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Viruses as agents of mass destruction

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Abstract
Recent events in the US, with the release of Anthrax Bacillus from as yet unknown sources, have for the first time in most people's lifetime focussed the world's attention on the threat of biological warfare. However, such attacks are not new. From time to time throughout history peoples and governments around the world have used microorganisms as efficient and cost-effective weapons of mass destruction. Starting in a rather crude but effective way, the Greeks and Romans deposited dead animals into their enemies' drinking water. Later dead soldiers were added to this, and the technique was further refined in Medieval times when bodies of people who had died of infectious diseases were catapulted into towns under siege.

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Once the true nature of microorganisms became clear in the nineteenth and early twentieth centuries, the ability to grow large stocks of bacteria and viruses meant that biological warfare assumed global significance. Although there are no clearly documented incidences of the use of biological warfare during World War I, the threat was fully appreciated, and accusations, counter-accusations and denials abounded. Hence the 1925 Geneva Protocol prohibited the use of biological methods as well as poisonous gases in warfare; but it did not ban their further development [1].

In 1929 the Russians set up a biological warfare research station north of the Caspian Sea, prompting Britain, Japan, the USA and Canada to do the same. The Japanese developed the most extensive programme, and in the years leading up to and during World War II, they used human subjects in open field trials to test out their lethal agents including the bacteria causing plague, cholera, glanders and typhus. Manufacture continued in some countries until The Biological and Toxic Weapons Convention came into effect in 1975. This certainly reduced the threat, but did not entirely eliminate it, and the problem of treaty verification has continued ever since [2].

In the modern world the threat of biological warfare comes mainly from terrorist groups and third world dictators. For them biological weapons have many advantages over their conventional counterparts, being cheaper and relatively easy to prepare. Although new restrictions are in place, seed cultures of many dangerous microorganisms can still be obtained relatively easily from national collections. And since researching and preparing vaccines (defensive research) is a legitimate reason for growing microbes on a large scale, biological weapons factories (offensive research) can masquerade as vaccine production plants. Clearly, Iraq is a case in point; six such facilities are known to have existed, including the Daura Foot and Mouth Disease Vaccine Facility at Al Manal. In 1991 when Iraqi troops occupied Kuwait, it was well known that they had a stockpile of weapons laden with biological agents including 200 bombs and 25 ballistic missiles. Combat troops in Operation Desert Storm were vaccinated, provided with protective equipment, and given prophylactic antibiotics. Thankfully, in the event, none of these were required [3].

Microorganisms are ideal for selective attacks on individuals or for targeting large metropolises.

They can be smuggled undetected through all traditional security devices, and tiny volumes can kill huge numbers of people. Furthermore, since they are invisible, odourless, tasteless and have a delayed action, so they can be released into the air without immediate detection. A major biological attack would place untold strain on medical services which are not designed to cope with such an incident. As we have no previous experience dealing with this type of attack, it is likely that panic and psychological trauma would lead to total confusion [4].

Many different organisms have been tested for their potential as agents of biological warfare, including bacteria which cause anthrax, TB, typhoid, plague, cholera, gas gangrene. Candidate viruses include the haemorrhagic fever viruses, like Ebola, and smallpox. The remainder of this review will focus on these two organisms.

Smallpox

Smallpox virus was probably the first microbe to be used as a weapon of mass destruction. It is likely that deliberate release of smallpox virus occurred on several occasions during the North American Indian Wars, but the best documented incident was in 1763. At the time Indian scalping-parties were devastating European settlements in the area surrounding Fort Pitt (now Pittsburgh) causing widespread fear and panic. Sir Jeffrey Amherst, British Commander-in-Chief in North America, knowing that troop reinforcements would not be forthcoming, feared that the whole of Western Pennsylvania would soon be lost. In the knowledge that the Indians were particularly susceptible to smallpox, he authorised smallpox-contaminated blankets to be distributed among the Native American tribespeople [1].

Until the twentieth century smallpox was a killer on a world-wide scale. The virus spread rapidly in large and crowded cities causing devastating epidemics. Case fatality rates reached 30%, or even higher in populations who had not previously encountered smallpox. The virus spread from person to person primarily through the air via droplets from the oropharynx; more rarely from direct contact with materials contaminated with pock fluid or scabs. In most communities smallpox epidemics occurred regularly, and since nearly all adults were immune, children were the main victims. However, unlike the other air-borne childhood infections (such as measles, mumps, chickenpox), smallpox tended to spread within households rather than in the population at large. This was probably due to the fact that sufferers only became infectious when the rash appeared, by which time they were likely to be confined to bed.

Inhaled virus particles infect cells of the upper respiratory passages, and after an incubation period of 12-14 days victims develop high fever and malaise with head- and back-aches. The characteristic pustular rash appears 1-2 days later, beginning in the mouth and pharynx and thereafter spreading to the face, arms, trunk and legs (see figure). The pustules begin to crust after 8-9 days and eventually the scabs separate leaving pitted scars, particularly on the face [5].

From the point of view of the aggressor, one of the main features of smallpox which make it a desirable agent for biological warfare is the fact that it remains infectious for relatively long periods of time, particularly in cold, damp conditions. This means that it could be packed into

Effects of smallpox

war-heads of guided missiles and sent to its destination still in a viable condition. Also, since smallpox was eradicated in 1977, almost half of the World's population is non immune and would by now be susceptible. Furthermore, the amount of protection afforded by a vaccination given over 20 years ago is unclear. The infectious dose of virus is thought to be very low (1-2 virus particles), and so disease would occur in almost everyone who became infected. In addition to this, although the threat of a deliberate smallpox release is well recognised by governments and stocks of vaccine have been retained for this eventuality, in reality it would not be possible to vaccinate an entire population in time to prevent an epidemic spreading, probably on a world-wide scale.

Ebola Haemorrhagic Fever

Viral haemorrhagic fever is a syndrome which can be caused by a number of RNA viruses from different virus families. The syndrome characteristically begins abruptly with a high fever, headache, malaise, myalgia, fatigue, diarrhoea and bleeding. Increased vascular permeability resulting from viral infection of vascular endothelium initially causes petechial haemorrhages, which progress to generalised bleeding into mucous membranes and internal organs. Depending on the particular organs affected, patients develop neurological, pulmonary and/or hepatic features, with eventual hypotension, cardiovascular collapse, shock and renal failure. Disseminated intravascular coagulation is another prominent feature, and with no specific treatment to offer, mortality is very high.

Ebola virus was first isolated from an outbreak of haemorrhagic fever in Yambuku, a remote jungle village in Northern Zaire, in 1976. However, it is probable that the virus had caused localised outbreaks in rural Africa prior to this time, and several subsequent outbreaks have been documented. On each occasion the virus has infected man from an unknown source, and this suggests that there must be a reservoir of infection, probably an animal in the rain forest which carries the virus as a harmless passenger. Until this animal is identified sporadic, unpredictable outbreaks will continue to occur.

The first outbreak of Ebola was typical. The index case was a school teacher who had just returned from a trip through the bush when he became unwell with fever and malaise. He went to the local mission station, where the Belgian nuns assumed he had malaria and gave him an injection of antimalarials. As was their practice, they then used the same needle throughout the day to inject others. By the time the school teacher died a few days later there were many other cases, including his family and several of the nuns. In all 318 people contracted the disease and 280 died. The outbreak was only brought under control when the necessary control measures were implemented.

Ebola is not endemic in the human population, and therefore any outbreak requires an initial infection, probably through a bite from the animal which harbours the virus naturally. However, once the virus has crossed the species barrier and infected man, it can spread from person to person very effectively by direct contact. Patients are highly infectious since all body fluids contain large amounts of infectious virus. Thus in the Yambuku outbreak the virus spread via a contaminated needle to other patients and through routine contact and nursing procedures to the nuns and family members.

As a weapon of mass destruction Ebola virus certainly has its attractions, in particular it's high infectivity, the devastating nature of the disease, the high mortality, and the lack of preventive or therapeutic measures. But although devastating, Ebola outbreaks generally remain localised. This is because the virus is spread by direct contact and not by aerosol, and the short incubation period (may be only 4 days) and severe symptoms prevent patients travelling far from the site of infection. Thus once the necessary isolation precautions (strict barrier nursing) are in place, it is relatively easy to bring the outbreak under control.

Conclusions

Biological weapons are primarily designed to destroy all vital activity but not necessarily to wipe out the whole human race. In this regard, smallpox, while it would certainly incapacitate,

would probably not kill all those infected because of our inbuilt resistance which developed and strengthened over the centuries when the virus was rife. We have no such inbuilt resistance to Ebola, but a world-wide epidemic of this virus would be very difficult to engineer because of its localised method of spread.

After the world-wide elimination of smallpox, the World Health Organisation (WHO) recommended that all laboratories destroy their stocks of the virus, and two WHO reference laboratories were set up: The Institute of Virus Preparations in Moscow, Russia, and the Centre for Disease Control in Atlanta, USA. These remaining stocks were due to be destroyed by the end of the twentieth century, but were in fact retained for further research when the potential threat was realised. According to a former Deputy Director of the Soviet Union's Civilian Bioweapons program, smallpox virus from these stocks has been used to grow up large quantities for use in bombs and missiles. And, to end this review with the most frightening information (hopefully only a rumour), work was apparently underway to produce more virulent and infectious strains, perhaps even a hybrid combining the worst features of Ebola and smallpox. With the break up of the Soviet Union there are now fears as to whose hands these potentially highly lethal weapons may fall into [5].

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Some of the material in this review is contained in the author's book, The Invisible Enemy: A Natural History of Viruses, OUP, 2000.