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Combatting Bioterrorism

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Glossary

Active Defense Interdicting or intercepting an opponent's weapons when the attack is underway (e.g., weapons in flight) before the weapons detonate on their targets.

Biodefense Any passive defense measure intended to protect humans, livestock, or agriculture from intentional attacks using pathogenic microorganisms or toxins.

Biological and Toxin Weapons Convention A treaty introduced in 1972 that bans the development, production, stockpiling, acquisition, and transfer of biological agents of types and in quantities that have no justification for prophylactic, protective, or other peaceful purposes.

Geneva Protocol A treaty introduced in 1925 after World War I that banned the first use of chemical and bacteriological weapons in war.

Medical Prophylaxis Medical treatments, for example, antibiotics, antiviral drugs, and vaccination, that either kill the microorganism in the host or boost the host's immune system to help combat the disease.

Passive Defense Protecting the target of attack from the effects of a weapon after it has detonated.

Preemption Thwarting an opponent's ability to strike first by destroying his weapons before they can be launched when the threat of their use is imminent.

Concern that a terrorist group might attack civilian populations or agriculture by releasing deadly pathogens has grown in the past decade. Failed attempts by the Japanese cult Aum Shinrikyo to release botulinum toxin and anthrax in Tokyo on several occasions in the early 1990s, and the 2001 anthrax letter attacks in the United States seem to confirm these fears. However, there were only five fatalities in the US case and none in the Japanese case. The question naturally arises: How serious is this threat and, if it is serious, what strategy should states take to combat it? This article draws on US experience to outline a strategy for combating bioterrorism that is general enough to apply to most states, especially ones with well developed public health and medical infrastructures.

The Nature of the Threat

Historically, attacks using biological agents are rare. This is not surprising given the relative ineffectiveness of biological weapons as a military weapon due to the difficulty of infecting opposing forces, the availability of protective clothing (a simple mask will do in most cases), prompt medical treatment for troops, and the risk that the attacker's troops may also become infected. The centuries-old revulsion to killing people with poison or disease codified in the 1899 Hague Convention, the 1925 Geneva Protocol, and the 1972 Biological and Toxin Weapons Convention (BTWC) is perhaps the best explanation for why we have not witnessed more deaths due to biological attack. Norms have a powerful, albeit imperfect, influence over human behavior. Finally, with respect to terrorist use, the traditional view has been that "terrorists want lots of people watching, not lots of people dead." To the extent this is true, terrorists have little incentive to attack civilians indiscriminately because they would loose political support within their community and the attack would likely provoke a draconian response by the state to eliminate the group.

The question is whether this trend will continue. There is reason for concern regarding bioterrorism because the knowledge, materials, and equipment to make biological weapons are spreading worldwide; the incentives for states or terrorists to acquire and use such weapons may be increasing; and civilians, as well as agricultural sectors, remain quite vulnerable to such attacks.

The knowledge, materials, and equipment to manufacture biological weapons are spreading due to advances in biomedical technology, the dual-use character of this

technology, the global nature of the biotechnology and pharmaceutical industries, and the pervasive access to knowledge through rapid global information sharing. Unlike nuclear weapons, where 5–15 kg of fissile material is required to build a rudimentary fission bomb, no such barrier exists for biological weapons. In fact, biological weapon proliferation is governed more by the spread of knowledge than the spread of material and equipment. Traditional biological agents can be found in the environment or in numerous unprotected strain collections around the world and large batches of bacteria or virus can be grown in simple fermenters.

Former state biological programs represent another potential source of materials, equipment and, especially, knowledge. The remnants of the former Soviet biological weapon program, estimated by some accounts to have once employed over 50 000 scientists and technicians, represents an avenue by which states or terrorists might acquire biological weapons without the painstaking research and development required to create them *ab initio*. President Yeltsin declared in 1992 that the former Soviet biological weapon program had been dismantled and that Biopreparat, the civilian biomedical research organization that conducted much of the biological weapons research, would be converted solely to peaceful pursuits. Due to a lack of transparency, concerns remain that a covert biological weapons program may still exist in Russia. Cuba, Iran, North Korea, and Syria are also believed by the US government to have biological weapon programs, at various levels of development, and South Africa and Iraq formerly had programs from which materials or expertise could leak. In addition, numerous countries have biological weapon defense programs, which produce small quantities of pathogens for peaceful purposes (e.g., testing prophylaxis efficacy), which is allowed under the BTWC, from which knowledge or materials could also leak.

Biological weapons of varying degrees of sophistication clearly are within a state's means to acquire covertly. The dual-use nature of the equipment and supplies make biological weapon programs easy to hide under the guise of legitimate biomedical activities. Only small quantities of pathogens are required for seed stocks, and biological agents emit no detectable signal, making them virtually impossible to detect remotely. The fact that biological weapon facilities can be small and have no distinct physical features makes their identification difficult even with intrusive on-site inspections, as the UN Special Commission charged with locating and destroying Iraq's weapons of mass destruction discovered after the 1991 Iraq War. It took the Commission 4 years to locate most of Iraq's biological weapon facilities and then only after Kamel Hussein divulged the scope of the secret Iraqi program after defecting to Jordan in 1995. Finally, legitimate peaceful activities such as vaccine and biopesticide production can be converted to biological weapon production within weeks to months.

It is less clear whether terrorists can acquire effective biological weapons without state support. Terrorists operating rudimentary laboratories face challenges obtaining lethal pathogen strains, extending pathogen shelf life and, in particular, mastering the 'weaponization' hurdles – agent drying, stabilization, and aerosolization (i.e., creating a respirable aerosol of viable agent less than 5 μm in diameter so it does not settle out of the atmosphere close to the release point and so it can penetrate the alveolar region of the lungs where pathogens are most infectious). Wet pathogen slurries are relatively easy to produce but difficult to disseminate in a 5-μm aerosol. Dry powders can be ground to less than 5 μm prior to dispersal (although clumping and electrostatic charge can be a problem), but dry agent is more difficult to produce and handle in a safe manner. Thus, each path has its hurdles. Most terrorists lack the practical knowledge required to circumvent these hurdles, even if they have trained microbiologists in their ranks, unless they receive outside help. (Aum Shinrikyo failed to kill anyone with anthrax because they used a nonlethal vaccine (Stern) strain in 1993 and attempts to aerosolize the spores failed. This led the cult to carry out its more infamous Sarin gas attack on the Tokyo subway in 1995.) Of course, terrorists may not strive for highly efficient weapons. Causing panic, if not terror, is possible even with a rudimentary biological weapon.

Not only are the means for acquiring biological weapons spreading but the incentives to acquire, and possibly use, them are increasing as well. The United States emerged from the Cold War as the world's unrivaled conventional military power, while the collapse of the former Soviet Union left its allies to fend for themselves. Consequently, opponents of the United States must search for 'asymmetric' means – including, possibly, biological weapons – to counter US military might. The suicide bombings in Iraq and Afghanistan are a current example of this approach. Terrorists' incentives to use such weapons may be changing as well. The 11 September 2001 attack in the United States and subsequent indiscriminant attacks in Bali, Madrid, Beslan, and London suggest that terrorists may wish to inflict mass casualties. Biological attacks can also devastate sectors of the US or world economy – an attractive goal to some terrorists. Still, some constraints may exist. For example, terrorists may be reluctant to use contagious agents because the subsequent contagion might spread to their home country or social group, which may have less access to public health. They may also eschew biological attacks because the operation is more likely to fail, preferring conventional explosives instead. To divinely inspired perpetrators, failure can be a deterrent because it suggests that God does not support their actions.

The vulnerability of civilian populations and agriculture may encourage bioterrorism. While modern military forces are relatively invulnerable to biological attack, civilians are quite vulnerable because they do not have protective clothing, would not know when to put it on if they had it, and they do not routinely receive prophylaxis against common biological warfare agents. The agricultural sector in most countries is also vulnerable because farms, animal pens, animal feed, and even finished agricultural products (e.g., milk) typically are not very secure against malevolent actors. The sudden appearance of diseases such as foot and mouth disease, bovine spongiform encephalitis, wheat rust, or similar plant or animal diseases can shut down an agricultural sector very quickly, preventing exports if not domestic consumption, as demonstrated by natural outbreaks of these diseases in the past.

The bioterrorism threat is complex and diverse. Biological weapons may be toxins or living pathogens. They may target humans, livestock, or crops and, hence, be aimed at mass murder or economic impact. Pathogens may be lethal or nonlethal, contagious or noncontagious, and they may infect the host via contact with openings in the skin, animal or insect vectors, ingestion of contaminated food or water, or inhalation, giving rise to a wide range of delivery mechanisms and attack outcomes that vary by many orders of magnitude in terms of their consequences. The current threat largely involves naturally occurring pathogens and toxins. In many ways, biological attacks are similar to the scourge of disease that has wrought havoc on human, animal, and plant populations for millennia, the main difference being that the consequences are greatly compressed in time if not scope. In the future, genetically altered or synthetic pathogens may be possible because the science of genetic manipulation and DNA synthesis is evolving rapidly. This diversity of threats makes it difficult to comprehend bioterrorism as a singular phenomenon requiring a singular strategy.

Strategies for Combating Bioterrorism

The complexity of the bioterrorism threat suggests a multifaceted approach. To simplify the remaining discussion, this article focuses on the elements of a strategy for combating bioterrorism aimed at humans, especially airborne releases because they have the potential for creating the greatest number of casualties. The strategy for protecting the agricultural sector will have similar elements but requires a separate analysis.

The strategy for coping with any proliferation problem involves four complementary elements: diplomacy, deterrence, preemption, and defense. Diplomatic initiatives may help prevent the spread of proscribed weapons, thereby eliminating the problem at its source. If weapons proliferate, deterrence may dissuade their use. If deterrence is about to fail, preemptive attacks may destroy the weapons before they can launch and, if preemption is not a viable option, 'active' defenses may interdict weapons before they arrive and 'passive' defenses may protect people from their effects after detonation. This framework applies to any proliferation problem – nuclear, biological, chemical, or ballistic missile. All four elements are important, with different emphasis depending on the nature of the proscribed weapon. For example, the Cold War nuclear threat was principally addressed by deterrence, complemented by diplomatic (i.e., arms control) efforts to circumscribe the threat and limited efforts at preemption and defense. For biological weapons, the main emphasis should be on defense, complemented by diplomatic efforts, preemption, and deterrence.

Diplomacy

Diplomatic efforts to prevent the proliferation of biological weapons include the 1925 Geneva Protocol, which bans the first use of biological (and chemical) weapons; the 1972 BTWC, which bans the development, production, stockpiling, acquisition, and transfer of biological agents "of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes" and their means of delivery; the Australia Group, which coordinates the export control policies relating to chemical and biological weapons materials and equipment among the 40 or so member states; and UN Security Council Resolution 1540, which calls upon states to "refrain from providing any form of support to non-State actors that attempt to develop, acquire, manufacture, possess, transport, transfer, or use nuclear, chemical or biological weapons and their means of delivery," to adopt and enforce domestic legislation to prevent non-State actors from engaging in these activities, and to establish domestic controls to prevent such proliferation.

The fundamental problem with monitoring biological weapon proliferation is that biological agents, material and equipment are quintessential dual use items, making it difficult to separate benevolent from malevolent applications, and covert biological weapon facilities have few unique signatures that would allow for identification without intrusive inspections. Even with intrusive inspections, it can be difficult to identify covert facilities. For this reason, the BTWC did not include any monitoring or verification provisions, common to most arms control treaties, because member states could not agree on inspection provisions. This difficulty is compounded by the fact that the BTWC allows states to acquire small quantities of pathogens for prophylactic and other peaceful purposes. The difference between a small pathogen sample used to test antibiotics or vaccines and one used as seed stock in a biological weapon production facility is solely one of intent.

Attempts during the 1990s to strengthen the BTWC with an inspection protocol ended in 2001 when the Bush Administration withdrew its support; arguing, with some justification, that covert biological weapon programs could easily be hidden even if this protocol entered into force; that legitimate facilities could be converted to produce biological weapons in a short period of time (weeks to months); and that any inspection regime that was intrusive enough to detect covert programs could compromise proprietary information crucial to commercial companies. Similarly, the Australia Group faces an enormous challenge distinguishing between legitimate and illegitimate end uses for exported biological material and equipment. At best, export controls may impede large-scale acquisition or activities, but it probably cannot thwart small-scale operations.

Future diplomatic efforts should extend beyond traditional arms control treaties and export control regimes. For example, the US–Russian Cooperative Threat Reduction Program, which has focused principally on securing nuclear weapons, materials, and scientists in the former Soviet Union, should be expanded to cover a wider range of former Soviet biological weapon facilities and activities. Material protection, accounting, and control would help prevent the spread of pathogens, equipment, and materials; and funding to employ key former Soviet personnel on peaceful biomedical research would discourage them from selling their expertise to foreign bidders. The latter is particularly important because biological weapon acquisition is largely an issue of acquiring the tacit knowledge, as opposed to the equipment and materials, to build such weapons.

An international code of conduct for biomedical researchers could help reinforce the norm against biological weapons development. The promulgation of international standards and shared best practices for safety and security at pathogen collections or biocontainment facilities that work with deadly pathogens, for example, could reduce the risks associated with accidents or diversion and would help promote interaction among biomedical practitioners engaged in potentially dangerous research. International association and collaboration among biologists, medical professionals, and public health practitioners would help address emerging infectious diseases and the transparency produced through such collaborations would have, as a collateral benefit, the potential to detect covert activities. The Soviet biological weapons program would have been more difficult to conceal had there been international collaboration with Soviet biologists, medical and public health practitioners during the Cold War. Detecting covert biological weapon activities increasingly will be a matter of detecting the people involved, not the weapons.

Improving international disease surveillance, specifically improving public health laboratories in less-developed countries and their connectivity to the international health community, is a worthy objective that also has security benefits. If an attack with a contagious agent occurs in a foreign country, the sooner this is detected, the better governments will be able to limit its entry into their state by monitoring borders and ports of entry, and restricting travel. Improved international disease surveillance might also detect the presence of covert biological weapon programs in the event of an accident that infects the local population. The 1979 accidental anthrax release in Sverdlovsk, Russia would have been readily detected if such a surveillance system were in place at that time. Of course, hiding covert programs, as well as avoiding political embarrassment from natural disease outbreaks, is precisely why some states will resist disease surveillance that is not under their control. Still, efforts by the World Health Organization (WHO) to implement the Global Outbreak Alert and Response Network are well placed and the recently revised WHO International Health Regulations, which require reporting of any disease of international public health concern within 24 hours, when fully implemented, will have public health and security benefits for all nations. These efforts need sustained diplomatic and financial backing. Ultimately governments must recognize that the spread of disease does not respect international boundaries. Hence, public health is not solely a sovereign issue, especially in an age of rapid international travel and commodity transport.

However, diplomacy alone ultimately cannot prevent the spread of biological weapons. Revelations about the size and scope of the covert Soviet biological weapons program during the Cold War, much of which existed under the guise of legitimate biomedical research, demonstrates the limited utility of diplomatic means. Diplomacy's greatest benefit may be to reinforce the widely held norm against the use of disease as a weapon of war or terror. Reinforcing this norm is important not because one hopes to convince malevolent actors to abide by the norms to which the status quo powers adhere, but rather for deterrence; it convinces malevolent actors of the sincerity with which the United States and other like-minded states abhor biological weapons and, hence, the resolve with which they will respond if attacked.

Deterrence

Despite the best diplomatic efforts, biological weapons may still spread. The question then becomes whether states can dissuade other states or terrorists from using them. The efficacy of deterrence against 'rogue' states or terrorists has been questioned because their leaders are believed to be irrational and, hence, cannot be dissuaded by retaliatory threats. This argument distorts the character of regional leaders. Authoritarian leaders may be ruthless, unsavory characters with little regard for their

civilian population; however, generally, they are not suicidal. Similarly, terrorist groups often have clear strategic and tactical goals, with an infrastructure that supports their operations logistically and financially. While those who carry out acts of terror may be suicidal, the top- and mid-level leadership frequently is not. Therefore, in principle, one may be able to identify targets against which retribution will dissuade some terrorist groups from acting. In practice, this often is more difficult, especially if one wants to avoid civilian casualties.

Effective deterrence depends upon the ability to identify the perpetrator of an attack. Therefore, attribution, especially against terrorists or state-sponsored terrorists, is crucial for effective deterrence. By holding states responsible for terrorists who acquire material from them, states will have greater incentive to secure any biological agents they might possess and they will be more reluctant to provide them to terrorist groups with whom they sympathize. Unauthorized acquisition is a problem and will be the obvious cover for any state that contributes to a terrorist's biological weapon capability, UN Security Council Resolution 1540 notwithstanding.

Deterrence relies upon clearly communicated, credible retaliatory threats whose consequences outweigh any benefits the attacker might hope to gain. Credibility, in turn, depends on a state's capability and resolve to retaliate. Public commitment to the Geneva Protocol, the BWTC, and UN resolution 1540 helps convey resolve, in conjunction with statements by top government officials. However, states often lack the capability to respond, in part, because they lack biological weapons themselves with which to make tit for tat retaliatory threats. Nuclear threats, for those states that can make them, are less credible because they require nuclear first use – a difficult political/strategic decision under any circumstances. The United States may be alone in having sufficient conventional military power with which to threaten retaliation, for example, to topple the regime that aided or carried out the attack. Although nuclear response options cannot be ruled out, the United States clearly should emphasize conventional military capabilities to deter biological attack.

Such threats may help deter biological attacks by states, but they are bound to be less effective than deterrence of nuclear attacks during the Cold War. Deterring terrorists may have common elements with deterring states, assuming one can locate enough of the top leadership and infrastructure that supports their operations. However, terrorists have less to lose so the cost-benefit calculus is more difficult to shift in the deterring state's favor. Perhaps the best way to dissuade terrorists from attacking is to deny the success of the attack. Terrorists often are risk averse when it comes to the success of their mission, preferring tactics, techniques, and targets that assure success. Dissuading an opponent by convincing him that his chances for success are slim is referred to as 'deterrence by denial'. However, this terminology confounds deterrence with defense. True, defenses may divert an attack to less well defended targets or dissuade a terrorist group from attacking altogether because of the reduced chance of success. However, the objective of a defense is not to influence terrorist calculations, but to protect the defender regardless of their calculations.

Preemption

Preemptive attacks, that is, thwarting an opponent's ability to strike first when the threat is imminent by destroying his weapons before they can be launched, is frequently practiced in conventional war and was considered by both the United States and the former Soviet Union with respect to nuclear war. Preemption will play less of a role against biological attacks because it is impractical – biological facilities and weapons are easy to conceal and, even if located, they are not easy to destroy without the risk of collateral damage, whether this is from the radioactive fallout from a nuclear blast or the dispersal of pathogens due to their incomplete destruction in a conventional strike. Against terrorist attacks, preemption certainly will be attempted if a state knows where biological weapons are located but, again, this is unlikely unless intelligence or law enforcement agencies get lucky. Efforts to improve intelligence on suspect groups or individuals are useful; however, there are no technical fixes in the offing that will allow intelligence agencies to improve their ability to detect covert biological weapon programs in the future. Better human intelligence is imperative. Therefore, while states should be alert to the opportunity to preempt state or terrorist attacks, it is impractical to rely upon preemption for coping with biological attacks because of the demands it places on accurate, timely intelligence.

Defense

Active Defense/Interdiction

'Active' defenses interdict weapons before they reach their targets. Interdiction frequently is cited as a preferred strategy against terrorists. However, interdiction is difficult against covert biological delivery because pathogens have no signature that allows one to detect them in transit on a person, in luggage, or in any other container. Moreover, biological agents can be released in a myriad of ways, complicating surveillance efforts. Again, there are no clear fixes that will allow intelligence agencies to improve their ability to determine who, when, where, and how a biological attack might occur. Therefore, interdiction programs like the Proliferation Security Initiative – a US effort to create international agreements

and partnerships with other countries to allow the United States and its allies to board airplanes or ships suspected of carrying weapons of mass destruction or their components – may have some deterrent role but without accurate and timely intelligence, it will likely be of limited effectiveness against biological threats, unlike chemical, nuclear, or ballistic missile threats where the cargo is easier to detect.

Examples of efforts to improve border and transportation security in the United States either focus on identifying potential terrorists (e.g., the United States Visitor and Immigrant Status Indicator Technology (US-VISIT) program) or dangerous cargo (e.g., advance electronic cargo manifests, the Container Security Initiative, and the Customs-Trade Partnership Against Terrorism program). Screening travelers at ports of entry is useful because it potentially detects malevolent actors, not their weapons. Screening cargo is much less useful for biological threats because, again, biological agents emit no detectable signature. Not surprisingly, most cargo screening efforts focus on detecting nuclear or radiological materials.

Traditional forms of defense such as air and ballistic missile defense will be of limited use against bioterrorism attacks. Air defenses can be effective provided air defense networks are alerted to the attack, but covert air delivery using a commercial or private airplane will be very difficult to detect without prior intelligence. Ballistic missile defenses are of limited use because terrorists are unlikely to have ballistic missiles at their disposal, except possibly very short-range missiles or rockets. Against the latter, defenses such as Patriot Advanced Capability-3 (PAC-3) interceptors or the Mobile Tactical High Energy Laser (MTHEL) may have some utility, assuming they can prove their effectiveness on the test range. Against biological weapon attacks by a state, ballistic missile defenses also will be of limited value because biological submunitions released early in flight, a technology the United States and the former Soviet Union mastered in the 1950s, can easily overwhelm missile defenses.

Passive Defense

'Passive' defenses protect a population from the effects of weapons after they detonate. Against biological weapons, passive defenses can be quite effective.

Physical protection

Inhalation is the most infectious method of exposure for biological agents. Therefore, a simple mask can provide considerable protection if one knows when to don it. Standard, inexpensive N95 or N99 masks filter out 95% or 99%, respectively, of the submicron particles from inhaled air, thereby substantially reducing the inhaled dose. Their use, for example, would substantially reduce the scale of an epidemic if donned immediately after a contagious disease outbreak is detected, thus increasing the effectiveness of any medical response because it could focus on a smaller infected population.

In principle, homes could be outfitted with High-Efficiency Particle (HEPA) filters, although this would require substantial modifications to most home heating, ventilation, and air conditioning (HVAC) systems and would require positive overpressure systems to prevent infiltration through cracks. However, hermetically sealed office buildings frequently have HEPA filters and positive overpressure HVAC systems, making it easier to 'harden' such buildings if they are likely targets of attack or if they perform critical functions in the midst of an emergency.

Despite the simplicity and relatively low cost associated with most physical protection schemes, they all suffer from the fact that, to be effective, protection must either be in place at all times (e.g., hermetically sealed office buildings) or individuals must know when to seek shelter or don masks. The latter relies upon adequate warning and the ready availability of shelters and masks, both of which currently are not available in most countries. During the 1991 Iraq War, most Israeli citizens carried gas masks which they donned each time their ballistic missile surveillance system warned of an incoming Iraqi Scud missile attack. However, most countries do not have such plans or provisions and, in any case, at best they work only in war and not against covert bioterror attacks in peacetime.

Preattack vaccination

Preattack vaccination conceptually is the simplest approach to preventing disease from a biological attack. This is the approach taken for most infectious diseases of public health concern. For example, almost all children in the United States are vaccinated against Polio, Measles, Mumps, Rubella, Pertusses, and Varicella; and large segments of the population who may be at risk are vaccinated against pneumococcal infection, Hepatitus A, Hepatitus B, Tetanus, and Influenza. The reason this approach has not been widely adopted as a defense against bioterrorism is twofold. First, unlike Mother Nature, terrorists are strategic opponents. When it becomes known that a population has been vaccinated against specific pathogens, terrorists will choose an alternate pathogen or, if sufficiently sophisticated, they may design the pathogen to circumvent the vaccine.

Second, some vaccines have serious medical side effects in a very small percentage of cases. Vaccinating the entire population prior to an attack could produce several hundred severe reactions, possibly including death, and hence is an option of which political leaders will be chary unless the threat of attack is imminent, which as noted above will be difficult to determine. Postattack medical prophylaxis, on the other hand, does

not suffer from this political liability and, hence, is the preferred strategy, assuming it can be effective. If, however, postattack medical intervention is not effective against some pathogen or if the threat of attack from a particular pathogen is a clear and present danger, then a case can be made for preattack vaccination against this particular agent, assuming the vaccine exists. Otherwise, preattack vaccination is contraindicated until safer vaccines become available.

Postattack medical response

All biological agents, with the exception of toxins, incubate in their hosts for a period of days to weeks, depending on the pathogen and the dose to which the individual is exposed. Moreover, medical intervention – antibiotics and vaccines in the case of bacterial agents, and antiviral drugs and vaccines in the case of viral agents – can be very effective if administered prior to the development of symptoms in the host, or shortly thereafter under some circumstances. Therefore, a window exists inside of which medical intervention can be very effective at saving lives. This is the basis for the most important element of a biodefense strategy, namely, rapid postattack medical response.

Postattack medical response involves three elements: biological agent detection and identification, medical logistics to deliver supplies to the exposed population, and a prophylaxis campaign that can dispense the appropriate medications to the entire exposed population in a short period of time, including to a potentially large number of people who believe they have been exposed but are not. All three steps must occur before too many people become symptomatic if this strategy is to provide a high degree of protection. The incubation period for a given disease sets the timescale on which these activities must occur.

The medical efficacy of postattack antibiotic treatment against inhalation anthrax, for example, is illustrated in **Figure 1**, which plots the percentage of hypothetical victims that can be saved as a function of the time at which medical intervention begins. The airborne anthrax release upon which this calculation is based is one for which the exposed population is approximately 300 000 people, 8000 of which would become infected in the absence of medical treatment. The medical intervention posited here consists of antibiotic distribution to 95% of the exposed population over a period of 48 hours (possibly followed by vaccination), that antibiotic treatment prior to the onset of symptoms is 98% effective, and that postsymptomatic antibiotic treatment is approximately 50% effective if delivered within 4 days of symptom onset, assuming intensive medical care is available of the sort provided to the victims of the fall 2001 US anthrax letter attacks (i.e., multidrug regimens and pleural fluid drainage). (Different curves are required for different attack sizes and different diseases, and, in the case of contagious diseases, one must account for secondary transmission.) From Figure 1, one observes that over 90% of this exposed population can be saved if treatment begins within 3 days after exposure. The maximum medical efficacy asymptotes at 93% due to assumptions embedded in the model. Clearly, the sooner one can provide prophylaxis to the exposed population, the better. As the detection and identification time is reduced, more time is available to implement the medical response. And, some functions can overlap in time; for example, the logistics associated with activating the Strategic National Stockpile (warehouses in the United States that currently store medical supplies for a massive infectious outbreak) and setting up and staffing the points of distribution (PODs) where people will eventually queue up to receive treatment can occur simultaneously and immediately after an attack is detected but before the agent has been identified.

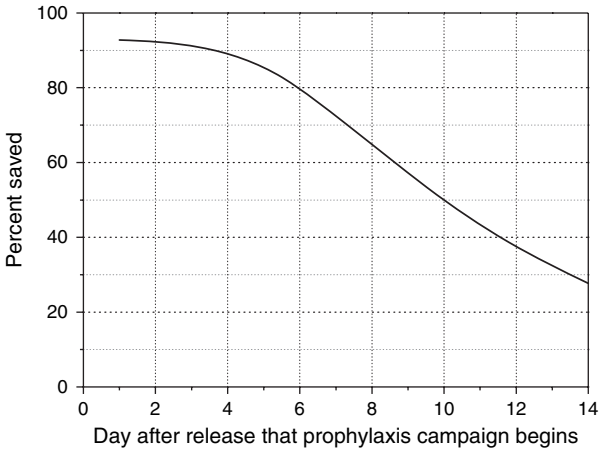

Figure 1 Efficacy of medical response as a function of the time it begins.

This figure should be interpreted with care because it is based on optimistic assumptions, given current US preparedness, regarding the detection time, the speed with which medical logistics can deliver antibiotics to the PODs within the affected area, the speed with which queues can be processed at these PODs, and the effectiveness of the prophylaxis regime (e.g., certain medications may be contraindicated for some subpopulations such as children, pregnant women, and immunocompromised individuals and other victims may not comply with the entire prophylaxis regimen). But, Figure 1 does represent the level of protection that, in principle, can be achieved. Moreover, a 90% effective medical response against an attack that hypothetically infects 8000 people, still leaves 800 people infected, which in the case of inhalation anthrax implies close to 800 deaths, a horrific outcome compared to any bioterrorism witnessed to date. This will likely be viewed as an unacceptable outcome. Thus, the tendency will be to

strive for medical effectiveness well above 90%. To achieve levels of protection above 90%, it will be very important to implement policies that reduce the percentage of people who do not receive prophylaxis (assumed to be 5% of the exposed population in **Figure 1**) or that do not adhere to the full antibiotic regimen over time – both of which are important social, as opposed to technical, challenges for a prophylaxis campaign.

Finally, it is important to note that this strategy overlaps with efforts to improve public health. Consequently, some of the cost for biodefense will have benefits even if an attack never occurs. Given the low, albeit uncertain, likelihood of a biological attack, emphasizing those biodefense programs and activities that have substantial public health benefits is a prudent way to proceed, although some important biodefense programs will not meet this criterion (e.g., developing an improved smallpox vaccine). Moreover, given that infectious diseases are the leading cause of death in many developing countries, a strategy for coping with bioterrorism that does not address the legitimate public health concerns of the developing world will gain little sympathy, support, or cooperation. Contrariwise, the developed world stands to gain tremendous good will if it helps the governments of developing countries solve their public health problems – a commodity not irrelevant in the global struggle against terrorism.

Attack detection and identification

Two issues are important with respect to detecting a bioterrorism event: low false alarm rate and speed. False alarms quickly erode confidence in any detection system, not to mention their economic costs, and consequently should be very infrequent (e.g., on the order of one per decade for a given facility or urban area being monitored). The false positive rate depends on the detection technology, the detection threshold (lower thresholds give more false positives), and background biological aerosol levels in the environment that cannot readily be discriminated from the agents one wishes to detect. As a rule, using two or more different detection technologies, with uncorrelated noise and background signals, reduces the false alarm rate considerably. These detection methods can be sequenced in time to reduce cost, with the first detector cueing the second; however, this increases the detection time.

Rapid agent detection and identification is important because medical treatment is most effective if delivered prior to a victim becoming symptomatic. Prophylaxis efficacy drops rapidly after symptoms appear and intensive supportive care is required to ward off death, making medical intervention more burdensome and costly and, hence, less likely to reach as many people. Real-time detection is not required, unless physical protection – donning masks or entering protected buildings – is part of the defensive strategy. Detection within 24 hours is a reasonable goal for rapidly incubating diseases such as anthrax, thus leaving 1–2 days to conduct an effective medical response. For diseases that incubate more slowly (e.g., smallpox) or for contagious diseases where preventing secondary infections is an important part of preventing a widespread epidemic, slower detection speeds are acceptable. Finally, detailed DNA analysis and trace element detection is important for forensic evidence; however, this can be collected and analyzed within days or weeks after an attack.

The US government has funded the development of a wide range of biological agent detectors. They fall into two categories: environmental sampling and detecting the host response to infection. Environmental sampling involves collecting air, water, food, or swab samples and analyzing them for the presence of pathogens using antibody tests, or matching DNA sequences to known pathogens. Environmental sampling has the virtue that it can, in principle, be rapid (on the order of a fraction of a day, depending on how frequently samples are taken) and it can be used to identify the pathogen, though not necessarily whether the pathogen is virulent. The US BioWatch program, which currently monitors the air in approximately 20 American cities for a range of pathogens, is an example of this approach. If a pathogen plume passes one of the BioWatch air sampling stations in sufficient concentration, it would be detected within approximately 1 day.

The disadvantage of environmental sampling is that a large number of sensors, or air collection stations, must be deployed to ensure that small releases are detected with high probability. If intelligence is available, mobile sensors can be deployed to the area of concern. However, without reliable intelligence, the system costs become prohibitive if one wishes to monitor the air for small releases in hundreds of cities all the time. Finally, such a sensor network provides little benefit to public health because it cannot detect contagious diseases of public health concern, for example, Severe Acute Respiratory Syndrome (SARS) or influenza, because the concentration of these microorganisms in the open environment is well below any detection threshold.

Methods to detect the human response to infection currently involve clinical diagnosis and syndromic surveillance, the data from which would be sent over a nationwide alerting network. Clinical diagnosis relies upon symptomatic patients visiting a physician or hospital emergency room. Not all symptomatic victims would seek medical care immediately because the early symptoms of diseases caused by biological agents are frequently similar to those for influenza – fever, nonspecific cough, congestion, etc. Physician aids can improve differential diagnosis of the relatively uncommon diseases caused by biological warfare agents, thus reducing the time for detection and identification; however, one must still wait for the first few victims to present which may take on the order of 1–2 days. Moreover, laboratory

cultures commonly used to confirm the infectious agent take an additional 1–2 days, although antibody tests such as Enzyme Linked Immunosorbent Assays (ELISA) can reduce this to a fraction of a day if the test is conducted immediately. Therefore, clinical diagnosis currently cannot warn of an attack within 24 hours.

Syndromic surveillance systems monitor clinical reports, pharmacy sales, school absentee rates, and other data to detect an above-normal rate of symptoms in a geographic area. These systems, for example, BioSense in the United States, have detected unusual increases in local infection levels from natural outbreaks. However, they detect events only when the number of symptomatic cases rises above the background level which, by definition, is late for effective medial intervention in the event of a biological attack. Hence, while syndromic surveillance systems may have public health benefits, they cannot provide sufficient warning (i.e., within 24 hours) of a biological attack to implement a highly effective medical response.

Veterinary and wild animal disease surveillance may detect disease among animal and bird populations before they become apparent in the human population, as was the case with the West Nile virus natural outbreak between 1999 and 2001 in the United States. However, monitoring animal disease outbreaks benefits public health more than defense against intentional attacks, where exposure of animal and human populations would be simultaneous, because the incubation period in animals and birds frequently is comparable to that in humans, implying that animal disease detection is unlikely to precede the detection of zoonotic diseases in humans. In any case, rapid veterinary and wild animal disease detection, and its integration with human disease surveillance systems, has not occurred in the United States.

Future research and development in the area of attack warning should emphasize improving the detection time for the host's response to infection, as opposed to environmental sampling, because the latter will be expensive and have very limited benefits for public health. Automated laboratory testing, for example, using ELISA techniques or DNA chips, can reduce detection and identification times to a few hours (from the time samples enter the laboratory); however, clinical diagnosis still requires the presentation of symptomatic patients. Presymptomatic diagnostic techniques that detect the early host immune response to infection, for example, mRNA transcription of the genes involved in the host's immune response which begins within approximately 24 hours of exposure, would be more useful, assuming further research demonstrates that gene expression patterns are reliable fingerprints for the presence of a given pathogen or small class of pathogens. Such techniques could reduce the warning time to approximately 1 day, assuming it is used routinely in hospitals and medical clinics, by detecting asymptomatic victims who visit for other reasons. Presymptomatic diagnostic methods would have tremendous benefits for routine medical diagnosis of common infectious diseases and the resulting economies of scale will reduce their cost.

The United States currently can probably detect and correctly identify a bioterrorism event within approximately 4 days of the initial release by clinical diagnosis. Note, however, that it took 7–10 days to diagnose cases from the 2001 anthrax letter attacks, including the time for blood culture confirmation. Diagnosis information would then be conveyed to the US Center for Disease Control (CDC) via the Public Health Information Network in a matter of hours from most major urban areas, although this network has not been fully implemented. In the future, the US National Biosurveillance Integration System is being designed to provide warning of disease outbreaks of natural or terrorist origin, integrating food, agriculture, public health (clinical diagnosis and syndromic surveillance), and environmental sampling data. The speed with which this system will be able to detect an outbreak will be constrained by the above-mentioned limits associated with the different detection methodologies. Again, real-time detection is not required. Twenty-four hour warning should be sufficient to mount an effective medical response. Since medical prophylaxis should begin within approximately 48 hours of an atmospheric release (in the case of anthrax), a 24-hour detection capability would leave at least one day to implement medical logistics and to begin providing prophylaxis to a large number of exposed and worried citizens.

Medical logistics and the prophylaxis campaign

Providing prophylaxis to a large number of people requires the delivery of large quantities of medical supplies to the exposed population. The suggestion that people keep supplies of the necessary medications at home, thus obviating the need for rapid distribution, have been rejected because some people will take the medications inappropriately (e.g., antibiotics when they have the flu), they may take inappropriate doses, a large selection of medications would be needed to protect against all possible biological agents, and self-vaccination would not be possible. Consequently, current US plans call for stockpiling the necessary medical supplies (antibiotics, antiviral drugs, vaccines, syringes, intravenous supplies, ventilators, etc.) in central warehouses referred to collectively as the Strategic National Stockpile, with the intent to rapidly dispense these supplies after an attack has been detected.

Palletized 'push packs' of medical supplies can be delivered to any local staging area in the United States by aircraft or truck within 12 hours of a decision to deploy them. The greater challenge is to distribute these supplies from the local staging area to the PODs where people queue up to receive medications. These PODs could be

local schools, fire stations, or shopping malls, but not hospitals. Hospitals should remain free from congestion to handle acute cases of victims who have passed into the symptomatic disease phase.

The United States has little hospital surge capacity due to managed healthcare. However, hospital surge capability is important only for those victims who need intensive care. The principle challenge for effective medical response is to provide prophylaxis prior to the appearance of a large number of symptomatic cases. If hospitals become overwhelmed with acute cases, surge capacity is not the answer but rather more rapid and effective presymptomatic prophylaxis. Therefore, POD surge capacity is more important, in particular, augmenting the personnel capable of servicing queues to increase POD throughput. Diagnostic techniques to triage noninfected individuals will greatly reduce the number of people requiring prophylaxis because the number of people concerned about exposure will exceed the actual number of people who become infected by a factor of 10 to 100, if not more.

The time it takes to transfer medical supplies from the local staging area to the PODs depends on the time required to repackage supplies into smaller quantities and to transport them to individual PODs, most likely via small trucks. Efforts clearly should be made to minimize the extent to which repackaging is necessary. Helicopter backup may be required if roads are congested with people fleeing an exposed area. Depending on the size of the urban area, several tens to several hundred PODs will be required to minimize the time required to treat the exposed population. Local officials must identify suitable POD locations, transportation, and staff for each POD, and exercise these logistics plans so they go smoothly in an emergency. This is beginning to occur in the United States.

The prophylaxis campaign requires medically trained personnel to triage individuals according to their medical status and prescribe the appropriate prophylaxis regimen. Paperwork is required to track individuals and the mediations they receive, and to provide information about the medications and possible side effects. Security personnel will be required to ensure order.

If detection occurs within 24 hours, and it takes 12 hours to distribute supplies from the Strategic National Stockpile to local staging areas, 12 hours to distribute supplies from there to the PODs, and 24 hours to set up the PODs (this can occur concurrently with stockpile dispersal), then prophylaxis can begin within 48 hours of a release. If 40 urban PODs can process 500 people each per hour around the clock, then such a rapid medical response can, in principle, provide prophylaxis to approximately 1 million people within 2 days, thereby saving over 90% of a population exposed to anthrax according to **Figure 1**. Again, these numbers do not reflect current capability but rather the level of protection that is possible with sufficient effort.

Medical research and development

Effective medical treatment depends on stockpiling the appropriate medications in sufficient quantity. While antibiotics have an efficacy of approximately 98% for healthy individuals, they may be contraindicated for certain subpopulations (e.g., children, pregnant women, and immunosuppressed individuals). In the United States, the immunosuppressed population is growing due to cancer treatments, human immunodeficiency virus (HIV), organ transplants, and other medical interventions, which is cause for some concern if a highly effective medical response is desired for all significant subpopulations.

Vaccination is an effective defense against many infectious diseases. However, vaccines often take 3–4 weeks for primary seroconversion, and may require one or more booster shots thereafter to achieve full protection. Consequently, they are generally less effective for post-attack prophylaxis unless antibiotic or antiviral drugs are available to control the disease until vaccination takes effect. Moreover, vaccines do not exist for some biological agents and they do not exist in sufficient quantity for others because they are not routinely stockpiled for diseases that are not current public health concerns.

Therefore, research and development should focus on new broad spectrum antibiotics, antiviral drugs, and safe, effective vaccines against known biological agents that can be administered to most segments of the population. Medical research in these areas will also have important benefits for public health as new treatments are discovered for emerging infectious diseases. Concern with antibiotic or antiviral resistant pathogens is best addressed by limiting the overuse of these drugs and by having multiple medications on hand that are effective against a given pathogen strain, again highlighting the importance of medical research and development.

Finally, genetically engineered pathogens that have enhanced effects, circumvent detection systems, or circumvent medical countermeasures may become more widespread in the future. However, increasing the virulence of pathogens through genetic manipulation is not trivial, notwithstanding the Australian mousepox experiment. Nor would terrorists need to go to this trouble since natural pathogens are terrifying enough. At the current time, bioterrorism countermeasures should focus on naturally occurring pathogens. However, biotechnology is in its infancy and powerful discoveries lie ahead. Hence, any defensive policy must strike a balance between developing countermeasures to current versus possible future pathogens.

Research on new prophylactic drugs and vaccines should be carried out largely by private biotechnology and pharmaceutical companies because they have the resources and the expertise to create new drugs, with government sponsored financial incentives to encourage them to develop countermeasures that otherwise would be unprofitable. The US Bioshield Act of 2004 and

follow-on Bioshield II legislation currently under Congressional review illustrate the kinds of incentives that may be effective, for example, tax credits, patent extension, and liability limitations.

Debates have also surfaced about the wisdom of censorship in biomedical publications. The world has a lot more to gain from improved public health than it stands to lose from bioterrorism by allowing unfettered access to scientific advances in biology and medicine. Thus, censorship or classification schemes to keep certain information from malevolent actors should be carefully scrutinized, with open access being the norm unless a clear and present danger exists. This is the best hope for having the medical countermeasures available if and when the need arises while at the same time providing benefits to public health. The US government has established the National Advisory Board for Biosecurity, a group of 25 biologists, physicians, and security experts from outside the government, to help maintain the balance between scientific openness and preventing bioterrorism. In addition to developing guidelines for research and publications in the life sciences, they have helped draft a code of conduct for life science professionals and fostered international cooperation to help define these issues.

Decontamination

Decontamination is required to prevent bioterrorism from becoming a threat to physical infrastructure by rendering buildings unusable for months or years because public officials cannot certify that they are safe for occupancy. An effective decontamination policy must determine safe public exposure levels, which depend on site use and individual susceptibility to infection. Little data exists on environmental background levels for common pathogens. Moreover, the scientific debate regarding the effects of low-level exposure to pathogens may be as contentious as the low-level radiation debate. Therefore, the seemingly simple question of how clean a site must be to ensure public safety will, in fact, be difficult to answer with existing scientific data. Answering this question should be the first priority for decontamination research. Pathogen levels will have to be monitored for months to years after an event, which is both expensive and complicated by the fact that some detection techniques (e.g., DNA sequence matching) do not distinguish living from dead pathogens. In addition, communicating the risks associated with residual contamination to the public in a credible way is vital to allay public anxiety and the economic consequences that flow from these fears. This will be a nontrivial challenge for federal, state, and local authorities working in conjunction with the media.

Postattack vaccination of the local population is an important adjunct to any decontamination strategy because vaccinated individuals can live safely with much higher residual contamination. However, not everyone can be vaccinated due to health risks and vaccinating all visitors to a contaminated area will be inconvenient.

Decontamination strategies differ for outdoor and indoor contamination. Outdoor contamination can be partially removed by washing surfaces with water and, in any case, will decrease with time due to environmental degradation of the agent (e.g., ultraviolet light reduces anthrax spore viability by 10- to 100-fold each day). Locating 'hot spots' will be important but costly because all possible outdoor locations where pathogens might collect in quantity must be sampled initially and monitored thereafter. Outdoor chemical decontamination is expensive and, therefore, will be feasible only for areas on the order of a few square kilometers.

Indoor contamination is a more serious problem because of the absence of ultraviolet light, thus slowing environmental degradation, and because of the amount of time people spend indoors, thus increasing exposure. Indoor remediation can be very expensive, as demonstrated by the experience with the Hart Senate Office Building and the Brentwood Postal Facility after the 2001 US anthrax letter attacks, the latter of which took 1 year at a cost of approximately $130 million to clean up. Moreover, current decontamination chemicals (e.g., chlorine dioxide, methyl-formaldehyde, para-formaldehyde, methyl-bromide, hydrogen peroxide, and household bleach) are corrosive, carcinogenic, and/or toxic. Safer, more effective decontaminants are an important area for research and development, for example, gaseous germination agents that cause anthrax spores to germinate whereupon the vegetative bacillus becomes much more vulnerable to environmental degradation. Combining advanced decontamination agents with high-efficiency particulate air (HEPA) vacuuming could reduce the indoor decontamination problem to a manageable level, especially when combined with vaccination of the local population. Ultimately, a mixed decontamination strategy that takes advantage of environmental degradation, washing, chemical decontamination, and vacuuming where appropriate should be able to render public areas usable, but the cost may be quite high depending on the extent to which future decontamination technologies can avoid a repeat of the 2001 US anthrax decontamination experience.

Conclusion

The logic behind the belief that bioterrorism is a serious emerging threat is sound, although reasonable people can disagree about its urgency. Moreover, this threat is multifaceted and complex, owing to the range of pathogens, delivery modes, and targets for attack. Substantial uncertainties exist in predicting the outcome of any hypothetical biological attack, which implies that attack outcomes can look bleak or relatively benign depending on one's assumptions. The tendency to focus on worst case scenarios, which

leads one to the conclusion that biological weapons are the poor man's nuclear weapon, originate, in part, from exaggerations by those trying to move governments to action, which may have the unintended consequence of convincing some that defense against bioterrorism is too hard and others that pathogens are an ideal weapon of terror. Hence, states must develop a coherent strategy for combating bioterrorism at reasonable cost.

Such a strategy involves diplomacy, deterrence, preemption, and defense, with the emphasis on defense. Arms control and export controls may constrain large-scale biological weapon programs. More importantly, they reinforce the norm against the acquisition or use of pathogens in war or as weapons of terror. This helps reinforce deterrence, which may be effective against states but is less likely to be effective against terrorist groups. Attribution will be crucial to deter states from aiding terrorist groups. However, neither diplomacy nor deterrence is sufficient alone, or in combination, to reduce the biological weapon threat to a satisfactory level. In terms of limiting damage from such threats, preemption, attractive as the concept might be, will be impractical because it relies on accurate, timely intelligence. Interdiction of covert biological attacks also will be very difficult because one must detect the malevolent actors since one cannot detect the biological weapons themselves. Consequently, the emphasis should be placed on passive defense, which involves detecting the release of pathogens in a timely manner, rapid postattack medical intervention, and effective decontamination to restore contaminated areas to a usable state. In principle, postattack medical response can protect over 90% of an exposed population if pathogens can be detected within 1 day of their release, medical logistics can deliver appropriate medical supplies to the exposed population within 1 day, and a prophylaxis campaign can be mounted to treat the exposed population, potentially numbering into the millions, within 2 days. While no state currently can claim to have such an effective defense in place, except possibly against small outbreaks, such a defense is possible. Moreover, to the extent biodefense overlaps with efforts to improve public health, the expenditures may be justified because resources are not wasted even if a biological attack never occurs.

See also: Chemical and Biological Warfare; Health Services, Effects of War and Political Violence on; Health Consequences of War and Political Violence; Public Health Models of Violence and Violence Prevention

Further Reading

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http://www.bt.cdc.gov – Strategic National Stockpile, Emergency Preparedness and Response.