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BIO-TERRORISM

In the last 10 years, policymakers have become increasingly concerned over the threat of terrorist attack using biological weapons (BW). Recent anthrax attacks in the US have intensified those concerns. This briefing note outlines the nature of the various BW and their effectiveness, assesses which agents are most likely to be available and looks at UK plans to manage the consequences of BW attacks.

Background

Even before the recent anthrax attacks in the US, the Royal Society[1] had identified reasons for increasing concern over possible terrorist use of BW:

- The possibility that genetic modification could be used to produce new biological threats. While all sorts of 'designer' weapons have been proposed, simply engineering a bacterium to be antibiotic resistant could significantly increase its effectiveness as a BW.
- BW are relatively easy and cheap to make. In addition, only very small quantities are needed to cause enormous disruption. Such factors may make BW particularly attractive to terrorists.

BW agents

Any organism that causes human disease can potentially be developed into a BW; living microbes and natural toxins of particular concern are outlined in the box opposite. These include agents that can be spread as fine airborne particles (aerosols) such as the bacterium that causes anthrax, as well as other microbes that can be used to contaminate food or water (e.g. the bacteria that cause cholera and typhoid fever).

Dispersal and effectiveness

Contagious agents

Some of the microbes (e.g. the smallpox virus and the bacterium that causes plague) are highly contagious and may thus spread from one person to another. In such cases, widespread dispersal of the biological agent may not be necessary: a small quantity of the agent initially infecting just a handful of people has the potential to start an epidemic affecting millions. While such agents may appear ideally suited for terrorist use, the unpredictability of the outcome – for instance, the possibility of an epidemic spreading to countries other than those targeted in the initial attacks – may dissuade some against their use.

Non-contagious agents

Other biological agents, most notably the anthrax bacterium (see box, page 2) used in the current attacks in the US, are not transmitted from one person to another, so the number of people affected depends on how widely the agent is dispersed in the first place. In practice the most effective method of dispersal is as an aerosol of fine particles. However, the technology to achieve this is far from straightforward. It requires the

Biological weapons agents

The Royal Society report identified 4 main classes of agents that could be used in BW.

Bacteria – any bacterium that causes human disease is a potential BW. These include *Bacillus anthracis*, the cause of anthrax, as well as the causative agents of plague (*Y. pestis*), tularaemia (a plague-like illness caused by *F. tularensis*), cholera (*V. cholerae*) and typhoid (*S. typhi*).

Viruses – commonly cited examples of possible viral BW include the Ebola and Marburg viruses and those causing yellow fever, smallpox, flu, Congo Crimea haemorrhagic fever and various forms of encephalitis.

Toxins – are naturally occurring poisons isolated from bacteria, fungi and plants. Examples include the bacterial botulinum, perfringens and *Staphylococcus* entertoxin B toxins, as well as fungal mycotoxins and ricin (which can be isolated from castor beans).

Rickettsia/Coxiella – are classes of bacteria that are harboured by lice and other parasites. Of most concern are the causative agents of epidemic typhoid and Q fever.

capability to manufacture particles of 1-5μm, small enough to remain suspended in the air as an aerosol and to be inhaled deep into the lung. It also requires a mechanism for generating the aerosol. This may involve 'weaponising' the BW into munitions or missiles that generate aerosol on detonation, or spraying it from aeroplanes or specially adapted vehicles.

Overall effectiveness of BW

Various attempts have been made to assess the likely impact of BW in the hands of terrorists, using models based on studies of aerosol spread and data from animal studies to estimate the lethal dose of anthrax spores required[2]. As outlined in the box below, such worst case scenarios suggest that a single attack using 50-100kg of anthrax aerosol released over an urban area could result in between 100,000 and 3 million deaths. However, experience of exposure of human populations to anthrax spores suggests the risks may be considerably lower. For instance, an accident at a Russian military facility in Sverdlovsk in 1979 exposed 15,000 workers at the plant and at least 50,000 people living in the surrounding area to an aerosol of anthrax spores. The number of reported anthrax cases (79) and resulting deaths (68) were low in proportion to the size of the exposed population[3].

Worst case scenarios for anthrax attacks

In 1970, a World Health Organisation (WHO) expert committee[4] estimated casualties following a theoretical release of 50kg of anthrax spores from an aircraft over an urban population of 5 million people. It estimates there would be 250,000 casualties, of which 100,000 would die without proper treatment.

A later (1993) report by the US Congressional Office of Technology Assessment[5] looked at a scenario involving release of 100kg of anthrax aerosol upwind of the Washington DC area. It estimated that this would cause at least 130,000 deaths and possibly as many as 3 million. An economic model developed by the Centers for Disease Control and Prevention[6] recently estimated a cost of $26.2 billion per 100,000 people exposed to a bioterrorist attack.

The current anthrax attacks in the US are more limited in their scope than the scenarios above. For instance, the method of distribution – sending contaminated letters through the post - targets small numbers of people rather than populations. It also means that infection may be more likely to occur via skin contact (seldom fatal), rather than inhalation into the lung (usually fatal).

Issues

Availability of BW agents

Terrorists may obtain such agents through various means. For instance they may steal them from research laboratories, buy them on the black market or from legitimate sources such as a reference laboratories that hold a collection of different strains, or receive them from sympathetic states. In theory, terrorists may be unlikely to have access to viruses such as Ebola or smallpox since these are supposed to be strictly controlled and held only in a small number of secure laboratories. For instance, the smallpox virus legitimately exists in only two laboratories in the world – one in the US and one in Russia. However there has been much recent speculation that the then USSR developed BW containing smallpox. If this speculation is true, then stockpiles of this virus may be more extensive and widely distributed than was previously thought.

Bacterial BW agents may be more readily available. It is not inconceivable that terrorists could attempt to isolate harmful bacterial agents from their natural environments

Anthrax

The bacterium – is found naturally in farm animals and other mammals around the world. It exists in 2 forms:

- Spores - in the absence of nutrients, the bacterium form small spores, ~1μm in diameter. These are very hardy, and can survive for decades outdoors.
- Growing cells - when anthrax spores find themselves in suitably nutrition-rich surroundings – e.g. in the blood or tissues of an animal or human host – they germinate into bacterial cells capable of rapidly multiplying and infecting the cells of the host.

Virulence - there are numerous different strains of the bacterium, some of which are more virulent than others. The most virulent strains have a capsule that protects the cells from attack by the body's immune system, and also produce a toxin that causes swelling and bleeding.

The disease – anthrax can occur in three forms depending on the route by which the bacterium enters the body:

- Inhaled – if spore-bearing particles of 1-5μm are inhaled deep into the fine airways of the lung, the body's immune system transports them to the lymph nodes. They may germinate here up to 60 days after exposure. Toxins produced by the cells result in the onset of disease within a few days. Initial symptoms resemble those of the common cold, but rapidly progress to severe breathing difficulties and shock. This is the least common naturally occurring form of anthrax but is often fatal (~86-90% fatality rate).
- Via cuts or scratches in the skin – spores entering by this route usually germinate within a few days causing localised swelling. This develops into an ulcer a few days later, with a characteristic black scab at the centre. Fatalities can occur if the infection is not treated with antibiotics and spreads throughout the body, but are rarely seen in cases that receive appropriate treatments. This type of anthrax accounts for the majority (95%) of naturally occurring cases.
- Eaten – spores that are eaten (e.g. via contaminated raw meat) may germinate in the gastrointestinal tract. Toxins produced by the cells cause blood loss and inflammation, giving rise to symptoms such as vomiting, severe diarrhoea, fever, etc. Mortality rates vary between 25-60%.

Treatment – naturally occurring anthrax strains are sensitive to most major classes of antibiotics including penicillins, tetracyclines and fluoroquinolones. Penicillin is normally the treatment of choice. But reports suggesting that Russian scientists have engineered a virulent strain of *B. anthracis* to resist the effects of tetracyclines and penicillins led a US working group to recommend treatment with ciprofloxacin (a fluoroquinolone). Early administration of antibiotics after exposure is essential – with inhaled anthrax, a delay of just a few hours is enough to significantly reduce the chances of survival. Because spores can take a long time to germinate, antibiotic treatment should continue for 60 days.
Source: JAMA, 1999. 281, 1735-1745.

and culture them. Pure *B. anthracis* could be isolated from (say) infected farm animals, although obtaining a stable, virulent strain would involve the evaluation of many such samples. The equipment needed to grow such a strain, harvest the spores and process them into 'weapons-grade' anthrax (particles of 1-5μm) is readily available, although the operation would have to be conducted in an enclosed facility.

In practice, terrorists may be more likely to seek to acquire BW agents 'ready-made' on the black market or from sympathetic states. At least one country (Iraq) has admitted to developing anthrax weapons; the Sverdlovsk incident described previously makes it highly likely that Russia was also developing anthrax BW. Some 15 other countries around the world are thought to have offensive BW programmes, although the BW agents involved are unknown.

Just prior to the Gulf War, UK intelligence analysts identified the most likely BW threat as coming from bacterial sources, notably anthrax, plague and botulinum toxin (BTx). UK forces were vaccinated against both anthrax and plague; serum for treating exposure to BTx was also taken to the Gulf. US planners did not concur with the UK analysis over the risk of exposure to plague, but US forces did receive both anthrax and BTx vaccines. Neither UK nor US planners saw a credible threat of smallpox attack at that time.

Tracing BW agents

Experts in the US are currently examining samples of the powder used in the anthrax attacks. These analyses could reveal the original source of the anthrax. For instance, pure preparations of highly virulent strains that have been modified to resist antibiotics and consist of particles in the optimal size range may be suggestive of material originating from a state-sponsored BW programme. However, such studies will not reveal anything about the route by which the anthrax was acquired from the original manufacturer.

UK arrangements for deliberate release of BW

Co-ordination

The UK has well-tried arrangements for detecting, investigating and controlling natural outbreaks of microbial disease (see box opposite). Arrangements for managing deliberate releases of BW against civilians use the same basic surveillance and response framework, co-ordinated by contingency plans drawn up by the Civil Contingencies Secretariat within the Cabinet Office, Department of Health (DH) and Public Health Laboratory Service (PHLS). DH drew up guidance on the "Deliberate Release of Biological and Chemical Agents" in March 2000, which forms the basis of its contingency planning. PHLS published interim guidelines for anthrax, botulism, plague and smallpox in October 2001[7]. As noted by the Royal Society, the emergency planning process is informed by military intelligence about the likely availability of the various different BW agents.

UK framework for dealing with microbial disease

- Health/local authorities. Each HA employs a Consultant in Communicable Disease Control (CCDC), trained in the epidemiology of infectious disease.
- PHLS maintains 50 regional laboratories providing diagnostic services and expertise and runs a central laboratory in London, which houses reference laboratories with expertise on specific microbes. It also has a centre for the surveillance of microbial disease that provides epidemiological expertise in managing outbreaks of disease anywhere in the country.
- NHS hospitals and family doctors are responsible for clinical care of those affected. More serious outbreaks will also involve regional directors of public health, regional PHLS epidemiologists and the DH.

Detection of natural outbreaks may occur locally (e.g. if doctors detect a rise in the number of cases of a disease or PHLS labs notice a new type of microbe), or through PHLS national surveillance. Handling an outbreak involves:

- co-ordinating the response via an outbreak control team consisting of the CCDC and various experts;
- care of affected patients;
- identification of risk groups;
- finding all cases of people affected;
- identification of the causative agent and the route (air, food, water, etc.) by which it is transmitted;
- decontamination of the source and control measures;
- use of vaccines and antibiotics to protect from infection;
- provision of information to the public and the media.

Detecting an attack

Covert release of a BW may only become apparent once the first cases of the disease arise. Some diseases occur so infrequently in nature that the appearance of just one case may be suggestive of deliberate release. For instance, PHLS interim guidelines note that deliberate release should be considered as a cause in the event of a single case of inhaled anthrax. For diseases such as botulism, it may be more difficult to distinguish between deliberate release and (rare) natural occurrence. The public health impact of the anthrax attacks in the US has been minimised through good clinical awareness and early notification to the public health authorities. DH contacted all GPs in October 2001 reminding them how to access the latest advice on diagnosing anthrax; UK clinicians are also being alerted to watch out for tell-tale symptoms and presentations.

Response/treatment

All individuals exposed to a deliberate release of BW need to be traced, decontaminated and offered treatment with antibiotics or vaccines. PHLS recently published advice for doctors on investigating and managing outbreaks of unusual illness. DH is currently reviewing the adequacy of UK stockpiles of treatments for chemical and biological incidents. No information is publicly available on the extent of UK stockpiles, but therapeutics likely to be part of this review are outlined in the box on page 4. The US government has a stockpile of ~15M doses of smallpox vaccine, much of it made 20 years or more ago (production for civilian purposes ceased in the early 1980s). It recently sought funding from Congress to increase this to 300M doses (see box for details). A Cabinet Committee has been set up to review UK supplies of smallpox vaccine and to assess whether

Preventing and treating exposure to BW

Plague vaccine – the vaccine given to UK troops in the Gulf War is no longer available. Its effectiveness in protecting against certain forms of the disease (notably pneumonic plague) had been questioned, it had not been comprehensively tested in humans and the long time it took to confer resistance would make it ineffective against a deliberate release. Newer vaccines have been developed but have not been comprehensively tested in humans.

Anthrax vaccine – an effective vaccine exists, but is currently given only to those at risk of exposure (a small number of laboratory workers). PHLS guidelines advise that the vaccine may be used to reduce the risk of disease after exposure to anthrax in some cases. Although the vaccine is not routinely used in civilian populations, more than half a million doses have been given to US armed forces with no evidence of serious adverse effects.

Smallpox vaccine – an effective vaccine was used in mass immunisation on a global basis to eradicate the disease in the 1970s. WHO now recommends vaccination only for those at risk of exposure and recently reiterated advice not to vaccinate entire populations. The vaccine is also effective when given to people that have already been exposed to smallpox, reducing the severity of the symptoms in some cases and preventing the disease altogether in others. WHO estimates there are ~90M doses available worldwide for civilian use, the potency of which will depend on how it has been stored since it was originally made (commercial production was discontinued in the early 1980s and facilities dismantled). The US government has asked Congress to approve funds to increase the US stockpile from ~15M to 300M doses. It is negotiating with companies to supply the vaccine and has commissioned development (and ordered 54M doses) of a new vaccine, although the first batch will not be delivered until 2002.

Antibiotics – used to treat disease caused by bacteria, and to prevent symptoms in those thought to have been exposed. Ciprofloxacin is the antibiotic of first choice for anthrax, plague and tularaemia.

better vaccines are needed against plague. The Royal Society report suggested that the DH arranges emergency access to stockpiles of therapeutics held by other countries, and noted there may be a need for more isolation/treatment facilities.

Use of vaccines

Vaccines can be used in one of two main ways. First, they can be given to people prior to exposure, to protect them against a disease. They may be targeted at people identified as being at increased risk of exposure (e.g. the plague and anthrax vaccines given to UK soldiers prior to the Gulf War), or used to protect entire populations. Of the vaccines described in the box, only the smallpox vaccine has been used in mass immunisation. However, WHO now advises[8] against using the vaccine in this way, partly because of safety concerns (the risk of adverse reactions to the vaccine). Second, they can be given to people after exposure to an agent that causes disease to reduce the severity of symptoms, or prevent the disease entirely. Anthrax and smallpox vaccine can both be used in such a way. In the event of a smallpox outbreak, WHO recommends the vaccine is given to all people with the disease, and all those they have been in contact with.

Providing information to the public

As noted by the Royal Society, attempts should be made to reduce panic by issuing accurate information to the public and media; this should be prepared in advance for release in the event of an incident. PHLS has already prepared such fact sheets for anthrax, plague, botulism and smallpox. There is also the issue of whether more information should be provided to the public to prepare them for any such attack. To date, the government has sought to reassure the public that the chances of a biological attack are low, and that the UK is well prepared to deal with any such occurrence, without revealing details of UK preparedness.

International efforts to stop BW proliferation

The development, testing, production and stockpiling of BW are all prohibited under the Biological Weapons Convention (BWC) agreed in 1972, which has been signed by 144 nations; the BWC does not include a mechanism for verifying that nations are complying with its terms. Efforts to establish a verification protocol are underway, but have been hampered by the 'dual-use' nature of BW technology. The challenge is to find a way of preventing the development of BW, without restricting legitimate/beneficial applications of the technology. Measures envisaged for the protocol include: declarations of information about all facilities that could be used for developing/producing BW; checking declarations by on-site visits by internationally appointed inspectors; and procedures for investigating possible infringements (including internationally agreed procedures for dealing with transgressors). The US also recently proposed that BWC signatories enact strict national laws against BW activities, with strong extradition requirements.

Overview

While the deliberate release of BW agents is a frightening prospect, it is important to keep the likely consequences in perspective. So far, the attacks in the US have led to few deaths, and only a handful of confirmed cases of infection. But they have led to disruption of the US Congress and postal service, and caused widespread alarm around the globe. While the prospect of a large-scale release of a highly contagious pathogen cannot be discounted, the evidence to date suggests that continued small-scale anthrax attacks targeted at individuals are unlikely to cause significant numbers of fatalities.

Endnotes

1 "Measures for controlling the threat from biological weapons", the Royal Society, July 2000.
2 Estimates put the lethal dose needed to kill half the people exposed to it at between 2,500 and 55,000 inhaled anthrax spores.
3 "The Sverdlovsk anthrax outbreak", Science, 266, 1202-04, 1994
4 "Health aspects of chemical and biological weapons", WHO, 1970.
5 "Proliferation of weapons of mass destruction", OTA, 1993.
6 "Economic impact of a bioterrorist attack", Emerg Infect Dis, 3, 83-94, 1997.
7 see www.phls.co.uk/advice/index.htm
8 see www.who.int/inf-pr-2001/en/state2001-16.html

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