Risk of disease spread through bioterrorism

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Summary

Bioterrorism is seen as a clear and present danger, although historically, acts of bioterrorism have been relatively unpredictable, rare and, thus far, small-scale events. The risk of an event is elevated by increasing contact among species and a global connectivity that provides rapid dissemination of infectious diseases regardless of origin. Virtually any pathogenic microbe could be used by bioterrorists. An attack may be difficult to distinguish from a naturally occurring infectious disease outbreak; however, consequences are likely to be similar. The agricultural sector is extremely vulnerable to bioterrorist attacks because animals and plants have little or no innate resistance to foreign pathogens and are not vaccinated or otherwise protected against these diseases. It is also important to note that weapons or delivery systems are not an issue because the animals and plants themselves are the primary vector for transferring agents. Many bioterrorism agents are zoonotic in origin, thus an attack on animal populations could pose a health risk to humans. Additionally, disease outbreaks resulting from bioterrorism could jump to wildlife species, persist in the environment, replace locally adapted enzootic strains, expand their range, or emerge as a new zoonotic disease in naïve human and animal populations.

Keywords

Agro-terrorism, Biological weapons, Bioterrorism, Bioterrorists, Pathogens, Zoonoses.

Rischio di diffusione di malattie attraverso il bio-terrorismo

Riassunto

Il bio-terrorismo è da vedere come un pericolo serio e attuale benché gli atti di bio-terrorismo siano stati, storicamente, eventi su scala ridotta, relativamente imprevisti, rari e, pertanto, lontani.Il rischio di un evento aumenta a causa della diffusione dei contatti tra le specie e della possibilità di comunicazione globale, che permette una rapida diffusione delle malattie infettive qualunque sia la loro origine. *Teoricamente, qualunque microrganismo patogeno* potrebbe essere usato da bioterroristi. Può essere difficile distinguere un attacco dal diffondersi di una malattia infettiva che si manifesta in modo naturale; tuttavia, è possibile che le conseguenze siano simili. Il settore agricolo è estremamente vulnerabile agli attacchi del bio-terrorismo, perché animali e piante hanno ridotta o nessuna resistenza nei confronti di agenti patogeni estranei e non sono vaccinati o protetti in altro modo contro queste malattie. Inoltre, è anche importante osservare che le armi o i sistemi di trasmissione non rappresentano un problema in quanto gli stessi animali e piante sono il principale vettore per la trasmissione degli agenti patogeni. Molti agenti legati al bio-terrorismo sono in origine agenti di zoonosi, quindi un attacco rivolto alla popolazione animale potrebbe rappresentare un rischio sanitario per gli esseri umani. Inoltre, l'insorgenza di patologie derivanti dal bio-terrorismo potrebbe estendersi a specie selvatiche, persistere nell'ambiente, sostituire ceppi enzootici locamente

Biological Sciences Division, Pacific Northwest National Laboratories, P.O. Box 999, K9-81, Richland, Washington 99354, United States of America Dick.Weller@pnl.gov adattati , espandere il loro raggio d'azione, o emergere come una nuova zoonosi nelle popolazioni umana e animale autoctone

Parole chiave

Agroterrorismo, Armi biologiche, Bioterrorismo, Bio-terroristi, Patogeni, Zoonosi.

Introduction

'In comparison to the real and enormous threat of emerging, re-emerging and transported infectious diseases, the problem of deliberately caused disease is almost insignificant. From a public policy perspective, it would make sense to pay more attention to the larger problem while not neglecting the smaller. There is a need to place the threat of bioterrorism in perspective the greater biological threat facing the United States is not terrorists armed with biological weapons; it is, as it always has been, diseases of natural origin. If we can successfully meet and defeat the real threat of emerging, re-emerging, and transported infectious diseases, then we have also gone a long way towards being able to handle whatever manifestations of bioterrorism that will occur' (35).

The attacks on the World Trade Center in New York and the Pentagon in Washington, DC, in September 2001 were followed in October by the release of weapons-grade anthrax spores in postal facilities and the Capitol buildings. With the arrival of actual bioterrorism – not just the threat of it – a major change occurred in the way in which the world views infectious diseases. Bioterrorism, defined as 'the use by non-state actors of microorganisms (pathogens) or the products of living organisms (toxins) to inflict harm on a wider population' (1), adds a new dimension to our concern. Non-state actors include, but are not necessarily limited to, rebel opposition groups, local militias and warlords, as well as vigilante and civil defence groups, when such are clearly operating without state control. It should be remembered that:

- bioterrorism is not biowarfare, and extensive epidemics are not a prerequisite for creating great public anxiety
- while it has been said before, it is still true that the only significant difference between a naturally occurring epidemic and one that has arisen through bioterrorism is motive
- there is always a possibility that bioterrorism could arise through a novel recombinant virus created specifically for that purpose (12).

Many interconnected factors are influencing the increasing rate at which diseases have emerged in recent years. The ever-increasing human population brings the species into greater contact with animals and great global connectivity can rapidly disseminate infectious diseases from the initial focus. Whereas in previous centuries, a disease focus might have died out by failing to establish a chain of transmission, it now has the opportunity to rapidly recruit susceptible hosts on a global stage.

Ackerman and Moran note in a report prepared for the Weapons of Mass Destruction Commission (1): 'The widespread attention that bioterrorism receives today is significant and new. Up until the past decade, the prospect of someone, other than a state, using biological weapons (BWs) was largely confined to speculation and a small cadre of biowarfare experts. The use of sarin by the Japanese cult Aum Shinrikyo in the Tokyo subway system in 1995 alerted both policymakers and counterterrorism experts to the possibility that at least some terrorists and other non-state actors were willing and able to engage in mass-casualty attacks using unconventional weapons. However, it was only in late 2001, when an as-yet-unidentified

perpetrator sent weapons-grade preparations of *Bacillus anthracis*, the organism that causes anthrax, through the mail that the world accepted the notion that violent non-state actors might seek to use harmful biological agents in terrorist acts.

The 2001 'anthrax attacks' were not by any means the first bioterrorism incidents. In 1984, for instance, the Rajneeshees, a religious cult located in Oregon, contaminated several salad bars with the nonlethal pathogen Salmonella enterica serotype Typhimurium causing more than 750 people to fall ill. Occurring as close as they did to the 11 September attacks, the anthrax attacks reinforced many of the concerns that had accompanied earlier revelations about the advanced level of the secret Soviet biological weapons programme and the Aum cult's attempts to develop biological weapons. The intense media and public interest surrounding the 2001 anthrax attacks had predictable effects. What was already a major security issue in the United States quickly achieved the status of a global threat as policymakers worldwide were galvanised to address the possibility of bioterrorism' (1).

One would assume that a thorough understanding of the bioterrorism threat underlies policy decisions associated with preventive and response-related measures which often involve resource limitations and tradeoffs between existing programmes. Yet this has repeatedly been shown not to be the case. At every level, from the local to the national to the international, approaches to countering bioterrorism have been fragmented and distorted by political or parochial institutional concerns.

Background

Huxsoll noted that biological warfare is defined as the deliberate use of microorganisms or toxins derived from living organisms to induce death or disease in humans, animals, or plants (16). Until the anthrax events in October 2001, the world was somewhat complacent about the bioterrorism threat. Now we realise that livestock, crops, tourism and transportation are all possible terrorist targets. Even small outbreaks of exotic disease in livestock or crops could remove a country from global markets for its agricultural products.

According to Hickson by understanding the ways and means of strategic, indirect warfare, in light of military history and intentionally ambiguous cultural subversions, we may better anticipate and strategically counteract subtly maturing forms of bioterrorism and longer-range forms of psychobiological warfare, which may also be intensely dislocating new manifestations of economic warfare (14). By indirectly attacking and infecting unprotected 'soft targets', such as seeds, a strategic aggressor or trans-national criminal syndicate or terrorist could have many disproportionately adverse effects upon a whole culture and its way of life. This may be but one new form of 'asymmetrical warfare' against sophisticated interdependent societies. The developments from research in molecular biology and its variety of manipulative applications in biotechnologies offer many new capabilities to the malevolent.

Bioterrorist attacks could be covert or announced and could be caused by virtually any pathogenic microbe. A bioterrorist attack may be difficult to distinguish from a naturally occurring infectious disease outbreak. Investigators must first examine the aetiology and epidemiology of an outbreak to identify its source, mode of transmission and targets at risk. Certain clues might indicate whether an outbreak is the result of purposeful release of microorganisms. Naturally occurring diseases are endemic to certain areas and involve traditional cycles of transmission; some diseases occur seasonally and the appearance of sentinel cases in domesticated animals and wildlife is not uncommon. In contrast, a disease outbreak caused by bioterrorism could occur in a non-endemicdisease area, at any time of the year, without warning and, depending on the aetiological agent and mode of transmission, in large numbers – thousands of cases might occur abruptly. Public health officials must be appropriately sensitised to the possibility of bioterrorism when investigating disease outbreaks.

However, despite their high profile and potentially devastating consequences, bioterrorist acts are relatively unpredictable, rare, and thus far smallscale events. In contrast, biological invasions are occurring daily in the United States and have a significant impact on human health, agriculture, infrastructure and the environment, yet they receive far less attention and fewer resources. Scientists throughout the world must work together to implement a comprehensive approach to biosecurity that addresses not only bioterrorism, but also the more common incursions of invasive alien species such as the zebra mussel or monkeypox virus into the United States and the potential for deliberately using them as agents of bioterrorism. To achieve these goals, it will be necessary for the relevant international organisations and government institutions to acknowledge and include prevention, early detection and rapid response to species incursions as central mission themes. In addition, the scientific community, industry and the public must work together to ensure that the necessary technology and information systems are readily available (23, 24).

Short history of biological terrorism

Biological weapons specialists agree that bioterrorism has a long history, from the poisoning of arrows and wells to the dispersion of toxins on the battlefield to the contamination of food and mailing of letters laden with anthrax spores. However, some point out that such weapons have never been used in a widespread manner in any form of conflict, with the exceptions of the sporadic German sabotages in World War I and the greater, but geographically contained, Japanese use before and during World War II. In any event, it is useful to recount some of the history of bioterrorism (20).

Over the centuries, pathogens such as smallpox, botulinum toxin, bubonic plague and anthrax have been used for terrorism. These have mainly been used in military situations, primarily to disable or terrorise civilian populations. However, given the dual-use nature of microbes, the line between military use and terrorism has always been arbitrary at best.

An early case of an attempt to spread infectious disease occurred in 1346 in the Crimea. Tartar forces were besieging the town of Caffa when an outbreak of plague occurred. The Tartars loaded the freshly dead into catapults and launched them into the city. The defenders of Caffa tried to rapidly dispose of the bodies by throwing them into the sea, but eventually a plague epidemic broke out within the walls. Ultimately, the defenders were forced to abandon the city and retreat to the west. It is hypothesised that this retreat helped spread the plague to Italy, creating one of the first waves of the Black Death (33).

Using smallpox as a weapon was not unprecedented for the British military; Native Americans were the targets of attack earlier in the 18th century. One infamous and welldocumented case occurred in 1763 at Fort Pitt on the Pennsylvania frontier. British General Jeffery Amherst ordered that blankets and handkerchiefs be taken from smallpox patients in the fort's infirmary and given to Delaware Indians at a peace-making parley. A smallpox epidemic quickly overwhelmed the tribes causing very high mortality. Some tribal groups virtually vanished, and the rest suffered severe population losses (33).

By the time of World War I, the germ theory of disease was well established; scientists grasped how microbes such as bacteria and viruses transmit illness. During the war, German scientists and military officials applied this knowledge in a widespread campaign of biological sabotage. The first substantially supported allegations of the use of biological warfare agents against livestock were made against the Germans during World War I. German agents employed anthrax and glanders against cattle, sheep, mules, horses and reindeer in Romania, Spain, France, Norway, Argentina and the United States (31). By infecting just a few animals by injection and by pouring bacteria cultures on feed, German operatives hoped to spark devastating epidemics. Secret agents waged this campaign in Romania and the United States from 1915-1916, in Argentina from roughly 1916 to 1918, and in Spain and Norway (dates and details are obscure) (15, 32).

A more methodical case of terrorism was 'Unit 731,' a special germ-warfare unit of the Japanese Army that is notorious for conducting experiments on humans to develop BWs. In 1939, Unit 731 of the Kwantung Army set up a topsecret, biological warfare research base in Harbin, capital of Heilongjiang Province. This unit conducted germ warfare experiments on prisoners of war and launched mass terrorist attacks on Chinese civilians using plague and anthrax bombs. At least 3 000 people, mostly Chinese civilians and victims from Russia, Mongolia, and Korea died in the experiments between 1939 and 1945 (8).

Following World War II, a number of nations pursued large offensive BWs programmes including the former Soviet Union, United Kingdom, Canada and the United States. The scope and ambition of these efforts has become better known since the break-up of the Soviet Union in 1991 and the illumination of the scale of Iraq's BWs programme following the first Gulf War. At its peak the Soviet programme included more than 50 laboratory locations and involved more than 100 000 people, 40 000 of whom were employees and 1 000 of whom were highly qualified research scientists specialised in dangerous pathogen research, while the agricultural BWs programme is reported to have employed 10 000 staff at eight known locations that were conducting an offensive BW programme targeting livestock, poultry and crops (34). It is little wonder that non-state groups have become very interested in BWs.

Attraction of biological weapons for terrorists

Terrorism experts have warned that BWs pose new global threats through possible attacks on livestock and crops or through the deployment of yet unknown pathogens produced by genetic modification. Governments have taken steps to defend their citizens against possible attacks from weapons such as anthrax, but experts have warned that diseases targeting livestock and crops could expose many countries to potential economic ruin. Furthermore, because many priority bioterrorism agents are zoonotic in origin, an attack on human populations would likely pose a health risk to animal populations in the target area and vice versa so the attackers could potentially accomplish several goals with one attack (29).

One problem in containing the threat posed by BWs is that they are difficult to detect because they piggyback on the same technology used to produce legitimate products. Many countries also lack basic laws against BWs. Singapore, for example, only recently made the creation of BWs punishable by life imprisonment. The nearly exponential rate of scientific development also introduces the risk that formulae and emerging technologies that could be used to produce new weapons will fall into the hands of terrorists. Others have warned that terrorists wanting to unleash economic chaos would be well served by targeting livestock and crops, which have traditionally gone unprotected. In addition to the danger from the weapons, BWs have certain other advantages for a terrorist (28), as follows:

- they are undetectable by traditional anti-terrorist sensor systems (and hence by conventional countermeasures)
- the time-lag (in many cases) between release of an agent and its perceived effects on humans and/or animals can allow the perpetrator(s) to escape
- in at least some cases, the lack of an agent 'signature' can enable an assassin, for example, to disguise the cause of death
- they are adaptable to small demonstration attacks as an indication of resolve and ability to carry out the threat of a much more devastating attack
- they have the capacity unobtainable by other means - to inflict heavy casualties on the military forces of a state or to seriously damage its economy
- they can instil sheer terror (and hence societal disruption) in a target population because of the particularly insidious nature (microscopic, colourless, and/or odourless) of the agents in question
- they are relatively easy and cheap to produce or acquire, particularly in comparison with nuclear weapons.

Risk of disease spread by bioterrorism

To consider the risk of disease being spread through acts of bioterrorism, how the risk itself is assessed and defined needs to be understood. A standard dictionary defines risk as 'the qualitative or quantitative

estimation of the likelihood of adverse effects that may result from exposure to specified health hazards or from the absence of beneficial influences'. A risk assessment is a report that shows assets, vulnerabilities, likelihood of damage, estimates of the costs of recovery, summaries of possible defensive measures and their costs, and estimated probable savings from better protection. A 'risk analysis' is the process of arriving at a risk assessment, which is also called a 'threat and risk assessment.' A 'threat' is a harmful act such as the deployment of a virus or deliberate adulteration or contamination of food or food products. A 'risk' is the expectation that a threat may succeed and the potential damage that can occur. Simply put, risk is the product of the perceived threat multiplied by the vulnerability of the target.

Defining the problem

According to Ackerman and Moran (1) the first step in assessing any type of threat is to properly define the scope and nature of what is to be assessed. They define bioterrorism as 'the use by non-state actors of microorganisms (pathogens) or the products of living organisms (toxins) to inflict harm on a wider population'. They assert that the three following key issues flow from this definition:

- it avoids debate about the nature of 'terrorists' and 'terrorism' by focusing on the use of BWs by non-state actors
- non-state actors will not necessarily use BWs only to cause mass death, but for a variety of other purposes from the strategic to the tactical
- humans are not the only targets of bioterrorism; crops and livestock can be attacked with bioagents, or can be used to disseminate biological agents to human populations (so-called 'agroterrorism').

The following characteristic of bioterrorism is also important; biological agents are not BWs. Merely

possessing biological agents with the theoretical potential to cause harm is insufficient (1).

The potential use of microbes as weapons and agents of terrorism is of great concern. The ability of such agents to cause mayhem was demonstrated in October 2001 when five envelopes containing weapons-grade Bacillus anthracis spores resulted in 11 cases of inhalational anthrax, disrupted the functioning of the United States government and caused widespread fear and anxiety. In the United States, agents with a high potential for use as BWs have been included in a 'Select Agents List' that categorises them as A, B or C, depending on the assessed threat posed by the agent (4). However, the designation of a microbe as a potential BW poses the interesting question of how such a decision is made given the many pathogenic microbes that cause disease.

Analysis of the properties of microbes that are currently considered BWs against humans has revealed no obvious relationship to virulence, except that all are pathogenic for humans. What does this say regarding microbes that are considered potential BWs against livestock and crops? Notably, the weapon potential of a microbe, rather than its pathogenic properties or virulence, appears to be the major consideration when categorising certain agents as BWs. Efforts have been made to standardise the assessment of the risk posed by microbes as biological warfare agents using the basic principles of microbial communicability and virulence.

The weapon potential of a microbe is a function that includes such variables as its virulence, the delay before the occurrence of signs of disease and susceptibility of possible target populations. Although communicability functions as a threat amplifier, it is not always a desirable quality in a BW because the aggressor cannot control the agent once it is released, and there is always the potential that person-to-person communicability would affect friendly, nontargeted populations. Similar concerns would not exist for agents that are strict livestock or crop pathogens. Clearly, the weapon potential formalism is a first approximation for a very complex relationship, and the basic formula can be further modified to consider other variables. For example, one can add a terror modifier based on the judgment that the agent would cause panic and social disruption. Such a systemic approach could help when determining policies for vaccinations and other interventions (3).

Assessing the threat of bioterrorism

Chalk has written that the threat of bioterrorism cannot be evaluated exclusively in terms of the hazards posed by the various biological agents themselves or in terms of the likelihood of an attack taking place (7). Even the most dangerous pathogen presents little threat in terms of bioterrorism if there is no one willing or able to use it. Conversely, even the most extreme terrorists require a biological agent capable of causing the harm and terror they seek to inflict.

Ackerman and Moran (1) have suggested the following formulation for constructing an initial bioterrorist threat:

 Bioterrorist threat = consequences of attack x likelihood of attack.

Each of these elements can be further subdivided as follows:

- Consequences = value of assets being defended x hazard posed by agent(s) x vulnerability of asset being defended, and
- Likelihood of attack = motivation x capability of attacker(s).

This formulation shows that the threat of bioterrorism is a function of the value and vulnerability of the asset at risk, the harm that could be caused by a particular biological agent or toxin and the capabilities and intentions of the bioterrorists. These elements are interdependent (1).

Vulnerability to biological weapons

International vulnerability to disease is increasing, especially disease used as a weapon. Increased globalisation, which promotes the rapid movement of people, animals and products around the globe; the emergence of new pathogens as human populations invade previously pristine environments; increasing contact between people and domestic animals and wildlife leading to new zoonoses jumping from animals to humans; urbanisation; the appearance of antibiotic and pesticide resistance by diseases and disease vectors of global concern; lack of effective vaccines; and termination of vaccine programmes for diseases that have been eradicated contribute to this increased vulnerability. The global trade in wildlife also provides pathways for transmitting diseases that threaten not only humans, but livestock, international trade, agriculture, native wildlife populations and the health of ecosystems (18). The next step in conducting a threat assessment for bioterrorism is a vulnerability analysis. This involves searching for ways in which the target can be attacked by non-state actors using BWs (1, 23). The agricultural sector is extremely vulnerable to bioterrorism attacks against livestock and crops. Agriculture has several characteristics that pose unique problems for managing the threat. Production is geographically disbursed in unsecured environments and livestock are frequently concentrated in confined locations and then transported and mingled with other herds. Pest and disease outbreaks can quickly halt economically important exports. There is also a significant lack of national expertise in the diagnosis and management of exotic foreign animal diseases (FADs). Although

vulnerability does not equate to risk, what makes the vulnerabilities inherent in agriculture so worrying is that the capability requirements for exploiting those weaknesses are not significant and are certainly considerably less than those needed for a humandirected biological attack.

The following illustrates why there is a vulnerability to these animal agents. First, there is a large menu of potential agents that have the potential to severely effect agricultural populations and/or trade. Many are environmentally hardy, able to exist for extended periods in organic or inorganic matter, or to access available vectors or wildlife reservoirs. The most important are listed by the Office International des Épizooties (OIE: World organisation for animal health) (25). Second, most FADs are non-zoonotic, meaning there is little risk to the terrorist when handling these agents. This eliminates the need for special protective measures and biosecurity practices that could indicate a developing threat. Third, animal and crop diseases can be spread rapidly to large numbers of herds or fields over wide geographic areas because of the intensive and concentrated nature of modern farming practices and the increased susceptibility of livestock and crops to viral and bacterial agents. Of critical importance is the fact that no 'weaponisation' or delivery systems are required - the animals and plants themselves are the primary vector for agent amplification and transmission. Vulnerability is further increased by an inefficient, passive disease reporting system that is further hampered by a lack of trust between regulators and producers.

Another area of vulnerability is represented by emerging infectious diseases (EIDs) (11). This subject is discussed in detail by Brown in this journal (2). Emerging infectious diseases of free-living wild animals can be classified into

three major groups on the basis of key epizootiological criteria:

- EIDs associated with 'spill-over' from domestic animals to wildlife populations living in proximity and vice-versa
- EIDs directly related to human intervention, via host or parasite translocations
- EIDs with no overt human or domestic animal involvement.

Two major biological implications are that first, many wildlife species are reservoirs of pathogens that threaten domestic animals and human health and, second, wildlife EIDs pose a substantial threat to the conservation of global biodiversity (9).

Most human EIDs result from exposure to zoonotic pathogens, that is, those transmitted naturally between animals and humans, with or without the establishment of a new life-cycle in humans. Wildlife plays a key role in their emergence by providing a 'zoonotic pool' from which previously unknown pathogens can emerge. This occurs classically for the influenza virus which causes pandemics in humans after periodic exchange of genes between the viruses of wild and domestic birds, pigs and humans. Searches for new zoonotic pathogens have become part of the strategy to counter emerging disease threats to humans and domestic animals and knowledge from studies of known pathogens can assist in this surveillance (9). In addition, as noted earlier, many bioterrorism agents of major concern are zoonotic in origin (29). Several diseases that threaten human and livestock health can be carried by different species of wildlife. Often the wildlife species are migratory, increasing the risk of spreading the diseases over larger geographic areas and across borders that are invisible to these travellers. Increasing the contact rate between infected wildlife and humans is one potential risk of human infection and disease spread and only rarely can domestic animals be regarded as fully isolated from wildlife. In most cases, livestock are maintained in environments and direct physical contact with wildlife is obvious. Wild, migratory waterfowl, for example, have been observed feeding among grazing cattle in the Netherlands. Wild ducks feed with domestic ducks in many parts of the world and shore birds get in close contact with chickens in Malawi. Across the globe, wild waterfowl share feed with turkeys raised on range and with free-range chickens. Eventually these domestic animals will contact humans and the probability of spreading disease is real. Hunting and harvesting of wildlife create a very direct contact between humans and wildlife because of the handling of bagged animals (17, 18).

Motivations for engaging in bioterrorism

For a bioterrorism attack to be significant, terrorists must be both capable of conducting a biological attack and motivated to do so. Ackerman and Moran (1) identified a variety of ideological, strategic and tactical factors that provide important motivational incentives and constraints that shape the inclination of terrorists to embrace or reject such action.

The literature is filled with articles, essays, monographs, studies and editorials that attempt to describe and explain those factors that motivate terrorists, such as culture and religion, poverty, repression, psychological (i.e. personal dissatisfaction), strategic and political objectives. However, what appears to bind these groups together is belief in a core ideology. The term ideology implies a comprehensive vision, a body of ideas reflecting the social needs and aspirations of an individual, group, class or culture. Simply stated, it reflects what a group is 'for' and what is 'against' (1).

The motivating factors of terrorism also include a rational strategic consideration of goals and

options – a cost-benefit analysis – as acts of terrorism are planned events, not random acts of violence. As such, they require tactical consideration (evaluation) of vulnerabilities and gaps in biosecurity of the intended target. In societies with a free press, those vulnerabilities are often revealed and reinforced in media coverage of bioterrorism-related topics that may encourage exploitation of those vulnerabilities using bioterrorism (1). For example, the United States food supply is widely seen as a target of opportunity by terrorist groups. A March 2005 Government Accountability Office report (13) noted that while some progress had been made, fundamental channels of communication and coordination have yet to be established in attempting to prevent an agro-terror attack. In December 2004, former secretary of the United States Department of Health and Human Services, Tommy Thompson, noted, 'For the life of me, I cannot understand why the terrorists have not attacked our food supply because it is so easy to do. We are importing a lot of food from the Middle East, and it would be easy to tamper with that' (26). Lastly, Michael Blackwell, Dean of the College of Veterinary Medicine of the University of Tennessee, has opined that the next terrorist attack is 'probably going to involve the food supply since agro-terrorism is certainly the easiest scheme to accomplish because of the way food moves. How do you guard food products from the farm or pasture all the way to the table?' (21).

As noted previously, BWs are extremely well suited for covert development and deployment and can leverage the availability of dual-use technologies that can be easily acquired by legitimate channels. Terrorists might be constrained by the perceived challenges of developing and using BWs, the unpredictability of a desired outcome, and the ease of acquisition and reliability of conventional alternatives, such as explosives and small arms.

As already noted, the capabilities and motivations of potential perpetrators for engaging in bioterrorism has often been given insufficient attention in threat assessments. Although there are likely to be few external indicators of a non-state BW programme, law enforcement and intelligence analysts could look for any indicators that might appear (e.g. group members becoming ill with rare diseases or evidence of acquisition of dangerous pathogens). However, it is primarily by examining general characteristics and patterns of behaviour of non-state actors that analysts will be able to discern a capability or motivation for bioterrorism.

Case studies

To illustrate the potential for bioterrorism to spread disease, it is worth examining a couple of recent examples of diseases that appeared without warning and have steadily expanded their range, established endemicity, and pose substantive threats to livestock and humans.

West Nile virus

The recognition of West Nile virus (WNV) in the Western Hemisphere in the summer of 1999 marked the first introduction in recent history of an Old World flavivirus into the New World (Fig. 1) (5). Humans who contract WNV usually experience only mild symptoms-fever, headache, body aches, skin rash and swollen lymph glands. If WNV enters the brain, however, it can cause life-threatening brain inflammation or meningitis.

The appearance of WNV in the United States and Canada was possibly a result of animal transportation or migration. The WNV is a flavivirus maintained in nature by a bird-mosquito

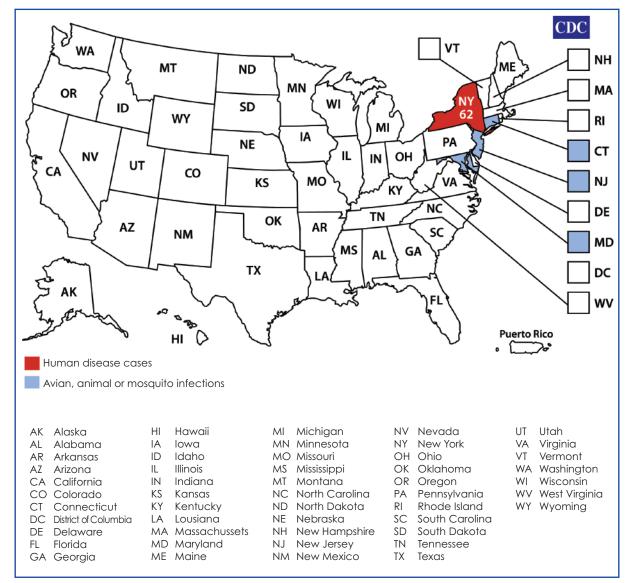


Figure 1

The extent of West Nile virus spread in the United States following its introduction in 1999 (5) Source: Centers for Disease Control

cycle. Lack of aggressive attempts to control mosquito vectors allowed the virus to successfully over-winter (12) Each subsequent year, the virus spread (Fig. 2) (6) and by 2004, it had extended widely across the contiguous states of the United States, several provinces of Canada and south to the Caribbean and Mexico (12).

The United States, however, is not alone in reporting new or heightened activity in humans and other animals and incursions of flaviviruses into new areas are likely to continue through increasing global commerce and travel. Similar expansion of other flaviviruses has been documented. Dengue viruses have spread from their roots in Asia to all tropical regions. Japanese encephalitis virus recently encroached on the northern shores of Australia and may soon become endemic on that continent. With this recent history of flavivirus incursions

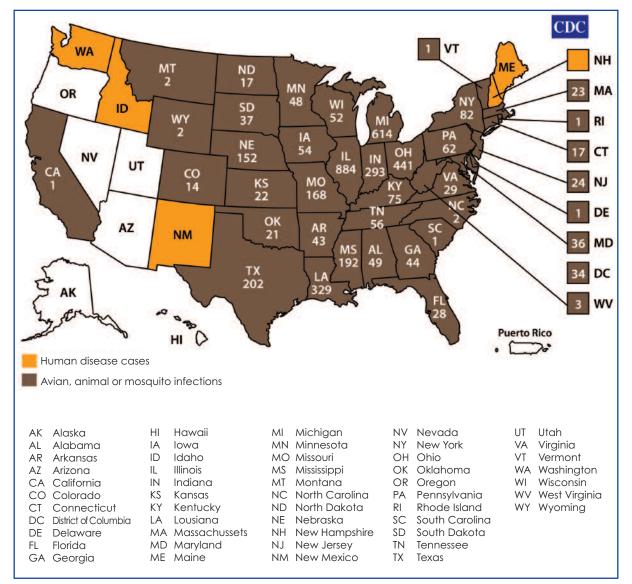


Figure 2

in the United States and elsewhere, it is highly likely that other microbes of public and veterinary health concern might follow (27).

The first step in the transmission cycle of WNV occurs when a mosquito bites an infected bird or other infected animal. More than 138 bird species and more than 43 mosquito species have been identified as WNV transmitters. With so many susceptible hosts to amplify it, WNV has spread rapidly across the United States. The disease is most commonly found in Africa, West Asia, Europe and the Middle East. In the course of a single year (2004), there were 2 470 cases of WNV reported, including 88 deaths (17).

Foot and mouth disease

A strain of foot and mouth disease (FMD) virus serotype O (FMDV type O) named PanAsia has spread from India throughout southern Asia and

The extent of West Nile virus spread in the United States by 2002 (6) Source: Centers for Disease Control

the Middle East. It was responsible for an explosive pandemic in Asia and extended to parts of Africa and Europe from 1998 to 2001. It was first identified in northern India in 1990 and spread westwards into Saudi Arabia during 1994 and, subsequently, throughout the Near East and into Europe (Turkish Thrace, Bulgaria and Greece) in 1996. In 1993 it was reported in Nepal and later in Bangladesh (1996) and Bhutan (1998). In 1999, it was reported from mainland China (Tibet, Fujian and Hainan) and then detected in the Taiwan Province of China. In late 1999 and in 2000, it reached most of South-East Asia. Most recently, it has been introduced into the Republic of Korea, Japan, the Primorsky Territory of the Russian Federation and Mongolia (areas free from FMD since 1934, 1908, 1964 and 1973, respectively).

The FMD virus has been isolated from a wide variety of host species (cattle, water buffalo, pigs, sheep, goats, camels, deer and antelope). In February 2001, the PanAsia strain spread to the United Kingdom where, in just over seven months, it caused outbreaks on 2 030 farms. From there, it quickly spread to the Republic of Ireland, France and the Netherlands. Shortly after the outbreak in the United Kingdom, genomic analyses revealed the virus responsible was related to the virus that spread from India in the early 1990s to the Far East. The sequence data suggested that the closest relative of the United Kingdom outbreak virus was an isolate from an outbreak in the Republic of South Africa, which appeared to have resulted from the introduction of an Asian virus into the port of Durban (22). Although the virus has been controlled or eradicated in all of these normally FMD-free or sporadically infected countries, it appears to be established throughout much of southern Asia, with geographically separated lineages evolving independently. It also appears to have, in some areas, replaced the enzootic strains of FMDV type O. A pandemic such as this is a

rare phenomenon but demonstrates the ability of newly emerging FMDV strains to spread rapidly across a wide region and invade countries previously free from the disease (Fig. 3) (19, 30).

Consequences of an act of bioterrorism on agriculture

Agro-terrorism will be viewed as an act of economic warfare. In this age of global agribusiness, any country that has its livestock or crops infected by endemic or exotic pathogens, either naturally or intentionally, is rapidly barred from export markets (31). Agricultural targets are not just animals or plants; they can include transportation systems, water supplies, farm workers, producers, food handlers, grain elevators or other storage facilities, restaurants, grocery stores and food and agriculture research laboratories. Infectious, chemical or radiological agents could be introduced at any point in the farm-to-table continuum. Direct harm to humans is more likely to occur if terrorists contaminate finished food or food products rather than target livestock or crops. While the cases of bovine spongiform encephalopathy (BSE) in the United States are not a result of terrorism, they serve to illustrate how agricultural business is interconnected and how key stakeholders, such as farm suppliers, transportation companies, grocery stores, restaurants, equipment distributors and, ultimately, consumers all pay the price in an agricultural crisis.

An attack against animals and crops is generally viewed as more benign and less offensive than if humans are killed from a direct assault such as the anthrax mailings. Agriculture terrorism is not about killing animals, it is about crippling a nation's economy (10). To that end, pathogens foreign to United States livestock, poultry and crops would possibly be targeted by terrorists for use. Many pathogens readily available in nature could be

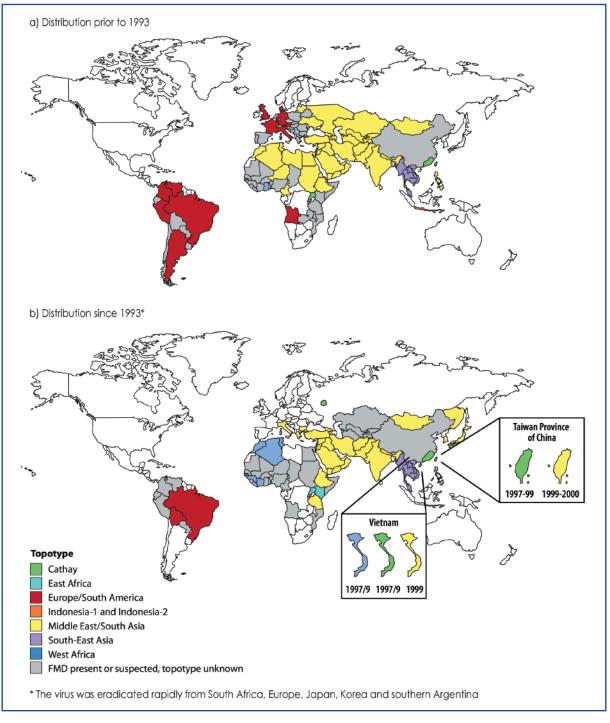


Figure 3

Distribution of foot and mouth disease virus type O topotypes in 2001 (30)

used against livestock and crops and require little effort or risk to smuggle into the United States. These same agents could be acquired from lowsecurity laboratories or commercial sources located outside of the country. Most FAD agents pose no risk to human health, so terrorists could safely and freely handle and disperse these pathogens. Once released, an agro-terrorism attack might go unnoticed for days to weeks or, in the case of crops, months, and by that time attribution may be impossible for law enforcement agencies.

Conclusion

While it is unlikely that a bioterrorist attack would increase the risk of a disease spreading beyond what has already been observed for diseases like West Nile virus and other emerging or re-emerging diseases, the environmental consequences and public health impact of an attack on agriculture should not be underestimated. The fact that the agents used in agro-terrorism pose a minimal zoonotic threat to human populations does not mean there are no public health consequences to a terrorist attack. The psychological trauma resulting from the loss of the family farm would be significant. Farmers and producers may feel inadequately prepared to perform well in other occupations, leading to a sense of failure. Stress on families would be very high, which could lead to serious depression, anguish, substance abuse, domestic violence, loss of insurance benefits and suicide. Results of agro-terrorist attacks could include major economic crises in agriculture and food industries, loss of confidence in government and some human casualties. Once the agent has transgressed prevention measures, time becomes one of the most important predictors for the significance of effects. The longer the agent goes undetected, the greater the costs for management and the fewer the opportunities and options for eradication, containment or control (23). In addition to the immediate effects of a bioterrorist event, the persistence of introduced agents in the environment could have profound long-term effects leading to the creation of new or unbalanced ecosystems that in and of themselves could prove harmful to indigenous human, animal and plant species.

References

- Ackerman G.A. & Moran K.S. 2004. Bioterrorism and threat assessment. Prepared for the Weapons of Mass Destruction Commission (WMDC), No. 22, 1-18 November. WMDC, Stockholm, 19 pp (www.wmdcommission.org/ files/No22.pdf accessed on 18 July 2006).
- Brown C.C. 2006. Risks from emerging animal diseases. *In* Worldwide risks of animal diseases (J.E. Pearson, ed.). *Vet Ital*, **42** (4), 305-317.
- Casadevall A. & Pirofski L. 2004. The weapons potential of a microbe. Trends Microbiol, 12 (6), 259-263.
- Centers for Disease Control and Prevention (CDC) 2000. Biological and chemical terrorism: strategic plan for preparedness and response. Recommendations of the CDC Strategic Planning Workgroup. MMWR Recomm Rep, 49, 1-14.
- Centers for Disease Control (CDC) 2006. Final 1999 West Nile virus activity in the United States (map). CDC, Atlanta (www.cdc.gov/ncidod/dvbi d/westnile/Mapsactivity/surv&control99Maps.htm, last updated13 February 2006, accessed on 25 April 2006).
- Centers for Disease Control (CDC) 2006. Final 2002 West Nile Virus Activity in the United States (map). CDC, Atlanta (www.cdc.gov/ncidod /dvbid/westnile/Mapsactivity/surv&control02Maps.

R.E. Weller

htm, last updated 13 February 2006, accessed on 25 April 2006).

- Chalk P. 2004. Hitting America's soft underbelly: the potential threat of deliberate biological attacks against the U.S. agricultural and food industry. Rand National Defense Research Institute, Santa Monica, California, MG-135-OSD, 68 pp.
- Cody E. 2006. War lives on at museum of the macabre, A14. washingtonpost.com, 17 April (www.washingtonpost.com/wp-dyn/content/ article/2006/04/06/AR2006040602022.html accessed on 18 July 2006).
- Daszak P., Cunningham A.A. & Hyatt A.D. 2000. Emerging infectious diseases of wildlife – threats to biodiversity and human health. Science, 287, 243-249.
- Davis R.G. 2001. Agricultural bioterrorism. New frontiers: global threats. Iowa State University, Ames (www.actionbioscience.org/newfrontiers/ davis.html accessed on 25 April 2006).
- Fauci A.S., Touchette N.A. & Folkers G.K. 2005. Emerging infectious diseases: a 10-year perspective from the National Institute of Allergy and Infectious Diseases. *Emerg Infect Dis*, **11**, 519-525.
- Gibbs E.P.J. 2005. Emerging zoonotic epidemics in the interconnected global community. *Vet Rec*, **157**, 673-679.
- Government Accountability Office (GAO) 2005. Oversight of food safety activities: Federal agencies should pursue opportunities to reduce overlap and better leverage resources. Washington, DC, 30 March (www.gao.gov/highlights/d05213high.pdf accessed on 18 July 2006).
- 14. Hickson R. 1999. Subtle forms of strategic indirect warfare: infecting 'soft' biological targets; some psychological, economic, and cultural consequences. *In* Abstracts of the 1999 American Phytopathological Society (APS) Annual Meeting Symposium: Plant pathology's role in anti-crop

bioterrorism and food security, 10 August, Montreal. APS, St Paul, Publication No. P-1999-0150-SSA (www.apsnet.org/meetings/abstract/ 1999/sp99ab51.htm accessed on 18 July 2006).

- Hugh-Jones M. 1992. Wickham Steed and German biological warfare research. Intell Nat Security, 7, 379-402.
- 16. Huxsoll D.L. 1999. Biological terrorism: Identifying and protecting our infrastructure. *In* Abstracts of the 1999 American Phytopathological Society (APS) Annual Meeting Symposium: Plant pathology's role in anti-crop bioterrorism and food security, 10 August, Montreal. APS, St Paul, Publication No. P-1999-0146-SSA (www.apsnet.org/meetings/abstract/1999/ sp99ab47.htm accessed on 18 July 2006).
- 17. Kanstrup N. & Wollscheid K. 2005. The role of hunters and hunting in management of diseases spread by wildlife. Presentation given at United Nations Environment Programme (UNEP) Conference on Migratory Species of Wild Animals (CMS) Roundtable on Wildlife Diseases, 19 November, Nairobi. UNEP Headquarters Gigiri, Nairobi, 5 pp (www.cic-wildlife.org/uploads/media/UNEP _CMS_Roundtable_on_Wildlife_Diseases.pdf accessed on 18 July 2006).
- Karesh W.B., Cook, R.A., Bennett E.L. & Newcomb J. 2005. Wildlife trade and global disease emergence. *Emerg Infect Dis*, **11**, 1000-1002.
- Knowles N.J., Samuel A.R., Davies P.R., Midgley R.J. & Valarcher J.-F. 2005. Pandemic strain of foot-and-mouth disease virus serotype O. *Emerg Infect Dis*, **11**, 1887-1893.
- Labanca N. 2000. Key points in the history of biological warfare, Conference on biosecurity and bioterrorism. Instituto Diplomatico 'Mario Toscano', Villa Madama, 18-20 September, Rome. Istituto Nazionale di Fisica Nucleare, Milan, 20 pp (www.mi.infn.it/~landnet/Biosec/ labanca.pdf accessed on 18 July 2006).

- Loveday Y. 2004. The best offense is a strong (bio)defense, *Tenn Alumn Mag*, 84 (2) (pr.tennessee.edu/alumnus/alumarticle.asp?id= 480 accessed on 18 July 2006).
- Mason P.W., Pacheco J.M., Zhao O-Z. & Knowles N.J. 2003. Comparisons of the complete genomes of Asian, African and European isolates of a recent foot-and-mouth disease virus type O pandemic strain (PanAsia). J Gen Virol, 84, 1583-1593.
- Meyerson L.A. & Reaser J.K. 2002. Biosecurity: moving toward a comprehensive approach. Bioscience, 52 (7), 593-600.
- 24. Meyerson L.A. & Reaser J.K. 2003. Bioinvasions, bioterrorism, and biosecurity. *Front Ecol Environ*, 1 (6), 307-314 (www.ecos-systems.org/downloads/ Bioterrorism.pdf accessed on 18 July 2006).
- Office International des Épizooties (OIE) 2006. Diseases notifiable to the OIE. OIE, Paris (www.oie.int/eng/maladies/en_classification.htm accessed on 22 September 2006).
- 26. Pear R. 2004. U.S. Health Chief, stepping down, issues warning, New York Times, 4 December, Washington (www.nytimes.com/2004/12/04/politics/04healt h.html?ei=5090&en=011a6bc57616fb58&ex=12 59816400&adxnnl=1&partner=rssuserland&adx nnlx=1145894452-9/ tGkC2Gc92q7o36SGwNng accessed on 24 April 2006).
- Peterson L.R. & Roehrig J.T. 2001. West Nile virus: a reemerging global pathogen. *Emerg Infect Dis*, 7 (4), 611-615.
- Purver R. 1995. Chemical and biological terrorism: the threat according to the open literature. Canadian Security Intelligence Service Report, Ottawa(www.csis-scrs.gc.ca/en/publications/ other/c_b_terrorism01.asp accessed on 18 July 2006).
- 29. Rabinowitz P., Gordon Z., Chudnov D., Wilcox M., Odofin L., Liu A. & Dein J. 2006. Animals as

sentinels of bioterrorism agents. *Emerg Infect Dis*, **12** (4), 647-652.

- Samuel A.R. & Knowles N.J. 2001. Foot-andmouth disease type O viruses exhibit genetically and geographically distinct evolutionary lineages (topotypes). J Gen Virol, 82, 609-621.
- Weller R.E. 2001. Agricultural pathogens, biological containment and the Biological and Toxin Weapons Convention. *In* Anthology of biosafety. IV. Issues in public health (J.Y. Richmond, ed.). American Biological Safety Association, Mundelien, 281-290.
- 32. Wheelis M. 1999b. Biological sabotage in World War I. *In* Biological and toxic weapons: research, development, and use from the Middle Ages to 1945 (E. Geissler & J.E. van Courtland Moon, eds). International and Peace Research Institute, Stockholm. Oxford University Press, Oxford, 35-62.
- Wheelis M. 1999a. Biological warfare before 1914. *In* Biological and toxic weapons: research, development, and use from the Middle Ages to 1945 (E. Geissler & J.E. van Courtland Moon, ed.). International and Peace Research Institute, Stockholm. Oxford University Press, Oxford, 8-34.
- 34. Wilson T.M., Logan-Henfrey L., Weller R.E. & Kellman B. 2000. Agroterrorism, biological crimes, and biological warfare targeting animal agriculture. *In* Emerging diseases of animals (C. Brown & C. Bolin, eds). ASM Press, Washington, DC, 23-57.
- 35. Zilinskas R.A. 1999. Assessing the threat of bioterrorism: Congressional testimony by Raymond Zilinskas before the House Subcommittee on National Security, Veterans Affairs, and International Relations, US House of Representatives, 20 October, Washington DC. Center for Nonproliferation Studies, Monterey, California (cns.miis.edu/pubs/reports/zilin.htm accessed on 18 July 2006.