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THE THREAT OF PLANT PATHOGENS AS WEAPONS AGAINST U.S. CROPS

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■ **Abstract** The U.S. National Research Council (NRC) concluded in 2002 that U.S. agriculture is vulnerable to attack and that the country has inadequate plans for dealing with agricultural bioterrorism. This article addresses the vulnerability of U.S. crops to attack from biological weapons by reviewing the costs and impact of plant diseases on crops, pointing out the difficulty in preventing deliberate introduction of pathogens and discovering new disease outbreaks quickly, and discussing why a plant pathogen might be chosen as a biological weapon. To put the threat into context, a brief historical review of anti-crop biological weapons programs is given. The argument is made that the country can become much better prepared to counter bioterrorism by developing a list of likely anti-crop threat agents, or categories of agents, that is based on a formal risk analysis; making structural changes to the plant protection system, such as expanding diagnostic laboratories, networking the laboratories in a national system, and educating first responders; and by increasing our understanding of the molecular biology and epidemiology of threat agents, which could lead to improved disease control, faster and more sensitive diagnostic methods, and predictions of disease invasion, persistence, and spread following pathogen introduction.

INTRODUCTION

> *Using [biological weapons] to attack livestock, crops, or ecosystems offers an adversary the means to wage a potentially subtle yet devastating form of warfare, one which would impact the political, social, and economic sectors of a society...*
>
> *Kadlec (42)*

> *The United States is vulnerable to bioterrorism directed against agriculture ... The nation has inadequate plans to deal with agricultural bioterrorism.*
>
> *NRC report on Countering Agricultural Bioterrorism (60)*

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The attacks on September 11, 2001, and the subsequent anthrax infections in the fall of 2001 abruptly reminded Americans that the United States is vulnerable to attack (45). As expected, the press has emphasized the public health and medical aspects of bioterrorism since then, but the country's vulnerability to attack is much broader (22, 87, 88). Here we address the threat of plant pathogens as weapons against crops. We do this by giving a brief historical context to the concerns about bioterrorism, addressing the impact of diseases on crops, reviewing past efforts at developing plant pathogens as weapons against crops, and showing that there is no consensus on the most serious biological threats to U.S. crops. We then address U.S. preparation (or lack thereof) for biological attack against crops. Much of our analysis is based on the recent National Research Council report "Countering Agricultural Bioterrorism" (60).

We use the term "bioterrorism" fairly broadly. There are at least two useful definitions of terrorism: a policy intended to strike with terror against whom it is adopted (Oxford English Dictionary); and the unlawful use or threatened use of force or violence by a person or an organized group against people or property (American Heritage Dictionary of the English Language, 4th edition). The former definition focuses on acts that specifically cause terror or fear in a population, whereas the latter definition encompasses all nongovernmental acts of aggression. The distinction between warfare, terrorism, and criminal behavior can become difficult at the boundaries. Here we use the term bioterrorism as the intentional use, by any human agent other than uniformed military personnel, of organisms (or their products) to cause harm (or death) to humans, animals, or plants (74, 75).

GENERAL CONCERNS

Fear about the threat of biological weapons has been episodic throughout the past century, with the 1930s and the 1950s being times of particular concern. The most recent cycle began in the late 1990s (1, 7, 13, 15, 46, 86). This was based on the knowledge that several countries or groups were, or recently had been, developing or trying to acquire biological weapons (5, 10, 13, 29, 41, 46, 63, 64, 83, 85). Moreover, because the United States is a free and open society, with little restriction on movement of individuals, it was quite clear that the country was vulnerable to attack with biological weapons (46, 60). Popular and technical books published in 1999 dealt with many aspects of the threat. Of particular importance were the revelations by Ken Alibek, a principal figure in the former Soviet Union's bioweapons program, of the extent and magnitude of that country's program on what is sometimes called the "poor man's weapon of mass destruction" (5). There is concern that the scientists involved in the former country's bioweapons program, which was concentrated in regions that are now independent countries, could be hired to use their expertise and facilities to prepare terrorist weapons (38).

The seriousness of the threat of bioterrorism was emphasized in a theme issue of the *Journal of the American Medical Association* (*JAMA*) in 1997, and the themes were expanded in a book edited by Nobel Laureate Joshua Lederberg in 1999 (46). The National Research Council (NRC) issued a report on Chemical and

Biological Terrorism in 1999 (58). The references make the strong point that the threat is real and that countries in general, and the United States in particular, have not made adequate plans to prevent or respond to attack. Several popular books (e.g., 52) have also sounded the alarm, and bioterrorism has become a prominent theme in novels and films. Because of the perceived threat, U.S. Executive Orders and Presidential Decision Directives were issued in 1998 and 1999 addressing the problems of weapons of mass destruction, and preparedness against biological and chemical weapons (91–93).

The fears that emerged in the late 1990s about bioterrorism in general also coincided with cautions regarding potential bioterrorism directed against agriculture. In a conference on Food and Agricultural Security in late 1998, many of the issues discussed were related to the threat of attack, and the lack of U.S. preparedness. A report on the conference proceedings was published in 1999 (29). In 1999, the American Phytopathological Society (APS) held a symposium on "Plant Pathology's Role in Anti-Crop Bioterrorism and Food Security" (70) that received considerable media coverage in the United States and Canada. Both *Scientific American* and *New Scientist* published articles that discussed past offensive programs using crop pathogens and the threat of new attacks by terrorists (48, 67). The initial plans for a NRC study on agricultural bioterrorism also began in 1999 (60). A workshop entitled "Agro-Terrorism: What is the threat?" was held at Cornell in the fall of 2000, sponsored by Cornell's Peace Studies Program, The Center for Global Security Research, and The Center for Nonproliferation Studies. Both the Association of Conservation Districts and the USDA Annual Outlooks Conferences held sessions on agricultural bioterrorism. It is likely that there were other workshops on the topic.

Despite the rising fears about the use of biological weapons against agricultural and nonagricultural sectors of the United States, and the increased discussion that began in the late 1990s, little progress was made in preparing to either prevent or respond to attack. The organizer of the Agricultural Security conference in 1998, T.W. Frazier, stated, "some organizations with keen interest were unwilling to even be listed as a sponsor organization or to send a speaker to this conference" (28). Moreover, he continued, some "friendly governments are reluctant to discuss WMD [weapons of mass destruction] terrorist issues in public" (28). The events during the fall of 2001 clearly caused public perception to consider bioterrorism (in some form) as a threat. It remains to be seen how this highly visible and intense consideration of the topic at governmental and extra-governmental level will translate into better preparation.

VULNERABILITY

U.S. agriculture is vulnerable to attack precisely because it is so economically important, representing 13% of the gross domestic product and 17% of employment (80). Crops are vulnerable because they are grown over large areas, cannot be protected (in a military sense), and are poorly monitored. For instance, soybeans are grown over 31 million hectares in the United States (77), making detailed

surveillance virtually impossible. Most of the crop cultivars grown are susceptible to many pathogen species and strains, especially to those that are not endemic (49), and genetic diversity is low for most species grown (27). Obviously, we could not, and would not, place walls around fields to prevent the introduction of microorganisms. Thus, one can think of crops as easy targets for attack, since there is little chance of a perpetrator being observed releasing microbial agents or pests in an area, and there is little that can be done initially to limit disease spread as infections occur unobserved and uncontrolled. In a military sense, crops can be considered soft targets (37).

Another consequence of the low surveillance of crops is the long lag between introduction of a pathogen and discovery of the resulting disease. Epidemiological theory and practice indicate that successful eradication or containment of a disease of any host requires action very soon after the start of the epidemic (26). However, with many crop pathogens, the disease may be present for months or even years before it is identified. Because most individual plants are not observed by anyone, a new disease problem likely will not be reported until after many generations of infection, when disease prevalence exceeds the threshold for being noticed. For instance, *Plum pox virus* was probably introduced into Pennsylvania at least 5 years before it was reported in 1999 (F. Gildow, personal communication); citrus canker was introduced into Florida 2.5 years before it was discovered (72). Moreover, a new disease may be initially misdiagnosed, further delaying appropriate response.

Adding to the vulnerability of crops is the relative ease of introducing a pathogen into the United States, given the long borders with two countries and the impossibility of observing all products in transnational commerce. Port inspectors can observe only a small percentage of actual products (60). Furthermore, they focus on agricultural commodities when searching for pests (e.g., weeds, insects, pathogens), but a terrorist would not likely smuggle pathogen inoculum using declared agricultural products. The port inspectors may well serve as a valuable reminder to law-abiding individuals of the dangers in bringing in unapproved or uninspected products, but they cannot be effective in detecting deliberate smuggling of pathogens. Given the inability of the U.S. government to eliminate the importation of large volumes of illegal drugs into the county, interdiction of the tiny amounts of material that would be carried by bioterrorists is clearly hopeless.

Because spores of many plant pathogens can be dispersed long distances from a source (11), a terrorist might not even have to enter the country. Releasing spores from the other side of the border, or from offshore, may be just as effective. Contaminating seed with inoculum is another way of introducing a pathogen. This pathway of introduction may be of high importance since an increasing proportion of seed used for U.S. crops is produced in other countries (16).

PLANT DISEASES: COSTS AND IMPACT

There are many thousands of plant diseases in the United States, and an exact number is probably impossible to determine. Over 13,000 unique fungal pathogen species are listed by Farr et al. (24), and over 75,000 plant-fungus combinations

(because a single pathogen species may infect many host plant species). A given crop species such as wheat may be affected by over 200 different diseases worldwide; however, in a given region, there are generally about 5–20 serious diseases to control on an annual basis (e.g., 94). Many of the pathogens causing serious problems in crops are not native to the United States, not surprisingly as most of the crop species were introduced from other parts of the world, and the pathogens (slowly or rapidly) followed. In contrast to animal diseases, eradication of the most contagious plant diseases from a region has rarely been accomplished or even attempted (30, 73). Rather, crop production practices involve management of diseases at a low incidence or severity. Despite the existence of many plant pathogens within the country, several potentially serious ones have not yet taken hold here (49).

Pimentel et al. (66) estimate that plant diseases cost the U.S. economy $33 billion/year. Although such estimates are hard to derive, and are based on many assumptions, they are useful for showing the seriousness of crop diseases. These costs include the reduction in quantity and quality of yield, as well as short-term and long-term costs of control. Short-term costs include the purchase and application of pesticides, whereas long-term costs include the breeding for resistance and the development of new pesticides. Harvesting and grading differently because of the presence of disease, replanting, and growing less desirable crops in a given area all add to the overall cost. Trade disruptions can occur because the presence of some diseases can (drastically) restrict exports. A good example is Karnal bunt. Although many plant pathologists consider the disease to be of minor importance in terms of reduction in yield, the pathogen (*Tilletia indica*) is of quarantine significance. When the disease was discovered in Arizona (and subsequently in a few other states) in 1996, there was an immediate threat to the national wheat export market even though incidence of the disease was limited to a small geographic area (9). Although the disease was initially contained and markets preserved, it has subsequently been found in other states, and once again, wheat exports are threatened by a "minor" pathogen of limited distribution.

There is also a cost to animal and human health associated with plant disease, because some pathogens produce detrimental toxins (e.g., mycotoxins) and alkaloids (3). The important mycotoxins include the alflatoxins produced by *Aspergillus* species (which can cause acute necrosis, cirrhosis, and cancer), and the trichothecenes (i.e., T-2 mycotoxin) produced by *Fusarium* species (which can cause dermal irritation, and pulmonary and bronchial hemorrhage) (65). T-2 toxin is sometimes known as "yellow rain" in the BW (biological warfare) literature, after the term for alleged [but (now) largely discredited] allegations of use in S.E. Asia as a biological weapon (76).

Plant diseases develop over time—over a single or multiple growing season—through the multiplication of the pathogen (11). In some cases, complete defoliation can result, but substantial losses can occur with much lower disease intensities. The rate of spread of a disease depends on the dispersal mechanisms of the pathogen, as well as other epidemiological components (96), and can be either slow or fast. The spread of chestnut blight from a point source in New York in

1904 throughout the region east of the Mississippi river over less than 50 years is well documented (11), as is the within-season transport of spores of the stem rust pathogen (*Puccinia graminis* f.sp. *tritici*) from southern USA to Canada. Each year, the sporangia of the tobacco blue mold pathogen (*Peronospora tabacina*) are disseminated 1000+ km in a matter of hours from Cuba and Florida to more northern parts of the eastern United States (44). A recent example of disease invasion is barley stripe rust, caused by *Puccinia striiformis* f.sp. *hordei*. First discovered in one location in Texas in 1991, the disease had spread throughout the western United States by 1995 (14), and it is now one more disease for which resistance must be bred in order to grow barley economically.

PLANT PATHOGENS AS BIOLOGICAL WEAPONS

Because of the effects of diseases on crops, and high costs attributed to plant diseases, several countries in the twentieth century have, not surprisingly, explored the use of pathogens as weapons against crops. Moreover, dissident groups have threatened to use pathogens, "agents," or "compounds" against crops for a range of purposes. Finally, the objective of controlling the source of illegal drugs has prompted serious consideration of using plant pathogens as biological herbicides of crops. We discuss each of these topics below and present some of the information in terms of the broader topic of agricultural bioterrorism. However, we do not address the history of the use of products of plant pathogens (e.g., aflatoxin, T-2 toxin) as biological weapons against humans.

State Programs

Simon Whitby has written extensively about state-sponsored anti-crop biological weapons programs over the past century, especially those of the United States, Europe, and Iraq (89). He concludes:

> ". . . where states are intent on acquiring a capability to wage biological warfare and have access to modern biology, such activities are likely to include investigations into biological warfare against crops" (page xi).

Historical experience thus validates the current alarm about anti-crop biological weapons.

In World War I, Germany, and to a much lesser extent France, had programs of attacking military animals with biological agents (84). Horses and mules (very important for military operations at that time), and to a lesser extent cattle and sheep, were the principal target, with the attacks performed by secret agents operating in neutral trading partners of the Allied Powers (including Romania, Spain, Argentina, and the United States) and trans-shippers (Norway). Despite the concentration on animal targets, there is some sparse mention in surviving documentation of attacks on grains. This strategy most likely involved attempts to spoil harvested

wheat stored prior to shipping. Geissler (31) suggested that fungal spoilage agents were used; chemical spoilage agents (mercaptans in capsules that would rupture during milling) are also mentioned in the records (84).

After the war, a number of countries became actively involved in developing biological weapons. Most of these programs included an anti-crop component, albeit minor in some cases. In 1939, the French discussed using both Colorado beetle (*Leptinotarsa decemlineata*) and *Phytophthora infestans* (late blight) as agents to attack German potato crops from the air (47). However, it is unclear if any research was ever initiated. The French program ended suddenly in 1940 when the laboratories at Le Bouchet fell into German hands. In Germany, biological warfare research and development was severely curtailed by Hitler's 1942 prohibition of any offensive BW activities (32a). Nevertheless, under the rubric of defensive research, experiments on a number of plant diseases and pests were conducted, and work on Colorado beetles advanced to the point of field trials of aerial dissemination of live beetles or wooden models in 1943. Preparations for offensive use seem to have begun (i.e., mass production of beetles). The United Kingdom also had a BW program beginning before the war and continuing throughout, conducted in collaboration with Canada—and the United States after 1942—but it appears that there was little consideration of anti-crop BW, despite active development of anti-crop chemical agents (12, 84). The United States was different (57, 89); anti-crop agents were actively considered from 1942, and production of several agents [of rice blast (*Pyricularia oryzae*) and brown spot (*Cochliobolus miyabeanus*) of rice] were at the pilot plant scale by the end of the war, with several other agents under study. Aerial dispersal was tested, but the results were not encouraging.

The only country known to have used biological weapons in the Second World War was Japan (35, 36). There was extensive, albeit rather primitive, use of diseases as a weapon against Chinese troops and civilians, beginning in 1939 (the R&D program began early in the 1930s), with a death toll probably in the hundreds of thousands. Most scholarly attention to this program has focused on the anti-human efforts, and on the use of human subjects in the R&D process, but there was clearly an anti-agricultural component as well, involving both crop and animal disease agents. A wide range of plant pathogens, including fungi, bacteria, and nematodes, affecting a wide range of grains and row crops, were studied in experimental plots. However, delivery devices were never developed, and the anti-crop biological agents were apparently never used (although chemical herbicides were used against Chinese crops on several occasions).

After World War II, several countries had biological weapons programs; most important are the United States, the Soviet Union, and Iraq. The U.S. program was the largest and most successful BW program ever, until President Nixon dismantled it by executive order in 1969 (67, 89). Although it was a continuation of the U.S. wartime BW program, the program really took off only in the early 1950s under the stimulus of the cold war and the Korean conflict. In addition to developing and stockpiling munitions filled with anti-human agents for possible retaliatory use, a number of plant agents were developed for strategic use. Principal agents were

fungi that cause stem rusts of wheat and rye (*P. graminis* f.sp. *secalis*), rice blast, and late blight of potatoes. Methods of large-scale culture, harvesting and drying, storing, and dissemination were studied. By 1954, the United States had developed stem rust into a usable weapon, delivered by cluster bombs containing turkey feathers heavily dusted with spores (aerial spray devices were developed later). Spores were produced year-round, and munition fills were replaced periodically to maintain spore viability. Rice blast subsequently entered large-scale production as well. By the time Nixon renounced offensive BW, the United States had stockpiled the agents of stem rust of wheat, stem rust of rye, and rice blast. All were destroyed by 1973, pursuant to President Nixon's executive order.

The Soviet BW program, which started in the 1920s, also probably did not produce a militarily significant capability until after World War II. Even then it appears to have been less effective than the U.S. program. However, when the United States renounced its offensive BW program in 1969, the Soviet Union was on the verge of a dramatic expansion of its program, and over the next 20 years became the only biological-weapons superpower (5). Their program involved an extensive anti-crop program, which began in the late 1940s or early 1950s (5). Although few details of the anti-crop program are known, the principal agents were those causing rice blast, wheat stem rust, and rye stem rust. The agents were not stockpiled, but rather a short-notice production capacity was maintained in case of need. Use of the agents was anticipated to be strategic, in an all-out war, delivered by ICBMs. The anti-crop program was discontinued in the late 1980s, before the anti-personnel program, when strategic considerations suggested it to be unnecessary.

UNSCOM inspections following the 1991 Gulf War disclosed's the development of biological weapons in Iraq in the late 1980s (the program began in 1974). Although here, as in other known programs, attention focused on anti-human agents, covered smut (caused by *Tilletia tritici* and *T. laevis*) of wheat was being actively developed as an anti-crop weapon (89, 90). There is some evidence that other pathogens of grain crops were also investigated as weapons. (The Iraqi program also involved the *Aspergillus*-produced aflatoxin as a biological weapon.) Although Iraq did not succeed in developing covered smut into a functional weapon, they were probably close, given their experience in weaponizing other agents. Large-scale production had been achieved, and there may have been small-plot field trials. The Iraqi BW program was ended by the Gulf War and the subsequent UNSCOM inspections. At present, it is not known if Iraq has rebuilt its capacity.

Thus, as indicated by Whitby (89), the historical evidence suggests that countries serious about developing a military capability to wage biological warfare usually include an anti-crop capability as part of the program. Anti-crop weapons have always been of lower priority than anti-human weapons, and in all known cases have been notably less successful. Nevertheless, any country with the military and scientific sophistication to successfully develop a biological weapons capability is likely capable of developing an effective anti-crop biological weapon. Given that there are at least half a dozen countries suspected of actively developing

biological weapons, there is a real possibility that secret military interest in anti-crop weapons poses a serious risk to security in today's world.

Allegations

In addition to the documented military development of anti-crop biological weapons, there have been sporadic allegations that nations or subnational groups have used them, or have threatened to use them [reviewed in (54)]. None of these allegations is supported by convincing evidence, and the likelihood is that all are erroneous; there is no evidence that any of the threats have been implemented. However, the allegations demonstrate that the threat of biological weapons against such crops can be used for political purposes. Here we summarize the only allegation with more than anecdotal importance: by Cuba against the United States in 1997.

Cuba has made recurrent public accusations that the United States has deliberately introduced pathogens and pests into its territory (97). Most of these complaints were clearly intended largely for domestic consumption, and were contained in speeches by Castro reported principally in domestic news media, but some were repeated to international media or in the UN General Assembly. With one exception (see below), none was the subject of consideration in any formal process. The numerous allegations included charges that sugarcane rust (*Puccinia melanocephala*) had been introduced in 1978, and that blue mold of tobacco had been introduced in 1979 and 1980. No supporting evidence was provided.

The one allegation in which evidence was adduced, and that was subject to formal consideration in the international political arena, was that the insect pest *Thrips palmi* was deliberately released one October during a legal overflight of Cuba by a U.S. crop duster en route to Columbia to participate in the coca interdiction program. A Cuban commercial pilot in the same airspace reported the release from the crop duster of a misty substance at about 3300 m. In December, Cuba detected *T. palmi* for the first time in the area of the release. Cuba requested a formal consultation under the provisions of Article V of the BWC (Biological Warfare Convention), which obliges States Parties to consult with each other on matters of contention under the Convention, charging that the United States had deliberately released *T. palmi* by air. The U.K. was appointed chair of a consultative meeting in August 1997, in which the Cuban allegations and U.S. response were presented. All parties to the BWC were invited to submit opinions (only 11 did so), and a final report was issued in December. Although no official conclusion was reached, the majority of States Parties responding held that the infestation was natural, caused by wind-blown insects from neighboring islands. A few respondents found the evidence to be inconclusive.

Drug Control Program

Plant pathogens can cause harmful effects to undesirable plants (i.e., weeds) as well as to desirable plants (crops). Consequently, there has been extensive R&D on using fungi as mycoherbicides, with mixed results (68, 69). One of the most successful

programs is the control of skeleton weed in Australia with the rust fungus *Puccinia chondrillina* (68, 69). A closely related concept, biological control of illicit drug crops, has been studied by the United States for over a decade. In particular, R&D has been conducted on controlling coca, cannabis, and opium poppy with fungal pathogens.

In the 1990s, the United States persuaded the United Nations Drug Control Program (UNDCP) to sponsor the anti-coca and anti-poppy programs (40). Strains of *Fusarium oxysporum* have been tested for all three crops (17), and the fungus *Pleospora papaveracea* has been studied as a mycoherbicide for poppy in ARS research (8). This idea of using plant pathogens in the war on drugs has even made it into fiction (18, 50). The relevance of this drug-control program to bioterrorism and biowarfare is that the methods used are essentially the same as those used in programs by the United States and the former U.S.S.R. that were aimed at legal crops. That is, the anti-drug program involves the preparation and storage of large amounts of inoculum and the delivery of the inoculum clandestinely over "unfriendly" territory for the purpose of destroying a cultivated crop.

After all Andean countries in which coca is cultivated had expressed their official objection to the use of mycoherbicides, the program against coca was discontinued. Strong opposition in the press and from political activist groups may have also influenced the decision to discontinue (40, 43). The eradication program against poppy has continued, with the development and testing being done in Uzbekistan. Use against Afghan poppy fields is probably imminent.

It is valuable to address the paradox: How could biocontrol be successful in controlling coca and other drug plants when biological control of weeds has proven so difficult? Plant diseases are often (but not always) most severe when plants are grown in dense and uniform conditions (as in typical crop production), and weed populations may be considerably more diverse genetically than a crop population. Furthermore, a weed biocontrol agent must work under a wide range of conditions to be commercially successful, but a pathogen (including a newly introduced one) can be a serious constraint on crop production overall even when high disease severities occur only in some years and locations.

WHY TARGET CROPS WITH PLANT PATHOGENS?

The first finding of the NRC report on "Countering Agricultural Bioterrorism" is that there is a real threat of biological weapons aimed at agriculture, including crops (60). Furthermore, the report concluded that it "is not feasible to be specifically prepared or have all the scientific tools for every contingency or threat to agriculture" (60). We agree with this assessment in terms of crops. An individual, group, or country might choose to target U.S. crops for several reasons, and the possible motives were discussed recently by Wheelis et al. (88). Crops would most likely be targeted because of their economic importance. Even though there is little possibility of a pandemic and food shortages following a pathogen introduction, especially in the year of the attack, even a small outbreak could have far-reaching

repercussions on trade. The example of Karnal bunt in the United States demonstrates this point (9). Containing and controlling the (new) disease could become a permanent cost to society. Reports in the news media of an alleged bioterrorist attack could cause loss of faith in the food supply, even if it was all perfectly safe for consumption. This psychological effect would be especially relevant if there were a multi-pronged attack against people, crops, and livestock.

Unlike the situation with human pathogens, there are few obstacles to weaponization of many highly contagious plant pathogens (88). Moreover, plant pathogens are not harmful to perpetrators, and attribution can be difficult because of the potentially long time to discover and identify the pathogen. Because most plant diseases have not been eradicated, it is relatively easy to obtain diseased plants around the world, to either culture in the laboratory or directly introduce into a field in the United States. The database of genetic fingerprints for plant pathogens is much less extensive than that for human pathogens, so determining the origin of an introduced pathogen would be a slow process. All of these factors make U.S. crops highly vulnerable to attack.

THREATENING PATHOGENS

General Comments

A list of pathogens or pathogen groups identified as most threatening to U.S. agriculture would help in planning the responses for disease outbreaks, including the best way of containing the outbreak and perhaps eradicating the disease (60, 88). Intelligence and Defense agencies could use the list to deter or prevent others from using the pathogens as weapons. Such a list also would help guide research on the development of methods for rapid and sensitive detection and in the genetic characterization of the most threatening pathogens. Additional epidemiological research would indicate the potential magnitude of disease spread. Much of the research could be useful for forensic purposes—determining if a disease outbreak was caused by a deliberate or accidental introduction. This information, if properly used, could also indicate to which microorganisms access should be restricted.

Lists

There is no consensus on the most threatening pathogens that could be used as biological weapons against crops (70). For animals, the List A and B microorganisms of the *Office International des Epizooties* (61) are generally considered the greatest threats (88). These pathogens cause highly contagious diseases, and tremendous effort in developed countries has gone into eradicating them. Any introduction has a major effect on the infected or exposed animals and on society as a whole (e.g., foot and mouth disease virus). No organization has been formed to categorize plant pathogens in the same formal way, partly because even the most contagious plant diseases have generally not been eradicated from a country or region, as discussed above.

Various lists of threatening plant pathogens have been produced by either groups or individuals, for a range of purposes. For instance, there are lists of pathogens (pests in general) that are restricted for international trade (23, 78). These are the quarantine-significant pathogens. Because all pathogens of crops do not yet occur in all regions growing the crop, countries can place restrictions on the entry of products that may harbor high-impact pathogens based on the World Trade Organization's Sanitary and Phytosanitary agreement, ratified in 1996 (49). The decisions on the restricted pathogens are supposed to be based on sound science and risk analysis, but no global consensus yet exists. It is very easy for political considerations to be involved since the decisions can greatly affect international trade.

Other lists have been prepared of pathogens that are threats if introduced (70). These lists come from both individual authors and (official and unofficial) groups such as the U.S. Departments of Commerce and Defense and the so-called Australia Group (19, 70, 82; L.V. Madden, unpublished). It is not always clear which criteria were used in deriving the lists, or if the criteria were uniformly applied. The list makers also seem to borrow from each other. One common criterion for inclusion on the list apparently is that the pathogen was previously used in a biological weapons program; however, just because a pathogen was studied and tested in BW program does not mean that it is actually a threat, or if used by a terrorist, would be of significant consequence. For instance, stem rust of wheat is often listed as a potential weapon, probably because the United States, U.S.S.R, and others used this pathogen in their BW programs. The disease is highly contagious, with short generation times, the spores are transported very long distances, and infection has a large effect on yield. However, the disease is endemic in the United States and is controlled with resistance and other practices, so its effectiveness as a terrorist weapon is questionable. Of course, strains not currently occurring in the country could be introduced in which the currently grown cultivars are susceptible. Similarly, Iraq's BW program included the *Tilletia* species causing covered smut in wheat (90). Compared to many other fungi, however, these pathogens are not very contagious and are fairly easily controlled (89). Thus, covered smut arguably is not a threat to U.S. agriculture.

Table 1 contains a list of the threatening plant pathogens developed by the so-called Ad Hoc Group (2) of the BWC. The table also lists pathogens approved by USDA-APHIS as Select Agents (2a) that must be restricted in the United States (which is just one of the uses for a threat list). This latter list is a response to the Agricultural Bioterrorism Protection Act of 2002 (2a), a direct consequence of the attacks of 2001. It is our belief that the readers of this article will have mixed opinions about the choices of pathogens as serious threats. For instance, the inclusion of the pathogen causing maize smut (*Ustilago maydis*) in the Ad Hoc Group list is very surprising. Clearly, a formal and rigorous analysis is needed to evaluate the magnitude of the threat from particular pathogens and develop plans for preventing, deterring, detecting, and responding to attack. Moreover, different lists may be needed for different purposes. For instance, a restricted-access list probably

TABLE 1 Plant pathogens selected by the Ad Hoc Group of the Biological Weapons Convention (BWC) (2) and U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA-APHIS) (2a)

BWC, Ad Hoc Group	USDA-APHIS select agents
Citrus greening bacteria	*Liberobacter africanus, L. asiaticus* (citrus greening bacteria)
Colletotrichum coffeanum, var. *virulans*	*Peronosclerospora philippinensis*
Cochliobolus miyabeanus	*Phakospora pachyrhizi*
Dothistroma pini	Plum pox potyvirus
Erwinia amylovora	*Ralstonia* (formerly *Pseudomonas*) *solanacearum*, race 3, biovar 2
Microcyclus ulei	*Sclerophthora rayssiae* var. *zeae*
Phytophthora infestans	*Synchytrium endobioticum*
Pseudomonas solanacearum	*Xanthomonas oryzae* pv. *oryzicola*
Puccinia erianthi	*Xylella fastidiosa* (citrus variegated chlorosis strain)
Puccinia graminis	
Puccinia striiformis	
Pyricularia oryzae	
Sugarcane Fiji disease virus	
Tilletia indica	
Ustilago maydis	
Xanthomonas albilineans	
Xanthomonas campestris pv. *citri*	
Xanthomonas campestris pv. *oryzae*	
Sclerotinia sclerotiorum	

Minor spelling mistakes in the AHG list were corrected; two insects on the pathogen list of AHG are omitted here. Recent updated scientific names not necessarily included in the BWC list.

should just contain pathogens that are not indigenous to the United States, or those not readily obtained from naturally infected plants in the field; however, a list for strategic planning purposes probably would contain indigenous and nonindigenous threat agents that can have serious consequences for U.S. agriculture.

Risk Analysis, Epidemiology, and Models

The threat of a given pathogen by deliberate introduction can be determined by various types of risk analysis, coupled with appropriate experimental research and modeling. An outline of the approach is given here.

The risk (R) of pathogen X could be defined as:

$$R = A \times E \times S \times H \times (1 - C),$$

which is an expanded version of the model presented by Madden & Scherm at the 1999 APS symposium (70). A is the probability that the pathogen will be introduced (i.e., arrive) in the United States, dependent, in part, on the motivation and capability of perpetrators and accessibility of appropriate inoculum. Determining

A certainly must involve intelligence agencies and groups not commonly associated with plant pathology. *A* is also dependent on how easy it is to isolate, culture, and store the pathogen; in other words, how easy it is to work with it. Because plant pathogens typically are not harmful to humans (except for those producing toxins), it is much easier to prepare plant pathogens as weapons than human (and some animal) pathogens as weapons (88).

E is the probability of initial disease establishment, dependent, among other things, on the susceptibility of the crop and favorableness of the environment. In other words, if pathogen *X* were introduced into a field, how likely is it that infections would occur initially and that there would be a sufficient pathogen reproduction over time and sufficient degree of pathogen survival between seasons for the disease to persist? Determination of *E* requires knowledge of the disease epidemiology, including the effects of environment on the components of the disease cycle (e.g., 71). From epidemiological theory (33, 34, 51), *E* can be predicted from the so-called basic reproduction number, R_0, the mean number of new diseased individuals (plants, leaves, roots, etc.) infected from an infected individual introduced into a disease-free population over the lifetime of the infected individual (21, 54, 55). Disease can become established only if $R_0 \geq 1$. In general epidemiological terms, establishment is equivalent to disease "invasion," although those working on invasive species (59) would use the term invasion somewhat differently. Although less so than with *A*, *E* is partially dependent on the capability and knowledge of the perpetrators, because the probability can be maximized ($E < 1$) by placing inoculum at the "right" place at the "right" time.

S is the probability of spread from the initial established focus of disease and widespread high incidence of disease. This depends, in part, on the dispersal of the pathogen and high infection rate. The so-called contact distribution can be calculated as a measure of effective spore dispersal; this distribution indicates the probability of a spore (or other unit of inoculum) originating at one location causing an infection at a location *y* distance units away. The rate of disease spread from a focus (*v*; meters/day or kilometers/day) is directly proportional to the parameters of the contact distribution and (typically) to $\log(R_0)$. That is, increasing R_0 (>1) and mean (or median) distance of the contact distribution leads to increasing *v* (81, 96). The final level of disease intensity for a fixed host (non-growing) or the equilibrium level of disease intensity for a dynamic host (growing and dying) is also directly proportional to R_0 (20, 39). There is an extensive literature in general epidemiology (i.e., nonplant diseases) for determining these key population parameters in terms of life-cycle components, and some of this work pertains directly to plant diseases. The models are generally used for a host that is continuously present so that the biological processes are not interrupted. The major food crops are annuals, however, with an abrupt elimination of the host at regular times (i.e., at harvesting), and then a reintroduction of the host after a host-free period (i.e., planting or transplanting). This complicates the mathematics of determining thresholds for invasion, persistence, and spread. New research is now shedding light on how to adapt general epidemiological theory to annual crops (33, 51, 81). For instance,

Madden & van den Bosch (51) recently showed how to develop a multiseason R_0 for determining invasion and persistence of an introduced pathogen.

H is the probability of the introduced disease causing major economic damage (i.e., hazard). This involves all the costs associated with the disease, including the reduction in yield and loss of markets (11). As mentioned above, costs of a disease may still be very large even when disease intensity is low and little direct yield loss occurs. *C* is the probability of practically controlling or containing the disease. Many diseases can be controlled quite easily (e.g., with seed treatment), but others are difficult to control even with pesticides (73). Moreover, since aerial application of fungicides is expensive for field crops, the use of chemicals may not be of practical long-term value.

The concept of the general risk analysis described here is similar to that used by USDA and others for regulatory purposes (62, 95). Use of the equation for *R* above implies that all terms are equally important, and that the highest risk occurs when all the probability terms are high. Alternative models can be constructed in which one term may supersede one or more of the others. It may take a considerable amount of work to determine reasonable values for the probabilities. As mentioned above, some of the terms are dependent on the epidemiology of the disease, and it may be difficult to quickly ascertain the magnitude of R_0 for a particular disease. There are alternatives, fortunately, to determining these probabilities. Schaad et al. (70) introduced a prototype scoring system for pathogens, where experts for a particular crop or group of pathogens can answer questions about a particular pathogen species or strain (Table 2). A weighting system is then used to derive

TABLE 2 Prototype pathogen scoring system from Schaad et al. (70) for quantifying the threat of pathogens to the United States

Scoring criteria	Weight
Easy to obtain, handle, deliver (*A*)	10
Easy to grow in large amounts (*A*)	10
Highly infectious (under many environments) (*E,S*)	10
Survives long periods (without crop) (*E*)	5
Systemic infection (*E*)	10
Spreads quickly (*S*)	5
No chemical control or plant resistance (*C*)	10
No method for rapid & accurate detection (*E, S, C*)	10
Quarantine significance (*H, C*)	10
High crop losses (*H*)	5
Produces toxin (*H*)	15

Letters in parentheses refer to the corresponding terms of the risk model in the text. Text description slightly altered from Schaad et al. (70) for consistency with current article.

a composite score. The method was developed by having a panel interactively decide on the criteria relevant for determining a threatening pathogen. A newer set of questions has recently been developed (based on a more thorough analysis) (N.W. Schaad & L.V. Madden, unpublished).

The letters next to the scoring items in Table 2 are the probability terms in the equation for R. The items in the scoring system correspond to one or more of the risk probabilities. The next step needed is to put into practice use of the scoring system in Table 2, the risk analysis model, and the epidemiological models in order to evaluate the specific threats to U.S. agriculture. None of the lists currently available for plant pathogens as potential biological weapons has been based on such rigorous analyses.

PREPAREDNESS

As stated in the NRC report, "... no publicly available, in-depth, interagency or interdepartmental national plan had been formulated for defense against the intentional introduction of biological agents directed at agriculture" (60). In other words, the United States is not prepared for attacks of this type. As expected from this finding, the major recommendation in the NRC report is that

> "... the US government should develop a comprehensive plan to respond to the threat of agricultural bioterrorism that does the following: Integrates elements of deterrence, prevention, detection, response, and recovery; ... Includes domestic and international strategies for recognition, prevention, and control; ... Defines legal and jurisdictional authority and lead roles at the federal, state, local, and private levels ...; [and] ... Defines a categorical priority list of threat agents for planning."

Furthermore, the NRC report recommends significant improvements in surveillance, laboratory diagnosis, and electronic reporting of threat agents; coordination among agricultural and other agencies, including law enforcement, national intelligence, defense, emergency management, and environmental and wildlife programs; and development of public information, education, and outreach strategies for dealing with potential and actual attacks (60). This need for a comprehensive plan was also recently emphasized by Meyerson & Reaser (53). These recommendations are consistent with the recommendations made by the APS ad hoc committee on biosecurity through two white papers (6). Because the current plant disease and pest diagnostic labs are underfunded and understaffed, it was recommended that an integrated distributed system of diagnostic labs be developed as first responders to a bioterrorist threat. Interestingly, USDA is now spearheading an initiative to improve the capability of the individual diagnostic labs and provide an integrated reporting and communication network for disease outbreaks (79). APS also recommended the formation of a national plant disease center that can provide ongoing risk assessment, updating of threat agents to crop plants, maintenance of databases of plant pathogens, and standardization of diagnostic techniques and

certification of laboratories. The national laboratory, possibly modeled on the Center for Disease Control and Prevention (CDC), could exist as an actual facility or a virtual center within the USDA.

The stated need for enhanced educational and public information programs in the NRC report (60) is also consistent with an APS recommendation (6) to expand the educational programs for first responders, those individuals most likely to first notice a new or unusual disease outbreak. It was also recommended that more graduate students be trained in diagnostics, plant health management, and applied plant pathology. Implementing these recommendations will not be trivial, however. Declining federal resources for extension will make it difficult to pay for new educational programs. Moreover, to educate more students in applied fields requires that there are individuals who wish to pursue careers in these areas, that there will be positions available for them, and that there are resources to fund their graduate education.

Many of the changes called for in the NRC report can be made with our current science and technology base. However, preparedness can be improved with new scientific information. The NRC explicitly calls for increased understanding of the biology and epidemiology of threatening agents and the development of improved tools for detection, diagnosis, and identification, as well as basic research on bioinformatics and genomics, and applied and basic research on control (60). These recommendations also are consistent with those of APS in its white papers (6). The basic research could lead to the development of novel methods of pathogen detection, plant cultivars with durable resistance to multiple pathogen species or strains, and novel pesticides for disease control. Furthermore, determination of sequences of plant pathogens would aid in forensic investigations of newly discovered disease outbreaks. Basic epidemiological research can lead to better predictions of disease invasion, persistence, and spread, and aid in upgrading optimum control strategies.

Improved preparedness for possible attack against U.S. crops with biological weapons will require additional resources and redirection of current activities by those in the plant protection field. Because one could argue that individual acts of bioterrorism are low probability events, whether directed against people, animals, or crops, staying focused on preparation over many years, especially if there are no new (major) acts of terrorism, will be challenging. However, we believe it is precisely the responsibility of the federal government to protect the United States from attacks that have high consequences, whether the probability of the attack is high or low. Thus, the U.S. government should maintain its current direction to improve our ability to counter acts of bioterrosim.

CONCLUSIONS

There is clearly broad interest in the threat of microorganisms as weapons against the United States, prompted by the demonstrated vulnerability of some parts of the country to attack in the fall of 2001. As discussed in this article, awareness of the

danger existed before September 11, 2001, although the major public discussion has occurred primarily since then. Biological threats to crops have received relatively little attention relative to human bioterrorism or even animal bioterrorism, but recent analyses confirm that U.S. crops are susceptible to attack and that adequate plans to prevent and respond to an attack have not been made. Although the deliberate introduction of a plant pathogen into the United States is very unlikely to result in a pandemic and/or major food shortages, there can be major economic fallout from such an introduction. In particular, global trade could be greatly compromised by an even minor crop epidemic. The United States can become much better prepared through structural changes—such as establishment of a national center of plant disease control—and through additional research at the molecular and population (epidemiological) levels. Risk assessments and modeling can suggest strategies for optimum disease control, containment, or eradication if a pathogen is deliberately introduced.

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LITERATURE CITED

1. Abelson PH. 1999. Biological warfare (editorial). *Science* 286:1677
2. Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction. 1997. *BWC/AD HOC GROUP 38, Rolling Text, Annex I*, p. 117

2a. Agricultural Bioterrorism Protection Act of 2002. Possession, use and transfer of biological agents and toxins. Dep. Agric. Anim. Plant Health Serv. *Fed. Regist.* 67(240):76926–38

3. Agrios GN. 1997. *Plant Pathology*. New York: Academic. 4th ed.
4. Alibek K, Handelman S. 1999. *Biohazard: The Chilling True Story of the Largest Covert Biological Weapons Program in the World, Told from the Inside by the Man Who Ran It*. New York: Random House
5. Alibek K. 1999. The Soviet Union's anti-agricultural biological weapons. See Ref. 28, pp. 18–19
6. APS. 2002. Crop biosecurity and countering agricultural bioterrorism: responses of the American Phytopathological Society. *APSnet.* http://www.apsnet.org/online/feature/bioterrorism/
7. Atlas RM. 1999. Combating the threat of biowarfare and bioterrorism. *BioScience* 49:465–77
8. Bailey BA, Apel-Birkhold PC, O'Neill NR, Plaskowitz J, Alavi S, et al. 2000. Evaluation of infection processes and resulting disease caused by *Dendryphion penicillatum* and *Pleospora papaveracea*on *Papaver somniferum*. *Phytopathology* 90:699–709
9. Bandyopadhyay R, Frederiksen RA. 1999. Contemporary global movement of emerging plant diseases. See Ref. 28, pp. 28–36
10. Brown CC, Slenning BD. 1996. Impact and risk of foreign animal diseases. *J. Am. Vet. Med. Assoc.* 208:1038–40
11. Campbell CL, Madden LV. 1990. *Introduction to Plant Disease Epidemiology*. New York: Wiley
12. Carter GB, Pearson GS. 1999. British biological warfare and biological defense, 1925–45. See Ref. 32a, pp. 168–89
13. Casagrande R. 2000. Biological terrorism targeted at agriculture: the threat to US

national security. *Nonprolif. Rev.* 7(3):98–99

14. Chen X, Line RF, Leung H. 1995. Virulence and polymorphic DNA relationships of *Puccinia striiformis* f.sp. *hordei* to other rusts. *Phytopathology* 85:1335–42
15. Christopher GW, Cieslak TJ, Pavlin JA, Eitzen EM. 1999. Biological warfare: a historical perspective. See Ref. 46, pp. 17–36
16. Condon M. 1997. Implications of plant pathogens to international trading of seeds. In *Plant Pathogens and the Worldwide Movement of Seeds*, ed. DC McGee, pp. 17–30. St. Paul, MN: APS Press. 109 pp.
17. Connick WJ Jr, Daigle DJ, Pepperman AB, Hebbar KP, Lumsden RD, et al. 1998. Preparation of stable, granular formulations containing *Fusarium oxysporum* pathogenic to narcotic plants. *Biol. Control* 13:79–84
18. Cook W. 2001. *Buzzword*. Boalsburg, PA: Public Policy Press
19. Dando M. 1994. *Biological Warfare in the 21st Century*. London: Brassey
20. Diekmann O, Heesterbeek JAP. 2000. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis, and Interpretation*. Chichester, UK: Wiley
21. Diekmann O, Heesterbeek JAP, Metz JAJ. 1990. On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *J. Math. Biol.* 28:365–82
22. Dudley JP, Woodford MH. 2002. Bioweapons, biodiversity, and ecocide: potential effects of biological weapons on biological diversity. *BioScience* 52:583–92
23. FAO. 2002. *International Plant Protection Convention*. http://www.ippc.int/cds_ippc_prod/IPP/En/default.htm
24. Farr DF, Bills GF, Chamuris GP, Rossman AY. 1989. *Fungi on Plants and Plant Products in the United States.* St. Paul, MN: APS Press
25. Deleted in proof
26. Ferguson NM, Donnelly CA, Anderson RM. 2001. Transmission intensity and impact of control policies on the food and mouth epidemic in Great Britain. *Nature* 413:542–48
27. Finckh MR, Wolfe MS. 1998. Diversification strategies. In *The Epidemiology of Plant Diseases*, ed. DG Jones, pp. 231–59. Dordrecht, Neth.: Kluwer
28. Frazier TW. 1999. Natural and bioterrorist/biocriminal threats to food and agriculture. See Ref. 29, pp. 1–8
29. Frazier TW, Richardson DC, eds. 1999. *Food and Agricultural Security: Guarding Against Natural Threats and Terrorist Attacks Affecting Health, National Food Supplies, and Agricultural Economics*. New York: NY Acad. Sci. 233 pp.
30. Fry WE. 1982. *Principles of Plant Disease Management*. New York: Academic
31. Geissler E. 1997. “Anwendung von Seuchenmitteln gegen Menschen nicht erwünscht.” Dokumente zum Einsatz biologischer Kampfmittel im Ersten Weldkrieg. *Militärgesch. Mitt.* 56:107–55
32. Geissler E. 1999. Biological warfare activities in Germany, 1923–45. See Ref. 32a, pp. 91–126

32a. Geissler E, Moon J, eds. 1999. *Biological and Toxin Weapons: Research, Development and Use from the Middle Ages to 1945*. Oxford: Oxford Univ. Press

33. Gubbins S, Gilligan CA. 1997. Persistence of host-parasite interactions in a disturbed environment. *J. Theor. Biol.* 188:241–58
34. Gubbins S, Gilligan CA, Kleczkowski A. 2000. Population dynamics of plant-parasite interactions: thresholds for invasion. *Theor. Popul. Biol.* 57:219–33
35. Harris SH. 1994. *Factories of Death: Japanese Biological Warfare 1932–45 and the American Cover-Up.* New York: Routledge

36. Harris SH. 1999. The Japanese biological warfare programme: an overview. See Ref. 32a, pp. 127–52
37. Hickson RD. 1999. Infecting soft targets: biological weapons and Fabian forms of indirect grand strategy. See Ref. 29, pp. 108–17
38. Horn FP, Breeze RG. 1999. Agriculture and food security. See Ref. 29, pp. 9–17
39. Jeger MJ, van den Bosch F. 1994. Threshold criteria for model plant disease epidemics. I. Asymptotic results. *Phytopathology* 84:24–27
40. Jelsma M. 2001. *Vicious Circle: The Chemical and Biological War on Drugs*. Amsterdam: Transnatl. Inst. www.tni.org/drugs/
41. Kadlec RP. 1995. Twenty-first century germ warfare. In *Battlefield of the Future: 21st Century Warfare Issues*, ed. BR Schneider, LE Grinter, pp. 227–50. Maxwell Air Force Base, AL: Air Univ. Press
42. Kadlec RP. 1995. Biological weapons for waging economic warfare. See Ref. 41, pp. 251–66
43. Kleiner K. 1999. Operation eradicate. *New Sci.* 163(2203):20
44. LaMondia JA, Aylor DE. 2001. Epidemiology and management of a periodically introduced pathogen. *Biol. Invasions* 3:273–82
45. Lawler A. 2001. The unthinkable becomes real for a horrified world. *Science* 293:2182–85
46. Lederberg J, ed. 1999. *Biological Weapons—Limiting the Threat*. Cambridge, MA: MIT Press
47. Lepick O. 1999. French activities related to biological warfare, 1919–45. See Ref. 32a, pp 70–90
48. MacKenzie D. 1999. Run, radish, run. *New Sci.* 164(2217):36–39
49. Madden LV. 2001. What are the nonindigenous plant pathogens that threaten U.S. crops and forests? www.apsnet.org/online/feature/exotic/.
50. Madden LV. 2002. Plant pathology fiction: Buzzword. *BioScience* 52:619–20
51. Madden LV, van den Bosch F. 2002. A population-dynamics approach to assess the threat of plant pathogens as biological weapons against annual crops. *BioScience* 52:65–74
52. Mangold T, Goldberg J. 1999. *Plague Wars*. New York: St. Martin's Press
53. Meyerson LA, Reaser JK. 2002. Biosecurity: moving toward a comprehensive approach. *BioScience* 52:593–600
54. Mollison D. 1986. Modelling biological invasions: chance, explanation, prediction. *Philos. Trans. R. Soc. London Ser. B* 39:283–326
55. Mollison D. 1995. The structure of epidemic models. In *Epidemic Models*, ed. D. Mollison, pp. 17–33. London: Cambridge Univ. Press
56. Monterey Inst. Int. Stud. 2002. Chronology of CBW attacks targeting crops & livestock. http://cns.miis.edu/research/cbw/agchron.htm
57. Moon JE. 1999. US biological warfare planning and preparedness: the dilemmas of policy. See Ref. 32a, pp. 215–45
58. NRC. 1999. *Chemical and Biological Terrorism: Research and Development to Improve Civilian Medical Response*. Washington, DC: NRC, Natl. Acad. Press
59. NRC. 2002. *Predicting Invasions of Nonindigenous Plants and Plant Pests*. Washington, DC: NRC, Natl. Acad. Press
60. NRC. 2002. *Countering Agricultural Bioterrorism*. Washington, DC: NRC, Natl. Acad. Press
61. OIE. 2000. OIE disease classification. www.oie.int/eng/maladies/en_classification.htm
62. Orr RL, Cohen SD, Griffin RL. 1993. *Generic Non-Indigenous Pest Risk Assessment Process.* Washington, DC: USDA APHIS. 40 pp.
63. Osterholm MT. 1999. Bioterrorism: media hype or real potential nightmare? *Am. J. Infect. Control* 27:461–62

64. Pearson GS. 1999. BTWC security implications of human, animal, and plant epidemiology. *Rep. NATO Adv. Res. Workshop, Cantacuzino Inst. Bucharest 3–5 June. Brief. Pap. No. 23.* http://www.brad.ac.uk/acad/sbtwc/briefing/bw-briefing.htm
65. Peraica M, Tadic B, Lucic A, Pavlovic M. 1999. Toxic effects of mycotoxins in humans. *Bull. WHO* 77:759
66. Pimentel D, Lach L, Zuniga R, Morrison D. 2000. Environmental and economic costs associated with non-indigenous species in the United States. *BioScience* 50:53–65
67. Rogers P, Whitby S, Dando M. 1999. Biological warfare against crops. *Sci. Am.* 280 (June):70–75
68. Rosskopf EN. 2001. Biological control of weeds. In *Encyclopedia of Plant Pathology*, ed. OC Maloy, TD Murray, 1:136–38. New York: Wiley
69. Rosskopf EN, Charudattan R, Kadir JB. 1999. Use of plant pathogens in weed control. In *Handbook of Biological Control*, ed. TS Bellows, TW Fisher, pp. 891–918. San Diego: Academic
70. Schaad NW, Shaw JJ, Vidaver A, Leach J, Erlick BJ. 1999. Crop biosecurity. *APSnet* 15 Sept.–31 Oct. www.apsnet.org/online/feature/Biosecurity/Top.html
71. Scherm H, Yang XB. 1999. Risk assessment for sudden death syndrome of soybean in the north-central United States. *Agric. Syst.* 59:301–10
72. Schubert TS, Rizvi SA, Sun X, Gottwald TR, Graham JH, Dixon WN. 2001. Meeting the challenge of eradicating citrus canker in Florida—again. *Plant Dis.* 85:340–56
73. Strange RN. 1993. *Plant Disease Control.* London: Chapman & Hall
74. Tucker JB. 1999. Bioterrorism: threats and responses. See Ref. 46, pp. 283–320
75. Tucker JB. 2000. *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons.* Cambridge, MA: MIT Press
76. Tucker JB. 2001. The “yellow rain” controversy: lessons for arms control compliance. *Nonprolif. Rev.* 8(1):25–42
77. USDA. 2001. National Agricultural Statistics Service. http://www.usda.gov/nass/
78. USDA-APHIS. 2001. Regulated plant pest list. http://www.aphis.usda.gov/ppq/regpestlist/
79. USDA-CSREES. 2002. Diagnostic labs receive from CSREES. http://www.reeusda.gov/1700/whatnew/02/diagnosticlabs.htm
80. USDA-ERS. 2002. Agricultural Outlook, Jan.–Feb. http://www.ers.usda.gov/publications/AgOutlook/Jan2002/
81. van den Bosch F, Metz JAJ, Zadoks JC. 1999. Pandemics of focal plant disease, a model. *Phytopathology* 89:495–505
82. Weller RE, Lyu CW, Wolters C, Atlas RM. 1999. Universities and the biological and toxin weapons convention. *ASM News* 65:403–9
83. Wheelis ML. 1992. Strengthening biological weapons control through global epidemiological surveillance. *Polit. Life Sci.* 11:179–89
84. Wheelis M. 1999. Biological sabotage in World War I. See Ref. 32a, pp. 35–62
85. Wheelis M. 1999. *Outbreaks of Disease: Current Official Reporting. Strengthening the Biological Weapons Convention.* Brief. Pap. No. 21, Dep. Peace Stud., Univ. Bradford. 14 pp. http://www.brad.ac.uk/acad/sbtwc/briefing/bp21.htm
86. Wheelis M. 2000. Agricultural biowarfare and bioterrorism. Edmonds Inst. Occas. pap. Updated at http://www.fas.org/bwc/agr/main.htm
87. Wheelis M. 2002. Biotechnology and biochemical weapons. *Nonprolif. Rev.* 9(1):48–53
88. Wheelis M, Casagrande R, Madden LV. 2002. Biological attack on agriculture: low-tech, high-impact bioterrorism. *BioScience* 52:569–76
89. Whitby SM. 2002. *Biological Warfare Against Crops*. Hampshire, UK: Palgrave
90. Whitby SM, Rogers P. 1997. Anticrop biological warfare-implications of the Iraq

and U.S. programs. *Def. Anal.* 13:303–18

91. White House. 1998. Proliferation of weapons of mass destruction. Executive Order 13094, White House Off. Press Secr. July 28. *Wkly. Compil. Pres. Doc.* 30(46):2386–89. http://www.ustreas.gov/offices/enforcement/ofac/legal/eo/13094.pdf
92. White House. 1998. *Combating Terrorism: Presidential Decision Directive 62*. Fact Sheet. http://www.fas.org/irp/offdocs/pdd-62.htm
93. White House. 1999. *Keeping America Secure for the 21st Century: President Clinton's Initiative on Biological and Chemical Weapons Preparedness*. Fact Sheet, White House Off. Press Secr. 22 Jan. http://clinton4.nara.gov/WH/New/html/19990122-7214.html
94. Wiese MV. 1987. *Compendium of Wheat Diseases.* St. Paul, MN: APS Press. 2nd ed.
95. Yang XB, Dowler WM, Royer MH. 1991. Assessing the risk and potential impact of an exotic plant disease. *Plant Dis.* 75:976–82
96. Zadoks JC, van den Bosch F. 1995. On the spread of plant disease—a theory on foci. *Annu. Rev. Phytopathol.* 32:503–21
97. Zilinskas RA. 1999. Cuban allegations of biological warfare by the United States: assessing the evidence. *Crit. Rev. Microbiol.* 25:173–277