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SMALLPOX, BIOTERRORISM AND THE WORLD HEALTH ORGANIZATION

Introduction: This paper sets out the historical background of the debate about the possible use of smallpox as an instrument of bioterrorism since its eradication. It traces growing national and international concern about a terrorist attack employing smallpox, gives examples of public health protection measures, and explains the role of WHO in global preparedness.

The conquest of smallpox is generally regarded as one of the greatest victories in public health, and there were understandable celebrations at the World Health Assembly on May 8, 1980, when WHO formally declared the eradication of the disease.

Director-General Halfdan Mahler, writing in a special issue of World Health magazine, said: “What is common to all (of those involved) is a sense of fulfilment, pride of participation in what can justly be called a noble and historic endeavour. Smallpox eradication is a sign, a token of what can be achieved…it comes as a glimpse into the future.” (1)

Twenty six years later, we are now all part of that future. Unfortunately, while the disease can still be declared clinically dead, the fear of its resurrection as a terrorist weapon has never been greater. According to a recent WHO report:

"The greatest fear is that in the absence of global capacity to contain an outbreak rapidly, smallpox might re-establish endemicity, undoing one of public health's greatest achievements." (2)

The world is greatly changed since 1980. One of the most profoundly disturbing changes is the international spread of terrorism, itself a syndrome from which no country seems immune. Next week will see the first anniversary of the July 7 suicide bombings in London. In just over 2 months' time, the fifth anniversary of the 9/11 attacks in the United States will be commemorated.

There have been mercifully few uses by terrorists of chemical or biological agents in attacks on civilians. In Japan in 1994, the Aum Shinrikyo religious cult released the deadly nerve gas sarin in Matsumoto, killing seven people and injuring more than 200 others. The group released sarin again on a Tokyo subway train in 1995.
Twelve people died and hundreds were hospitalized. In 2001, the dissemination of anthrax spores through the United States postal system in 2001 killed five people.

Nobody knows when, where and how terrorists will strike next, but we do know that bioterrorism is one of the forms an attack might take. That it might involve the use of smallpox is a risk being taken more seriously today than perhaps at any time in the history of the disease. It is a continuing preoccupation of governments, the scientific and public health communities, and not least, the World Health Organization.

Although the risk is still generally considered small, huge efforts are being made to reduce it further. National and international plans to counter and contain a deliberate smallpox outbreak are being established in many countries. Examples of these efforts and preparations will be given later in this presentation.

The possibility that smallpox might reappear as an instrument of biological warfare or of terrorism already cast a long shadow over the eradication victory celebrations of 1980. Throughout most of the Cold War, the major protagonists were known to be, or at least suspected of, stockpiling biological and chemical warfare agents: the very same weapons of mass destruction of such recent global concern.

Donald A. Henderson, who had led the eradication campaign, wrote with his colleagues in *Smallpox and Its Eradication*, published in 1988: “It is melancholy but perhaps realistic to suggest that the possibilities of biological warfare or terrorism now constitute the chief reason for holding reserves of vaccine and for maintaining epidemiological and laboratory expertise for the diagnosis and control of smallpox.” (3)

That rationale is even more compelling today than it was then. The remaining known stocks of smallpox virus continue to be contained in high security laboratories in the USA and Russia, their storage monitored by the World Health Organization.

Arguments for their destruction have been raised during many successive World Health Assemblies. Today these arguments look much less persuasive when viewed in the context of international terrorism. At the most recent Assembly in May 2006, the issue was deferred for further consideration until the WHO Executive Board meeting next January.

However, concern has been expressed that the virus might be held clandestinely and less securely elsewhere.

In April 1999, US President Bill Clinton said: “While we fervently hope smallpox would never be used as a weapon, we have a responsibility to develop the drug and vaccine tools to deal with any future contingency – a research and development process that would necessarily require smallpox virus.” (4)
His comments signalled the American government’s intention to delay destruction of the world’s remaining stocks of the virus - held in high-security facilities in Atlanta, Georgia, and in a Russian government laboratory in Koltsovo, in the Novosibirsk region. - so that virus samples could be used for scientific research. A month later, in May 1999, at the World Health Assembly in Geneva, the US successfully pressed this argument during a debate on the subject.

Writing in the *Journal of the American Medical Association* (5) in June 9, 1999, Henderson and colleagues warned: "If used as a biological weapon, smallpox represents a serious threat to civilian populations because of its case-fatality rate of 30% or more among unvaccinated persons and the absence of specific therapy. Although smallpox has long been feared as the most devastating of all infectious diseases its potential for devastation today is far greater than at any previous time.

"Routine vaccination throughout the United States ceased more than 25 years ago. In a now highly susceptible, mobile population, smallpox would be able to spread widely and rapidly throughout this country and the world.

"The specter of resurgent smallpox is ominous, especially given the enormous efforts that have been made to eradicate what has been characterized as the most devastating of all the pestilential diseases. Unfortunately, the threat of an aerosol release of smallpox is real and the potential for a catastrophic scenario is great unless effective control measures can quickly be brought to bear."

Just one week later, *The New York Times* on June 13 1999 carried a report citing a US government intelligence analysis which concluded that North Korea, Iraq and Russia were probably keeping secret of smallpox virus intended for military use. (6)

Clearly the United States government was taking the smallpox risk seriously. About this time, outbreak control plans were being updated and key staff, particularly hospital workers, immunized. Stocks of vaccine were being greatly increased.

In June 2001, the American government staged a huge exercise, named *Dark Winter* (7) which simulated a smallpox attack in the United States. The exercise was a stunning revelation of how poorly prepared and equipped the nation - perhaps any nation - was to deal with such an event.

The scenario was a covert smallpox attack that began in Oklahoma and spread rapidly. Within two weeks, there were 14,000 smallpox cases in 25 states, 1,000 deaths (with 5 000 more anticipated in the following two weeks), the medical system was completely overwhelmed and the outbreak had led to cases occurring in 10 countries. "A biological warfare attack on America with a contagious pathogen could potentially cripple the country…government responses will pose enormous challenges to civil liberties:"
In their BMJ paper of 2002, *Biological warfare and bioterrorism* (8) Nicholas Beeching and colleagues wrote: "In a military setting, biological warfare agents are most likely to be delivered by aerosol…In the bioterrorist setting aerosols could be disseminated…by direct delivery into ventilation or air conditioning systems or via letters or parcels. Suicide attacks would be extremely effective for disseminating diseases such as smallpox." They added: "The infection is highly contagious. Modelling has confirmed the potentially disastrous effects on the general population if smallpox were to be released."

By mid-2002, less than a year after the September 1 terrorist attacks in the US, the Bush administration was reported to have ordered 209 million doses of smallpox vaccine, enough to increase its supply to cover every American citizen, at a cost of US$ 428 million. The British government was reported to have ordered 20 million doses, at a cost of 32 million pounds in case of a terrorist attack. (9) *The Times*, London, July 30, 2002), and has said it has enough to protect the entire population.

In April 2003, the British government set up the Health Protection Agency, a successor to the Public Health Laboratory Service. The HPA's Centre for Emergency Preparedness and Response is based conveniently adjacent to the Ministry of Defence laboratories at Porton Down, Wiltshire, where for decades scientists have been conducting research on biological and chemical agents, for defensive purposes. Staff at the centre coordinate planning for attacks involving smallpox, and other diseases including anthrax and plague. The HPA has nine regional centres, employing more than 2000 people.

In September 2003, another smallpox exercise was staged. Code-named *Global Mercury*, it was organized by 8 countries - Canada, France, Germany, Italy, Japan, Mexico, the United Kingdom and the United States - together with WHO and the European Commission. Conducted over a 56-hour period, the exercise aimed to evaluate the communications protocols between and among the countries in the face of an outbreak of an infectious disease. (10)

The training objectives of the exercise were to evaluate international communications generated as a result of the discovery of a case of smallpox; record international aspects of national smallpox plans for later analysis; review national and international smallpox communication control challenges; and develop lessons learned.

In the scenario, a traveler collapses at Vancouver airport with a suspicious looking rash. Quarantine officers issue an international alert. Soon the man's companion also becomes ill and confesses they are members of a terrorist group who have infected themselves with smallpox and dispersed to 14 countries just as their infectivity is peaking. Frantic communications ensue among the affected countries, but there are many problems, including cross-border coordination, language difficulties and equipment failures. However, the exercise was described by all participants as being well coordinated, realistic and valuable as a test of international communications. "Participants believe that similar exercises should be scheduled regularly, possibly annually."
In their report, the participants concluded: "Exercise Global Mercury proved a very positive experience from the point of view of the national controllers, evaluators and players. It helped to highlight existing gaps in the preparedness and response to bioterrorism at the international, national and state levels, but it also helped participants to realize both the importance and usefulness of carrying out exercises of this sort in order to achieve adequate levels of organization and coordination between institutions. Finally, rather than an end point, we should consider Exercise Global Mercury as a stepping stone for generating a useful, effective organization for responding in an adequate and timely manner to the threat of bioterrorism worldwide."

The World Health Organization found the Global Mercury exercise very useful in refining further the established internal response protocols in the post-SARS environment.

"The issues and problems arising during the conduct of the exercise served to confirm and reinforce the WHO role as the lead agency for information collection and dissemination. The exercise also helped us to audit and validate our internal working practices devised and implemented since the SARS outbreak, and to identify areas requiring enhancement, including augmentation and redirection of human, communications and logistical resources for response to a global health event."

In an article entitled *Smallpox and bioterrorism*, published in the *Bulletin of the World Health Organization, 2003 (11)*, Hugh Pennington, of the Department of Medical Biology, Aberdeen University, said growing large amounts of the virus, while not very difficult, would be a much more challenging task than preparing weapons-grade anthrax, which would be hugely more stable in the environment. There was no unequivocal evidence that of smallpox exhaled by patients could carry infection further than a few metres.

“None of these factors favour smallpox as a weapon of mass destruction,” he said. “but none of them rule it out as a weapon that – even if lethal to only a few – is still so feared that even a small deliberate release would cause enormous panic and have a political impact totally out of proportion to its size.”

He went on: “The measures taken in the US and the UK will undoubtedly recreate systems that would control an outbreak caused by a deliberate release of the virus. Awareness of contingency plans may even reduce the likelihood of such an event by discouraging possible perpetrators. By raising public confidence in the ability of government agencies to protect public health, panic may be averted as well.”

In late 2004, against a background of growing concern expressed by countries, the WHO called together its Ad Hoc Committee on Orthopoxvirus Infections, which in its subsequent report, published in December, 2004, proposed the establishment of a global smallpox vaccine reserve. (2)
The proposal was based on the principle of the sharing of supplies and resources during epidemic emergencies, and acknowledged the leadership role of WHO, through its enhanced epidemic alert and response activities, in the direct delivery of interventions to affected areas.

"Such a vaccine reserve would be a rational way to enhance international response capacity…Having such a reserve could also serve as a global deterrent against use of the smallpox virus in a biological attack," the report said. It went on:

"The health consequences of such an event could be especially serious for several reasons. Smallpox was a severe disease with high fatality and no cure. As most countries have not experienced endemic smallpox for several decades, lack of clinical familiarity with signs and symptoms increases the likelihood that early cases will be missed.

"The long incubation period and contagious nature of smallpox facilitate rapid international spread. Population immunity following mass vaccination during the eradication era has waned, leaving much of the world's population vulnerable.

"The greatest fear is that in the absence of global capacity to contain an outbreak rapidly, smallpox might re-establish endemicty, undoing one of public health's greatest achievements. All these concerns have prompted consideration of rational measures for increasing global preparedness to respond to a smallpox emergency."

The global vaccine reserve proposal has two components that are intended to give WHO rapid, flexible access to vaccine supplies. The first is the maintenance of a strategic vaccine stock by WHO in Geneva for emergency use after confirmation of a smallpox outbreak. This would involve doubling the existing stock of 2.5 million doses of vaccine. As of now, an additional 1.3 million doses have been ordered.

The second component consists of vaccine stocks amounting to 200 million doses pledged to WHO by countries from their own national stocks. This is the same amount as the stockpile recommended by WHO after the certification of smallpox eradication. Pledged stocks - 31 million doses as of today - would remain under the control of the donor country, and held in its territory, until needed. At that point, donated vaccines would be delivered to recipient countries by or on behalf of WHO.

To strengthen global preparedness further, WHO is encouraging those of its Member States with vaccine-production capacity to reserve standby capacity for the manufacture of smallpox vaccines. Ideally, at least two such facilities, each able to produce a minimum of 20 million doses, would be identified globally.
In its 2004 report, *Public health response to biological and chemical weapons*, WHO said the development, production and use of biological weapons pose "serious hazards to those who would seek to use them... Even so, the magnitude of the possible effects on civilian populations of their use or threatened use obliges governments both to seek to prevent such use and to prepare response plans, which can and should be developed as an integral part of existing national-emergency and public-health plans."

The report continues: "Public health authorities, in close cooperation with other government bodies, should draw up contingency plans for dealing with a deliberate release of biological or chemical agents intended to harm civilian populations. These plans should be consistent with or integral with existing plans for outbreaks of disease, natural disasters, large-scale industrial or transportation accidents, and terrorist incidents."

The report points out that WHO can provide technical support to countries "in developing or strengthening preparedness for, and response to, the deliberate use of biological and chemical agents to cause harm."

Preparedness should be based on standard risk-analysis principles, and can be markedly increased in most countries by strengthening the public health infrastructure, and particularly public health surveillance and response. Measures should be taken to this end, the report says. It adds that managing the consequences of a deliberate release may demand more resources than are available, and international assistance would then be essential.

This and other related reports and information can be found on the "Preparedness for Deliberate Epidemics" section of the WHO web site.

In particular, there is a link describing the WHO Global Outbreak Alert and Response Network (GOARN). This is a technical collaboration of existing institutions and networks that pool human and technical resources for the rapid identification, confirmation and response to outbreaks of international importance. The Network provides an operational framework to link this expertise and skill to keep the international community constantly alert to the threat of outbreaks and ready to respond.

In the event of the intentional release of a biological agent, WHO's global alert and response activities and operational framework together with the technical resources of the Network would be vital for effective international containment efforts in responding to potential use of biological agents.

In an article in The Times in August 2005, the head of Emergency Strategic Planning, HPA, Dr Gordon MacDonald said: “In the event of a biological release, we would begin to see a picture emerge in the same way as we would monitor, for example, a flu outbreak.
"We have systems in place for GPs to report people displaying certain symptoms…the Department of Health’s Emergency Operations Centre in London would then coordinate a response based on the analysis of pathogens at the labs here…We then initiate a programme of tracing people with whom victims have come into close contact. People most closely exposed are treated with the relevant medicines, while we give prophylactic vaccines to stop the disease spreading… We are not saying there might not be fatalities, but we could prevent any widespread disaster.” (13): *The Times* August 24, 2005).

To conclude, while opinions inevitably vary about the likelihood of a smallpox attack or the scale of its impact should one occur, it is clear that the risk of such an attack is taken very seriously indeed by many countries including the US, the UK, France and Japan, and by organizations such as WHO.

As a result, elaborate exercises are continuously being planned and staged to test national and international responses, and WHO plays a central role in organizing a global vaccine reserve, a global information network, and in providing countries with technical expertise.

We all hope it never happens. If it does, let us also hope that the consequences are no worse, and perhaps even better, than described by Dr Nigel Lightfoot, director of the HPA’s Emergency Response Capability. In the same article in *The Times* last August, he said the HPA had carried out many simulations of an attack in various parts of the UK:

“From each exercise we’ve learned new lessons and implemented them. We are improving all the time, but if you were to ask are we ready, I would say yes. We shouldn’t be complacent but it is important for the public to realise that while there would be deaths, as there would be in a conventional attack using explosives, there would not be the kind of widespread catastrophe that they might imagine.”

References:


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(4) White House press statement


(6) *Nature* 399, 628 - 629 (17 June 1999); doi:10.1038/21287)
(7)  http://www.upmc-biosecurity.org/pages/events/dark_winter/dark_winter_slides.html


(9) *The Times*, London, July 30, 2002

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(13) *The Times*, London, August 24, 2005