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BIOTERRORISM: WHAT IS THE REAL THREAT?

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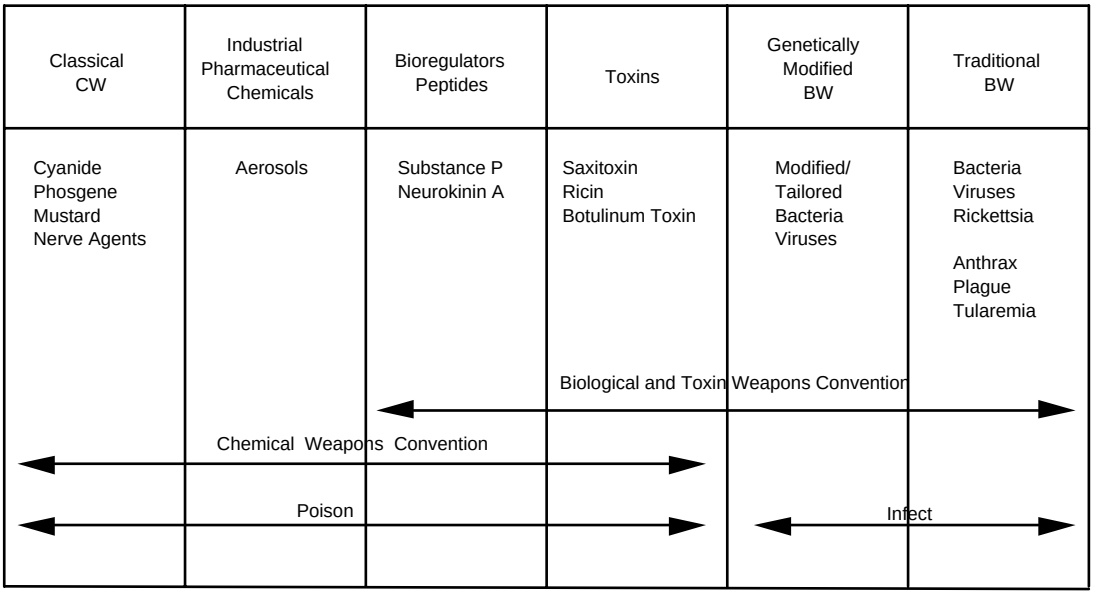
1. Introduction

The latest report *Mapping the Global Future* on US national security by the National Intelligence Council suggests that a major threat to the country right through to 2020 will be a terrorist biological weapons attack.[1] Given the recent intelligence failures concerning biological weapons in Iraq, it might be considered that there are reasonable grounds for suspicion about that conclusion. This paper attempts to answer the question of what the real threat of bioterror is by reference to the open scientific literature. Section 2 of the paper discusses the nature of the agents of concern and in section 3 various potential attack scenarios are reviewed. The overall conclusion is that there are real threats from terrorists with the capability to carry out a range of attacks with biological agents today, but that these threats do not include the one most commentators probably have in mind when they discuss the issue – a weapons of mass destruction scale of attack on people. In the final section of this paper the implications of the analysis for the risk questions we have been posed are addressed.

2. Biological Agents

Biological weapons are best regarded as part of a biochemical threat spectrum that ranges from so-called classical (lethal) chemical weapons through poisonous industrial chemicals and mid-range agents such as toxins and bioregulators to traditional biological agents and genetically modified agents (see Figure 1). Within this spectrum biological agents include well-known pathogens like anthrax, the toxins produced by bacteria such as botulinum toxin, and normal signalling molecules of living organisms (bioregulators) which, in unusual amounts, can cause massive disruption of normal physiology.

Figure 1: The biochemical threat spectrum



When concerns about possible biological weapon attacks grew in the 1990s, the Centers for Disease Control and Prevention (CDC) in the United States were asked to review what the most dangerous threats to the civilian population were. They made their judgements using criteria such as:[2]

> "1. public health impact based on illness and death;
>
> 2. delivery potential to large populations based on stability of the agent, ability to mass produce and distribute a virulent agent, and potential for person-to-person transmission of the agent;
>
> 3. public perception as related to public fear and potential civil disruption; and
>
> 4. special public health preparedness needs based on stockpile requirements [for example vaccines], enhanced [disease] surveillance, or diagnostic needs."

Using these criteria, a list of agents posing the greatest threat to civilian populations was drawn up. The most dangerous of these were designated Category A agents and included such things as smallpox and anthrax (see Table 1: CDC Category A agents).

Table 1: CDC Category A agents*

Biological agent(s)	*Disease*
Variola major	Smallpox
Bacillus anthracis	Anthrax
Yersinia pestis	Plague
Clostridium botulinum (botulinum toxins)	Botulism
Francisella tularensis	Tularemia
Filoviruses and Arenaviruses (e.g. Ebola virus, Lassa virus)	Viral haemorrhagic fevers

* From reference 2

The CDC also produced a list of Category B and C agents which, though not as dangerous as those in Category A, nevertheless presented a considerable risk. However, when the United States National Institute of Allergy and Infectious Diseases (NIAID) began its programme to develop countermeasures, it used a slightly more developed listing for its research agenda in which the individual agents were organised into various groupings (see Table 2: Category B and C agents).[3] The broad grouping of agents in the B and C categories shown in Table 2 is obviously much easier to understand than if the individual agents had just been presented in a very long list.

Table 2: NIAID Category B and C priority pathogens*

Group	*Biological agent (examples)*	*Disease/Common name*
INHALATION BACTERIA		
	Brucella species	Brucellosis
	Burkholderia pseudomallei	Melioidosis
	Burkholderia mallei	Glanders
	Coxiella burnetii	Q-fever
	Rickettsia prowazekii	Typhus
	Rickettsia rickettsii	Rocky Mountain spotted fever
ARTHROPOD-BORNE VIRUSES		
Alphaviruses	Venezuelan equine encephalitis	VEE
Flaviviruses	West Nile virus	WNV
	Yellow fever virus	YF
Bunyaviruses	California encephalitis virus	CE
TOXINS		
	Ricinus communis	Ricin toxin
	Clostridium perfringens	Epsilon toxin
	Staphylococcal enterotoxin B	SEB
FOOD- AND WATER-BORNE PATHOGENS		
Bacteria	*Salmonella typhi*	Typhoid fever
Viruses	Caliciviruses	(e.g. Norwalk)
Protozoa	*Toxoplasma gondii*	Toxoplasmosis
EMERGING INFECTIOUS DISEASES		

	Multi-drug-resistant tuberculosis	MDR-TB

* From reference 3

There are clearly many potential pathogens and toxins that could be used in various kinds of biological attacks against people. The essential characteristics of the more important of these agents will be reviewed and some of the lesser known bioregulators will be considered. At the end of the section some of the main agents that could be used to attack staple and economically valuable crops and animal husbandry will also be briefly reviewed.

Anti-personnel BW agents

The organisms listed as Category A and also, to some extent, those in Categories B and C of Tables 1 and 2 obviously include those which were weaponised in the offensive biological warfare programmes of the last century. It must be appreciated that the agents weaponised were not chosen by chance but because they had certain characteristics useful to an attacker.[4] Some of these characteristics are shown in Table 3. Thus for an attacker it clearly makes sense if the agent produces its effect at a low dose and if the target population cannot be protected via immunity or medical treatment.

Table 3: Characteristics useful in a biological weapons agent

1. An agent should produce a certain effect consistently.
2. The dose needed to produce the effect should be low.
3. There should be a short and predictable incubation period.
4. The target population should have little or no immunity.
5. Treatment for the disease should not be available to the target population.
6. The user should have the means to protect troops and civilians.
7. It should be possible to mass produce the agent.
8. It should be possible to disseminate the agent effectively.

9. The agent should be stable in storage and transportation in munitions.

A further complication arises, of course, because not all agents would kill. Some would certainly have very high rates of mortality (such as inhalation anthrax if not quickly treated) but others, some of which were in fact weaponised, would cause incapacitation rather than death in most victims. One such incapacitant is Staphylococcal enterotoxin B (SEB), which was extensively studied in the US offensive programme. Such an incapacitant might be considered useful, for example, if enemy troops were mixed with civilians or if the intention was not only to disable enemy forces but also to overload their capacity for dealing with the injured.

Finally, it is crucial to differentiate between agents which are not contagious person-to-person after first use and those which are. Clearly, agents such as smallpox which are highly contagious in this way are much more difficult for a defender to handle. From an attacker's stance, such agents could be expected to have greater effects, but their use carries with it the potential drawback of creating uncontrollable epidemics.

From a military point of view, therefore, individual agents are viewed against a certain matrix of possibilities (Table 4). Against that wider background, it is possible to see why certain agents have been and are so much favoured, in spite of the vast range of available pathogens known to cause illness in humans. For simplicity, we will deal first with Category A agents and then with some of those in Category B.

Table 4: A military classification of agents

Principal characteristics	*Examples*	*Militarily significant features*
Potentially contagious from first victim		
Incapacitating	Influenza virus	Limited use because of possible lack of control
Lethal	*Yersinia pestis* (plague)	
Not contagious from		

first victim

Incapacitating	*Coxiella burnetii* (Q-fever)	Decay rate in air; incubation
Lethal	*Bacillus anthracis* (anthrax)	period; length of illness etc.

Category A agents

Anthrax *Bacillus anthracis*, the causative agent of anthrax, is a natural pathogen of grazing mammals. Until the development of effective vaccines against the disease for these animals it was a major cause of fatal illness and it continues to kill domestic and wild animals where vaccination programmes are not maintained, for example during the disruption caused by warfare. The environmentally-resistant spore form of the organism is found in the ground where infected animals have previously died. Grazing animals can therefore ingest the spores or inhale them. Once inside an animal's body the vegetative form of *Bacillus anthracis* develops, grows and multiplies and produces several toxins which together kill the infected animal. When the animal dies and its body decays, nutrients run out, oxygen becomes freely available and the environmentally-resistant spores form again and can remain for long periods in the soil ready to infect other animals. With these characteristics, it is not surprising that in the past anthrax was also known as 'woolsorter's disease' in England since it was a hazard for workers involved in processing fleeces and wool.

Humans can contract three different forms of anthrax disease. If the spores get into a skin cut then cutaneous anthrax can develop. Eating infected meat can result in gastrointestinal anthrax. In a bioweapons attack, however, the aim would be to spread the spores on the air so that they were taken into the lungs to cause inhalation anthrax. This disease develops over a period of one to seven days and is deadly if untreated. The disease begins with non-specific influenza-like symptoms that make early diagnosis difficult, but rapidly worsens with many dangerous symptoms appearing. Death rates for untreated cases are at least 90 per cent.

Anthrax is not contagious person-to-person so there is no need to quarantine those infected. Various means can be used in the laboratory to diagnose the presence of

Bacillus anthracis in the body and antimicrobial therapy is effective if begun early enough. There is also a vaccine available in the West for people at risk of contracting the disease, but it requires a series of injections over time. It is uncertain whether it would be effective against a heavy aerosol inhalation assault. The dose needed to infect someone is also the subject of great uncertainty. The standard measure used is the dose required to infect 50 per cent of a population and this, the LD_{50}, can only be estimated from animal experiments.

Anthrax has been a standard choice for those interested in causing disease in animals and people. It was used in the German anti-animal campaigns of the First World War and was weaponised as a retaliatory anti-animal weapon by the British in the Second World War. It was later weaponised as an anti-personnel agent by both sides in the twentieth century east-west cold war. More recently, of course, anthrax has come to public attention following the deaths caused by leakage of the agent from a Soviet military facility in Sverdlovsk in 1979 and the anthrax letter attacks in the United States in late 2001.

As will become apparent, preparing an agent like *Bacillus anthracis* for use in an airborne biological weapons attack is not an easy technical task. It certainly appears to have taken years of experimentation to perfect in the state offensive biological weapons programmes of the last century. Such 'weapons grade' material would have had a very high concentration of spores, uniform particle size, low electrostatic charge and would have been subject to other treatment to reduce clumping of the material. There is, however, a prior problem for the would-be attacker. Because of the natural processes of mutation and geographical isolation in different environments, there are many different strains of anthrax in various parts of the world and these have different levels of lethality for humans. The first problem for a weaponeer, therefore, would be to find a virulent strain of anthrax.

It is a little-known fact that before their unfortunately successful attack on the Tokyo underground with sarin nerve gas in 1995, the Aum Shinrikyo sect had attempted to use anthrax to attack their fellow citizens. It has been suggested that one of the reasons they failed in their biological weapon attacks was that they did not have access to a lethal strain of the organism.

Smallpox There are two kinds of smallpox. That caused by the virus *Variola major* commonly kills 25 to 30 per cent of those infected while infection caused by the vaccine strain *Variola minor* has a death rate of 1 per cent or less. Closely related diseases such as cowpox and monkeypox exist, but smallpox appears to be uniquely an infection of humans. Smallpox caused by *Variola major* is an acute viral disease usually contracted by breathing in airborne droplets which carry the virus. In the past it seems likely that as many as 90 per cent of people exposed contracted the disease. It affected people of all races and did not discriminate between young and old or male and female. The infection had only two possible outcomes - death or very long-lasting immunity. With no known animal reservoir, the disease could only exist as an active infection causing waves of epidemic disease at different times and places in history.

With these characteristics, it seems unlikely that the disease could have existed in the sparse populations of early human history. However, it is possible that it was present in ancient Egypt. Epidemics which might well have been smallpox also raged across the Roman Empire in the second and third centuries AD, but the descriptions of the victims are not clear enough to be sure. Certainly by the ninth century AD though there are clear descriptions by a physician in Baghdad which leave no doubt that he differentiated between measles and smallpox. Historically, therefore, the populations of the Old World, in Europe and the Middle East, were accustomed to smallpox as a disease by the sixteenth century but as these peoples began to expand and migrate to the New World and Asia, they encountered populations which had had no contact with the disease. In those circumstances the effects of smallpox could be devastating and Europeans knew enough about the disease - even though they did not understand it scientifically - to use it for hostile purposes against the North American Indians.

Our modern techniques of vaccination had their origin at this time in efforts to prevent smallpox. The practice of *variolation* arose in which people were deliberately infected by obtaining material from an active case and scratching it into the skin. Practiced people who did this expertly were said to be able to keep the disease in a mild form with a very low consequent death rate. It was Edward Jenner in England, of course, who noticed that variolation failed to produce the symptoms of smallpox in people who had previously suffered the mild disease cowpox. He then vaccinated people with cowpox and showed that later variolation reliably failed to produce the smallpox disease.

Jenner published his findings in 1798 and vaccination was rapidly taken up around the world. Eventually, a campaign organised by the World Health Organisation eradicated the disease in 1979.

After the eradication campaign it was intended that stocks of the virus be kept in secure storage in just two places - the United States and the Soviet Union. Unfortunately, if the accounts of some of those involved are to be believed, as part of its illegal offensive biological weapons programme the Soviet Union weaponised massive amounts of smallpox as a lethal anti-personnel agent. Since very few people now have effective protection from vaccination against smallpox (having been vaccinated long ago or never having been vaccinated at all), an outbreak of this very contagious lethal disease could be devastating.

The infective dose for smallpox is not known, but is thought to be just a few virions lodged in the oropharyngeal or respiratory mucosa. At the end of an incubation period of 7-17 days, the patient experiences a high fever and is prostrated with head- and backache. A rash then appears which, within a couple of days, turns vesicular and then pustular. The pustules are deep in the skin and leave pitted scars if the patient survives. The patient is most infectious to others for 7-10 days after the rash appears. Although 90 per cent of cases follow this characteristic pattern, there are two other forms of the disease. In haemorrhagic smallpox there is widespread haemorrhaging into the skin and mucous membranes and the patient invariably dies about five days after formation of the rash. In the frequently fatal malignant variant, the pustules do not appear and the skin takes on a reddish-coloured rubbery form.

Diagnoses of smallpox in its characteristic form were made from the nature and distribution of the rash. Haemorrhagic and malignant smallpox were much more difficult to diagnose. Just one case of smallpox now would, of course, be the cause of a worldwide emergency. At present, all the treatment available to someone with smallpox would be supportive care and antibiotics to prevent secondary infection. There are currently no antiviral agents which are effective against smallpox but vaccination administered within a few days of exposure may prevent or ameliorate the disease. A major problem arises from the known difficulty of preventing smallpox transmission in hospitals. Not only is the virus capable of airborne infection, perhaps for 24 hours, but it can remain viable on laundry from infected people for extended periods of time.

Furthermore, though many people were safely vaccinated in the past, there is always the danger of major complications for a few.

Plague The non-motile, non-spore-forming bacterium *Yersinia pestis* is the cause of plague. Although it can remain viable for some days in water or moist soil, it is killed within a few hours by direct sunlight. Plague is still a problem disease in some parts of the world and there were outbreaks of plague in humans in Africa, Asia and South America during the 1990s.

Yersinia pestis is a natural pathogen of rodents such as the black rat, *Rattus rattus*, and the brown rat, *Rattus norvegicus*. The pathogen is transmitted between rodents and other animals through the bites of infected fleas. Major outbreaks of plague can occur in cities when many rats are infected and the disease spreads to humans. The normal human disease is bubonic plague, caused when the pathogen enters the body via regurgitation during a flea bite or through broken skin. If the lungs become infected, then a much more deadly, pneumonic, form of plague develops. It is this pneumonic form that would result from an aerosol attack if the agent was used in a biological weapon. Because there are natural reservoirs of the disease in rodent populations around the world, because it can be mass produced and disseminated, because there is a high fatality rate in untreated cases and because pneumonic plague is contagious through airborne spread, it is readily apparent why there is great concern about the possible use of *Yersinia pestis* as a biological weapons agent.

The Black Death is the name given to the great pandemic of plague which occurred in Asia, the Middle East, North Africa and Europe in the middle of the 14th century. With the centuries that have elapsed, it is difficult today to judge the death rates during the pandemic, but historians generally agree that it was in the range of 30 to 50 per cent of the population. The effects of this mortality rate on a society that had not suffered such an outbreak for centuries was enormous. The available control measures were largely ineffective against a disease whose cause was unknown, and there was considerable social disruption and change as a result of the pandemic. The Black Death was, in fact, the peak of a second pandemic of plague. The first pandemic occurred in the mid-sixth century AD and the third began in China in 1855, killing some 12 million people in India and China alone.

People develop symptoms of bubonic plague between two and eight days after being bitten by an infected flea. They suddenly experience fever and weakness and the characteristic bubos (swollen tender lymph nodes) appear a day or so later. A small number of people do not develop bubos but have primary septicaemic plague. Septicaemia can also develop following the appearance of the bubos. The name 'Black Death' may have derived from the appearance of gangrene in the nose, digits and other extremities following the onset of septicaemia. Secondary pneumonic plague may also develop in a minority of people suffering from bubonic plague. As mentioned earlier, following an aerosolised biological attack people would exhibit primary pneumonic plague and there would be no tell-tale bubos to aid diagnosis nor, unfortunately, any widely-available, rapid, diagnostic tests.

Until 1999 there was a licensed vaccine available in the United States but its production has been discontinued. In any case, it apparently did not prevent or ameliorate the development of primary pneumonic plague and this is probably also true for other vaccines available around the world. Vaccination during an epidemic would not be of much help anyway as immunity takes a month to build up. It *is* possible to treat people suffering from plague successfully with antibiotics, but if this treatment is not begun within 24 hours of the onset of symptoms the fatality rate remains very high.

Under modern conditions the outbreak of a new plague pandemic seems improbable. It should not be forgotten, however, that Japan tried to use plague-infected fleas to cause an outbreak amongst the Chinese during their mid-20th century offensive biological weapons programme, or that the Soviet Union later succeeded in mass-producing *Yersinia pestis*. Furthermore, it is clear that antibiotic resistance can be built into the organism using modern techniques of genetic engineering. Plague well deserves its place in the Category A list of potential biological threat agents.

Botulinum toxin Botulism is caused by the extremely potent toxin produced by the bacterium *Clostridium botulinum*. Botulinum toxin is, in fact, the most poisonous substance known to man. It has been estimated that, if evenly dispersed and inhaled, a gram could - theoretically - kill more than one million people. *Clostridium botulinum* is a spore-forming bacterium whose spores are found naturally in the soil. The toxin is produced by the growing (vegetative) form of the bacterium when it is in oxygen-limited

environments such as a wound or in canned food which has not been properly sterilised to kill the organism.

Seven distinct antigenic types of the toxin (A-G) have been recognised. This means that an antitoxin to the A type does not neutralise the B-G types and so on. Botulism in humans is generally caused by the A, B, E or F toxins. Types C and D have been shown to cause disease in other animal and bird species. The toxin is not absorbed through intact human skin but can enter through a wound or through mucosal surfaces such as those of the gut or lung. Distressing signs of the disease then follow rapidly within 12 to 72 hours of, say, eating contaminated food.

People suffering from botulism experience dysfunction of their motor nerves so, for example, they may have blurred vision and difficulty in speaking or swallowing. If not treated rapidly and effectively, they eventually die because general muscular paralysis also affects their respiratory muscles and they are unable to breathe. In the twentieth century botulinum toxin was soon recognised to be a potential lethal biological weapons agent. The Japanese tested its effects on prisoners in their offensive biological weapons programme, and because of concerns that Germany might use it against the Allies on D-Day, more than 1 million doses of botulinum toxoid vaccine were prepared. Curiously, the toxin has recently been licensed for treating certain medical conditions such as types of muscle spasm, and for cosmetic reasons to remove wrinkles.

The major concern is that aerosolised botulinum toxin might be used to cause widespread inhalation botulism, but contamination of the food supply could also result in a large number of cases for the medical services to deal with. Botulism is, unfortunately, easily confused with other diseases of the nervous system and laboratory tests which take days to complete are needed to confirm diagnosis. Modern medical care can greatly diminish the death rates from botulism; antitoxins are available and if administered early can limit the damage to the nerves. However, if damage does occur, the patients may require prolonged treatment, including feeding and mechanical ventilation, until their nervous systems recover. In theory, it would be possible to eliminate the hazard of botulinum toxin by mass immunisation but this is unlikely to happen, partly because of the scarcity of the required toxoid.

Tularemia The disease caused by the bacterium *Francisella tularensis*, tularemia, is much less well-known to the general public than the other potential

biological weapons agents in Category A. Yet it was an agent investigated by the Japanese and by both the United States and the Soviet Union in the last century. The bacterium is normally an infection of a wide range of wild animals and for that reason is known in different parts of the world as an animal fever, for example, rabbit fever. It also causes disease in humans, often through an insect bite.

Tularemia was first described as a potentially severe and fatal disease for humans in 1911. Large-scale human epidemics occurred in the 1930s and 1940s in Europe and in the Soviet Union, and the bacterium began to be recognised as a significant laboratory hazard for those working with it because of its extreme infectivity. There are two predominant sub-types of the organism with subtype A being much more virulent than sub-type B. We now know that it is one of the most infectious of the pathogenic bacteria with perhaps as few as 10 organisms being sufficient, if inhaled, to cause the disease in a human. Person-to-person transmission of the disease has not been documented. Although the bacterium does not form a spore, it can survive for weeks in moist soil, hay, straw and the like if temperatures are low.

Clinical manifestations of the disease vary with the route of entry and virulence of the organism. Infection through the skin, for example, usually produces an ulceroglandular form of the disease with an ulcer at the point of entry and swelling of the local lymph nodes. There is also an abrupt onset of fever, malaise and joint and muscle pains. Infection via an aerosol could produce a variety of symptoms such as pharyngitis or it might just be manifest as a systemic illness without such signs. An outbreak of this kind in a population would result from a successful biological weapons attack after about 3-5 days, and would be very difficult to distinguish initially from an outbreak of influenza or attack with a variety of other agents (see, for example, Q-fever below).

Vaccines are available to prevent tularemia infections and have been widely used in Russia since the 1930s. The development of better ones is hindered by the lack of detailed knowledge of the pathogenesis caused by the microbe. Antibiotics are effective against tularemia, but rapid confirmatory diagnosis is not simple. A source of much concern is that in both the Soviet and US offensive programmes antibiotic-resistant forms of the organism were studied. The overall mortality rate from the more virulent A strain is potentially as high as 60 per cent of untreated cases, so there is every reason for anxiety about this potential agent.

Viral haemorrhagic fevers (VHFs) The term viral haemorrhagic fever (VHF) refers to diseases which produce fever and bleeding as a result of infection by viruses from one of four different families (Table 5). The viruses are transmitted to people through contact with infected animals or by arthropod vectors. The course of the disease varies with each different virus, but there is still a great deal to be learned about their natural history and the pathogenesis they cause in humans.

Table 5: Some haemorrhagic fever viruses*

Family	*Virus*	*Disease*
Filoviridae		
	Ebola	Ebola haemorrhagic fever
	Marburg	Marburg haemorrhagic fever
Arenaviridae		
	Lassa	Lassa fever
Bunyaviridae		
	Rift Valley fever	Rift Valley fever
Flaviviridae		
	Dengue	Dengue fever
	Yellow fever	Yellow fever

* From reference 2

Of the 284 detected cases in the June 1976 outbreak of Ebola in the Sudan, 148 died - a 52 per cent mortality rate. In the subsequent September outbreak in Zaire there were 288 deaths out of the 318 cases - a 90.5 per cent mortality. A smaller outbreak in Zaire in 1979 resulted in a 66 per cent mortality rate. There were no substantial reported outbreaks through the 1980s until, in 1989, a shipload of monkeys from the Philippines, destined for the United States, was found to be infected. Sixty of the one hundred monkeys died but fortunately the outbreak was contained.

If the VHF viruses are considered as potential biological weapons agents, it is clear that some are not suitable. Dengue, for example, is not transmissible as a small-particle aerosol. Others certainly are the cause of great concern. In the Soviet Union's offensive biological weapons programme it was shown that just a few virions of Marburg were sufficient to cause infection and large quantities of this virus, along with Ebola and Lassa viruses, were produced. The United States investigated Yellow fever and Rift Valley fever viruses in its offensive programme. Rift Valley fever and the flaviviruses (Yellow fever etc.) are not transmissible person to person, but agents like Ebola can spread through close contact very effectively if special precautions are not taken.

There is, of course, an effective vaccine for individuals travelling to areas where Yellow fever may be present. However, this vaccine could not be used after a biological attack because the disease has a shorter incubation period than that needed for the development of antibodies and in any case, the vaccine is in relatively short supply worldwide. There is no licensed vaccine, even in the United States, against any other virus in the VHF group.

Filoviruses like Ebola and Marburg are extremely virulent in non-human primates and in man, and infection results in widespread damage to the viscera (such as liver, spleen and kidneys). However, the variable clinical picture that can result from infections with these viruses makes diagnoses very difficult. Confirmatory laboratory tests are available but cannot be completed within hours. The antiviral drug ribavirin may help in some cases, but the main treatment available is careful supportive medicine - which may not be possible if there are very many victims of an attack.

Studies have shown that viruses like Ebola, Marburg and Lassa can successfully cause infection in non-human primates when prepared in aerosols and inhaled into the lungs so there is every reason to believe that they could cause massive human casualties in a successful BW attack. Little wonder then that they are placed in the most dangerous - Category A - list of potential biological weapons agents.

Category B and C agents

As evidenced by the groupings of potential agents in the United States NIAID listing of Category B and C agents (see Table 2 earlier in this section) a wide range of different possibilities for attack were considered. The groups - inhalation bacteria, arthropod-

borne viruses, toxins, food-and-water-borne pathogens and even emerging infectious diseases - show just how different the mechanism of attack could be. In no sense can the threat from such agents be ignored. Indeed, a number of these pathogens were weaponised in the offensive biological weapons programmes of the last century. It is not possible to review in detail all the agents listed in Table 2 so some illustrative examples are presented here.

Brucellosis in humans results from infection by any of the four main species of *Brucella*. These bacterial species are normal pathogens of animals: *Brucella melitensis* infects goats; *Brucella abortus* infects cattle; *Brucella canis* infects dogs; and *Brucella suis* infects pigs. The cause of the disease was first worked out by David Bruce in Malta in 1887. He showed that the undulant (or Malta) fever prevalent among civilians and British troops on the island resulted from infection by *Brucella melitensis* originating from the island's goats. The bacterial cells are able to persist in the environment for weeks and human infections often result from eating raw animal products or drinking unpasteurized milk. In dried preparations the bacteria can remain virulent for years and infection by aerosol requires only a few organisms. Laboratory infections are therefore common among laboratory staff working with the organism, although person-to-person transmission is rare.

The incubation period for a brucellosis infection can be highly variable, usually between 5 and 60 days. Severe exposure would result in a shorter incubation period. Symptoms include an undulating fever, exhaustion, back and leg pains, headaches and so on. Without treatment, people usually recover after two to three months, but there can be cycles of remission and relapse over years and serious complications can result. Fatality rates are some 3 per cent or less, but the illness is debilitating and though antibiotic treatment can be a successful if begun early enough, no human vaccine is available to protect against the disease. With such characteristics, it is not surprising to find that *Brucella suis* was weaponised as an incapacitating agent in the US offensive biological weapons programme of the mid-twentieth century.

Q-fever Another pathogen weaponised as an incapacitant in the US programme was *Coxiella burnetii*. This causes so-called Q-fever in humans, the Q standing for 'Query' because of the initially uncertain nature of the disease. It was first identified in Australia and was initially recognised as an infection affecting abbatoir workers in

Brisbane. The scientific name of the organism honours Cox and Burnet, the scientists who made significant discoveries in the early work on the organism.

The pathogen is found in many wild animals as well as in livestock and its natural life-cycle includes transition through tick species. However, it is so infectious to humans in an aerosol and so stable in the environment that human infection usually occurs through inhalation of dust containing the organism. The clinical features of the disease begin after an incubation period of 18-21 days (again unless the dose is large when it becomes shorter) and include chills, fever, headache, muscle and chest pains. There can also be nausea, vomiting and diarrhoea. The mortality rate is less than one per cent, but the illness can persist for months. A vaccine is available in Australia and antibiotics can be successful if given early in the infection.

During the US offensive programme in the 1950s, members of the Seventh Day Adventist Church who did not wish to be conscripted into the armed forces could volunteer instead to be subjects for human testing of some biological warfare agents in what was called "Project Whitecoat." One of the agents studied in this way was *Coxiella burnetii* so there are good data on the infectivity of aerosols of this particular agent and every reason to believe that it would severely affect the health of a large percentage of those exposed to an attack. While it is not contagious and does not cause the high mortality of the Category A agents, Q-fever is obviously still a disease which could cause massive problems for a military organisation or a civilian population. Its causative agent well deserves its place in the Category B listing.

Venezuelan equine encephalitis (VEE) At the time when the US offensive biological weapons programme was in operation much more was known about bacteria than about viruses and so there was much more work done on bacterial than on viral agents. During the later cold war period we know that in the Soviet programme more attention was paid to viral agents. However, one viral agent, Venezuelan equine encephalitis (VEE) virus, was weaponised by the United States. This virus is on the NIAID Category B and C list in the arthropod-borne viruses group (Table 2).

Epidemics of VEE were first recognised in the 1930s and the disease is endemic in the central and northern parts of South America. The virus usually exists through a rodent-mosquito-rodent cycle but humans become infected naturally through the bite of infected mosquitoes when the disease spreads to an equine-mosquito cycle also. There is

no evidence of direct equine-to-human or human-to-human transmission. However, humans can be infected through an aerosolised agent and again it is clear that very few organisms are required to initiate the disease.

The disease manifests itself with an abrupt onset of influenza-like symptoms: severe headache, high fever, chills and muscle pains. It can also produce nausea, vomiting and diarrhoea. Most infections last 3 to 5 days and mortality rates are below one per cent. However, there can be major effects on the central nervous system with severe consequences for a few people. Fortunately, there are a number of vaccines available to prevent the disease in humans in affected regions of the world.

***Staphylococcus aureus* enterotoxin type B (SEB)** Although it was difficult to produce large amounts of many bacterial toxins at the time the United States, in its offensive biological weapons programme, did weaponise an incapacitating toxin in addition to the lethal botulinum toxin. This incapacitating toxin was *Staphylococcus aureus* enterotoxin type B or SEB as it became known. The five different types of staphylococcal enterotoxin are a frequent cause of food poisoning through improperly stored or cooked foods such as ham, processed meats, ice-cream and the like. Symptoms are usually nausea, vomiting and diarrhoea and normally occur within one to six hours of eating contaminated food. They are of relatively short duration - about 24 hours.

Inhalation of staphylococcal enterotoxin B causes a sudden onset of fever, headache, chills and a non-productive cough. The victim is likely to suffer these symptoms and be prostrated for up to five days and the cough can persist for weeks. The disabling dose for humans has been estimated to be very small in relation to body weight and the lethal dose to be at least 50 times greater. The toxin is known to trigger the release of massive amounts of cytokines (bioregulators) in the body which then produce the symptoms in the victim. It is readily apparent why SEB is on the list of Category B agents of concern.

BZ Another more direct interference with the body's chemical signalling system is caused by BZ - 3-quinuclidinyl benzilate. This is usually classed as a chemical incapacitating agent and appropriately, since it was weaponised by the United States during the cold war, is on one of the schedules of particularly dangerous chemicals subject to special international oversight in the Chemical Weapons Convention. BZ is one of a family of chemicals called glycollates and it interferes with the transmission of

information between nerve fibres. At particular types of synapses (junctions between the fibres), BZ blocks the receptor on the *post*-synaptic nerve fibre so that the synapse does not function and the signal is not transmitted. The Iraqis were said to have produced another glycollate named Agent 15. Such so-called *bioregulators* are also covered by the prohibition on toxins in the Biological and Toxin Weapons Convention.

Ricin Another toxin on the Category B list is ricin, a highly toxic glycoprotein which is found in the seeds (beans) of the widely-cultivated castor oil plant, *Ricinus communis*. Ricin can be dangerous if inhaled or ingested but does not cross intact skin. It acts by inhibiting protein synthesis in the body's cells and causes damage by killing the cells. At present the only treatment that can be given is supportive care and there is no vaccine available for human use. Ricin is a danger because it can be extracted relatively easily from castor oil beans. About one million tons of these beans are processed annually and ricin accounts for some five per cent of the residual waste. It is little wonder, therefore, that some of the terrorists arrested recently appear to have been trying to produce ricin since it is perhaps the easiest such agent to obtain in quantity.

Salmonellosis The importance of considering attacks other than with aerosolised agents is shown by events in Oregon, USA in 1984. On 17 September, the public health department there began to be notified of people falling ill with gastroenteritis after eating at restaurants in the small town of The Dalles. Because the affected people reported eating in salad bars, all salad bars were closed down on 25 September. It was eventually shown that at least 750 people had became ill with salmonellosis caused by the bacterium *Salmonella typhimurium*. There are many thousands of such cases caused by food contamination with the bacterium annually so nothing too unusual was suspected at the time. However, it was later discovered that the salad bars had been deliberately contaminated by followers of Bhagwan Shree Rajneesh.

The sect had purchased a large ranch in the region and was seeking to prevent people voting in a local election so that they could more easily gain permission for developments they wished to make on their land. Commune members were, in fact, just trialling a plan for making people ill on the forthcoming election day for county commissioners in November 1984. The sect had grown the bacteria in secret laboratories and then poured them onto items in the salad bars. Eventually, the FBI discovered vials

containing the bacteria on the sect's ranch and two members pleaded guilty and served prison sentences for their activities.

Though *Salmonella typhimurium* itself is not on the list of agents of concern, this criminal activity shows just why food- and water-borne pathogens such as *Salmonella typhi*, the cause of typhoid fever, and *Shigella dysenteriae*, the cause of bacillary dysentery, certainly are on NIAID's Category B and C priority list. Clearly, if the sect members had carried out widespread food contamination with a more virulent agent in a town, they could have caused many many more people to become ill - and they might well not have been detected as the perpetrators of the deliberate contamination.

Anti-agriculture biological warfare

The diversity of the anti-personnel forms of biological warfare should remind us that biological warfare need not only be directed against people. Microbial pathogens cause enormous problems in agriculture and some of these pathogens are clearly also suitable for deliberate use. Animal husbandry is particularly vulnerable, in part because it is often very intensive, with many animals kept in confined areas. It is also vulnerable because the animals reared are often from very limited genetic stock so that a large percentage of them could succumb to a single strain of pathogen. Finally, as is well known from disease outbreaks such as the recent Foot-and-Mouth disease (FMD) in the UK, the viral agents which cause disease in animal stocks are often particularly virulent.

Foot-and-Mouth disease is a very contagious disease of cloven-hoofed animals (cattle, pigs, sheep, goats etc). There are seven different serotypes of the virus and no cross immunity between these types. The disease can be highly lethal to young calves, but usually lethality is low. The problems lie in the serious production losses caused by the disease and, of course, in the measures that have to be taken to eradicate the outbreak. Natural infections have an incubation period of two to eight days. The symptoms of FMD are fever, loss of appetite and cessation of milk production in cows. Vesicles develop, particularly around the mouth and the feet, and then rupture to leave painful ulcers. FMD can be difficult to distinguish from a number of other infections, and collection and analysis of samples has to be done with great care because the organism is so contagious. Infected animals release the virus in saliva, milk, faeces, urine and

exhaled air. It is a hardy virus and is known to have survived kilometres of air-borne transmission to cause a new outbreak of disease elsewhere.

Newcastle disease is another very highly contagious viral disease and affects both domestic and wild birds. The different strains of the disease vary widely in virulence but some cause high lethality in domestic fowls, turkeys and pheasants. The incubation period of the disease is generally about five days. Its effects are variable but in its most virulent viscerotropic velogenic form (VVND) there is a sudden arrival and spread of the disease. Birds lose appetite and their egg production drops off very sharply. Profuse bright green diarrhoea is common and there is extremely rapid dehydration. Many birds die within a day or two and the mortality rate can be over 90 per cent. As with FMD, the virus is hardy and is excreted in faeces and in exhaled air. In affected areas there can be significant reservoirs of infection in wild birds, thus providing means for further disease outbreak to be initiated.

With effects such as these two diseases produce it is little wonder that anti-animal biological warfare was investigated thoroughly in the major offensive programmes of the last century. Indeed, biological warfare in the First World War was directed by both sides against the valuable draft animal stocks of the other. The first really viable biological weapon was produced by the British in their anthrax-laced cattle cakes for potential use against the German cattle industry. Pathogens like FMD and Newcastle disease are of interest today, when there are worries about possible bioterrorism, because they do not affect humans. The people producing and using such an agent would therefore be at little risk of infection in the process. Given the importance of animal husbandry, such means could be very attractive to those wanting to economically damage a country.[5]

Plant pathogens We just have to be reminded of the nineteenth century Irish potato famine to realise how devastating fungal diseases can be to staple crops. In fact, all staple and economically important crops have to be constantly guarded against the ravages of pests and diseases and even then there can be huge production losses. It is hardly surprising, therefore, that virtually all state-level offensive biological weapons programmes of which we have knowledge today carefully investigated anti-plant attacks.

In 1997, during the negotiations in Geneva aimed at strengthening the BTWC (which later failed), the South African delegation put forward a document[6] which discussed plant pathogens according to the following set of criteria:

- agents known to have been developed, produced or used as weapons;
- agents which have severe socio-economic and/or significant adverse human health impacts, due to their effects on staple crops, to be evaluated against a combination of the following considerations.

The considerations were:

- ease of dissemination (e.g. wind, insect, water etc.);
- short incubation period and/or difficult to diagnose/identify at an early stage;
- ease of production;
- stability in the environment;
- lack of availability of cost-effective protection/treatment;
- low infective dose;
- high infectivity;
- short life-cycle.

Ten plant pathogens were then identified as potential anti-plant biological weapons agents (Table 6).

Table 6: Potential anti-plant biological weapons agents*

Disease	*Agent*	*Comment*
Coffee berry disease	*Colletotrichium coffeanum*	Could cause serious economic damage
Blight of pines	*Dothistroma pini*	Could cause economic damage
Fire blight of apple, pear and related species	*Erwinia amyovora*	Could cause economic damage
Potato, tomato wilt, Moko disease of	*Pseudomona solanaceorum*	Could cause economic damage

banana etc.

Blast disease of rice	*Pyricularia oryzae*	Extremely destructive of this staple crop
Maize smut	*Ustilago maydis*	Could cause economic damage
Leaf scald of sugarcane	*Xanthomonas albilineans*	Could cause economic damage
Bacterial blight of rice	*Xanthomonas campestris*	Extremely destructive of this staple crop
Cover smut, stinking smut, common bunt of wheat	*Tilletia tritici*	Extremely destructive of this staple crop
Cottony soft rot, white mould and watery soft rot on vegetables, beans, soya etc.	*Sclerotinia sclerotorium*	Could cause economic damage

* From reference 6

The potential of plant pathogens was not lost on the bioweaponeers of the last century. The United States, for example, is known to have weaponised agents to attack wheat and rice staple crops. As can be seen from the comments in Table 6, such attacks on wheat and rice could be extremely destructive. The danger of attacks on crops has increased in recent years because of great advances in our understanding of biocontrol of plant pests and plant inoculants. Indeed, it has been suggested that efforts to develop fungal agents to attack drug crops such as poppies could be dangerous, at the very least in developing techniques that could be used in biological warfare. As with animal husbandry, the plant species used in agriculture are often of an extremely limited variety. Such monocultures are particularly open to attack with biological agents

Agent production and dissemination

In the early 1990s the US Congress Office of Technology Assessment (OTA) did a detailed open analysis of the technologies underlying weapons of mass destruction

(WMD).[7] For nuclear weapons, they concluded that the "[c]heapest overt production route for one bomb per year, with no international controls, is about $200 million." For chemical weapons, they concluded that an "[a]rsenal for substantial military capability...likely to cost tens of millions of dollars." In regard to biological weapons, however, their opinion was that "[e]nough for a large arsenal may cost less than $10 million." There is therefore a great difference in the resources required to obtain a nuclear as against a biological weapons of mass destruction capability.

An attacker who has obtained a pathogen with the required characteristics for the purpose intended (see Table 3) still faces considerable difficulties - for example, in mass producing the agent and effectively disseminating it. Mass production is difficult enough in itself but if a massive aerosolized attack is planned effective dissemination is extremely difficult.

To produce something like the anthrax bacterium there is a need for the seed stock (a small amount of the pathogen) and for standard fermenters such as those used in industry for the production of yoghurt, beer, antibiotics and vaccines. According to the OTA, in 1943 a pilot anthrax plant became operational at Fort Detrick, Maryland which was staffed by 500 scientists, engineers and technicians. Based on the experience of running this plant:

> "...the decision was made to build a full-scale plant at Vigo, Indiana, at a cost of $8 million, where 1,000 workers would manufacture more than 500,000 anthrax bombs a month..."

The plant was completed, but never actually went into production because the war had ended. However, the scale of productive capabilities cannot be misunderstood.

Fortunately, all the evidence in the open literature strongly suggests that is is very difficult to achieve effective distribution of an agent in order to cause mass human casualties. According to the OTA, the technical hurdles are these:

- the munition or delivery system must generate a cloud of aerosol particles with dimensions that allow them to be inhaled deep into the lungs of the target personnel;
- the agent must be physically stabilized so that it can survive the process of dissemination long enough to infect the target population;

- the agent must disseminate slowly meanwhile avoiding loss of viability or toxicity; and

- the overall size and shape of the aerosol cloud and the concentration of agent within it must be reasonably predictable, so that the dispersion pattern can be matched to the target.

These demanding technical hurdles have been overcome several times in state-level offensive biological weapons programmes, but they appear still to be beyond the capabilities of sub-state (terrorist or criminal) groups. Though WMD capabilities may be beyond sub-state groups today, nevertheless terrorists may still be able to do great harm through lesser capabilities without such demanding requirements.

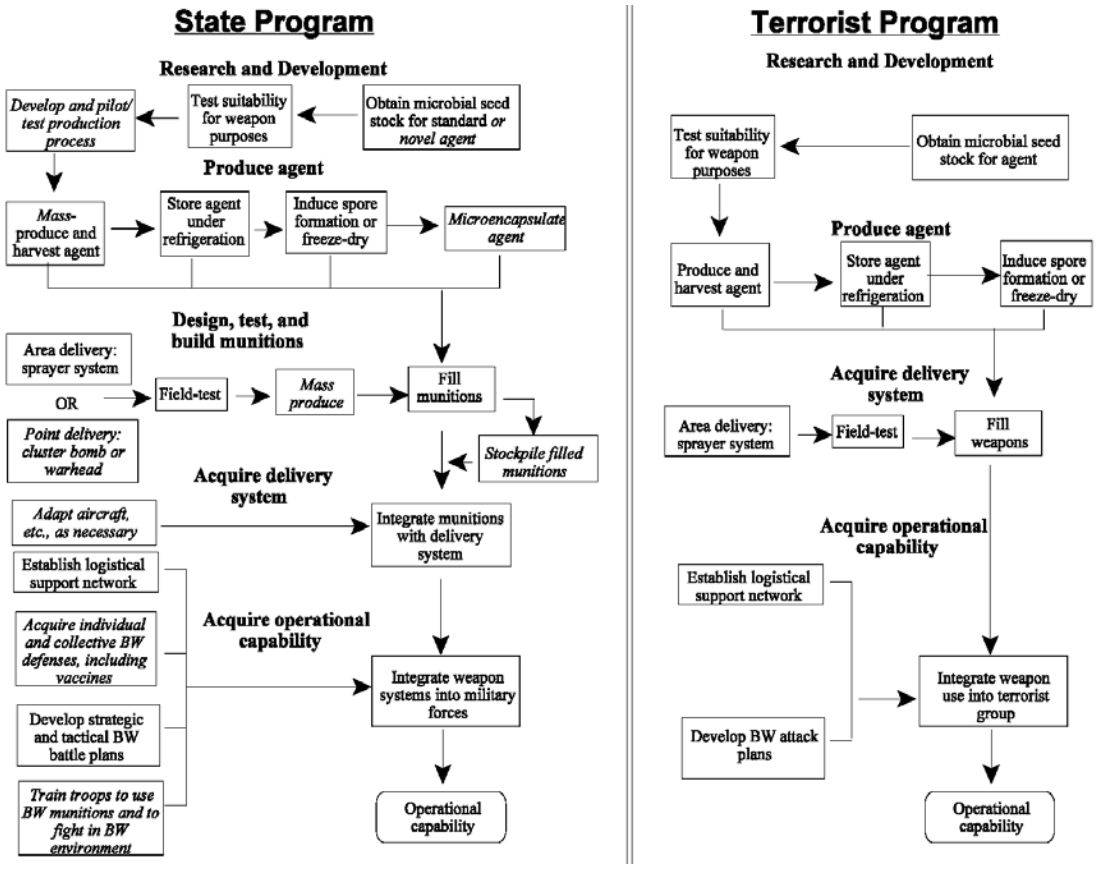
Non-WMD attacks on people

A May 2004 report by the US Congressional Research Service was titled *Small-scale Terrorist Attacks Using Chemical and Biological Agents: An Assessment Framework and Preliminary Comparisons*.[8] The report cautioned against thinking dominated by the requirements for a state-level offensive programme designed to achieve a capability for launching massive aerosolised attacks and causing WMD-level casualties. Since the information we have in the public record comes from such state-level offensive programmes, it is understandable if our thinking *is* dominated by state-level requirements. However, as the report points out:

> "…for terrorist distribution of a C/B [chemical/biological] agent, many steps considered to have a high practical difficulties may be nonexistent in the case of terrorist groups that wish to launch only a small-scale attack and that have a low regard for their personal safety…"

It then gives flow charts for a state programme and a terrorist programme (reproduced here as Figure 2) which show the sequence of steps required for these different types of programme to achieve their objectives.

Figure 2: Necessary steps for a programme to achieve its objectives



The report points out that the steps italicised in the state programme flow chart would not be needed in that of the terrorists. They would not need agents with a long shelf life, they would not need to optimise the functions of a large-scale dissemination device, to develop rigorous prophylaxis methods or to optimise the manufacture of large amounts of agent. The technical difficulties for the terrorists would clearly be very much reduced. If a terrorist group analysed the major disruptive effects of the very small scale use of anthrax (albeit lethal) in mail attacks in the USA in 2001, it might well decide that a relatively small attack using rather crude technology and at some risk to its own personnel would help it gain its objectives. So small-scale, low-level, technology attacks cannot be dismissed as totally unlikely in the future.

The Congressional Research Service report went on to analyse the agents which appear in standard lists such as those of the CDC, but not from the usual perspective of

which would be most dangerous coming from a state-level military programme, but rather from a terrorist's perspective. A virus like Marburg, for instance, would standardly be viewed as a high-level threat (in the Category A listing, see above), but since it is not easily obtainable in nature it gets downranked in this perspective. As the report notes:

> "…C/B agents that were considered high threats in other frameworks appear to present a lesser threat when viewed in the small scale attack context. Conversely, C/B agents that were considered of lesser threat when considering mass casualty attacks may be ranked more highly in the small scale context, as barriers to mass use may be missing when the agent is used on a small scale…"

Not surprisingly, therefore, the report went on to say "[b]ecause of the differences, policies designed to protect against catastrophic C/B attack may not provide equivalent protection against small scale C/B attack." It is not certain whether this view is widely held or if it is informing policies designed to counter terrorism.

3. Attack Scenarios Today

It is important to realise that an attacker could have any one of a variety of different objectives in carrying out a biological weapons attack. A criminal or terrorist group might use a small amount of agent in an assassination attempt, or a modest amount of agent in order to cause public fear and disorder. A state might use a large-scale release of biological agent for strategic military purposes or as a weapon of mass destruction against a civilian population (Table 7). So we are not dealing with just one type of 'biological bomb' but a very wide range of possible types and scales of attack. Furthermore, the target of the attack could be humans, animals or plants.

Table 7: Types of biological attack

Scale of agent release	**Nature of aggressor**		
	Individual	Subnational group	State

Point source	e.g. criminal act	e.g. assassination	e.g. assassination
Medium scale	e.g. criminal act	e.g. terrorism	e.g. military tactical
Large scale	not possible	e.g. national liberation army (use)	e.g. military strategic

Anti-personnel attacks

The well-known literature on use of biological weapons as weapons of mass destruction (WMD) by spreading an agent in an effective manner on the air over a large area will be considered first followed by a discussion of potential terrorist attacks on a lesser scale.

WMD attacks

In 1969, in the run-up to the eventual negotiation of the Biological and Toxin Weapons Convention, a report on *Chemical and Bacteriological (Biological) Weapons and the Effects of Their Possible Use* was produced by the United Nations Secretary General.[9] In its second chapter the report analysed the probable effects of biological weapons as against nuclear and chemical weapons. The relevant table is reproduced in part here (Table 8). It is immediately obvious from this table that in the right conditions a single bomber could affect a huge area with a biological weapons agent. The area would be much larger than that affected even by a large one megaton nuclear weapon (100,000km^2 as against 300km^2) and the expected death rate would be 25 per cent of the victims of the attack.

Table 8: Probable effects of the use of nuclear, chemical and biological weapons (carried on a single bomber) on an unprotected population*

Criterion	*Type of Weapon* *Nuclear* (one megaton)	*Chemical* (15 tons of nerve agent)	*Biological* (10 tons of biological agent)
Area Affected	Up to 300 km^2	Up to 60 km^2	Up to 100,000 km^2
Time to onset of effect	Seconds	Minutes	Days
Damage to structures	Destruction over 100 km^2	None	None
Maximum effect on man	90 per cent deaths	50 per cent deaths	50 per cent morbidity: 25 per cent deaths if no medical intervention

* From reference 9

Though the report was appropriately guarded in stressing that these probable effects were the result of judgements and much would depend on the prevailing conditions (e.g. the weather) during a biological weapons attack, the people involved in producing the report were of the stature, for example, of Sir Solly Zuckerman, Chief Scientific Adviser to the Government of the United Kingdom, who had access to the results of all experimentation done in the British offensive biological weapons programme in the years during and following the Second World War. The report should therefore leave no doubt in any reasonable mind that biological weapons could be used as weapons of mass destruction.

By the early 1990s it was possible to add to this United Nations report a variety of estimates from other open sources.[10] These all lead to the same conclusion - that biological weapons could, if used in an appropriate manner, cause huge levels of disease and death. Consequently, they have to be regarded as weapons of mass destruction

equivalent in many ways to nuclear weapons. Some of these estimates are set out in Table 9. The first case in the table was described by the Stockholm International Peace Research Institute (SIPRI) in volume two of its classic 1970s study, *The Problem of Chemical and Biological Warfare*. The second case was analysed in careful detail by Steve Fetter in the major journal *International Security* in 1991 and the third and fourth cases are taken from the 1993 US Office of Technology Assessment (OTA) study, *Proliferation of Weapons of Mass Destruction: Assessing the Risks*.

Table 9: Some publicly-available information comparing large-scale attacks using biological, chemical and nuclear weapons*

Study (case)	*Weapon System*	*Area Affected (km^2)*	*Fatalities*
I			
SIPRI			
Bomber	10-kt nuclear	30	n.a.
	biological agent	0-50	n.a.
	VX nerve gas	0.75	n.a.
	5-kt high explosive	0.22	n.a.
II			
International Security			
Missile on sparsely populated city	20-kt nuclear	n.a.	40,000 dead and 40,000 injured
	300 kg Sarin	n.a.	200-3,000
	30 kg anthrax spores	n.a.	20,000-80,000
III			
OTA			
Missile on sparse to moderately populated city	12.5 kt nuclear	7.8	23,000-80,000
	300 kg Sarin	0.22	20-200
	30 kg anthrax spores	10	30,000-100,000
IV			
OTA			
Line attack	100kg anthrax spores	46 (clear day)	130-460,000
		140 (overcast)	420,000- 1.4 million
		360 (clear night)	1-3 million

* From reference 10

What is clear from the first three cases is that they support the view put forward in the 1969 United Nations report, that a biological agent delivered effectively by bomb or missile would cause huge levels of casualties in the target population. Furthermore, during the state-level offensive biological weapons programmes of the last century the bioweaponeers made great advances in the effectiveness of their weapons. This is evident if we consider the fourth case in Table 9.

It had been shown that the most effective way to use a biological weapon was to spray it in a line (say from a plane) so that the material drifted across the target. This was best done at night so that ultraviolet (UV) light from the sun did not kill off the (anthrax) bacteria. The OTA example assumed that the attack was on Washington D.C. in the United States. The three sets of conditions under which the attack was carried out were: a clear, sunny day with a light breeze; an overcast day or night with a moderate wind; and worst of all, a clear calm night. Analysis of where various quantities of the 100kg of anthrax spores sprayed in a line on the windward side of the city would land, and the concentrations required to infect and kill, suggested that in the worst case some 1 to 3 million people would die.

As we have seen in section 2, it would be possible to treat people with antibiotics successfully if treatment started early enough. However, whether any public health system could cope with such numbers seems unlikely, even if the attack was detected. Additionally, if a genetically-manipulated organism with built-in antibiotic resistance were used, even early treatment might not work. We clearly have to accept that biological weapons could be used as weapons of mass destruction, even if the actual outcome of an attack might vary considerably in different weather conditions. It will also be noted from Tables 8 and 9 that the calculated effects of the use of a biological agent like anthrax far exceed those of a nerve gas.

Non-WMD attacks

Also in the run-up to the negotiation of the Biological and Toxin Weapons Convention the World Health Organisation (WHO) produced, in 1970, the first edition of its report on

Health Aspects of Chemical and Biological Weapons.[11] This is interesting because it analysed cases of weapons of mass destruction usage and also lesser-scale attacks using biological weapons.

The WHO report considered WMD-style attacks using *tularemia* as the biological agent against a city of 5 million people in a developed country with good medical resources and on a similar-sized city in a developing country, and against a city of 500,000 people, again in both a developed and a developing country. These cases do not change the overall conclusion derived from the earlier case studies discussed here, but they give more detail on the problems that would be encountered by the health and municipal authorities. A similar analysis was given for an attack using *plague* against a city of 5 million in a developed country (with antibiotics available) and against a similar-sized city in a developing country (with only a small supply of antibiotics). As might be expected, in the latter case for plague it was suggested that a total death toll of 250,000 could result from the successive waves of epidemic caused by the agent.

What is of particular interest, however, is that the WHO report went on to look at the sabotage of water supplies with biological agents. The authors considered contamination at the intake or treatment works, at the raw or treated water reservoirs and at a trunk or transmission main. They dismissed the idea of a takeover (or staff corruption) at the treatment plant as it would require the attacker to have very special access and favourable conditions – although it would obviously lead to a worst-case scenario. They also dismissed the idea of contamination of a water reservoir as a means of effective sabotage. In their opinion, controlled injection of an agent into a trunk main "would be potentially the most devastating in effect, difficult to prevent and detect, and feasible in practice in many water systems."

Two of the hypothetical cases considered in the report used, as the contaminating agents:

> "(a) the typhoid bacillus, which produces no recognisable symptoms for about 1 week; and
> (b) botulinal toxin, type A, which would produce no recognizable symptoms until 6 or 8 hours after ingestion and, in a stabilized form, would resist denaturation by the elements found in a normal water supply…"

The report noted that these agents would likely escape detection and could produce effects at low concentration so that only a small bulk of initial contaminant would be required. It also suggested that if there was a chlorine residue left in the mains its effect on the agents could be reduced by simultaneous injection of a dechlorinating agent.

The hypothetical attacks were deemed to take place without warning so that no special precautions were undertaken by the authorities, and the attackers were assumed to have knowledge of the mains systems layout so that they could achieve maximum effect. So that impossibly large amounts of agent were not required it was assumed that 1 kg of freeze-dried culture of *typhoid bacillus* was used to attack a city with a population of one million-plus and for *botulinum toxin* an attack with 0.24kg of toxin on a city of 50,000 was considered. Clearly, if the typhoid bacillus was used in such circumstances, with no recognizable symptoms for a week the authorities could take no immediate remedial action. For an attack with botulinum toxin, because symptoms begin to appear after 6-8 hours the authorities might be able to warn people not to drink the water until it had been flushed clear of contamination. For both agents two patternss of water consumption were considered. For two industrial communities, one of a million-plus and one of 50,000 in a temperate climate, it was assumed that 15 per cent of people would not drink water direct from the tap in the relevant period. For two non-industrialised cities of 1million-plus and 50,000 in a tropical area, it was assumed that everyone would drink the tap water in a 3-4 day period.

The percentages of people who would be infected by different levels of typhoid bacillus are known from other studies of human volunteers. In the first case of a large industrial city in a temperate climate, it was assumed that the amount of water drunk per person was 0.5 litre per day. The total number of typhoid cases was then calculated to be about 35,000 and assuming that early and effective use of antibiotics reduced the fatality rate to 0.6 per cent, a total number of 200 deaths was assumed. In the second case of a large non-industrialised city in a hot climate, water consumption was assumed to be 2.0 litres per person each day. It was calculated that 10^5 micro-organisms would be delivered to over 125,000 people (out of the million in the city) and cause many of them to become ill. If no facilities were available for mass treatment it was suggested that some 4,500 people might die.

In regard to the botulinum toxin attacks on two cities of 50,000 people, one industrial in a temperate climate, one non-industrialised in a hot climate, because of the rapidity of onset of symptoms and the extreme toxicity of the agent the figures assumed for deaths were much higher – around 30,000 people. There was little difference between the two cities because there was little chance in either – for the people who received lethal doses – to apply modern medical treatments**.**

Such hypothetical examples reinforce the conclusions drawn from studies of what happens when pathogenic contamination of food and water occasionally causes problems even in developed countries. These suggest that sabotage with pathogenic micro-organisms or their toxic products cannot realistically be ignored as a threat to the general population. Contamination of the food supply chain or soft drink production, for example, could also be considered by terrorists with malign intentions.

Anti-agriculture attacks

Plant pathogens cause huge losses in agricultural production so it is hardly surprising that the bioweaponeers of the last century gave careful consideration to deliberate destruction of the staple food crops of their potential enemies. A document dated March 1958 and released under the United States Freedom of Information Act, for example, was titled *The Importance of Rice and the Possible Impact of Antirice Warfare*.[12] The 185-page document was a study of how China might be attacked through destruction of its rice crop, thereby reducing the country's "capability and will to wage war." Among its conclusions, the report noted that:

> "A susceptible period for attacking rice exists shortly after transplanting, an operation readily apparent by aerial observation and suitable as a reference for timing an attack."

The idea was that by spreading a biological agent on the crop at this early stage the pathogen would cause a primary infection to grow and disperse spores which would then cause secondary infections. The amount of material that would have to be used by an attacker would therefore be quite small.

It is difficult to overstate the scope of the work. The document reported studies on the susceptibility of different rice varieties to different isolates of the chosen fungus.

The aim here was to use a mixture of different types of the fungal agent *Piricularia oryzae* so that any variation in the type of rice being grown would not affect the consequences of an attack. The main rice-growing areas of China at the time were analysed, as were the average contributions of the rice crop to the daily calorific intake of the Chinese population. The report suggested that a two-pronged attack would be effective, with a biologically active chemical agent being used where the environment was not suitable for use of the pathogen, but "[w]here the environment is suitable for the use of an antirice pathogen it should be used." *Piricularia oryzae* causes rice blast and its spores could be easily produced by methods perfected in the United States. The dried spores were stable in storage and resistant to environmental degradation.

The possibility of large-scale attacks on staple crops such as rice has to be taken seriously. As is clear from the discussion of available agents in Section 2, it would also be quite possible to direct attacks at economically important cash crops and at vital animal husbandry.

Current terrorism concerns

Following the attack on the twin towers in New York and other targets in the United States on the 11th of September 2001, and then the anthrax letter attacks soon after, worries about bioterrorism grew. An article in the 2002 *Annual Review of Microbiology* encapsulated many people's concerns. Titled "Bioterrorism: From Threat to Reality," the article began:[13]

> "The fears and predictions of attacks with biological weapons, which were increasing at the close of the twentieth century, were transformed into reality not long after September 11, 2001, when several anthrax-laden letters were sent through the U.S. postal system…"

The article pointed out that it was fortunate the material had not been used in a massive aerosol release which could have affected thousands, and noted that whilst the problem was dealt with by the authorities, "[f]ear gripped the nation." Undoubtedly, many people were fearful about what might happen if terrorists were to use biological weapons in earnest. National and international authorities reacted by reviewing and improving their safety precautions.

It is known that national biodefence communities had long considered the possibility of bioterrorism. In the United States tests had been carried out with pathogen simulants by the US Navy which released an aerosol off San Francisco and tested how far concentrations of organisms reached inland; simulants had been released on the New York subway and estimates made of how many people would be infected in a real attack and so on. Similar analyses had been made in the UK and, no doubt, in other countries.

A Technical Note[14] written by a member of the US Army at its main biodefence testing site (Dugway Proving Ground) recorded that:

> "The use of biological materials in conjunction with terrorist events has been addressed in various studies and reports (see Annex A)…"

Annex A to this 1986 report listed nineteen US Army reports on the subject over the previous eleven years, and a further eight studies by institutes such as the Rand Corporation over the same period! The introduction to the annex noted that the list of reports in the annex was intended to be a representative sample and pointed out that:

> "When, in 1973, DPG [Dugway Proving Ground] received a mission assignment…to maintain the program for technical assessments of foreign biological threats, one of the first studies was an assessment of the potential threat from the use of biological materials by terrorists. Since that time, consideration of terrorist employment of biologicals…has been a continuing part of the program…"

So in no sense did governments like those of the United States, the United Kingdom and others lack information on what terrorists might be able to do in biological attacks.

The second report in Annex A was titled *Covert Biological Weapons Literature Review*.[15] This 1975 report sought to review the possibilities for a subversive group carrying out a biological weapons attack in the United States. It specifically excluded large-scale, direct, aerosolised biological weapons as a means of covert attack by such a group, but concluded:

> "…BW agents can be used against man, animals, or plants. Reports reviewed here show plainly that a…subversive group could produce a variety of effective BW agents, and deliver them against the civilian population and

> agricultural and water resources of the United States by many covert and overt means…"

So there can be little doubt that a terrorist group at the present time could carry out some small to medium-scale biological weapons attacks. The situation in regard to a massive WMD aerosolised agent attack is quite different. All the technical literature and opinion maintain the view that although the problems of production and dissemination have been solved in state programmes in the past it is presently still unlikely that a sub-state group would have the necessary capabilities and resources. As Milton Leitenberg of the Center for International and Security Studies in the School of Public Affairs at the University of Maryland has emphasized:[16]

> "…threat assessment, most particularly regarding 'BW terrorism' – the potential for BW use by non-state actors - has been greatly exaggerated…"

Speaking at a meeting organised under the auspices of the Italian Ministry for Foreign Affairs in April 2002, Leitenberg went on to argue that this exaggeration was counter-productive both in suggesting to those with malign intent that they should be interested in biological warfare, and in distorting priorities for investment in public health. So it is necessary to be careful and to keep the threats in realistic proportion as we examine some recent analyses.

Anti-agriculture bioterrorism

As many experts have cogently argued, it is agriculture that is particularly vulnerable at present to bioterrorism. Potential attacks on agriculture have been characterised as "[l]ow-tech, high consequence bioterrorism." The reasons for this characterisation are not at all difficult to understand. Many studies suggest that this kind of bioterrorism would require relatively little in the way of specialist knowledge, technical expertise or technology. The diseases are highly contagious to the intended targets (but not to humans), would therefore spread rapidly, and would cost a great deal of money to eradicate. An added cost would come from the losses in international trade that would follow as other countries tried to protect themselves from the disease.

Taking the United States as an example, one recent analysis argued:[17]

> "…Pathogens that cause diseases such as FMD, rinderpest, African Swine Fever (ASF), soybean rust, Philippine downy mildew of maize, potato wart, and citrus greening, could, if introduced into the continental US, have serious consequences for the US economy."

After the first case of FMD was reported in the UK outbreak of 2001 the European Union and others immediately blocked imports of British beef, sheep and pigs and the products derived from them, and the authors noted that the scale of the US industry is much greater than that of the UK. They concluded that "with $37 billion of beef, $23 billion of dairy and $9.2 billion of pork sales annually (USDA, 1999), the trade consequences of an outbreak of FMD would be much larger." They emphasized this point by referring to a recent study using very conservative estimates of the impact of an FMD outbreak on Californian agriculture which suggested a $6-13 billion loss – even if confined just to California and eradicated within 5-12 weeks.

Taking another example, they pointed out that even though kernel bunt of wheat, caused by the fungus *Tilleta indica*, does not have a large direct effect on crop yield, about 80 countries ban wheat imports from regions infected with the fungus. The disease was discovered in Arizona in 1996, probably through an accidental introduction from Mexico, and produced an immediate threat to the $6 billion per year US wheat crop of which about 50 per cent is exported. The US Department of Agriculture's Animal and Plant Health Service therefore spent some $60 million on eradicating the disease between 1996 and 1998 while the growers in the small area affected were estimated to have lost over $100 million in sales and through extra production costs incurred.

Against that kind of background it is obvious that potential attacks against agriculture using biological weapons must be taken seriously. Whether they are taken sufficiently seriously today is an open question.

Catastrophic bioterrorism

Despite the arguments presented so far indicating that we may not have paid enough attention yet to biological weapons attacks on agriculture and to smaller-scale attacks on humans, it is obvious from the rapid evolution of biotechnology that we neglect to think about large-scale attacks in the future at our peril. One person who has tried to think this

issue through over a number of years is Richard Danzig, the former US Navy Secretary. He has been concerned with what he calls "catastrophic bioterrorism" and is far from sanguine about the problem.

Danzig argues, in part, that the aim of the terrorist is to disable good governance, enhance divisiveness and undermine the confidence of citizens in their government. Writing in August 2003, he argued strikingly that:[18]

> "…Biological terrorism affords the possibility of repeated attack, undermining confidence and forcing ever-escalating investments of resources to achieve a modicum of defence…"

He went on to point out that terrorists' ability to carry out repeated attacks could remain intact while a government's ability to manage the consequences of the attacks could be exhausted. Here we encounter the quite new concept of a terrorist *campaign* using bioweapons rather than the usual one of an isolated attack with biological weapons. This is the much more serious problem that Danzig wishes us to consider. He advises us to "Plan to defend against a campaign not just an attack."

But just how does a government go about planning to defend against such complexities – so many agents, so many targets, so many different scenarios? In Danzig's view, a way forward is to try to devise a representative range of possible attacks (planning cases) and to work out what capabilities would be required to deal with them. The planning cases have to be drawn up with care, but Danzig views the cases themselves as much less important than the process of trying to work out what those capabilities would be. The cases are, in short, "an anvil against which to hammer out our hypotheses…and test the validity of different strategies."

Working, of course, in the context of the United States, but presumably taking into account the thinking of experts in other countries, Danzig suggested four planning cases which he felt would "represent our most significant risks, illuminate how our systems would be taxed, and stimulate a broad range of preparations." The cases were:

1. A large-scale outdoor aerosol anthrax attack;
2. A large-scale outdoor aerosol smallpox attack;
3. An attack that disseminates botulinum toxin in cold drinks; and

4. An attack that spreads foot and mouth disease among cattle, sheep and pigs.

He argued that these cases will encompass most others we can think of. For example, plague is a bacterium like anthrax and is contagious like smallpox, so if we have the general capabilities required to deal with anthrax and smallpox we shall have gone a long way towards being able to deal with plague. An attack with plague is thus a included case as it is far less contagious than smallpox and more responsive to treatment than anthrax (although it will naturally require appropriate specific vaccines and treatment regimes).

Danzig's thinking, has a further suggestion that we should note. As biotechnology evolves and the strategic situation develops, we must be sensitive to the possibility that bioterrorism will also evolve. This suggests to Danzig the need for a "Case 5 Committee" deliberately tasked with analysing the evolution of the potential threat and with suggesting changes to the four planning cases when that becomes necessary.

4. Conclusion

Since the middle of the twentieth century it has been clear that if sufficient resources were to be applied to the problem biological weapons of mass destruction could be created. It has also been clear that lesser anti-personnel attacks on military or civilian targets would be possible without the application of such large resources and that agriculture would be particularly vulnerable to attack with biological agents.

We have been fortunate indeed that to date such resources have been applied only to a limited extent in major hostilities. It is often forgotten that the Japanese expended vast resources in attacking the Chinese with bioweapons before and during the Second World War and that the United States carried out a large-scale campaign of plant destruction during the Vietnam War using material such as Agent Orange – a synthetic bioregulator. In a sense then, the growing worries about military, and particularly terrorist use of biological weapons is just the reawakening of public concern about issues that were well aired decades ago.

In reality, very little has changed except the renewed perception of threat. However, the revolution in biology has greatly accelerated over those years and we face the threat in coming decades of a much more systematic application of the new biology to hostile purposes. Though today it remains almost certainly the case that an aerosolised WMD bioattack is only possible in a state programme, in the future - if we are unable to prevent the thoroughgoing militarization of biology - it seems likely that sub-state groups, and perhaps even deranged individuals, may gain the capabilities to cause mass human casualties.

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