JOURNAL OF THE ROYAL SOCIETY OF MEDICINE

October 2002 Volume 95 Number 10 ISSN 0141-0768

Bioterrorism: what can we do?

Bioterrorism is much in the news, mainly because of the incidents involving letters contaminated with anthrax spores sent through the post in the USA. Twenty-two people were infected and five out of the eleven with inhalation anthrax died. This episode was a clear warning of the power of biological weapons not only to kill but also to instil widespread fear. At the end of last year the RSM's Comparative Medicine Section had a meeting to discuss anthrax as a biological weapon against man and animals. It included a powerful film about the use of aerosols from bombs or grenades against sheep on Gruinard Island, off Scotland, during the Second World War. A more rounded discussion of the threat of bioterrorism was offered in June 2002 at the inaugural meeting of the South and West Region of the RSM.

For several reasons, defence experts have downgraded biological weapons as effective weapons of war[1]. In 1969, President Nixon stopped the offensive biological weapons programme in the US by executive order. This was mainly because nuclear and advanced conventional weapons had made biological weapons redundant for national security. The scale of damage that could be done by biological weapons was conjectural and there was no way in which training in the use of biological weapons could be developed for the military. There was also at that time a widespread feeling that, with chemotherapy and vaccines and an alert public health service, infectious diseases were controllable. The US was therefore happy to sign up to the Biological Weapons Convention when it was formulated in 1972, largely as a result of UK initiatives[2]. 140 countries signed the document banning biological weapons research, manufacture or use. The great weakness of this Convention was lack of enforcement.

There is no doubt that biological weapons could wreak havoc. In 1970 the World Health Organization estimated that 50 kg of anthrax spores released from aircraft along a line of two kilometres upwind of a population centre of 500 000 would cause 95 000 deaths and 125 000 incapacitated casualties[1]. Smallpox could generate similar devastation in a largely unprotected population under 40 years old, with an unknown number of secondary cases. Other possible targets for attack are farm animals and crops; the latest outbreak of foot and mouth disease in the UK gives an idea of the vast scale of infection that could result from deliberate releases of virus. What are the risks and what can we do about them?

It is clear that there is a real risk that terrorists careless of their own lives, and to a lesser extent 'rogue states', might be attracted to the use of bioterrorism. The costs are not prohibitive and the technology is readily available. Some agents—notably, anthrax and smallpox—are easily obtainable, and numerous others have been worked on in biological weapons programmes. The methods of control are similar for all biological weapons. The first requirement is a well trained and alert group of infectious disease physicians, supported by a network of laboratories (such as those operated by the Public Health Laboratory Service in the UK), and public health staff empowered to take decisive action in an emergency—for example, to commandeer beds and other necessities. These personnel need training in how to respond to suspicious events and must be constantly alert to the possibility of attack by biological weapons. In the UK, public health is in a poor state after endless reorganizations and the Public Health Laboratory Service is to be disbanded. The national and regional laboratories will join other bodies such as the National Radiological Protection Board in a new Health Protection Agency; other laboratories are to be transferred to local NHS trusts, and their future roles have yet to be defined. Will the network provide the strong leadership and possess the confidence to act promptly—for example, to isolate suspected cases of smallpox and to initiate contact vaccination where necessary? It needs to draw up a list of the agents most likely to be used for bioterrorism and to make clinicians aware of diagnostic tests and countermeasures. If the group is to have the power to act effectively, it will require special funding. The Royal Society inquiry[3] into infectious diseases in livestock stressed the need for similar training for veterinarians in the state service—perhaps recognized by the award of a Master's degree. Another important requirement is a reliable and accurate laboratory diagnostic kit. For foot and mouth disease and smallpox, tests based on polymerase-chain-reaction technology are already available; they only need refinement, validation and development so that they can be deployed close to the patient. A pen-side test for foot and mouth disease[4] shows the way such tests might go. Similar tests for anthrax are at an earlier stage of development, in use for epidemiological tracing of strains but not for routine diagnosis. The lytic enzyme from a

phage PlyG specific for *Bacillus anthracis* has been adapted as a test to detect both vegetative and spore stages of the bacterium[5].

The first step is diagnosis, which depends on clinical awareness and specific tests. The second is isolation, especially for diseases such as smallpox where secondary cases may occur. After isolation—difficult in the event of a large-scale attack—comes treatment. For anthrax, antibiotic treatment is effective if given early enough. For smallpox there is the antiviral agent methisasone, but this is no longer available and has a high incidence of side-effects. Since elimination of the wild virus there has been immense progress in antiviral research and some of the newer compounds should be tested against vaccinia and if possible against smallpox virus itself.

The final requirement is vaccine and vaccination. Ring vaccination is well established for the control of smallpox and was widely used in the end stages of the eradication campaign. There is also an anthrax vaccine. None of the existing vaccines is ideal. The anthrax vaccines now available in the UK and the USA are old-fashioned and an updated more clinically acceptable vaccine is urgently needed. (Only 2% of US postal workers agreed to have the anthrax vaccine when it was offered to them.) Although vaccinia was the key tool for the eradication of smallpox it is far from satisfactory as an agent for widespread use in populations free from smallpox. Some of the vaccination issues have lately emerged in the popular press, two of them being who to vaccinate and which 'strain' of vaccinia to use? There is little information on the biological characteristics of different strains and how these relate to vaccine performance in man. The variants considered for use in both the UK and the USA are the Lister Institute strain and the New York Public Health strain. Do these differ in protective efficacy? Do they differ in safety? The evidence for efficacy of vaccinia against smallpox does not come from controlled trials but from public health experience—the successful global eradication programme. At conservative estimates, vaccine was 90–95% effective in preventing secondary cases[6]; there are no comparative data on different strains of vaccinia. The most important known factor in efficacy of vaccinia is potency—a high count of viable virus.

Even before the eradication programme there were considerable doubts about the safety of vaccinia, especially for universal vaccination. It is for this reason that, in the UK plan, vaccination is to be used only for key personnel and for outbreak control. There are indications that the Lister strain gives rise to more encephalitis (about 30 cases per million vaccinations) than the New York strain, but the data were collected separately and differently for the two vaccines; it was not a direct comparison. The Lister strain was the bedrock of the smallpox vaccination programme when it was still running in the UK, and one can understand the British decision to stick with what is familiar. Clearly, however, a new vaccine against smallpox is required. The existing vaccinia strains cause too much encephalitis and are dangerous in immunocompromised patients and those with eczema. Moreover, the method of manufacture—by growing the virus on the shaved flanks of sheep or calves—is archaic. Much work has been done on vaccinia and its genetics in the hope that this virus could be used as a vector to deliver new molecules in medicine—notably rabies antigens. This means there is a substantial body of research data as a starting-point for vaccine development. Vaccinia virus has been produced on a large scale in cell culture under sterile conditions. Also, with modern techniques an observation by Appleyard *et al*.[7]—that the protective antigen of rabbitpox is on extracellular enveloped virus—might be exploited to provide a killed vaccine.

Much work needs to be done on the organization, training and research and development aspects of counter-terrorism, but effective defensive capabilities do exist.

A J Beale

The Priest's House, Sissinghurst Castle, Cranbrook TN17 2AB, UK

E-mail: jbeale@dircon.co.uk

REFERENCES

1 Lederberg J. *Biological Weapons: Limiting the Threat*. Cambridge, Mass: MIT Press, 1999

2 British Medical Association. *Biotechnology, Weapons and Humanity*. Amsterdam: Harwood Academic, 1999

3 Royal Society. *Infectious Diseases in Livestock*. London: Royal Society, 2002

4 Callaghan JD, Brown F, Osorio FA, *et al*. Use of a portable real-time reverse transcriptase-polymerase chain reaction assay for rapid detection of foot-and-mouth disease virus. *JAVMA* 2002;**220**:1636–41

5 Schuch R, Nelson D, Fischetti VA. A bacteriolytic agent that detects and kills *Bacillus anthracis*. *Nature* 2002;**418**:884–9

6 Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. *Smallpox and its Eradication*. Geneva: WHO, 1988

7 Appleyard G, Hapel AJ, Boulter EA. An antigenic difference between intracellular and extracellular rabbitpox virus. *J Gen Virol* 1971;**13**:9–17