

Comment

Anthrax

As terror strikes the hearts of US citizens due to the recent mailings of anthrax spores, Rick Titball reviews our current state of knowledge of the causative organism of this disease.

Further reading

Jackson, P.J. & others (1997). Characterization of the variable-number tandem repeats in *virA* from different *Bacillus anthracis* isolates. *Appl Environ Microbiol* 63, 1400–1405.

Jernigan, J.A. & others, and members of the Anthrax Bioterrorism Investigation Team (2001). Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. *Emerg Infect Dis* 7, 933–944.

● Please note that views expressed in *Comment* do not necessarily reflect official policy of the SGM Council.

Recent events in the USA have highlighted a problem that many have expressed concern about over the past decade – the use of *Bacillus anthracis* as an agent of bioterrorism. In comparison with the high world-wide incidence of ‘naturally occurring’ anthrax in humans and animals, the number of cases in the US over the past few weeks is relatively low. Yet the level of public concern remains high, and the impact on US society at all levels has been significant. Pneumonic anthrax as a consequence of human activities is not a new phenomenon – during the early and mid-20th century, cases of disease were reported in workers in wool mills who were exposed to air-borne spores of the bacterium. The disease was so common that it was termed ‘woolsorters’ disease’. The subsequent control of woolsorters’ disease was achieved by the disinfection of fleeces and by the vaccination of at-risk workers in wool mills.

The vaccine which was used to control woolsorters’ disease is still available in the UK and is manufactured at CAMR Porton Down. The evidence is that this vaccine is effective. The active component of the vaccine is one component of the anthrax toxin, the so-called protective antigen (PA). However, the full course of vaccination requires four doses of vaccine given over a period of 6 months. Also, the preparations may contain traces of oedema factor and lethal factor, which impart toxicity to the anthrax toxin complex and result in adverse side-reactions in vaccinated individuals. Recent research in the UK has focused on devising methods which yield purer forms of PA, and on developing vaccine delivery systems and adjuvants which will allow single-dose vaccines to be delivered non-invasively. Significant progress has been made in these areas and a recombinant PA-based vaccine devised at Dstl Porton Down will be evaluated in phase 1 clinical trials next year. In parallel, vaccine formulations which can be given intranasally, orally or by inhalation are being devised at Dstl Porton Down and the prospect of a single dose and mucosally delivered vaccine in the near future is good.

In the current outbreak of disease, the time between exposure and the onset of symptoms was between 4 and 6 days. Between 1 and 7 days then elapsed before individuals received appropriate healthcare. Prior to the current outbreak of disease, available evidence suggested that even with treatment the survival rate for individuals suffering from pulmonary anthrax (i.e. after symptoms had appeared) was < 15%. In contrast, 60% of the first 10 individuals suffering from pulmonary anthrax during the recent outbreak have been successfully treated using multidrug regimens and supportive care. Surprisingly,

the successful control of disease did not appear to be directly related to the period between the appearance of symptoms and the start of appropriate healthcare.

Of equal importance to the ability to prevent and treat disease is the ability to identify the strain of *B. anthracis* responsible for the current outbreak of disease. Most of the pioneering work in this area has been carried out in Paul Keim’s laboratory in the USA, where techniques for the rapid discrimination of individual strains of *B. anthracis* on the basis of differences in variable number tandem repeat (VNTR) loci have been devised. The finding that individual strains could be typed in this way was to some surprising, since *B. anthracis* is generally considered to be clonal. Prior to this outbreak a programme to sequence the genome of *B. anthracis* Ames strain had been initiated at TIGR in collaboration with Dstl Porton Down, and this project is close to completion. It has been suggested that the strain responsible for the current outbreak should also be genome-sequenced.

Although the worldwide community has been prepared for the illegitimate use of *B. anthracis* as a weapon, there is still more research required. During research carried out at Porton Down in the 1950s and 1960s it was noted that the treatment of anthrax-infected animals with antibiotics resulted in the eventual elimination of the bacteria, but that these animals subsequently died as a consequence of the release of pre-formed toxin from the dead bacterial cells. Control of this intoxication and the subsequent shock remains the greatest challenge in the treatment of late-stage anthrax infections. Judging by the response from the scientific community to this problem both in the UK and overseas over the past few weeks we can expect some major advances in this area over the next few years.

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