



Smallpox

A wide range of microbial pathogens of humans, domestic animals and crop plants are available as potential agents for biological warfare or, nowadays, bioterrorism. Among those that could be used to produce disease in humans, the smallpox virus is unique in that it produces a very severe disease that is contagious, i.e. transmissible from one person to another.

Why smallpox as a bioterrorist weapon?

Uniquely, the disease smallpox was eradicated globally, the last 'natural' case occurring in 1977. Why is there now a risk that it may re-emerge as a bioterrorist weapon? The answer is complex.

From early in World War II many of the 'advanced' countries set up biological warfare establishments, although bioweapons were not, in fact, used in that war. These establishments continued to be active in research until, in 1975, all these countries ratified a Convention to close them down.

However, in spite of having signed the Convention, the USSR greatly expanded its biowarfare programme, which had

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included smallpox virus since 1947. In 1980, the year in which eradication was announced, they greatly expanded the programme, and by the late 1980s the smallpox virus had been weaponised and a stock of 20 tonnes was maintained for distribution from airplanes or cruise missiles.

In 1992 President Yeltsin closed down the civilian section of this programme which included most of the biological research institutes, and hence the virologists. The suspicion that the smallpox virus may be used by terrorists derives from the fact that some of the unemployed scientists may have sold their services, as well as ampoules of several of the viruses and bacteria they had been studying, to other states or groups.



Global susceptibility

The World Health Organization initiated an intensified eradication programme in 1967 and the transmission of smallpox from one person to another was interrupted worldwide by October 1977. The basic discoveries and methods that made this possible were the demonstration that there was no animal reservoir for the virus, the use of highly potent, freeze-dried vaccine for general vaccination, and the establishment of high quality surveillance networks accompanied by containment vaccination of all case contacts.

The vaccine used was vaccinia virus, the value of which had first been demonstrated by Jenner in 1798. Unfortunately, even though the strains selected were the best available, they cause more adverse effects and deaths than any other vaccine. Hence its use in many countries where it was not endemic ceased in the early 1970s, except for overseas travellers.

The durability of protection varies, but many persons who were vaccinated 15 years before they were infected with smallpox suffered mild disease and some deaths have occurred in people vaccinated 20 years earlier. Since most people in the world have been born since 1980, the populations of all countries are





now highly susceptible. Further, there are now many more people with immune deficiencies, due to HIV or therapeutic immunosuppression, who are much more likely to suffer severe adverse effects.

Clinical signs and diagnosis

Infection occurs by the respiratory route, but smallpox is much less contagious than measles or chickenpox and most infections occur in close contacts of a patient. The incubation period, during which an infected person is completely well, is on average, 12 to 14 days.

The onset of illness is sudden, with fever, headache and backache severe enough to confine the patient to bed. The characteristic rash begins two or three days later and progresses through macules, papules and pustules to scabbing during the third week in the 70% who survive the attack. Importantly, patients become infectious as soon as the rash appears, because the macules in the mouth and

throat rapidly ulcerate and release virus. Diagnosis can be confirmed by visualisation of the characteristic virions by electron-microscopy of material from throat swabs or skin lesions, or by PCR on such material.

Use by bioterrorists

If indeed the virus became available to a bioterrorist, it would most likely be distributed by a nebuliser in some crowded place, such as an airport, railway station or supermarket. Because of the long incubation period, infected persons could travel anywhere in the world before the first case was recognised.

Response

It is highly likely that by the time the first case was diagnosed, some contacts would have been infected. Close contacts of a case should be vigorously sought, quarantined with respiratory isolation, vaccinated, inoculated with vaccinia-immune globulin and observed for some 17 days.

Public health response

The governments of some countries (USA, UK, Israel) have identified populations which are regarded as being at special risk. They are in the process of vaccinating medical response teams and some governments are offering mass vaccination of the whole population now, rather than after the occurrence of a case of smallpox. Other than for military personnel, vaccination requires informed consent and in the USA and UK a large proportion of the general public appears to be reluctant to consent before there has been a case of smallpox somewhere in the world.

Further reading

Alibek K. *Biobazard*. New York, Random House, 1999.
Henderson DA *et al*. Smallpox as a biological weapon. Medical and public health management. *Journal of the American Medical Association* 1999; 281:2127-2137.
Bremam JG & Henderson DA. Diagnosis and management of smallpox. *The New England Journal of Medicine* 2002; 346:1300-1308.

Smallpox Panel A: clinical manifestations.

Panel B: pathogenesis.

Panel C: immune response and period of infectiousness (Courtesy Breman & Henderson (2002) and WHO).

