

## Bioterrorism: an emerging threat

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Prior to the 1998 Vancouver Asian Pacific Economic Summit, emergency physicians were briefed on the possibility of terrorist-related biological or chemical weapons incidents. As part of a training exercise, the “victim” of a chemical weapon attack was brought to our ED. Because of confusion and ignorance, the “victim,” the physician, several members of the ED staff, and a number of other patients also became “casualties.”

### A history of biological warfare

Biological warfare is not just a twentieth century phenomenon. During the French and Indian War (1754–1767), Sir Jeffery Amherst, commander of the British forces in North America, devised the plan of using smallpox against hostile Native Indian tribes.<sup>1</sup> On June 24, 1763, one of Amherst’s officers acquired several contaminated blankets from a smallpox hospital and presented them, as a gift, to a group of Native Americans. Shortly thereafter, smallpox decimated tribes along the Ohio River Valley. This outbreak may or may not have been related to Amherst’s gift.<sup>2</sup>

Almost 2 centuries later, on a sunny spring afternoon in 1915, German troops at Ypres deployed chlorine gas against the French. Within minutes, thousands were overcome. During the next 3 years, all of the major powers

participated in a chemical arms race that culminated in the development of mustard gas by the Germans. By 1918, over 100,000 men had died from exposure to chemical weapons.<sup>2</sup> After the war, a backlash of moral revulsion led to the development of the Geneva Protocol (1925), which prohibited future use of chemical or biological agents.

Between 1932 and 1945, Japan conducted biological weapons research in occupied Manchuria. At least 10,000 prisoners died after being infected with anthrax, meningitis, cholera or plague. During this period, Japan launched biological attacks on at least 11 Chinese cities. Infectious agents were deployed by directly contaminating water and food supplies, by spraying cultures from aircraft, by dropping bacteria-filled bombs, or by releasing clouds of plague-infected fleas over major cities.<sup>2</sup> In a single attack on Changteh in 1941, 10,000 Chinese citizens and 1700 Japanese troops died, predominately from cholera.

During the 1950s and 1960s, nuclear, biological and chemical weapons proliferated, primarily in the arsenals of the United States and the Soviet Union. But the concept of biological weapons remained abhorrent to individuals and governments alike. This general disdain ultimately spawned an international treaty, the Biological Weapons Convention (BWC), which proscribed the development, production, storage, or acquisition of biological weapons. On April 10, 1972, 79 nations signed the

BWC, bringing an end to widespread biological warfare research.

### The modern era

Recent events in the former Soviet Union, Iraq, Japan, and Oregon have led industrialized countries to become increasingly concerned about the risk of bioterrorism.

Despite signing the BWC, the Soviet Union continued a vast biological weapons program,<sup>1,3,4</sup> producing and stockpiling several agents, including anthrax and smallpox. A former deputy chief of research for the biological weapons program reported that the Russian military had mounted smallpox virus in bombs and intercontinental ballistic missiles for strategic use.<sup>5</sup> In a related event on April 3rd, 1979, Soviet technicians at a Sverdlovsk military installation failed to activate critical air filters. Up to a gram of anthrax spores was inadvertently released, killing 68 people and rendering a 4000-square-mile area uninhabitable.<sup>1,3,6</sup> This event is testimonial to the hazards of working with biological agents.

Iraq remains a major concern. It is the only country since World War II that has deliberately released biological weapons against its enemies (Iran) and its own people (the Kurds). Between 1985 and 1991, Iraq accumulated a variety of biological agents including botulinum, *Yersinia pestis*, dengue virus, anthrax, and smallpox.<sup>1,2</sup> The Iraqis claim to have produced 90,000 litres of *botulinum toxin*, 8300

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litres of anthrax, and to have distributed 200 bombs and warheads containing these agents to various military bases.<sup>4,5</sup> Iraq has complied minimally with United Nations (UN) requests for nuclear and chemical weapons site inspections, and has resisted all attempts to locate biological weapons factories. Despite defeat in the Gulf War, Iraq's development facilities, scientific personnel, and biological warfare capability remain essentially intact.<sup>7</sup>

During the 1990s, a fanatical religious group, Aum Shinrikyo, made several attempts to aerosolize anthrax and botulism throughout Tokyo.<sup>2,3,5</sup> In 1992, group members travelled to Zaire, the site of an Ebola virus outbreak, to acquire samples for use as biological weapons.<sup>2,8</sup> In 1995, in one of the most notorious terrorist attacks in history, Aum Shinrikyo placed sarin nerve gas in 5 subway cars converging on central Tokyo. This attack affected over 5000 people, causing 1000 hospitalizations and 12 deaths.<sup>2</sup>

Biological incidents have also occurred in North America. In September of 1984, the Rajneeshee religious cult contaminated 10 restaurant salad bars in the Dalles, Oregon, area with *Salmonella typhimurium*.<sup>9</sup> Subsequently, 751 community members developed salmonella gastroenteritis, demonstrating the ease with which a motivated group can perpetrate an act of bioterrorism. Six years ago, in April of 1993, Canadian customs agents stopped an Arkansas man carrying weapons, ammunition, neo-Nazi literature, and enough ricin to kill 30,000 people.<sup>4</sup>

In the United States, the number of

anthrax threats has increased from 1 in 1997 to 37 in 1998. There were 10 additional threats during the first 2 months of 1999 alone.<sup>10</sup> While none have been associated with actual spore release, these incidents generate fear among the general population, strain public health resources, and undermine the urgency of response required by the medical, public health, municipal and provincial agencies.

Bioterrorism is a growing threat as we approach the millennium.<sup>4</sup> Today at least 17 countries are believed to have active biological weapons programs.<sup>3</sup> Recipes for biological agents

are available on the Internet, and groups with basic scientific knowledge can develop deadly biologicals at low cost. Several dissident groups have the

skills necessary to cultivate lethal pathogens<sup>8</sup> and the will to deploy them. Biological weapons will be deployed again, but we have no ability to predict or prevent an attack, little ability to detect one when it occurs, and limited ability to manage the consequences.

### **Bioterrorism and the emergency department**

It is crucial to understand the differing nature of biological and chemical agents (Table 1), since these differences mandate different public health, first responder, and medical responses.

Chemical agents produce immediate dramatic effects. In the Tokyo sarin gas attack, symptoms appeared within hours and thousands of people were affected. In such incidents, the key health care responders are firefighters, paramedics, police and military.<sup>5</sup> This medical response is typically practised and promoted by local

agencies as part of a disaster plan.

Biological events are different. They may be clandestine; there may be no recognition that an attack has occurred. Because biological agents have incubation periods, an immediate deluge of casualties is unlikely. Rather, victims are likely to present over a period of weeks with flu-like illnesses (anthrax) or chickenpox-like rashes (smallpox). Patients may be spread over wide areas and present at diverse health care facilities. Since few physicians have seen smallpox, anthrax or plague, recognition will be delayed. Days or weeks may pass before public health agencies become aware of the biological attack, during which time the outbreak can spread widely.<sup>5</sup> The potential for casualties is huge. Whereas conventional terrorist activities like bombings kill dozens or hundreds, a single act of bioterrorism may kill thousands or millions.<sup>11</sup>

Initial cases will present to emergency departments, and ED physicians will constitute the first line of defense.<sup>5,11</sup> Because biological agents threaten not only the lives of the primary victims, but also those of physicians and hospital staff, rapid diagnosis is important; therefore emergency physicians, particularly those in large cities, should be trained to recognize the syndromes caused by the most likely biological warfare agents.<sup>11</sup> Early syndrome recognition facilitates life-saving vaccination of high-risk populations (e.g., ED staff) and allows for early post-exposure therapy for victims. In the event of a smallpox release, rapid recognition and response could mitigate the effects by 100-fold, but only if initiative is shown. Early identification of a deadly pathogen may mean the difference between life and death for ED staff and patients, and could prevent thousands or tens of thousands of casualties over the ensuing months.

## Epidemiology of bioterrorism

Knowledge of basic epidemiological principles is important in dealing with biological warfare threats. The first requirement is to maintain a high level of suspicion, looking for the following clues:

- large epidemics of acutely ill patients
- unexplained animal deaths
- diseases that are unusual for the region
- multiple or simultaneous epidemics
- increased utilization of pharmacies, medications, ambulance services, emergency departments, physicians and funeral homes.

Claims by terrorist groups or prior intelligence about attacks may simplify the public health investigation.

The steps required to deal with a bioterrorism attack are the same as for any infectious outbreak. They include verifying that an alleged disease event has occurred, developing an objective case definition based on signs and symptoms, searching for unreported cases, describing the outbreak and comparing it to expected disease rates and other epidemics. Unfortunately it

can take months, as it did with the Pacific Northwest Salmonella outbreak, to confirm that an incident was, in fact, an act of bioterrorism.

## Biological weapons of mass destruction

An ideal biological agent is easily and rapidly produced, is environmentally stable, and can be concentrated or dried. Agents should be highly infectious (but not necessarily conta-

gious) in low doses, properly sized to cause infection (2 to 6 microns) by the aerosol route, and cause severe disease. In addition, it is advantageous if vaccines and toxoids are available to protect those working with or deploying the agent. There are thousands of possible pathogens but only a few meet the criteria listed above (Table 2). The 4 most likely to be used are smallpox, plague

and botulism. Of these, smallpox and anthrax are the greatest threats.<sup>5</sup>

### *Smallpox*

The last natural case of smallpox occurred 20 years ago in Ethiopia. Although it is difficult to obtain, smallpox virus is considered a high risk for use as a biological weapon.

Smallpox is spread person-person by droplets or aerosol (e.g., coughing). It is highly infectious and contagious at low doses. After a 10-

## Bioterrorism will demand the expertise of emergency medical staff and public health clinicians.

to 12-day incubation period, victims develop a flu-like illness with fever, joint pains, headache, and a pustular, chickenpox-like rash. Unlike chickenpox, the rash is centrifugally distributed and pustules develop on the palms and soles. The case fatality rate is 30% to 80%, and treatment is limited to isolation and vaccination. Vaccination within 3 days of exposure can prevent disease, and vaccination within 4 to 5 days may prevent death. Existing vaccine stores, in the United States, are adequate to immunize 6 to 7 million people, but further large-scale vaccine production would take at least 36 months.

### *Anthrax*

Anthrax, primarily a disease of grazing animals, is caused by gram-positive rods that may survive up to 40 years in spore form. Anthrax is transmitted to humans who are exposed to animal products in agricultural or occupational settings. Aerosolized anthrax disseminates easily over large areas, making it a dangerous biological agent. For example, while it takes 8

**Table 1<sup>5</sup>**

Parameter	Chemical agent	Biological agent
Onset of illness	Rapid: usually minutes to hours	Delayed: days to weeks
Patient distribution	Downwind; near release point	Widespread; perhaps international
First response	Paramedics, firefighters, police	ED physicians and nurses
Decontamination	Critically important	Usually unnecessary
Treatment	Chemical antidotes	Vaccines and antibiotics
Isolation	No need after decontamination	Crucial for communicable diseases

**Table 2. Biological agents**

Bacteria	Viruses	Toxins
Plague	Smallpox	Botulinum toxin
Anthrax	Viral hemorrhagic fevers	Ricin
Tularemia	Viral encephalitides	Marine toxins
Q fever		Venoms
Brucellosis		Staph enterotoxin B

tons of ricin to cover a 10-square-mile battlefield and achieve a 50% death rate, a few kilograms of anthrax will have the same effect. Although anthrax can be acquired via the aerosol route, the risk of secondary anthrax through re-aerosolization or person-to-person contact is low.

## **We should consider how our local and regional disaster plans will address the issue of biological terrorism.**

Cutaneous anthrax, the most common form, begins as a dermal vesicle that breaks down to form an eschar, sometimes with associated edema. It is easily recognized, susceptible to antibiotic treatment, and carries a low mortality.<sup>3</sup> Gastrointestinal anthrax, most common after ingestion of contaminated meat, produces hemorrhagic gastroenteritis followed by anthrax septicemia, which is generally fatal.

Inhalational anthrax is rare except after a biological weapon exposure.<sup>3</sup> Aerosolized anthrax spores penetrate terminal alveoli and are taken up by pulmonary macrophages. Nonspecific symptoms, including fever, malaise, headache and cough, occur 1 to 3 days after exposure. Spore germination (which may be delayed up to 2 months) leads to toxin production, edema, and tissue necrosis. Rapid deterioration ensues, characterized by dyspnea, stridor (if tracheal nodes are involved), and the *sine qua non*, hemorrhagic mediastinitis. Hemorrhagic meningitis is seen in up to 50% of cases, and death frequently occurs within 3 days of symptom onset. Given a compatible clinical presentation, a wide mediastinum on chest x-

ray is a classic finding of anthrax. The diagnosis is confirmed by history of exposure, a positive Gram stain of blood, nasal swabs, or environmental samples, and a positive culture or polymerase chain reaction (PCR) for anthrax DNA. A suspicion of anthrax should prompt immediate notification of public health authorities so that definitive testing can be arranged.

Pre-exposure prophylaxis involves 6 doses of anthrax vaccine at 0, 2 and 4 weeks, and at 6, 12 and 18 months.<sup>3</sup> Post-exposure therapy, which should begin within 48 hours of exposure, includes ciprofloxacin or doxycycline for 30 to 60 days in addition to anthrax vaccine at 0, 2 and 4 weeks.

Unfortunately, in a typical anthrax scenario, victims would develop non-specific symptoms 2 to 3 days after exposure and physicians would not think of anthrax. By the time definitive identification was made, treatment would likely be futile.<sup>8</sup> Infected individuals would become critically ill within 24 to 48 hours and die rapidly. The mortality rate for non-vaccinated civilians after pneumonic anthrax exposure would approach 100%.

There have been several recent hoaxes where individuals claim to have mailed anthrax in a letter. In such situations, "exposed" persons should remove their clothing and personal effects, place them in plastic bags and shower copiously with soap and water. Personal effects and anything that contacted the letter should be decontaminated with a 0.5% hypochlorite solution.

## **Vaccines**

Vaccines exist for anthrax, smallpox, cholera and plague, although the latter is only effective against flea-borne plague. The US military vaccinates its entire armed forces against anthrax, but there are no plans to vaccinate

against smallpox. Vaccine availability is very limited,<sup>3</sup> and there are no plans to vaccinate the general public. In the event of a bioterrorism attack, preferential vaccination would be provided for those exposed without symptoms, contacts of anthrax victims, first responders, laboratory workers, and (probably) government officials. Ongoing research is focused on the development of vaccines against smallpox (second generation), tularemia, Q fever, botulinum and viral equine encephalitis.

## **Planning for biological incidents**

Proactive mitigation is crucial to disaster planning. Recognizing that terrorist action can rarely be predicted or prevented, the greatest payoff will come from improving our response to biological attacks and the emergency medical community will play a critical role in this process.<sup>11</sup>

It is likely that a biological weapons incident would overwhelm community and medical resources, and many questions need to be considered. Who will coordinate outbreak investigation and control? How will communication occur between organizations, the media and the public? How will emergency health services, police, military, emergency medicine and ancillary medical personnel be coordinated? How will local disaster teams set up containment and command centres? Who will designate hospitals and how will they contain infection? How will hospitals obtain antibiotics and antitoxins for large numbers of patients? What are the plans to distribute vaccine? Who will authorize quarantines or martial law? Who will authorize the closure of airports and borders if necessary? How will panic be controlled within the population at large?

## But wait! This is Canada

The cash-strapped Canadian health care system can barely cope with “normal” health care problems. In most Canadian cities, public health budgets are stretched to the limit and probably inadequate. Few funds are available to address emerging infections. Yet bioterrorism is an emerging reality we cannot ignore. The Clinton administration appears ready to assign \$2.2 billion dollars in the 1999 and 2000 budgets toward preparing for this threat. More realistic goals in Canada are to develop appropriate plans to deal with this potentially devastating occurrence and to increase the awareness of key health care providers, managers and administrators — especially those involved with disaster plans and their implementation.

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Further information about bioterrorism is available at the Johns Hopkins Infectious Disease Web page ([www.hopkins-id.edu](http://www.hopkins-id.edu)) and at The Center for Civilian Biodefense Web site ([www.hopkins-biodefense.org](http://www.hopkins-biodefense.org)).

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