Muscatello, below and Playford[1]), tularaemia (from a possum bite in Tasmania; McGregor & Brown[1]) and monkey pox (the subject of a "hypothetical" which challenged a panel of experts to propose plans for investigation and management of a mysterious illness with vesicular rash that had potential links to bioterrorism and international crime; see Bagg & Pinto[1]).

References

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3.Duncan CJ, Scott S. What caused the Black Death. Postgrad Med J 2005; 81:315-20

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6.http://www.fbi.gov/about-us/history/famous-cases/anthrax-amerithrax.

Hendra virus outbreak of 2011

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Bats are reservoir hosts of some of the most significant recently emerging viral zoonoses (Calisher et al. 2006). In Australia, Pteropidus bats, commonly referred to as flying foxes or fruit bats, carry three noteworthy zoonotic viruses, the Australian Bat Lyssavirus (ABL), and two viruses within the *Paramyxoviridae*, Menangle virus and Hendra virus. Death from direct transmission to man from bat, in the case of ABL, or to man through an animal amplifier, in the case of Hendra virus has been observed.

Hendra virus is found in four species of fruit bat that range across the northern and eastern coast of Australia (spectacled fruit bat, black fruit bat, little red fruit bat and the grey-headed fruit bat). The horse is susceptible to Hendra virus and acts as an amplifier facilitating transmission to man. Transmission from bats to horse is through the ingestion of infectious biological fluids, such as placental tissue, urine, faeces and saliva, deposited under trees which bats roost. Regurgitated bat digest or 'spats' are highly palatable to the horse and are likely a significant infectious source. The incubation period in the horse ranges from 5 to 16 days. The horse presents with various clinical signs that may resemble colic in the early stages but rapidly progress into severe neurological and/or respiratory symptoms. Death is common within 48 hours of the first signs of illness. The horse begins to shed small quantities of the virus ~48 hours prior to clinical signs peaking as the horse become maximally ill, around the time of death. This reflects the elevated infectious risk ill horses represent to other animal and man. The virus can be detected in a range of equine secretions, including blood, urine, nasal and faeces. The virus is inherently fragile and is not highly contagious, transmission between horses and from horse to man requires intimate contact with secretions.

The loss of natural habit has resulted in bats finding alternative food sources. The recognition of abundant urban flowering resources has resulted in a growing urban fruit bat population encroaching upon man and horse. Consequently the likelihood of bat-horse interactions and viral spill-over events increases especially during winter, when shedding from late pregnant bats or bats giving birth peak (Plowright et al. 2011). Hendra incidents correlate with observations of bats roosting in flowering fruit trees such as Moreton bay figs, on incident properties or within the range of observed urban bat colonies. Exactly how bat colonies become infected is unclear. The little red fruit bat may play a key role in this due to its inability to mount lasting immunity to the virus. It is worth noting that a mixture of the 4 bat carriers is seen in SE Queensland and Northern NSW where Hendra predominantly occurs. Bat population dynamics may influence the likelihood of introducing Hendra and spill-over.

From 1994 – 2010, 14 incidents (a property with at least one case) of Hendra virus were seen, between June and January in coastal parts of Queensland and Northern NSW. These incidents resulted in 46 horses dying and 7 human cases diagnosed with 4 deaths. In 2011, bat surveillance showed elevated Hendra viral load in secretions and incidence of infection during the summer and autumn months. Consequently 18 Hendra virus incidents were observed between June and September, 11 in Queensland and 7 in Northern NSW with a total of 21 horses dying from the virus. The first incidence of Hendra in an inland Queensland town, Chinchilla, was observed this year and the southern most incident of Hendra in Macksville, NSW was recorded. The first document natural infection of Hendra in a dog was also observed this season. Despite observing the worst every year for Hendra virus in Australia's history we failed to observed any human cases. This remarkable observation highlights the increased awareness of the virus amongst the equine community, specifically veterinarians and horse owners and improved biosecurity measures at the human-horse interface.

A Hendra virus vaccine for use in horses is currently in the final phase of field trialling. This sub-unit recombinant vaccine contains soluble Hendra virus glycoprotein G. The vaccine appears to be able to protect horses experimentally infected with a lethal dose and importantly prevents viral replication and shedding. The ability for this vaccine to be made available and administered widely throughout equine populations in this country will probably be the key factor in effectively preventing a similar Hendra outbreak in years to come. The vaccine is likely to be released in 2012/13.

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I'm a veterinarian with an interest in microbiology. I completed my PhD at The University of Melbourne in 2005 investigating the ecology and epidemiology of *Rhodococcus equi* pneumonia in foals and am recognised as an international leader in *R. equi* research, spanning aspects of disease control and management, diagnostics and molecular and general epidemiology. I currently lecture in Applied Animal Microbiology at the Veterinary Faculty of the University of Sydney and am involved in a variety of research activities in food safety, the equine infectious disease field and the Thoroughbred industry. I also have an interest in climate change research; specifically the impact climate change will have on the prevalence and severity of infectious diseases in production animals and the emergence of novel zoonotic pathogens. I'm currently the animal production, biosecurity and health theme leader within the Primary Industry Adaptation Research Network (PIARN) a branch of the National Climate Change Adaptation Research Facility (NCCARF). Given my passion for horses and emerging infectious diseases impacting horses and man I've naturally been involved and actively consulted during this year's arbovirus and Hendra outbreaks. I hope to be able to provide a valuable veterinary microbiological insight into the various topics, discussions and forums provided by CIDM-PH/SEIB.

Biosecurity Policy and Ethics:

Australia and the Biological Weapons Convention

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In December this year the Australian Government will send a delegation to Geneva, Switzerland, for the Seventh Review Conference of the 1972 Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction (more commonly known as the Biological Weapons Convention or BWC).

From the early 1930s and throughout the Second World War, the Imperial Japanese Army deployed a large-scale biological weapons (BW) program against China. In the immediate aftermath of that conflict, it might have been considered patriotic for an Australian microbiologist to advocate an Australian BW program, but ethical standards have since shifted radically. When the United States under President Richard Nixon renounced its offensive BW program in 1969, it was the first time a major power had unilaterally eschewed an entire weapon category. Nixon's decision gave a huge boost to the norm against BW use and thus prepared the political and moral ground for the eventual entry into force of the BWC.

Article I of the BWC provides: "Each State Party to this Convention undertakes never in any circumstances to develop, produce, stockpile or otherwise acquire or retain: (1) Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes; (2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict."

Biosecurity Policy and Ethics: Australia and the Biological Weapons Convention

Identical words appear in Australian domestic law (section 8 of the federal Crimes (Biological Weapons) Act 1976), and a person convicted under this provision may be imprisoned for life. Australia's commitment to take any national measures necessary to implement the provisions of the BWC domestically is also demonstrated by the introduction of a scheme to regulate the handling, transfer and disposal of 22 listed "security-sensitive biological agents" under the federal National Health Security Act 2007.

The greatest strength of the BWC is the universality of its norm. It is widely accepted in the international community that BW are abhorrent, and the norm against their use has been internalised by individuals' and nations' value systems. Although the strong norm against BW use creates a powerful stigma, it nevertheless requires constant reinforcement in the face of new challenges. In particular, there is a danger that, as a result of technological advances and/or changed international security circumstances, some political decision-makers might convince themselves and others that BW are no longer an illegitimate means of protecting national interests. Prior to 2001, the idea attracting most political attention as a means of strengthening the BWC was that of a legal instrument for monitoring compliance by member states. An Ad Hoc Group (AHG) of member states had a mandate, granted at a Special Review Conference in 1994, to negotiate a verification protocol. Broadly speaking, greater confidence in BWC compliance was to be generated by: (1) declarations by member states of existing BW stockpiles and potentially BW-capable facilities; (2) routine and unannounced visits to declared or suspected BW-relevant sites; and (3) investigations of 'suspicious' disease outbreaks. However, the AHG negotiations were brought to an abrupt end after 2001 when the United States announced it would not support a draft protocol presented to the Fifth BWC Review Conference.

Since the last Review Conference in 2006, BWC member states have been participating in annual meetings to "discuss, and promote common understanding and effective action on": ways and means to enhance national implementation, and regional cooperation on implementation, of the Convention (2007); measures to improve biosafety and biosecurity, and oversight, education, awareness-raising, and adoption and/or development of codes of conduct for life scientists (2008); promoting capacity building in the fields of disease surveillance, detection, diagnosis, and containment of infectious diseases (2009); and provision of assistance and coordination with relevant organizations in the case of alleged use of BW (2010). At the 2011 Seventh Review Conference in December, most if not all BWC member states are likely to endorse these annual meetings as having been a valuable means of exchanging ideas and information. There is consensus that, given the fast pace of treaty-relevant developments in science and technology, it is better to meet at least annually rather than on a five-yearly basis. An important issue for debate, however, will be whether to allow member states to also make binding decisions about the Convention on an annual basis.

Among the other issues likely to generate discussion in December is the need for greater national transparency and participation in confidence-building measures. Unfortunately, doubts persist as to whether particular countries are adhering to their BWC obligations. Some member states might even advocate resurrecting the pre-2001 idea of a formal compliance protocol, but this is unlikely to succeed so long as the US Government remains firmly opposed to BWC verification. Education and awareness-raising for present and potential life scientists on the problem of BW is another important issue, and suggestions for pursuing this goal are likely to be pushed most strongly by non-government organizations attending the Review Conference. Lastly, there remains the challenge of universality. Among the 195 states in the United Nations, 164 are BWC members and there are 13 BWC signatories. Eighteen (18) states have neither signed nor ratified the Convention: Andorra, Angola, Cameroon, Chad, Comoros, Djibouti, Eritrea, Guinea, Israel, Kiribati, Marshall Islands, Mauritania, Micronesia, Namibia, Nauru, Niue, Samoa and Tuvalu. As many of these states lie in the Pacific region, Australia has a particularly important role to play as a regional leader in encouraging greater BWC participation.

News & Events

- Calls for Expression of Interest 'Workshop on Microbial Whole Genome Sequencing'. EOI closes 12 November 2011. For more information on workshop and application, visit : www.cidmpublichealth.org
- SEIB 2011
  23-24 November 2011, Sydney Law School, University of Sydney. For more information, contact: seib@sydney.edu.au
- CIDM-PH Colloquium
  Date TBA - Westmead Education & Conference Centre, Westmead Hospital. The annual CIDM-PH Colloquium provides a forum for CIDM-PH staff and students to showcase their research and project outcomes. For more information, contact: lou_orszulak@wsahs.nsw.gov.au

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