Chemical and Biological Terrorism

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Terrorists by definition seek to create fear and panic. Their motivations are legion and one rarely recognizes, until an incident happens, that the terrorist is in our community. Driven by ideology, grievance, anger and other sociological issues, they attempt to make their presence felt by sudden and dramatic means. Injury, disruption, and death are their goals. Other objectives include media attention, publicity for their cause, and retribution for real or imagined grievances. Terrorist activity is a type of guerrilla warfare. A terrorist may be part of a highly organized, well-funded unit or may be a single, disgruntled employee. Potential for terrorism exists in every community. Public awareness, education, and training will help foil some incidents and mitigate others.

Understanding the nature of chemical and biological terrorist incidents can be challenging to those charged with the responsibility for response and mitigation. It is the goal of this paper to shed some light on this controversial and misunderstood facet of emergency response. In order to understand the potential threats, consequences, and vulnerabilities resulting from the intentional releases of chemical and/or biological agents, a basic review is needed of environmental and agent components affecting toxicity/infectivity. Also, the terms toxicant and toxin as used in this paper mean two different things.

The first relates primarily to those synthetic chemicals produced by man (insecticides, solvents) while toxin refers to chemical metabolites produced by living organisms (T-2 mycotoxin, botulinum toxin). An understanding of toxicological and microbiological principles, choice of chemical weapon or biological weapon agent, ease of acquisition, efficient aerosolization and dissemination, are key ingredients of the terrorist equation for effecting mass casualties and emotional trauma.

Bioagents most likely to be used in terrorist attacks are anthrax, botulinum toxin, and ricin. Chemical agents may include cyanide blood agents; mustard gas-type vesicants; and organophosphate nerve agents. Less toxic substances could be used, however, to cause large-scale injuries to the community. Examples are off-the-shelf insecticides such as malathion or diazinon (cousins of the nerve agents). Carbamates such as carbaryl are also good candidates.

One of the principal advantages of chemical and bioterrorism agents is their extreme toxicity in small quantities. These agents must have the ability to form and be delivered in respirable aerosol concentrations (10 μm or less) to result in mass casualties. The settling rate of aerosol droplets of this size proceeds very slowly and will drift for enormous distances at low wind speeds. Consequently, the ability of chemical and biological agents to generate aerosol droplet clouds is a necessity in order to be effective.

Of major concern is the accessibility of specific related compounds such as the organophosphate (OP) insecticides and the use of peacetime delivery systems such as insect sprayers, dusters and ULV foggers to disseminate the agent. Target delivery systems would be heating/ventilation/air conditioning (HVAC) systems and/or water reservoirs in high use areas (governmental buildings, shopping malls, or community centers).

CHEMICAL AGENTS – Blood and Choking Agents

Chemical mass casualty threats are most likely cyanide products (blood agents) and chlorine/phosgene (choking agents). They are industrial chemicals with widespread application and widespread availability. A terrorist may choose to redirect legitimate chemical sources to criminal terrorist purposes.

Cyanides act rapidly, causing death in minutes. Intravenous therapy may prove effective, but it is unlikely to be available in time unless there is advanced warning and preparation for the attack. Treatment requires fixation of the cyanide ion. Drugs such as intravenous thiosulphate and DMAP (4-dimethylaminophenyl-hydrochloride) are needed to achieve this cure.

Pulmonary agents such as phosgene may not cause serious initial discomfort. However, over time (within hours), they produce pulmonary edema and acute respiratory distress. Phosgene releases hydrochloric acid as it breaks down in the body. Its major medical impact, however, comes from its acylation reactions in the lung at the alveolar/capillary membrane. This leads to leakage into the interstitial portion of the lung.

Phosgene is treated with supportive respiratory therapy, to battle hypoxemia (unoxygenated blood from fluid in the lungs) and hypovolemia (due to the internal blood loss). Although pulmonary agents are not considered priority battlefield threats, their large-scale use by terrorists would most likely saturate available respirators.

BLISTER AGENTS (VESICANTS)

Mustard gas was one of the first chemical warfare agents, and remains a staple in many arsenals today. Only a minority of victims dies from the initial exposure. However, they require a long period of treatment before recovery. Sulfur mustard agent does not irritate the skin, but rapidly penetrates it. Within hours, it can cause blistering, alkylation of DNA, and bone marrow suppression. Mustard dissolves rapidly to form extremely reactive ions that bind to intra- and extra-cellular enzymes and proteins. This leads to cellular death and inflammatory reaction, including protease digestion of anchoring filaments in the skin and the formation of blisters. Vesicant exposure requires extensive supportive therapy as provided by any hospital intensive care unit.

NERVE AGENTS

Acetylcholine is a biochemical neurotransmitter that links nerve cells to muscle and organ cells inside the body. When nerve cells are stimulated, they release acetylcholine into the space (synapse) between the different types of cells, stimulating muscle cells. An enzyme called acetylcholinesterase rapidly breaks down (hydrolyzes) the active acetylcholine, permitting its "reuptake" to the nerve cell. Chemical agents known as nerve gases prevent the acetylcholinesterase in the synapses from neutralizing the active neurotransmitter, assuring that the muscles or organs continue to be stimulated, leading to convulsions and death.

Nerve gas was invented in the 1930s in Germany and is based on organophosphates. Various insecticides, such as malathion, can be considered a weak form of nerve agent. Sarin is one of the most widely feared nerve agents because it is relatively simple to synthesize, as well as having high lethality. VX, while considerably more powerful, is commensurately much more difficult to produce. Its use would tend to indicate a state-sponsored attack.

Therapy for nerve agents is atropine and an oxime such as 2-PAM Chloride (2-pyridine aldoxime methyl chloride; also called pralidoxime chloride). Even after surviving challenge, patients may enter an epileptic state in which they require anxiolytics such as diazepam (valium). Oximes attach to the nerve agent inhibiting the cholinesterase and break the bond with the agent, enabling the enzyme to resume normal activity. Once atropine and oximes are administered, supportive respiratory therapy may be needed.

Valium may also be administered as an anti-convulsant. Pyridostigmine Bromide (PB) is also an interesting pre-medication. It acts as a relatively mild, reversible nerve agent. PB is a carbamate that temporarily binds to the molecular sites and denies the nerve agent a binding site. Later, PB comes unbound, and the cell resumes normal activity.

BIOLOGICAL TERRORISM

Leading biological agents are anthrax, tularemia, plague, viral hemorrhagic fevers and smallpox. Toxins are usually classed as biological agents, although they are chemical by-products of biological organisms. Toxins are powerful poisons, but they do not reproduce in the host's body, as bacteria and viruses do.

The major categories of biological agents are bacteria, viruses, and toxins. From a medical perspective, one may be vaccinated against either a bacterial or viral illness and build up immunity over weeks or months. However, bacteria are small living organisms that may be treated by antibiotics. Viruses, on the other hand, will run their course and are not susceptible to antibiotics. Viruses are also contagious from person to person, while many bacteria are infectious but not contagious. One has to be directly exposed to get the disease. Although there is much less that medical science can do to treat viruses, they are also much harder for potential terrorists to produce. For instance, viruses need to be grown

in eggs, animals, or a bioreactor, since they cannot survive and reproduce independent of a host. Bacteria, on the other hand, may be simply fermented in a growth medium and produced in quantity.

Terrorist-initiated scenarios that could intentionally expose citizens to biological agents are:

Bioaerosol development and dissemination via man-made delivery systems

Specific bio-agents such as bacterial and fungal agents are ubiquitous in the environment and routinely develop in man-made delivery systems. These systems include HVAC systems as well as water displays and reservoirs. Terrorist development and dissemination of bioaerosols containing anthrax, botulinum toxin, or fungal mycotoxins are feasible. High-use community areas such as domed stadiums, shopping malls, subways, and governmental complexes would be prime targets.

Hazmat incidents involving biomedical materials

This category would include the intentional discard of medical wastes and infectious tissue material into or onto a target site. These substances would be of a human and/or animal tissue/blood sample type utilized in drug/medical research. The health effect of these types of terrorist-initiated releases would be limited. The basic impact would be more of an emotional nature.

Shipment of Class III pathogens

Packaging containing Class III pathogens (anthrax, *C. botulinum*, and plague are examples) are routinely shipped throughout the country from type collection laboratories to medical and microbiological research facilities. It is estimated that 10 percent of the approximately 80,000 shipments of microorganisms throughout the United States are Class III pathogens.

Shipment is by common carrier. Shipments involving 50 ml (or less) may be by passenger aircraft or ground transportation. Shipments that are 4 liters (or greater) must be by cargo aircraft.

The concern for emergency responders is that a terrorist group, disgruntled graduate student, or angry medical researcher might target a shipment; intercept the package containing the bioagents; and use the contents as seed stock for biological weapons production. Even if this is not the case, the placement of the stolen container at a high-use area would result in citizen trauma and panic. Intensive media coverage would also be a goal of the terrorist group.

Use of biological agents for agricultural pest or public health pest control

Bacillus thuringiensis (BT) strains have wide use as an agricultural and public health (mosquitoes, black flies) insecticide. The BT organism and its delta-endotoxin toxin adversely affect the targeted insect and effectively control the pest. BT is not a human pathogen. However, BT is closely related to the anthrax organism, *B. anthracis*. BT is also a spore-former whose parasporal bodies are cuboid or diamond shaped as opposed to anthrax's cylindrical or oval spores. BT is mass-produced in the U.S. by a fermentation process. The resultant crystalline spores and delta-endotoxin are formulated as liquid concentrates, powders, or granules.

The concern from a terrorist standpoint is that spray and granular equipment designed for BT dispersion could be easily adapted to a bioaerosol dispersion of anthrax spores. Also BT formulations could be contaminated by anthrax and applied by air or ground spray equipment used in mosquito control and agricultural pest activities. This is particularly relevant to populated areas, as mosquito control is usually conducted in highly urbanized or recreational areas.

BIOLOGICAL AGENTS - BACTERIA

Anthrax is often considered the leading biological threat agent because of its unique combination of high lethality, relative accessibility, and relative ease of covert employment. Its inhalation form has a mortality rate once the infection sets in and symptoms are present. However, there is a vaccine to make one immune to anthrax. In addition, exposed individuals can start treatment with antibiotics to prevent onset of symptoms. This may be done while also getting vaccinated, so that natural immunity is achieved before discontinuing the antibiotic regimen (about eight weeks).

Anthrax is endemic worldwide and forms a robust spore. Animal outbreaks are usually associated with dry weather, when dust containing old spores is then inhaled or ingested by animals. About 8-10,000 spores are considered the minimal infective dose. Anthrax can manifest itself in cutaneous or gastrointestinal forms, if the microbe infects cuts on the skin or is ingested. However, inhalational anthrax is considered the most deadly.

Spores in the 1-10 micron particle size are inhaled deep into the lung alveoli. There the spores may germinate and become vegetative. They are identified by the immune system and transported to lymph nodes in the mediastinum; the area around the heart and lungs. Anthrax spores are then ingested by white blood cells known as macrophages (macro = large, phage = eat). However, instead of dying, the anthrax has a capsule that protects it and permits it to reproduce inside the macrophage. It effectively releases toxins from host cells, leading to edema and septic shock (meningitis in about half the victims). Once the infection takes hold, even antibiotics are not effective, since the major impact is from the released toxins. The incubation period of the disease is considered to be 1-6 days by USAMRIID experts.

Even at late onset, the course of the disease is similar. The first symptoms are nonspecific and flu-like. There may be an "anthrax eclipse" during which the patient feels better. However, within a day or so, breathing becomes extremely difficult (dyspnea) and the patient dies shortly thereafter (similar to septic shock). It is the start of this second stage when most patients would seek hospitalization.

Since there are virtually no cases of respiratory anthrax, emergency room doctors may not recognize it immediately. With dyspnea, a sputum culture and an x-ray will be ordered. The sputum culture will come back negative, since the disease has taken hold in the lymph system rather than the lungs. The negative finding will probably trigger significant curiosity, since influenza or pneumonia would come back positive. An x-ray will reveal an enlarged mediastinum due to the anthrax edema.

It is at this point that critical care specialists may suspect anthrax, and move to preventively treat patients with similar symptoms while awaiting results of dispositive tests. Such tests have to be done in special facilities and may take 24 hours. Other evidence for a differential diagnosis may be drawn from autopsies. About half of the victims will have meningitis (a destructive inflammation of the brain).

All persons in the impacted area may need antibiotic prophylaxis. The antibiotic of choice is ciproflaxacin, until sensitivity tests determine if the microbe is sensitive to the tetracycline family or ampicillin (oral penicillin). In general, antibiotics have a limited shelf life (about 3 years) and are purchased at the rate at which they are expected to be used. There are few stockpiles of large amounts of antibiotics, especially ciprofloxacin or other fluoroquinolones. The US Centers for Disease Control is working on the stockpile problem.

Another treatment approach is through bacteriophages ("eaters" of bacteria). They are viruses that attack bacteria. Bacteriophages attach to the cell, inject their DNA and reproduce. When the cell bursts, up to 200 new bacteriophages are released, which pursue the same type of host cell and repeat the process. There are bacteriophages that are specific to anthrax. Some bacteriophages have been tried against sepsis and have survived and reproduced in a living host. It may be possible to develop bacteriophages that are able to attack anthrax even when they are engulfed in the macrophages.

BUBONIC PLAGUE

Bubonic Plague is the disease that devastated Europe in the 14th century, killing perhaps one-third of the population. Plague is still endemic around the world, including the southwest U.S. However, it is susceptible to antibiotics. Bubonic plague is spread by fleas on rats that then infest humans. However, after the disease spreads from the buboes (certain lymph nodes) to the lungs, it becomes pneumonic plague. The pneumonic form can be spread by droplets from human to human (coughing) and is highly contagious.

VIRUSES

Smallpox is one of the most prolific killers in history. Over 100 million died in this century alone before smallpox was declared eradicated (around 1972) by the World Health Organization. Currently, the only legally declared stocks are held by the U.S. and Russia. The destruction of the last samples has been postponed at the request of the US, so that work may be done to find a medical treatment for the disease. This may be important if additional stocks have been withheld and remain viable.

The U.S.stopped vaccinating against smallpox shortly after its formal eradication was declared. We retain about 16 million doses of vaccine (basically vaccinia or cowpox pustules scraped from intentionally infected calves). However, these stocks are failing quality control checks as they age, and moisture appears to be penetrating the package seals. Nevertheless, authorities believe the vaccine is still effective. They have not used it lately, however, since an antidote supply has also become questionable. The US Food and Drug Administration (FDA) insists that vaccinia immunoglobulin (VIG) be available to anyone who takes the vaccine, especially since the vaccine strain is very reactinogenic.

A new smallpox vaccine and VIG are being created for the military. Smallpox vaccine is very important, in that it can prevent the onset of symptoms even if one has recently been exposed. Victims are considered to be contagious from the time their symptoms start to appear until their pustules scab over.

TOXINS

Toxins are poisons that biological agents produce. Small quantities can cause fatalities. However, most toxins will not penetrate the skin (exception: the fungal mycotoxin, *yellow rain*). Toxins do not reproduce themselves in the host, as biological agents do. Botulinum is one of the most potent toxins on earth. Interestingly, it tends to work in an opposite way to a nerve gas. It prevents the uptake of the neurotransmitter acetylcholine. Thus patients have a characteristic lethargy and drooping eyelids. Death occurs when the diaphragm no longer contracts, and breathing stops. Availability of artificial respirators is key to overcoming a botulinum attack. The effect wears off if breathing can be maintained.

Ricin is another potent toxin, which can be derived from the common castor bean. Ricin does permanent damage, even if the victim does not die. This plant toxin appears to have been used in the past as a bioagent weapon.

NATIONAL ACTION NEEDED

The effective dispersion of chemical and biological agents can be accomplished in a variety of ways. Chemical or bioaerosol dissemination over widespread areas is feasible through aircraft-mounted aerosol generators used in insect control. In a confined space area

such as a HVAC system or a discrete water supply, a more limited assault involving hand-held motorized spray application equipment would be highly successful. Direct contamination of food products and food preparation areas would be the easiest target for the terrorists.

Considering all the factors and the uneasy political times we live in, there is a very good possibility of terrorist attacks utilizing chemical and biological agents in the future. Most of the emergency response community agrees that this threat has to be taken seriously. Obviously, monitoring and responder training is most effective prior to an incident.

Serious consideration should be given to the development of "real-time" biological sensors; establishment of tighter regulations dealing with the acquisition and use of CB agents, as well as the equipment used for aerosol dissemination. Also, high on the priority list are increased public awareness and education as to the threat posed by BC agent assaults, coordination between all intelligence, training, and military communities and increased training of local emergency managers.

On a more practical note, vaccine, antibody and antidote research and development need to be adequately funded. The responder community also needs the development of adequate and "user friendly" protective equipment. Creation and maintenance of regional biological/chemical task forces would go a long way in assisting the local responders in mitigating "agents of mass destruction" incidents.

LOCAL HEALTH DEPARTMENTS: INITIATIVES FOR TERRORIST-SPONSORED ATTACKS

The role of the local health department is to provide leadership to the public health and medical communities in a coordinated effort to detect, diagnose, respond to, and prevent illness that could result because of chemical or bioterrorism. These tasks are an integral part of local health departments' overall mission to monitor and protect public health.

In this regard, a strong and flexible public health infrastructure is the best defense against any terrorist-initiated attack. Local initiatives should include the strengthening of disease surveillance and response at the local level to detect and contain injuries/diseases caused by chemical or bioagents. Rapid response with accurate information provided to the media helps to forestall panic.

A terrorist attack utilizing chemical and bioagents initially may be invisible and undetected. Chemical releases would be easier to detect, as the onset of symptoms would be relatively immediate. The release of a biological agent or chemical toxin might not have an immediately visible impact because of the delay between exposure and onset of illness. Initial responders to such attacks would include local health officers, hospital staff,

members of the outpatient medical community, and a wide range of response personnel in the public health system.

Thus, the local health department has a major responsibility to improve the public health community's preparedness to detect injuries or illness that are a result of a chemical or bioterrorism threat. Local health department initiatives therefore should include the development of the appropriate public health structure and contingency plans to respond effectively in the event of a terrorism-initiated incident. An integrated approach with public safety, police, and emergency responders is extremely valuable if instituted PRIOR to an event. This allows for efficient utilization of specific strengths toward effective management of the event.

Local Health Department Initiatives

1) Strengthen public health surveillance to ensure rapid detection of unusual outbreaks;
2) Strengthen epidemiological capacity to investigate and control health threats from terrorist events;
3) Enhance public health laboratory capability (both chemical and microbiological) to identify agents most likely to be used in intentional release events; and
4) Develop/coordinate communications with local government agencies and the general public to disseminate critical information and minimize unnecessary fear.

Public health agencies need improved public health infrastructures that can detect intentionally caused disease outbreaks early and provide treatment. An observant, well-trained local health official should recognize that something out of the ordinary has occurred and alert public health authorities through prearranged communication channels. In many instances there is only a short window of opportunity to determine the following:

1. That an attack has occurred;
2. To identify the toxicant/bioagent;
3. To prevent further exposures; and
4. To mitigate the event where possible

First and foremost, local communities must have a coordinated response plan to a possible terrorist attacks. These response plans should include law enforcement, medical first responders, and public health officials. While the FBI has jurisdiction for terrorism response, local communities must have trained personnel available for rapid response. If chemical or bioterrorism is suspected, the local emergency response system should be activated.

In the event of a bioterrorist attack, rapid diagnosis is critical to the immediate implementation of prevention and treatment procedures. Future events could involve organisms that have been genetically engineered to increase their virulence, possess antibiotic resistance, or evade vaccine-induced immunity. Due to the fact that many of the bioweapons are currently not major public health problems in the United States, there is a limited capacity to diagnose them. Therefore it is important that the local health departments work with state health laboratories to increase the capacity to identify possible disease agents.

Local health departments should have the capacity to detect outbreaks of food-borne diseases caused by deliberate contamination. The early detection of these types of disease outbreaks can help avert possible widespread consequences.

In this regard, CDC's Epidemiological and Laboratory Capacity (ELC) program can help local health departments develop the skills and resources to address whatever infectious disease challenges may arise. One of the specific aims of the ELC program is the development of innovative systems for early detection and investigation of outbreaks.

Early Detection

A sentinel disease detection system involving local networks of clinicians and health providers should be established. In this way the medical community will be alerted in a timely manner so that health workers can identify disease threats. Additional resources to aid the sentinel process should be established with local academic, government, and private sector organizations.

Rapid Communications and Information Access

In the event of an intentional release of a chemical or biological agent, rapid and secure communications will be crucial to ensure a prompt and coordinated response. Each hour's delay will increase the probability that another group of people will be exposed, and the outbreak could spread both in number and in geographical range. The establishment of a Health Alert Network (HAN) will result in a well-developed communication, information, distance learning, and organizational infrastructure for a rapid-response to chemical and bioterrorism. Such a network would incorporate the following:

1. Continuous, high-speed connection to the Internet;
2. Broadcast communications;
3. Satellite- and Web-based distance learning.

National Pharmaceutical Stockpile (NPSP)

Once the cause of a terrorist-sponsored outbreak was determined, specific drugs, vaccines, and antitoxins might be needed to treat the victims and to prevent further spread. Appropriate medical supplies may not be readily available to local responders, or in the

quantity needed, since many infections are uncommon causes of disease in the United States. Therefore local health departments should avail themselves of the CDC-sponsored stockpile of pharmaceuticals that are available anywhere in the continental U.S. within 12 hours.

About the Author

Dr. Wagner is a noted scientist with years of experience in environmental toxicology and medical parasitology. His experience includes "hot zone" assessment of health effects during catastrophic disasters, such as train derailments. He is an Assistant Professor of Environmental Health Science at Salisbury University, Maryland. He also teaches at FEMA's National Emergency Training Center, Emmitsburg, Md., and the Emergency Assistance Center, Mt. Weather, Va., with specialty areas that include chemical and biological agent releases and exposures.

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