TOXIC AND BIOLOGICAL TERRORISM

by

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INTRODUCTION

Terrorism is the unlawful use of force or violence against persons or property to intimidate or coerce a government or civilian population in the furtherance of political or social objectives. Terrorism's purpose is to threaten a society, political body, and economy and obtain shock value in their action. Terrorists seek unsuspecting victims using novel attacks that are damaging and symbolic in their scope and victimization. In seeking a strategic, symbolic and political shock effect, terrorists depend upon the media to provide a stage for their psychodrama.

Terrorism as a form of domestic and international political violence reached its peak in the 1970s with the kidnapping of foreigners, hijacking of aircraft, and organized attacks in foreign countries. "State sponsored" terrorism has also continued to grow as an international problem.

Explosive devices have long been the standard terrorist weapon, and the United States has not escaped this wrath: The World Trade Center bombing in 1993 killed six and injured more than 1,000 people; the bombing of the Murrah Federal Building in Oklahoma City killed 168 men, women, and children, and injured more than 750; in June of 1996, the bombing of Kohbar Towers in Dharhan killed 19 U.S. military servicemen; the explosion in Atlanta's Centennial Park in 1996 during the Olympics further rocked our domestic sense of security. Finally, the September 11, 2001 World Trade Center and Pentagon terrorist attacks galvanized the civilized world's resolve that terrorism must end and sponsors of terrorism must be brought to justice.

The risk of international and domestic terrorism using nuclear, biological, or chemical (NBC) weapons has escalated at the end of the twentieth century and the beginning of the twenty-first century. According to the Central Intelligence Agency and the Federal Bureau of Investigation (FBI), terrorists based in the Middle East or elsewhere will someday use chemical, biological, and possibly nuclear weapons against U.S. targets. This sentiment was echoed by previous Defense Secretary William Cohen, who warned, "This scenario of nuclear, biological, or chemical weapons in the hands of a terrorist cell or rogue nation is not only plausible, it's...quite real."

NUCLEAR, BIOLOGICAL, AND CHEMICAL TERRORIST WEAPONS

Humans have employed poisons and germs throughout history to inflict harm and death in warfare and in politics. During the Siege of Kaffa on the Crimean Coast in 1346, Mongol invaders hurled cadavers infected with the plague across city walls to infect its defenders (1-3). In 1763, Lord Jeffery Amherst, the British Commander of the American Colonies, infected rebellious Indians by giving them gifts of blankets contaminated by smallpox (1-3). One of the more media-focused events occurred in 1995, when an Armageddon religious sect unleashed a terrorist attack on a Japanese subway with highly lethal sarin nerve gas, killing 12 and sending 5,500 people to hospitals.

While nations, including the United States, have developed offensive biological and chemical weapons, none of these weapons have ever won wars. Their use appears to be tactical. However, since these agents have been stockpiled by the militaries of some nations since World War I, it was only a matter of time until terrorists came to possess these so called "poor man's nuclear weapons." Toxic and biological agents possess characteristics that make them ideal terrorist weapons:

- They are inexpensive to manufacture
- They are hard to detect
- They are easy to disperse
- They lack warning properties such as odor, color or irritancy
- Victims are unaware that they have been exposed, even after symptoms appear.
- They evoke terror of the unknown

Biological and toxic terrorist attacks have actually been occurring since the 1970s (Table 1). The thought of injury, infection or death from such invisible weapons generates the perception of an imperceptible evil power that may strike suddenly, generating fear and loss of personal safety, escalating terror and stress, not only in victims, but in the public. The unfamiliarity of such agents touches our deepest fears. The October, 2001 anthrax events in Florida, New York and Washington D.C. points alarmingly toward the potential of biological and chemical agents being employed in the United States as terrorist weapons.

HISTORICAL PERSPECTIVES

The Brussels Convention on the Law and Customs of War in 1874 prohibited the use of poison or poison weapons, arms, projectiles or material that caused unnecessary suffering. In 1899, an international peace conference in The Hague concluded with the prohibition of the use of poisonous gas projectiles. However, neither of these agreements prevented the use of chemical weapons by both the Allies and the Axis powers during World War I.

April 22, 1915 is the date widely accepted as the beginning of modern chemical warfare. French and Canadian troops gathered in trenches were the targets of a green cloud of chlorine gas released by the Germans (4). Horrified allies considered this attack a crime. Though casualties were small, the terror felt was huge. Soon the Germans realized that chlorine gas attacks were not very effective, and in August of 1916 they unleashed a phosgene attack against allied forces. German ingenuity also led to the development of gas artillery shells which contained a mixture of explosives and the toxic gases diphosgene, diphenyl chloroarsine and chloropicrin (4). In July of 1917 around Ypres, the German's first used mustard gas (dichloroethyl sulphide) which caused terrible respiratory, skin and eye burns and blisters (4). Allied reports confirmed that the Germans had used tetanus bacteria, anthrax and tuberculosis to infect animals and livestock, further horrifying the Allies (3).

Control of chemical weapons was again approached during the Versailles Treaty of 1919. Then in 1922, the Washington Disarmament Conference renewed negotiations for the elimination of chemical weapons. However, both efforts failed. But the outrage over chemical weapons continued, eventually leading to the 1925 Geneva Protocol which prohibited the use of asphyxiating poisonous or other gases as well as bacteriological methods of warfare. But the Geneva Protocol did not prohibit the development, production or possession of such weapons. Nations that signed the Geneva Protocol maintained the right to possess these weapons for retaliation. The United States did not ratify the Geneva Protocol until 1975.

Following World War I, a Japanese army surgeon, Shiro Ishii, became intrigued with biological weapons. He reasoned that such weapons would be inexpensive and easy to develop due to Japan's advanced biomedical expertise (1). Japan had already learned the value of vaccinating its soldiers, thus reversing the trend that more soldiers died of disease rather than battle. In the Russo-Japanese War of 1904-1906, vaccination proved effective and only one of four Japanese soldiers died of disease (1).

After Japan invaded China in 1932, Ishii started a biological weapons research program in the Chinese town of Ping Fan. Termed Unit 731, this research and medical facility was secretly dedicated to production and testing of biological weapons. Ishii chose smallpox, salmonella, typhus, botulinum, toxin, brucellosis, tuberculosis, tick encephalitis, anthrax, clostridium perfringens, and tularemia for his research (1). He conducted horrible experiments on prisoners of war and any other human unfortunate enough to be imprisoned. He rationalized his work by his need for data and the inferior social status of his victims (1). Dr. Ishii's research led to development of biological bombs which were tested against Chinese cities. On October 4, 1940, a plague bomb of infected fleas, wheat, and rice was dropped on a city in Chekiang province. Another bio-bomb was dropped on October 27 on a different city. Both resulted in plague outbreaks.

Following WWII, the truth about Ishii's atrocities during the Japanese occupation of Manchuria became known (1,5,6). Ten thousand prisoners had died as a result of Ishii's experimentation. Evidence that at least eleven Chinese cities were attacked with biological agents using delivery mechanisms from aircraft and directly tossing cultures of infectious agents into homes and buildings became known to the Allies (1,5,6). Due to poor preparation, the Japanese sustained 10,000 biological casualties and 1,700 deaths among their own troops, most cases due to cholera (6-8). None of the Japanese involved in biological weapons testing on humans were prosecuted for war crimes.

By 1942 the United States had started an offensive biological weapons program at a facility in Fort Deitrich, Maryland. Japanese scientists who had participated in the Unit 731 program were granted immunity from war crimes for providing data and information to the United States military on biological warfare agents (1,6). Following WWII, less attention was paid to these agents due to the explosion of the atomic bomb. However, the United States continued to expand its offensive biological and chemical program weaponizing these agents with delivery systems.

In the 1950s, the United States began to develop vaccines to counter biological agents. Unfortunately, covert testing of "innocuous" biological agents on U.S. civilian and military volunteers also occurred. Between 1949 and 1968, reports surfaced that the U.S. military biological offensive program had targeted certain American cities as test sights for aerosolization and dispersal methods of non-pathogenic bacteria (1,9). Outrage led to Senate investigative hearings in 1977 and the United States Army was severely criticized. But the United States military had already developed a biological arsenal that included bacterial pathogens, viral pathogens, fungal plant pathogens and botulinum toxin, and continued experimenting with other biotoxins.

Efforts toward termination of development of offensive biological agents and disarmament of countries with established offensive biological weapons began again during the late 1960s when world leaders accepted the ineffectiveness of the 1925 Geneva Protocol. President Nixon directed the National Security Council to assess America's policy toward these weapons. This assessment lead to the unilateral, unconditional renouncement of all methods of biological weapons by the United States. Nixon's executive order on February 14, 1970 stated the following:

> "The United States renounces offensive preparations for and the use of toxins as a method of warfare.
>
> The United States will confine its military programs for toxins, whether produced by bacteriological or any other biological method or by chemical synthesis, to research for defensive purposes only, such as to improve techniques of immunization and medical therapy. I have directed the destruction of all existing toxin stocks and weapons which are not required for a research program for defensive purposes only.
>
> The United States will have no need to operate any facilities capable of producing toxins either bacteriologically or biologically in large quantities and therefore also capable of producing biological agents."

The Biological Weapons Convention

International concerns about biological weapons led to the 1972 Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological and Toxin Weapons. Known as Biological Weapons Convention (BWC), this agreement prohibited development, production and stockpiling of pathogens or toxins in quantities that had no justification for prophylactic, protective or other peaceful purposes (1). The BWC also prohibited the development of delivery systems for these agents. It required parties to destroy stocks of biological agents, delivery systems and equipment within nine months of ratifying the treaty. Transfer of technology to develop biological weapons of warfare or expertise to other countries was also prohibited. The BWC was ratified in April of 1972 and took effect March of 1975 with more than 100 signatory nations including Iraq and members of the United Nations Security Council.

Despite the BWC, in the years between 1975 and 1981 allegations arose that the Soviet Union had employed aerosolized trichothecene, a mycotoxin known as "yellow rain," against humans in Laos and Afghanistan. Then in April and May of 1979, an unusual anthrax epidemic occurred in Sverdlovsk, a city of 1.2 million people in the Soviet Union (10). While officials in the Soviet Union attributed this outbreak to consumption of contaminated meat, the United States attributed it to inhalation of anthrax spores that were accidently released by a biological production's facility in the city. Epidemiologic studies showed that most of the victim's worked or lived in a narrow zone extending down wind from the military facility. In 1991, Russian President Boris Yeltsin admitted that the facility's biological warfare development program was the cause.

The magnitude of the development of the Soviet Union's offensive biological weapons and chemical weapons was further revealed in 1992 when Yeltsin admitted that the Soviet Union had violated the Biological and Toxin Weapons Convention numerous times despite signing it and making formal agreements with the United States.

After the Gulf War, the United States realized that the size and scope of the Iraqi offensive weapons program has been underestimated. The Iraqis had deployed bombs, rockets, aircraft spray tanks, and scud missiles with deliverable botulinum toxin, aflatoxin and anthrax spores. Iraq was also involved in research in other biological and toxic weapons including clostridium perfringens, rotavirus, echo virus 71, and camelpox virus (12, 13).

In 1994, a special conference of the Biological and Toxin Weapons Convention was established to consider effective verification measures. However, the issue of verification remains unresolved. Therefore, the U.S. Army's Medical Research Institute of Infectious Diseases (USAMRIID) continues the development of medical defenses against potential military biological attack.

Then in 1995, a terrorist attack on a Japanese city and a subway by the Aum Shinrikyo Cult pointed out the ability of terrorist groups to possess toxic and biological warfare agents. This religious sect also tried to produce botulinum toxin and anthrax (11). Shoko Asahara, the head of the cult had travelled to Zaire allegedly to help treat Ebola virus infected victims. But the group’s intention most likely was to obtain the virus for culture and future use as a biological weapon (12, 13).

The Chemical Weapons Convention

The Chemical Weapons Convention (CWC) was signed by President George Bush but not ratified by the U.S. Senate on April 25, 1997. The CWC bans the production, stockpiling and use of chemical weapons and prohibits parties to the treaty from assisting other states to engage in these outlawed activities.

Signatories to the CWC must account for all their chemical weapons and facilities, and destroy chemical weapon stockpiles and production facilities within a specified period of time. The goal of the CWC is complete elimination of chemical weapons by the year 2007.

The Chemical Weapons Convention became effective on April 29, 1997 and the Organization for the Prohibition of Chemical Weapons (OPCW) was established in The Hague to be responsible for implementation. Russia, which admits to possessing chemical weapons, has not yet ratified the CWC. Other countries that have signed the CWC but have not ratified it include China, Iran, and Pakistan. Iraq, Libya, North Korea and Syria have neither signed nor ratified the CWC.

The basic obligations of the CWC contained in Article 1 (14) requires States possessing chemical weapons to destroy them in a safe and environmentally friendly manner, and forbids the disposal of chemical weapons by open-pit burning, burial or dumping in any body of water. The destruction of chemical weapons must be verified by on-site inspection. Facilities used to produce chemical weapons must also be destroyed or converted for purposes not prohibited by the CWC.

Chemicals to be verified are listed in three schedules (14): Schedule 1, Schedule 2 and Schedule 3. Each schedule is divided into two parts: toxic chemicals and precursors to toxic chemicals. The question now becomes, When is a chemical a chemical weapon? The three schedules do not constitute a definition of chemical weapons, and chemicals not listed on the schedules obviously can be used to make chemical weapons.

Schedule 1 Chemicals: Chemical warfare agents and their precursors including nerve agents and nerve agent precursors - sarin, soman, GF, tabun and VX. Mustard agents and lewisites are listed and includes 15 agents of these types (9 sulfur mustards, 3 nitrogen mustards and 3 lewisites). Two biotoxins, ricin and saxitoxin, are included.

Schedule 2 Chemicals: Includes dual use chemicals of limited use - Amiton, which is an organophosphate too toxic for agricultural use; OFIB, which is perfluoroisobutylene, a gas formed as a byproduct during production of fluorinated polymer such as teflon and has a toxicity similar to phosgene; BZ, which is an incapacitating agent and an intermediate in the production of pharmaceuticals. Schedule 2 also includes precursors to nerve agents, mustard gas, lewisites, BZ, and chemicals containing a phosphorous atom with one attached methyl, ethyl or propyl group. Schedule 3 Chemicals: Includes dual use chemicals of extensive use - phosgene, cyanogen chloride, hydrogen cyanide, chloropicrin and nerve agent precursors such as phosphorous oxychloride and phosphorous trichloride. These chemicals can have applications in the chemical industry in the production of insecticides and chlorinating agents. Mustard agent precursors are also included - three sulphur mustard and three nitrogen mustard precursors, including triethanolamine. Sulphur monochloride is also included which is used in the production of dyes, pesticides and cold vulcanization of rubber, and in polymerization catalysts for vegetable oils.

The CWC requires a nation's chemical industry to meet obligations for declaration and verification under its provisions. This provision has led many industries to oppose the CWC. Chemical facilities, chemicals and plant sites listed on Schedule 1, Schedule 2 and Schedule 3 fall under the purview of the CWC. Many producers, processors, consumers, importers and exporting firms are affected by the CWC and their reporting thresholds and inspections thresholds which are contained in the CWC.

PROFILE OF TERRORISTS

The Department of Defense defines terrorism as the calculated use of violence, or threat of violence, to inculcate fear intended to intimidate or coerce governments, societies or individuals in the pursuit of political, religious or ideological goals (15). The Federal Bureau of Investigation's definition of terrorism is the unlawful use of force or violence against persons or property in order to intimidate or coerce a government, civilian population, or any segment thereof in further of political or social objectives. Both definitions distinguish terrorism from other forms of violence.

Despite treaties and international conventions to prohibit development and use of such weapons, terrorist groups and extremists have managed to gain access to toxic and biological agents and to potentially weaponize them. Biotechnology also provides terrorist groups and rogue nations the ability to develop newer and more horrific biological weapons. Terrorist attacks with such weapons can only be prevented or deterred by the vigilance and efforts of law enforcement agencies.

Psychological Motivations of Terrorists

There is no one psychological motivation found among terrorists; however, there is a universal element which describes them as a "true believer" in their cause (15). Terrorists have also been described as having personal dissatisfaction with some aspects of their life or accomplishments and project their own antisocial motivations onto others, creating a "we versus they" mentality (15). Terrorists tend to contribute evil motives to those they target outside of their group. Due to this belief system, terrorists dehumanize their victims, removing any sense of remorse. Terrorism appeals to individuals who crave violence in order to relieve aspects of their anger. They reject the notion that their acts are criminal.

Terrorists frequently seek group affiliation to support their cause. Acceptance can be a strong motivator, even stronger than political objectives and terrorists may define their social status by group acceptance (15). Terrorists align their internal motivations with the internal motivations of the organization. These motivations not only justify the group's existence but also the terrorist's existence. As such, the terrorist or their group commit violent acts to maintain group legitimacy. The group identifies their enemy as evil and feel pressured to escalate the frequency of violence perpetrated on that enemy. Group dynamics do not allow dissent from cause and purpose. The intense group dynamics and fear of reprisal discourages an individual terrorist from leaving the group (15).

The psychodynamics of a terrorist group make achieving their goals difficult, if not impossible. If stated goals are achieved, then the group is no longer needed, threatening the psychological well being of the group's members. Thus, as a terrorist or terrorist group approaches a stated goal, there is an inclination to redefine that goal. Goal redefinition allows continued group existence. Terrorists may suffer from fear of success. Sometimes terrorists are psychologically prone to define goals so broadly that they are impossible to achieve so that they can always continue to fight (15).

In terms of psychoanalytic approaches to terrorists, the terrorist feels him- or herself to be the personification of ethnic or national expressions of a group's liberation or destiny. They become the appointed martyr, savior or messiah (15-18).

Rational Motivations of Terrorists

Terrorist violence is not spontaneous nor is it random. It is a calculated act. Target selection is planned in terms of the effect terrorists seek. It is intended to engender fear in a wider audience other than the victims.

Terrorists cannot accept compromise because they have placed themselves forever beyond acceptance to society. Negotiation is dishonorable and, at times, treasonous. For this reason, terrorist groups are prone to fracturing and splintering into sub-groups which may be more violent than the parent group (15).

Terrorists think through their goals and their options and make concrete, rational analyses. Risk is weighed along with the groups capabilities to sustain their terrorist effort. The terrorist weighs the target's defensive capabilities versus his or her own capabilities to mount an attack (15). A terrorist's rational mind works similar to a company's CEO considering available courses of action. A terrorist or a terrorist group must induce enough anxiety and fear to attain its goals without causing a backlash that will destroy its cause and perhaps eliminate the terrorists themselves. This is particularly true in terms of the popular reaction to their terrorist activity.

Cultural and Religious Motivations of Terrorists

Terrorist goals are stated to be political but there are usually religious or ideological objectives underpinning theiroals. Extremists are often driven by religious or ideological beliefs, and seek political power to compel a society, a government, a group of people to conform to their views. These objectives of terrorism distinguish it from other violent acts which are aimed at more personal gains.

Americans often do not appreciate the effect that culture has on behavior. This is particularly true with foreign terrorist activity. While our western heritage rejects martyrdom and self destructive behavior, other cultures do not. Americans also tend to impose our cultural values and motivations on others, thus hampering our understanding of the cultural motivation of terrorists (15).

A person's values and treatment of life in general, including the life of that individual, is a cultural characteristic that influences terrorism. Terrorists recruit from the destitute and impoverished and from the highly educated. The closer people identify themselves in terms of a group membership such as a tribe, a family, a religious sect, the more there is willingness to perform self-sacrifice for that group. Terrorists are eager to give their lives for their organization and destroy the lives of others who are considered evil to their value system. Threats to religion, group membership, culture homeland or territory, and fear of losing these, can trigger terrorist actions.

The concepts of social organization are important to extremist and terrorist organizations. But some social and political systems have no effective means for the nonviolent transfer or succession to power. Some cultures, such as the United States, have a high tolerance for nonpolitical violence. But while America tends to be one of the more violent societies in the world, we abhor political violence. Other countries have very low tolerance for violent crime but have an extensive history of political violence such as those in the Middle East, France and Germany.

Religion is one of the most volatile of cultural identifiers because it involves deeply held values for the individual and society. Any risk or threat to one's religion places not only the individual at risk, but their past culture and future at risk. Many religions feel so confident that they are correct or right in their assertion of beliefs that they try to force conversion of nonbelievers. Thus, terrorism in the name of religion can be very violent.

Religiously motivated terrorists act with certain moral turpitude, feeling that they are divinely sanctioned to carry out violent acts. Such terrorists feel a duty to carry out these acts in the name of their religion even if it means death to themselves.

Terrorist Profiles

The FBI has published annual reports through its Terrorist Research and Analytical Center (TRAC) listing specific terrorist acts, or acts suspected of occurring because of terrorism which have resulted in indictment of officially designated terrorists. Such investigations allow accumulation of and profiling of characteristics of terrorist groups and organizations in the United States (21).

Terrorists differ considerably in their ideology, economic views, politics, approach to terrorism and their targets. While some terrorists adopt a political focus, other embrace ideologies combined with cultural and religious beliefs. Researchers have profiled American terrorist as being different from their European or Middle Eastern counterparts (18-20). American terrorists tend to be between the ages of 18 and 35, primarily male, although growing in percentage of women, better educated than others their age, and generally from middle or upper income families.

Leftist groups of the 1980s had aspirations of an American social system embodying the Marxist views while despising capitalism's "exploitation" of the working class and minorities. While the right leaning extremists viewed the social governmental programs with opposition, left leaning extremists viewed such efforts as attempts to pacify the masses of people and became frustrated in their inability to change the system without violence (21). The philosophical root of the terrorist act that destroyed the Oklahoma City federal building in 1993 had as its basis an intense hatred of the U.S. Government's role in the lives of American citizens and a protection of gun owners' rights.

The attack of September 11, 2001 on New York City's World Trade Center and the Pentagon using commercial aircraft revealed a highly organized and well funded terrorist network of Islamic fundamentalists who plotted the coordinated attack for ten years before its execution. This network was both secretive and known by federal authorities because of previous terrorist attacks. Extremists and terrorists of all profiles face the contradiction and dilemma of requiring secrecy and publicity at the same time (21).

Terrorist and extremist groups depend upon funding and may be involved in illegal activities such as drug trafficking and robbery for funding their missions. Terrorist groups differ in target selection reflecting the hallmark of their respective philosophy and ideologies. The symbolic nature of the target many times is just as important to a terrorist as the extent of the damage or death that the terrorist act inflicts (21).

UNITED STATES POLICY REGARDING TERRORISM

The United States considers all terrorist acts as criminal and intolerable, and condemns them all regardless of motivation. U.S. policy regarding terrorism encompasses acts against Americans at home and abroad. The United States will support all lawful measures to prevent terrorism and bring terrorists to justice. But, up until the 1980s, the United States considered terrorism to be a police matter. Now terrorism has become a matter of State and military defense. The Department of Defense defines five threat levels to reporting terrorism and terrorist activities:

1. Critical level: A terrorist group has entered the country or is able to do so and has the capability to attack and engage its target and target selection, although its history and intentions may or may not be known.
2. High level: This indicates that a terrorist group exists which has the capability, history and intention to attack.
3. Medium level: This indicates that terrorist group exists and has the capability, history and intention to attack but those intentions are unknown.
4. Low level: A situation in which terrorist groups exists and have a capability to attack. Their history may or may not be known.
5. Negligible level: A situation in which the existence or capability of a terrorist group may or may not be present.

Combating terrorism involves defensive measures (anti-terrorism) and offensive measures (counter-terrorism). Anti-terrorism is defined as a defensive measure because it reduces the vulnerability of individuals and property of terrorist acts. It also may include limited response by military forces. Counter-terrorism involves offensive measures taken to prevent, deter and respond to terrorism. Counter-terrorism methods are classified.

Terrorism as a form of political violence is expected to remain a prominent activity into the twenty-first century. Terrorists may take advantage of the wide array of weapons, explosive triggering devices, and more technologically advanced communication technology and computers to coordinate their activities. Computer technology has allowed terrorists to access secure data banks, access information or destroy information. However, such technology may also allow law enforcement authorities to better track and apprehend terrorists.

The 1995 sarin nerve gas attack in the Japanese subway is such an example. Another is the March, 1993 bombing of the World Trade Center in New York City which shocked the United States into realization that terrorist attacks perpetrated by individuals from other nations are possible. The terrorist leaders of this attack planned to attack the United Nation's headquarters in the Holland Tunnel which would have inflicted thousands of casualties. The Oklahoma City bombing of a federal building on April 19, 1995 perpetrated by an American citizen, killing 168 people and injuring more than 600. This was the largest known act of domestic terrorism in the United States until September 11, 2001.

The Federal Bureau of Investigation has data indicating that domestic and international terrorism is rising significantly. International terrorist acts amounted to 440 in 1995, which was an increase from 322 in 1994. Future terrorism is probably going to include higher levels of violence and more novel approaches, with weapons that have more devastating psychological effects on a population and that produce more mass casualties. Terrorist targets of the future may also be ecological such as the devastation rendered by Sadam Hussein in Kuwait by creating oil fires and chemical spills. Terrorism will continue to be practiced on a global scale to support social issues, ethnic conflicts, even criminal enterprises, religious beliefs and politics.

The Biological Weapons Act of 1989

The U.S. Congress passed the Biological Weapons Act of 1989 to implement Article IV of the Biological Weapons Convention (22) intended to protect U.S. citizens against biological terrorist attacks. The Act defines as a federal crime the knowing development, manufacture, transfer or possession of any biological agent, toxin or delivery system for use as a weapon. The Act provides that federal agents can seize materials and charge individuals with criminal activity without having to show that the materials are intended for use as a weapon (22). Only probable cause that the material has no peaceful purpose need be shown. The final version of the Act does not apply to any use of a biological agent for prophylactic, protective or other peaceful purposes, to allow legitimate scientific and medical research. Broad powers were vested in federal agents to intervene at the earliest time to prevent bioterrorism.

The Anti-Terrorism Act of 1996

Following the Oklahoma City bombing in 1995, Congress passed the Anti-Terrorism Act of 1996 which provides the federal government with the tools and abilities to fight domestic terrorism. A wide range of investigative prosecutorial and regulatory powers dealing with chemical and biological weapons was conferred on law enforcement agencies by this act. The Anti-Terrorism Act also established a new regulatory framework for controlling the use of hazardous biological materials. The CDC was directed to establish regulations that would identify biological agents that pose a threat to public health and regulate the transfer and use of these agents (23) (Table 2).

The Anti-Terrorism Act of 1996 promulgated that the CDC would create and maintain a list of biological agents having the potential to pose threats to public health and safety (Table 4). Also the Act directed the CDC to establish regulations governing the use and transfer of these restricted agents in an effort to prevent terrorist access to these agents.

The Act provides a broad regulatory framework for governing the acquisition, use, transfer and possession of biological agents which pose such as risk to public health and safety. The CDC has four goals regarding this new regulatory framework (24):

- The identification of biological agents that are potentially hazardous to public health,
- Creation of monitoring procedures for acquisition and transfer of these agents,
- Establishing safeguards for the transportation of restricted agents, and
- Creation of a system for alerting authorities when an attempt is made to acquire a restricted agents improperly.

The current CDC list includes 24 infectious agents and 12 toxins which include 12 viruses and 7 bacteria and accounts for recombinant organisms and genetic products. A university, company, or an individual that acquires any restricted or wants to acquire such an agent in this list, must register with the federal government. Also see Regulations to Establish Procedures for Tracking the Transfer of These Agents from One Facility to the Other. These regulations are enforceable by criminal penalties.

TOXIC TERRORISM

The religious group, Aum Shinrikyo, known as the "Armageddon" sect led by Shoko Asahara, acquired sarin nerve gas and conducted two separate terrorist attacks in Japan. The first attack was on a residential section in the city of Matsumoto, on June 27, 1994 and affected 600 residents. Seven people died and 58 were admitted to hospitals (25). Their second terrorist attack occurred in a Tokyo subway station. The choice of sarin nerve agent is particularly interesting in both situations:

- Matsumoto attack: The time was around midnight when most people would be asleep in this city of 200,000. Climate conditions were hot and humid with a low wind speed of 0.5 meters/second from the southwest. These meteorological conditions would allow for maximum vaporization of sarin in the vicinity of release with slow movement downwind. The first emergency call was from a man at 2309 hours. His wife had fallen unconscious and his dog had suddenly died. Most of the people affected were around the suspected release point. Sarin was verified as the cause by gas chromatography - mass spectrometry.

- Tokyo subway: The choice of an underground, low-lying confined space of a crowded subway maximized sarin's toxic and physiochemical properties. Sarin is much heavier than air and seeks out lower lying areas. The confined space restricts dispersion of vapor and allows concentrations to build up. Ten people died rapidly and multiple more were made ill.

The availability of war gas chemicals, their chemical precursors, and the ease of manufacturing them has made these agents attractive to terrorist groups. The nerve gas, Sarin, is produced by mixing isopropyl alcohol with halogenated methyl phosphonates (26). The production formula for sarin, tabun and soman are readily found in the literature (27-29). The access to chemists who can produce quantities of nerve agents has escalated concern that such agents may be used in terrorist attacks.

Nerve Agents As Terrorist Weapons

The original German Wehrmacht nerve agents possess unique properties sought by terrorists and are similar to those described by Sartori in his book, *The War Gases*, published in 1939:

- A high vapor pressure at ordinary temperature to supply a vapor form of the agent
- The ability to deliver the agent in a gas, liquid or an aerosolized form
- Persistent activity once delivered
- Resistance to environmental decomposition or hydrolysis
- Stability in storage
- Ease of manufacturing
- Vapors lack color and odor, thus no warning
- Small amounts are highly lethal via inhalation or skin
- Dispersal systems exist

War nerve gases possess a high lethality and can be dispersed to achieve maximal trauma and shock value (The original Wehrmacht war gases were coded "G" for German). Four potent organophosphate compounds have been stockpiled in the arsenals of many countries, including those sponsoring terrorism:

- Tabun (GA)
- Sarin (GB)
- Soman (GD)
- VX

Other chemical warfare agents, such as phosgene, lewisite, and mustard gases, are not as toxic as the nerve gases. Besides, they have warning properties, and may not inflict the psychological and lethal impact on a population that a silent, colorless, odorless gas would achieve.

Individuals exposed to nerve agents develop rapid onset of cholinesterase inhibition signs and symptoms. Depending on the agent, death may occur in 1-2 minutes. One case report involved a man cleaning a sarin contaminated area with full protective gear. Unfortunately, his gear had a small leak (30). Within minutes he had developed increased oral and nasal secretions and difficulty breathing. In 5-10 minutes he was cyanotic, convulsing and had profuse secretions.

Treatment with atropine and Pralidoxime (2-PAM) must be timely and aggressive. Cases of soman and sarin poisoning that survived had persistent neurobehavioral symptoms persisted: depression, fatigue, anxiety, restlessness. Compared to other organophosphates, sarin is more potent than tabun, TEPP, DFP, and parathion in terms of acetylcholinesterase inhibition. Sarin is 4,000 times more potent than DFP, 10 times more potent than TEPP, and five times more potent than tabun (31). But VX is the most toxic of all.

Tabun (GA)

Tabun (Ethyl N,N-dimethyl phosphoramicocyanidate) is a pale to dark amber liquid which releases a colorless vapor. It has no odor in a pure state. It gives off rotting fruit odor as it oxidizes (32).

Tabun was developed by Dr. Gerhard Scharder in 1937 who became poisoned from a single drop of the new chemical when it spilled onto his lab bench. The new agent was immediately transferred to the control of the Wehrmacht military chemical laboratory in Berlin for further testing. Tabun was the first German nerve agent developed, and twelve thousand tons were produced for use as a weapon but it was never deployed.

Tabun forms a stable vapor cloud over a persistent liquid and is rapidly absorbed via the skin as a liquid or as a vapor. Between 1-1.5 grams of liquid solution (0.01 mg/kg concentration) will cause death in two minutes after dermal contact (32). Tabun presents the least vapor hazard of the nerve gases in terms of spread, whereas sarin presents the highest vapor hazard (32).

Tabun as a liquid can persist for two days in areas of shade in temperate climate conditions. Its vapor density is 5.6 times that of air and thus it will spill into lower elevations, confined spaces and low lying areas in buildings and structures. Liquid skin exposure results in death in two minutes while vapor inhalation exposure results in death in ten minutes (32).

The manufacturing of tabun is by the interaction of dimethylamidophosphoryl dichloride and sodium cyanide in the presence of ethanol. Chlorine based decontaminants, which are recommended for organophosphate nerve gas skin decontamination, will release hydrogen cyanide on exposure to tabun residues. Microencapsulation of tabun would make it highly persistent in the environment.

Sarin (GB)

Sarin (isopropyl methyl phosphorofluoridate) is a colorless liquid that gives off a colorless vapor with no odor (32). In oxidizing states, sarin gives off a rotting fruit odor. Sarin was the second organophosphate nerve gas developed by Dr. Gerhard Schrader in 1938. It worked 10 times as fast as tabun. Small scale sarin production began but the Soviet army captured the production facility in 1945 at the end of the war.

Sarin is the most toxic of the three German-developed nerve agents. Death is rapid via skin or inhalation. Ingestion of 0.01 mg/kg causes death within one minute (32). Sarin is also the most volatile of the three original nerve agents and forms a vapor 36 times faster than tabun. Sarin has a vapor concentration 2.9 times that of air and will flow downward into low lying areas. Sarin may be thickened by oils or petroleum products.

Soman (GD)

Soman (l-methyl-2:2 dimethyl propyl methyl phosphorofluoridate) is the third Wehrmacht nerve gas produced. It is a colorless liquid, and gives off a colorless vapor (32). It may have a camphor-like odor or odor of rotting fruit as it oxidizes. Soman has a vaporization rate between tabun and sarin. Its evaporation rate allows it to persist in an environment for about one day while producing a lethal vapor cloud, thus producing a hazard downwind. When the Soviet military captured the sarin and tabun production facilities in 1945. They discovered the formula and plans for soman also.

Soman is the second most toxic German nerve agent. A dose of 0.01 mg/kg orally or 100 $mg/min/m^3$ causes death in one minute. Soman persists one to two days in an environment which increases the likelihood of mass casualties. Soman has a highly toxic affect on the brain and causes permanent damage. Soman is a clear, solvent looking poison with a vapor density six times that of air.

VX

VX (ethyl S-2-diisopropyl aminoethyl methyl phosphorothiolate) is the most toxic nerve agent known. It is a pale amber liquid that looks like motor oil and gives off a colorless vapor (32). VX was developed in 1952 by the British who decided to pursue other nerve agents, so they sent the formula to the United States military. But it was intercepted by the Soviets in route. The U.S. producted 2.5 tons of VX. Production was halted in 1968 because 20 pounds of VX leaked from a spray tank in Skull Valley, Utah and killed 6,000 sheep (32).

VX was designed to create casualties by skin absorption or from aerosolization by spraying. 0.001 grams is lethal (30). It has a low volatility and vapor pressure that minimizes inhalational routes of poisoning. However, VX is highly persistent in an environment and may last weeks. Vapors are nine times heavier than air and therefore vapor hazards exist for continued low lying spaces.

Recognition and Management of Attack by Nerve Agents

As in the attacks on the people of Matsumoto and the Tokyo subway, illness develops suddenly and rapidly to those exposed to high levels of the odorless, tasteless, colorless vapors. If the attack is outdoors, a downwind pattern of illness and death will be noted. More severe symptoms and rapid death will occur close to the release site. Milder symptoms beginning with visual disturbance, cough, rhinorrhea, nausea suggestive of cholinesterase inhibition will be noted further away and downwind (Table 3). Very few, if any, symptoms will be noted in areas upwind from the outdoor release. Individuals entering contaminated areas may experience symptoms based on the vapor concentration and their route of exposure. In confined spaces and low-lying areas, casualties will probably be greater due to the vapor pressure buildup, confinement, panic and increasing gas concentration. Signs and symptoms will vary depending on the concentration and route of exposure (Table 4).

Nerve agents are absorbed through the skin and by inhalation when dispersed as a spray or an aerosol. Droplets can also be absorbed through the eyes. Local effects may occur first, followed by generalized systemic effects. However, absorption of enough nerve agent by any route can result in rapid systemic effects and death. Liquid nerve agent penetrates clothing very rapidly but absorption through the skin requires minutes. Removing contaminated clothing quickly can reduce the toxicity (33). Systemic symptoms appear within one to two minutes with a moderate or severe exposure. Following mild exposure, symptoms may not develop for several minutes. Depending upon whether vapor or liquid agent is contacted, the time course of the effects of nerve agents can differ (Table 5).

Diagnosis of nerve agent toxicity can be made by evaluation of clinical signs and symptoms and relative resistance to atropine. Individuals with mild exposure can experience the following:

Rhinorrhea or unexplained runny nose

Unexplained sudden headaches

Sudden drooling

Dimness of vision caused by myosis

Chest tightness

Difficulty breathing

Localized sweating

Localized muscle twitching in the area of contamination

Stomach cramps and nausea

More severe symptoms include the following:

Confusion

Wheezing

Severe dyspnea

Pulmonary edema

Coughing

Pinpoint pupils

Tearing

Vomiting

Severe muscle twitching

Urination

Seizures

Unconsciousness

There are no other toxins that will produce this kind of combination of signs and symptoms. The red blood cell and plasma cholinesterase can document decreased cholinesterase activity but may not be diagnostic in all cases. Nor does red blood cell cholinesterase activity always correlate with signs and symptoms.

Emergency medical personnel responding to victims may become poisoned because they are not aware of the situation. Health care facilities may quickly be overwhelmed with victims and those who think they are poisoned. Panic may ensue once the situation of a chemical attack becomes recognized by the media. Emergency department personnel unfamiliar with decontamination techniques and management of victims may become victims themselves from contacting residue on clothing and skin of exposed individuals.

Nerve gas agent effects may range from death within minutes to illness lasting for days requiring large doses of atropine and oxime therapy. Long term effects on the central nervous system may occur in survivors (Table 6). These effects may also be delayed. Neurobehavioral and psychiatric late effects have also been described (Table 7). Eye medical problems secondary to organophosphate compounds are another delayed effect (Table 8). Delayed peripheral neuropathy has also been described as a complication.

Retrospective Detection of Nerve Agents

Currently methods are lacking to detect highly toxic organophosphate compounds in biological samples. Measuring acetylcholinesterase inhibition in blood does not identify the organophosphate and does not always reliably provide evidence of organophosphate exposure when enzyme inhibition levels are in the low normal range. Also, because the enzyme is being synthesized, exposure can be missed.

Nerve agents such as sarin tabun, soman and VX bind very rapidly to acetylcholinesterase and butyryl cholinesterase. Studies have shown that both acetyl cholinesterase and butyryl cholinesterase inhibited by sarin can be reactivated by high concentrations of fluoride ions (34). Fluoride ions have a high nucleophilic affinity toward the phosphoryl moiety in the organophosphate, thus it can release the organophosphate from the enzyme. This leads to the formation of a phosphofluoridate which can be assayed. By this method, retrospective biological monitoring of exposed humans to nerve gases can be accomplished to determine the identity of the compound.

The assay is based on the stability of the butyryl cholinesterase-organophosphate complex. This method was applied to serum from victims of the terrorist attack in Japan and generated sarin from the victims' samples. Analysis of the phosphoryl moiety of butyryl cholinesterase after its conversion to the corresponding phosphofluoridate compound represents a reliable procedure for biologically monitoring exposure to organophosphates and identifying the organophosphorus compound (34).

Management of Nerve Agent Exposure

Pharmacotherapy for nerve agents includes dosing with atropine, pralidoxime and diazepam. Atropine blocks the muscarinic effects of nerve agents: bronchospasm, excessive respiratory secretions, and intestinal hypermotility. Large doses of atropine are usually required in severe poisoning. Doses of more than 2000 mg/day have been required in agricultural organophosphate poisonings. These large doses would not be unusual in the treatment of exposure to the more powerful military agents. But atropine provides no protection from the effects of organophosphates on the nicotinic receptors which can result in skeletal muscle paralysis and respiratory arrest. To reverse nicotinic effects, pralidoxime is necessary.

Pralidoxime is an acetylcholinesterase regenerating agent. In 1951, the oximes (pralidoxime) were first proposed as a treatment of poisoning by nerve agents. These drugs were used to reactivate acetylcholinesterase bound by the nerve agent. However, there is no oxime available that is effective in reactivation of acetylcholinesterase that is bound by all four of the nerve agents. Secondly, after binding enzymes, the nerve agents undergo an aging process (Straver reaction) after which time enzyme regeneration is difficult or impossible to achieve.

Pralidoxime must be administered within 4-6 hours after sarin exposure, or within 60 hours following VX exposure or the bond to the enzyme becomes permanent. However, for most commercial organophosphates, aging reactions occur after 24-48 hours. For soman (GD), this aging period is about 2 minutes. Even self-administrated pralidoxime, given at the first symptoms of soman exposure, would not be completely effective.

Other oximes have been studied for efficacy in treating organophosphate toxicity: Obidoxime and asoxime. Asoxime shows promise in reversing toxic effects of soman (31). Also asoxime has fewer adverse side effects compared with other oximes.

The United States Army uses pralidoxime chloride (2-PAM) to reactivate cholinesterase for nerve agent poisoning. It is least effective against soman, which "ages" in two minutes (GD). VX, on the other hand, has an aging period of sixty hours and 2-PAM is efficacious. A single dose of pralidoxime commonly used in agricultural pesticide poisoning is one gram. Animal data suggest that a serum pralidoxime level of about 4 ug/ml may be the minimal level to offer protection against toxic effects of commerical and agricultural organophosphates (32). Therapeutic guidelines recommend administration of 1 gram pralidoxime chloride every 4-6 hours. Infusion of 500 mg/hour provides serum levels of about 15 ug/ml in steady-state simulation in adults and may provide better therapy (33).

United States soldiers are issued three Mark I Kits containing pralidoxime chloride autoinjectors (600 milligrams each), and three atropine autoinjectors (2 milligrams each). Soldiers are trained to administer kits through protective clothing and undergarments if any symptoms of exposure occur (20).

The addition of diazepam to the nerve agent treatment protocol is recommended to protect against seizures. Diazepam also improves morbidity associated with soman poisoning independent of its anticonvulsant effects (20,34). There is animal evidence that prolonged nerve agents-induced toxic convulsions produce irreversible brain damage. Benzodiazapine anticonvulsants appear to reduce the morbidity associated with these convulsions.

Nerve Agent Decontamination

Skin decontamination is accomplished with soap and water or with 0.5% hypochlorite solution (1:10 dilution of household bleach solution). Decontamination personnel should wear protective gear with self-contained breathing apparatus.

When animal skin is contaminated with sarin (GB) and then flushed with water, 10.6 times more sarin is required to produce the same mortality rate as when no decontamination occurred (34). Another study showed that water alone was even better than hypochlorite solution (20).

Nerve agents are subject to oxidation reactions since they contain phosphorus groups that can be hydrolyzed. Therefore, decontaminants are designed to hydrolyze VX and G-series agents. Oxidative chlorination occurs with the use of hypochlorite solutions CA (0.5%, hypochlorite solution is made by one part water mixed with 10 parts 5% clorox® bleach). The reaction is pH and temperature dependent and increases markedly at pH values greater than eight and by a factor of four for every 10°C rise in temperature (20).

Wounds should be copiously irrigated with soap/water or 0.5% hypochlorite. Avoid getting hypochlorite solution in the eyes. Do not irrigate open cavity wounds with hypochlorite. If hypochlorite solution is used in wounds, they should then be flushed with normal saline or water (20,34).

Nerve agents react slowly with water and rapidly with alkalis and chlorinating agents. Chlorinated bleach is used to decontaminate skin and equipment.

But since tabun may release cyanide during rapid hydrolysis in the presence of strong acids or alkaline substances, chlorine-based decontaminates have the potential of releasing hydrogen cyanide as a byproduct. Therefore, aggressive water flushing with use of chlorine based decontaminates is recommended if tabun is suspected (32, 33).

Health care providers must be in full protective gear at all times during care for the patient until an environmental health specialist who is trained to detect these agents can '"clear" the patient.

BIOLOGICAL TERRORISM

A biological weapon has four components: (1) The agent or payload, (2) A munition or a container that keeps the agent intact during delivery, (3) A delivery system, (4) A dispersal system such as an aerosolized spray device or an explosive force to dispense the agent. Classes of biological agents previously developed for warfare include pathogenic organisms (bacterial, fungal, viral, rickettsial), biotoxins, and bioengineered toxins.

To be effective at producing mass casualties, a biological agent must be weaponized. A 1970 World Health Organization (WHO) publication estimated the potential health impact of a biological weapon release on populations (35):

- 50 kilograms of aerosolized anthrax spores dispensed by airplane two kilometers upwind of a 500,000 population with ideal weather conditions would travel 20 kilometers and kill or cause illness in 220,000 people.
- Unleashing *Francisella tularensis*, the cause of tularemia, under similar conditions upwind would cause an estimated 155,000 casualties.

In either event, once an attack is recognized, medical resources could be overwhelmed from real cases of disease and those thought to be exposed. Anyone with any symptom would be prone to seek medical care. Lack of protective equipment, immunizations and antibiotics could cause the situation to rise to crisis proportions.

Since April of 1991, the United Nation's Special Commission (UNSCOM) and the International Atomic Energy Agency have been investigating Iraq's Weapons' Program. Operation Desert Storm interrupted the Iraqi military's weapons of mass destruction program - nuclear, chemical and biological. But whereas the nuclear and chemical threats have been drastically reduced, the biological weapons threat continues to exist. The Iraqi's were on the way to deploying ballistic missiles with a 2,000 km range and a one-ton payload (36). Unfortunately, Iraq's biologicals program infrastructure remained intact after the 1991 War and in 1997 UNSCOM inspectors have verified a resurgence of the Iraqi biological weapons program. Iraq had developed biological warfare potential of five bacterial strains, one fungal strain, five viruses and four toxins including the following (36):

Anthrax
Francisella tularenesis
Botulinum toxin
Clostridium perfringens
Congo-Crimean hemorrhagic virus
Yellow fever virus
Enterovirus 71
Human rotavirus
Camelpox virus
Aflatoxin
Ricin
Trichothecenes

Bacillus anthracis (anthrax) and *Clostridium perfringens* (gas gangrene) were extensively studied by the Iraqis. Some anthrax strains were imported from France and the United States. The main facility for the Iraqi production of biological agents was the Al Hakam facility which was destroyed in June of 1996. This facility contained huge fermenters used to produce biological toxins including botulinus toxin (36).

Eight thousand liters of solution with an anthrax cell count of 1×10^9 milliliter was produced at the Al Hakam facility and 6,000 liters of this biological material was used to fill weapons (36). During 1990, 340 liter of solution containing Clostridium was produced at Al Hakam (36).

During 1989 and 1990, twenty thousand liters of solution containing botulinum toxin was produced at the Al Hakam facility and Al Manal facility (36). A crop-destroying fungal agent called wheat cover smut was also developed as a weapon. Furthermore, the Iraqi biological weapons capability included aflatoxin, ricin and tricothecenes. Production of aflatoxin at the Salman Pak facility resulted in 2,200 liters of solution (36). Approximately 10 liters of concentrated ricin solution was also manufactured at another facility.

The Iraqis had developed 250 pound and 400 pound bombs containing biological solutions in 1990. Two hundred of the 400 pound biological bombs were produced. One hundred were filled with botulinum toxin, 50 with anthrax and 7 with aflatoxin, and these were deployed at two sites (36). Also, 155 millimeter artillery shells filled with ricin were used for testing.

Of more concern, was the Iraqi ability to deliver biological warfare payloads at great distances using SCUD missiles. SCUDs known as "Al Hussein's" were fitted with biological warheads containing botulinum toxin, aflatoxin and anthrax and were deployed in railway tunnels along the Tigris River (37). The Iraqis were also in possession of dispersal systems that could generate aerosols between 1-5 microns in size for production of aerosolized particles and they had modified fighter planes to carry spray dispersal mechanisms.

Under the United Nation's Security Council Resolution 687 of April, 1991, the Iraqis accepted a cease fire and their biological warfare program was to be destroyed. Biological warfare agents were to be treated with formaldehyde and potassium permanganate with the residual being poured upon the ground near the facilities (36). Resolution 687 also specifies that facilities and equipment supporting Iraqi's weapons program were to be destroyed UNSCOM or the International Atomic Energy Administration. But Sadam Hussein has stymied weapons inspectors from the United Nation in violation of the Security Council agreement. In November of 1996, Secretary of Defense William Cohen publicly asserted the resurgent dangers of Iraq's chemical and biological weapons capability (38).

Recognizing and Responding to Biological Terrorism

Hearings in 1995 and 1996 before the U.S. Senate Permanent Subcommittee on Investigations found that the United States did not have a coordinated plan to manage consequences of a biological or chemical terrorist attack. A particular concern was that a biological terrorist attack could produce a large number of casualties over widespread areas through the following means:

- Aerosolized pathogen or toxin sprayed over a population
- Contamination of water supplies with agents resistant to disinfection
- Contamination of food supplies
- Ventilation system contamination of a large building
- Innovative delivery of biotoxins or pathogens

Biological agents fit the terrorist's ideal of a weapon that can cause mass fear in addition to casualties (Table 9). Consider that 1×10^{-6} grams of anthrax is probably a lethal dose. A kilogram (2.2 pounds) in an aerosolized form can kill hundreds of thousands of people concentrated in a city or a building via its ventilation system. Also, very few physicians have diagnosed and treated anthrax.

Enhancing civilian and military cooperation for responding to terrorist attacks was the essence of the Congressional Defense Against Weapons of Mass Destruction Act of 1996. This act enhanced domestic preparation for preventing and responding to terrorist incidents involving weapons of mass destruction. Over 100 U.S. cities were recipients of federal efforts to train police, fire and emergency responders by the Department of Defense in preparing for detecting biologicals, neutralizing biologicals, triaging of exposed individuals, treating exposed individuals, reducing infection risk to exposed persons, reducing risk to population at large, and managing psychological sequelae.

The clinical recognition of illness due to biological warfare agents can be difficult because these agents cause signs and symptoms common to many other diseases (38). Biological warfare agents also tend to be more insidious than chemical exposures which produce acute onset of illness. One of the difficulties with biological agents is that the diseases caused by these agents are rare, even in underdeveloped countries. Depending upon the agent, treatment modalities may exist. While vaccines exist for some biological warfare agents, these are not always readily available.

Person to person spread may be an important transmission route for infectious biological agents. Clinical suspicion and epidemiological investigation may identify biological agents as causes of disease. The presentation of increased numbers of patients with signs and symptoms of disease or the appearance of a rare disease may be the first indicator of a terrorist attack (38). Epidemiologic investigation would determine whether or not the outbreak is a natural outbreak or artificially induced (38). The CDCs Epidemic Intelligence Service was created to train epidemiologists in the event of a biological warfare attack within the United States during the cold war period (39).

Since illness from biological agents presents with signs and symptoms that could be similar to many other diseases, the pattern of disease development may help discern the difference (Figure 1). In naturally occurring epidemics, there is a gradual rise in incidents as people are exposed in a progressive fashion to a spread of disease agents or vectors. As contrasted, biological warfare agent release would cause a number of casualties or identified exposures at the same time, without the gradual rise over time. A compressed epidemic curve with a peak in days or even hours would be evident. Point sources may be noticeable, such as food contamination, water contamination, or a delivery means. Case definition would be formulated by public health officials to determine the number of actual cases, thus verifying the epidemic and the attack rate. The question would be: Is the disease rate greater than the background rate that normally occurs?

Casualty location would follow a distinct pattern. Usually it would involve the medium of transport such as air, water or food. Individuals affected by aerosolized biotoxins or infectious agents would be within the downwind pattern of agent release. Other clues would be the occurrence of an unusual disease in a geographic area or the occurrence of a disease in an area that lacks appropriate transmission routes. Multiple epidemics occurring in different geographic locations is also a clue. Through observations of disease patterns and use of epidemiologic principles, health authorities can be made aware of a potential biological release (Table 10).

Information regarding diagnosis, treatment and vaccines is available by contacting, commanders, USAMRIID at 301-619-2833 (phone) or 301-619-4625 (fax) (Table 11).

An Example of A Biological Agent

In September and October of 1984, a total of 751 people developed Salmonella gastroenteritis by intentional contamination of restaurant salad bars by members of a religious commune (40). These two outbreaks demonstrate the nature of a biological attack and underscore the epidemiologic principles which helped to characterize the situation.

The outbreak occurred in Oregon area restaurants in two waves from September 9-18 and September 19 - October 10. Most cases were associated with ten restaurants. A criminal investigation revealed that members of a religious commune had deliberately contaminated the salad bars with *Salmonella typhimurium*. Linking the outbreak to the religious commune took over a year.

Law enforcement agents found a vial of commercial stock culture containing *S. typhimurium* in a clinical laboratory operated by the commune that was purchased prior to the outbreak. Also, the isolate found matched the outbreak strain of bacteria. The basis of the attack was a controversy surrounding construction of the religious commune and land use issues. This incident is indicative of the vulnerability of populations to biological agents and the ease with which these dangerous biological agents can be introduced into the mass populations.

Another case of intentional food contamination involved *Shigella dysenteriae* Type II, which is rare in the United States (41). From October 29 through November 1, 1996, twelve laboratory workers at a large medical center in Texas experienced severe gastrointestinal illness after eating muffins and doughnuts which were left anonymously in their break room. Investigation performed on the food and stool showed *Shigella dysenteriae* Type II (41). The source was determined to be the medical center stock culture of the organism. The culprit of this bioterrorism remains unknown.

Food supplies and water supplies are vulnerable to bioterrorism attack. Despite state of the art disinfection and water treatment, the city of Milwaukee in 1993 suffered a massive exposure to the parasite cryptosporidium. How the cryptosporidium entered the water source remains unknown but the source is thought to be sewage and contaminant runoff from agricultural lands through ground water.

Anthrax as a Terrorist Weapon

Anthrax is an infectious disease caused by the gram-positive bacillus bacterium, *B. anthracis*. Bacteria and spores of anthrax are found in soil worldwide. Humans may become infected by contact with an infected animal or contaminated animal byproducts. Anthrax is also known as "wool-sorter's disease." Anthrax spores can survive in adverse environmental situations and remain viable for decades. In 1943 the Gruinard Island off the coast of Scotland was the test site for anthrax bombs. The island remains too infested with deadly anthrax spores today to allow human visitation.

Anthrax has been researched as a biological weapon by the United States, Britain, Soviet Union, Japan and Iraq. Anthrax spores are hearty and retain their virulence, particularly in a dry state. Anthrax cells and spores dispersed in an aerosolized manner can cause large numbers of casualties by inhalation and skin infection. If appropriate antibiotic therapy is not begun soon after exposure, the mortality is high (42).

Anthrax used in weapons can be liquid or dry powder. Although the liquid anthrax slurry is easier to manufacture, it loses its virulence quickly. A terrorist attack would probably deliver anthrax by aerosol delivery to cause inhalation of respirable size spores. Spores deposited in the respiratory tract are phagocytized by macrophages and transported to pulmonary lymph nodes. The spores then germinate into infective bacteria and produce necrotizing hemorrhagic mediastinitis (43). Anthrax has three clinical forms of presentation depending on route of exposure: cutaneous, inhalation and gastrointestinal (Table 14).

Naturally occurring cases of anthrax tend to be cutaneous or gastrointestinal. Inhalational anthrax should raise suspicions of a deliberate act. An epidemic caused 66 admitted deaths in the city of Ekatrinburg, (formerly Sverdlosvk) in spring of 1979 and was traced to an accidental release of an airborne Russian bioweapon strain of anthrax (78).

Inhalational anthrax is particularly lethal. In its early presentation, inhalation anthrax could be confused with viral or bacterial respiratory illnesses. Following inhalation of at least 1 x 10^4 spores, alveolar macrophages ingest the anthrax spores and the bacteria germinate and are transported to regional lymph nodes where the microorganisms elaborate toxin. A tracheobronchial lymphadenitis develops. Within 1-6 days of exposure, there is a sudden onset of respiratory distress, nonproductive cough, fatigue, malaise, chest symptoms, dyspnea, stridor and cyanosis. Tracheobronchial nodes undergo necrosis which progresses to mediastinitis with or without a bloody pleural effusion. Pulmonary edema may occur. Up to 50% of cases have concurrent hemorrhagic meningitis with bloody CSF. Septicemia, shock and death occur in 24-36 hours. Mortality of inhaled anthrax is 80-90% despite treatment. Pleural effusions and a widened mediastrinum may be seen on chest x-ray.

Blood cultures may be positive for *B. anthracis* which can also be visualized by Gram stain of peripheral blood smears. Anthrax toxin begins to appear systemically by the second or third day after inhalation of spores, paralleling levels of anthrax bacteremia. An enzyme immuno-absorbent (ELISA) assay is available for rapid diagnosis of the toxin.

Anthrax strains are sensitive to erythromycin, gentamicin, chloramphenicol and ciprofloxacin. Ciprofloxacin 400 mg Q8-Q12 hours IV is the recommended therapy and should be instituted at earliest signs of an infection. Vaccination derived from culture fluid of attenuated strains is available but limited in supply. Prophylaxis with antibiotic, particularly ciprafloxacin or doxycycline is recommended for potential exposure to anthrax. Chemoprophylaxis should be continued for at least four weeks and until three doses of vaccine have been received by the exposed individual (38).

Anthrax toxin may be detected in serum by immunoassay. Autopsy cases have been diagnosed by a peculiar “cardinal’s cap” meningeal inflammation typical to anthrax.

Anthrax Vaccine

Two types of anthrax vaccine are available in the United States and United Kingdom. Both are based on the partially purified protective antigen of the *B. anthracis* adsorbed to an aluminum adjuvant. The usual immunization series is six 0.5 ml doses over a span of 18 months. A primary series of three 0.5 ml doses (0, 2, and 4 weeks) will be protective against both cutaneous and inhalation anthrax for about 6 months after the primary series (12).

A live anthrax vaccine is used in Russia to immunize both livestock and human beings (79). It is a spore vaccine with both STI-1 and strain 3 mixtures. The Russians feel that this vaccine is superior at stimulating cell-mediated immunity (80).

There is no available evidence that vaccines will adequately protect against an aerosol challenge. New vaccines with a highly purified protective antigen or designer attenuated strains have both been used in laboratories but are not commercially available (81,82).

Antibiotic prophylaxis with ciprofloxacin (500 mg PO bid), or doxycycline (100 mg PO bid) is recommended by the United States military for imminent attack by a biological weapon. Should the attack be confirmed as anthrax, then antibiotics should be continued for four weeks for all who are exposed. Those exposed who have not been immunized should be started on anti-anthrax vaccine with the standard schedule. Those who have received fewer than three doses of vaccine prior to exposure should receive a single “booster” injection. Then antibiotics should be continued until the patient can be safely and closely observed when the antibiotics are discontinued. Inhaled spores are not destroyed by antibiotics and may persist beyond the course of antibiotics recommended.

Botulinum Toxin as a Terrorist Weapon

The bacteria *Clostridium Botulinum* is a spore-forming obligate anaerobe naturally occurring in the soil. *C. Botulinum* has four genetically diverse bacterial groups that have a common characteristic of producing the botulinum toxin. There are seven distinct antigenic types assigned letters A through G. These toxins are distinguished by their absence of cross-neutralization, that is, anti-A antitoxin does not neutralize toxins in the other types. Other strains of Clostridium bacteria have the capacity to produce botulinum toxin besides *C. Botulinum*. While a lethal dose for humans is unknown, extrapolations are that a lethal amount of crystalline Type-A toxin in a 70 kilogram human is 0.09-0.15 micrograms intravenously, 0.70-0.90 micrograms inhalationally, and 70 micrograms orally. Therapeutic botulinum toxin such as Botox is an impractical weapon because it contains only about 0.3% of the estimated human lethal inhalational dose and 0.005% of the estimated lethal oral dose.

Botulinum toxin is the most toxic poison known with an estimated dose of 0.001 mg/kg of body weight and is 50,000 times more toxic than the nerve gas VX and 100,000 times more toxic than sarin (45). The aerosolized form of botulinum toxin is extremely deadly. It has been estimated that 3 kilograms, approximately a little under 2 pounds, of concentrated botulinus toxin dispersed over an area of 100 square kilometers would deliver a medium lethal dose to the entire population (46).

Botulinus toxin binds to the presynaptic nerve terminal at neuromuscular junctions and at cholinergic autonomic nerve sites and blocks neurotransmission through preventing the release of acetylcholine presynaptically. The toxin is a zinc proteinase that cleaves fusion proteins by which neuronal vesicles release acetylcholine into the neuromuscular junction. Onset of symptoms is within 12-36 hours following exposure and usually begin with bulbar palsies and ocular symptoms such as blurred vision, mydriasis, diplopia, ptosis and photophobia. Other signs and symptoms include dysarthria, dysphonia and dysphasia. Gastrointestinal symptoms usually occur upon ingestion of botulinus toxin: nausea, vomiting, cramping and constipation. Skeletal muscle paralysis follows in a descending and progressive manner, leading to respiratory failure. There is usually no fever, postural hypotension may occur, the gag reflex may be absent, and the pupils may be dilated and fixed yet the patient may be able to converse but have difficulty swallowing. Extraocular muscle weakness usually is present on physical examination along with skeletal muscle weakness. Tendon reflexes generally disappear through the course of disease. Botulism can be confused with Gullian-Barre syndrome or other neuromuscular disorders.

The toxin may be identified by enzyme-linked immuno-absorbent assays (ELISA). Respiratory failure usually leads to death unless respiratory support is instituted. Fatalities are less than 5% with ventilatory assistance. Antitoxin can be effective following exposure if given before onset of symptoms. A trivalent equine antitoxin is available from the CDC. The U.S. Army has prepared an $F(Ab)_2$ fragment which is equine source heptavalent antitoxin for types A-G. Immunization therapies are being investigated.

Botulism toxin is also one of the first toxins to become licensed for the treatment of human disease in the form of Botox injections and is licensed for the treatment of cervical torticollis, strabismus, and blepharospasm associated with dystonia. Between 1990 and 1995, the Japanese called Aum Shinrikyo attempted to use botulinum toxin as a terrorist weapon when they dispersed aerosols at multiple sites in downtown Tokyo, Japan and at U.S. Military installations in Japan on three occasions. While these attacks failed because of faulty delivery techniques, the terrorists had obtained their Clostridia Botulinum from soil collected in Japan. Botulinum as a biological weapon was known 60 years ago and was used by the Japanese in their occupation of Manchuria against prisoners.

The potential of botulinum toxin as a bioterrorist weapon has constraints. It must be concentrated and stabilized for aerosol dissemination. However, a deliberate release of botulinum toxin in a civilian population would lead to substantial fear and stress. Botulinum toxin can also be used as a deliberate contaminate of food. Estimates are that point source aerosol release of botulinum toxin could incapacitate or kill 10% of persons within a 0.5 kilometer downwind (Botulinum toxin is a biological weapon (Medical and Public Health Management, Journal of the American Medical Association, 2001;285(8):1059-1070.).

Three forms of botulism exist: (1) Food borne, (2) wound related, and (3) infant and adult intestinal botulism. All forms result from absorption of the toxin into the circulation from the site of inoculation. The toxin does not penetrate intact skin. Infections from C. Botulinum can produce the toxin that produces classical human botulism .

Inhalational botulism has occurred accidentally in humans and has been demonstrated experimentally in primates. Absorbed toxin is distributed to peripheral colinergic nerve synapses where it binds irreversibly to the neuromuscular junction. All forms of botulinus toxins display similar neurological signs, however, in the food borne source, neurological signs are generally preceded by abdominal signs and symptoms of cramping, nausea, vomiting, or diarrhea. These may not occur though if purified botulinum toxin is intentionally placed in foods since the gastrointestinal symptoms are thought to be caused by other bacterial metabolites and not the botulinum toxin .

Botulism is an acute afibrile symetric descending flaccid paralysis that always begins in the bulbar musculature. It is not possible to have botulism without multiple cranial nerve palsies. Rapidity of neurological onset and severity of paralysis depends on the dose absorbed. Recovery may take weeks to months and patients may be ventilatory dependent during that time. Initially, affected individuals present with difficulty seeing, speaking and/or swallowing. They have ptosis, diploplia, blurred vision, and sluggishly reactive pupils, dysarthria, dysphonia, and dysphasia. The pharynx may appear injected because of peripheral parasympathetic collinergic blockade. Sensory changes do not occur except for occasional circumoral and peripheral parasthesias from hyperventilation due to stress and fright caused by the onset of paralysis.

As the paralysis extends beyond the bulbar musculature, loss of head control, hypotenia and generalized weakness become prominent. Dysphasia and loss of protective gag reflex occurs. The patient at this point may require intubation and mechanical ventilation.

Deep tendon reflexes generally remain intact but diminish or disappear in the ensuing spread of the toxin. Death results from airway obstruction and respiratory muscle paralysis . Patients are not confused or stuperous or in a coma because the toxin does not penetrate the brain cells. Patients appears lethargic though and have communication difficulties because of their cranial nerve palsies. The classic triad of botulism is: (1) Symmetric descending flaccid paralysis with prominent cranial nerve palsies, (2) an afibrile patient, (3) clear synsorium(?). The cranial nerve palsies are summarized as diploplia, dysarthria, dysphonia, and dysphasia (the four D's).

Rapidity of neurological sign and symptom onset and severity depends on the dose absorbed. Food borne botulism can begin as early as two hours following ingestion or as long as eight days after ingestion of the botulinum toxin. Cases typically present within 12 to 72 hours after eating . Primates show signs of botulism 12-80 hours after aerosol exposure. The three known cases of human inhalational exposure, the symtpoms began 72 hours after exposure but this was to an unknown, small amount.

Botulinum toxin in solution is colorless, odorless and tasteless. It is inactivated by heat greater than 85° C for five minutes and thus food that is not heated may transmit the poison .

Laboratory documentation of botulism requires specific testing and days to complete. It may be misdiagnosed as Guillan Barre, myasthinia gravis or some other central nervous system disease. Botulism differs from other forms of flaccid paralysis in its prominent cranial nerve palsies disproportionate to milder weakness and hypotonia below the neck in its symmetry, in its absence of sensory nerve damage. Diagnostic testing is available at the CDC and in some state and municipal public health laboratories. Serum samples for testing must be obtained before therapy with antitoxin which will nullify one of the bioassays used . Other samples include gastric aspirate, vomitous in suspected foods if available . Consult with the laboratory about the specimen they require . The cerebral spinal fluid (CFS) remains normal in botulism but may be abnormal in other central nervous system diseases.

Therapy consists of supportive care and passive immunization with equine antitoxin . The optimal outcome depends on early use of the antitoxin and will minimize subsequent nerve damage and severity of disease . However, it does not reverse paralysis that already has occurred . Antitoxin should be given as early as possible after clinical diagnosis . Treatment should not be delayed for laboratory testing . Botulinum toxin is available from the CDC and state and local health departments . The trivalent antitoxin contains neutralizing antibodies against Types A, B, and E, the most common causes of human botulism . If another toxin type is suspected, there is an investigational heptavalent A, B, C, D, E, F, G, antitoxin possessed by the United States Army . The dose of the trivalent antitoxin is a single 10 ml vial per patient diluted 1 to 10 in normal saline administered by slow intravenous infusion . The amount of neutralizing antibody in both the licensed trivalent and the heptavalent vaccine far exceeds the highest serum toxin levels found in food borne and naturally occurring botulism . Additional doses are generally not required . Use of antitoxin for post-exposure prophylaxis is limited by its scarcity and its high reaction rate . The United States also has an investigational pentavalent A, B, C, D, E botulinum toxoid distributed by the CDC, the laboratory workers and those at high risk of exposure . A recombinant vaccine is also under development . The pentavalent toxoid has been used for more than 30 years to immunize high risk workers but mass immunization is not feasible due to the scarcity of the toxoid . The toxoid induces immunity over several months and is ineffective for post-exposure prophylaxis.

Despite its potency, the toxin is easily destroyed by heating to an internal temperature of 85° C for five minutes . This will detoxify all contaminated food or drink . Extremes of temperature and humidity will degrade aerosolized toxin and, depending on the weather, aerosolized toxin can decay between 1% - 4% per minute with substantial inactivation occurring by two days following aerosolization . The intact skin is impermeable to the toxin. Washing skin and clothes after an aerosolized exposure with soap and water and cleaning with a 0.1% hypochloride bleach solution should provide adequate decontamination.

Plaque as a Terrorist Weapon

Plague is a zoonotic disease caused by the Gram negative bacteria *Yersinia pestis.* It is naturally found on rodents and prairie dogs and carried by their fleas. Fleas spread the plague from rodents to humans in the natural disease cycle. Under normal conditions three plague syndromes are recognized:

• Bubonic: Plague bacteria are inoculated into human by fleabite. The bacteria are transported to regional lymph nodes where they cause necrotic lymphadenitis (bubo). Incubation period of two to three days precedes symptoms. Malaise, high fever, buboes, and in 25% of cases pustules develop along lymph node distribution. Can progress to septicemia, pneumonia and CNS involvement. Contact with buboes can cause person to person spread.

• Pneumonic: A two to three day inoculation period is followed by high fever, myalgias, chills, headache and cough with bloody sputum. Pneumonia and sepsis develop acutely and may be fulminant. Patients develop stridor, cyanosis and circulatory collapse. Patchy infiltrates on chest x-ray. Secondary transmission possible. Respiratory precautions are necessary for 48 hours until sputum culture is negative or pneumonic plague is ruled out.

• Septicemic: Either the bubonic form or pneumonic form may result in sepsis, shock and death. Hematogenous spread can occur to the CNS, lungs and other organs. Vasculitis and purpuric thrombosis can occur resulting in gangrene.

Plague bacteria can retain viability in water for 2 to 30 days, moist areas for up to 2 years, and in near freezing temperatures for several months to a year.

Plague could be spread by either infected vectors such as fleas, or by an aerosol spray. Person to person transmissibility is high and the bacterium is highly infective.

Clinical Presentation

In bubonic plague, the incubation period is from 2 to 10 days. The onset is acute with malaise, fever and purulent lymphadenitis. The lymphadenitis is most often inguinal because of the bite of a flea on the legs, but cervical and axillary nodes are also involved. As the disease progresses, the nodes become tender, fluctuant, and finally necrotic (bubo). The bubonic form may progress to the septicemic form with seeding of CNS and lungs. If the organisms spread to the lungs, then the pneumonic form follows and the person becomes contagious through coughing and respiratory droplet spread. The course of the disease is 2-3 days. The mortality of untreated bubonic plague is 50%.

In primary pneumonic plague, the incubation period is 2 to 3 days. The onset is acute and fulminant with malaise, fever, chills, cough with bloody sputum and toxemia. The pneumonia progresses rapidly to respiratory failure with dyspnea, stridor and cyanosis.

Clinical laboratory findings reveal a WBC count over 20,000/mm^3 with bandemia, increased fibrin split products and a DIC-like picture. In the pneumonic form, the mortality approaches 100%. The terminal events are circulatory collapse, hemorrhage and peripheral thrombosis in septicemic plague. In pneumonic plague, the terminal event is often respiratory failure as well as circulatory collapse.

Diagnosis

A presumptive diagnosis can be made by finding the bipolar staining bacteria in Giemsa stained specimens. Appropriate specimens are lymph node aspirate, sputum, or CSF. Immunofluorescent staining is available and helpful if readily accessible. Y. pestis can be readily cultures from any of these sources (Table 23).

Therapy

The plague is contagious and strict isolation of the patients is essential. Therapy with antibiotics must begin within 24 hours of symptom onset to be effective. Treatment is with streptomycin (30 mg/kg/day IM DIB x 10 days) (Table 23). Doxycycline may also be used. Chloramphenicol is recommended for plague meningitis (12).

Prophylaxis

A plague vaccine is available, but probably does not protect against an aerosol exposure and subsequent pneumonic plague. The plague vaccine is a whole cell formalin-killed product. The usual dose is 0.5 ml given at 0, 1, and 2 weeks (Table 22 and 23).

Plague vaccines providing protection against aerosol exposure are not yet available, but are under development (84). Current whole-cell plague vaccines stimulate immunity against the bubonic form but are probably not effective for the pneumonic form (85,86).

Cholera

Cholera is a diarrheal disease caused by the gram negative curved bacillus, *Vibrio cholera*, acquired by humans through ingestion of contaminated water. The organism causes a profound watery diarrhea by the action of an enterotoxin on intestinal epithelium.

All strains of bacteria elaborate the same enterotoxin. The bacteria do not invade the intestinal epithelium. Cholera is a toxigenic diarrhea which is secretory in nature. Fluid loss originates in the small intestines. The colon is insensitive to the enterotoxin. The large volume of fluid generated by the small intestines overwhelms the capacity of the colon to absorb it. Recovery from cholera grants temporary immunity which may last for years. Cholera organisms are not viable in pure water, but survive 24 hours in sewage and up to six weeks in contaminated water containing organic material (12). The organism withstands freezing for three to four days and is readily killed by dry heat at 117°C, by steam, or by boiling, or by exposure to disinfectants. The cholera organism is a facultative anaerobic and grows best at a pH of 7.0 (12). The incubation period is 12-72 hours before sudden illness onset with vomiting, headache, intestinal cramping and diarrhea. Without treatment, death can result from hypovolemic shock.

Although cholera can be spread by aerosols, more likely terrorist or military employment would be contamination of food or water supplies. There is negligible direct human to human transmissibility. The bacterium does not have long persistence in food or pure water and not persistent when applied by aerosols.

Diagnosis

Gram staining of the stool sample will show few or no red or white cells. Renal failure may complicate severe dehydration. Electrolyte abnormalities are common with the profound fluid loss, generally hypokalemia predominates.

E. coli, rotavirus, and toxic ingestions such as staphylococcal food poisoning, Bacillus cereus, or even Clostridia species can all cause similar watery diarrhea. Bacteriologic diagnosis of cholera diarrhea has been well studied for decades. Vibrio species can be seen and identified readily with darkfield or phase contrast microscopes. Culture will prove the diagnosis but is not necessary for the treatment.

Therapy

Treatment of cholera is mostly supportive with fluid replacement and antibiotics. The WHO oral rehydration formula is appropriate, but generally not stocked in sufficient quantities in most cities. Pedialyte™ and sport drinks as Gatorade™ can provide interim oral hydration. If a cholera epidemic is treated, then intravenous fluids should be reserved for those patients who are vomiting and cannot tolerate oral rehydration, those patients who have more than 7 liters per day of stool, and those patients who are in hypovolemic shock.

Tetracycline (500 mg QID x 3 days) and doxycycline (100 mg BID x 3 days) have both been found to shorten the course of the diarrhea. Other effective drugs include ampicillin (250 mg every 6 hours for 5 days), TMP-SMX (1 tablet every 12 hours), Ciprofloxacin (500 mg BID x 3 days) and norfloxacin (400 mg BID x 3 days).

Prophylaxis

The currently available vaccine (Wyeth-Ayerst) is a killed suspension of *V. Cholera*. It provides incomplete protection and lasts for no longer than 6 months. It requires two initial injections with a booster dose every 6 months (0.5 ml IM at 0, 7-30 days, then boosters every six months) (12).

Tularemia as a Terrorist Weapon

Tularemia is a disease caused by the gram negative, intracellular coccobacillus, *Francisella tularenesis*. Tularemia is acquired from infected animals such as rabbits or from bites of infected deerflies, mosquitoes or ticks (32, 38). Inhaling contaminated dust or ingesting contaminated food may also cause disease. Aerosolized bacteria would produce pneumonia.

Clinical presentations take three forms: ulcerglandular, oculoglandular and typhoidal (46):
Ulcerglandular: Via the skin transmission, fever, chills and headache lasting weeks. Bacteria invade lymphatics system near point of inoculation. Regional lymphadenopathy with purulent filled lesions.
Typhoidal: Via respiratory transmission. Mortality around 30%. Fever, prostration, nonproductive cough, bloody sputum.
Oculoglandular: Via eye and mucous membranes around the eye. Eye pain, lacrimation, photophobia and regional lymphadenopathy. Corneal perforation and loss of sight can occur.

As few as 50-100 bacteria will result in disease if inhaled or injected intradermally (37). The ulcerglandular form of tularemia is caused by skin injection by contaminated animal biological fluid or blood. The typhoidal form occurs following inhalation of microorganisms.

The diagnosis of tularemia is made by blood culture, sputum culture or from skin lesion culture. Serologic diagnosis is available (Table 13). Streptomycin is the treatment of choice. Tetracycline and chloramphenicol are also effective therapy, but are associated with relapse.

VIRUSES AS TERRORIST WEAPONS

Small Pox

Smallpox is a disease caused by the Variola virus. It is an orthopox virus which affects primates, particularly man. The disease was declared eradicated in the world in 1977, and the last reported human case occurred in a laboratory in 1978. Theoretically, the virus exists in only 2 laboratories in the world in the United States and in Russia. The virus can cause major and minor forms of smallpox disease and is highly contagious via secretions, and aerosols. Smallpox infection has a 20%-40% mortality in unvaccinated persons. It is remotely possible that it is still living outside of the repository labs. A very closely related disease, Monkeypox cannot be easily distinguished from smallpox.

Following inhalation of the virus, replication occurs in the airway and regional lymph nodes. Viremia occurs after a 10-17 day incubation. The illness has a prodrome of 2-3 days with malaise, fever, headache, and backache. Over the next 7 to 10 days, all of the characteristic lesions erupt, progress from macules to papules to vesicles to pustules and then crust and scarify. The lesions are more numerous on the extremities and face than on the trunk. Some patients will develop disseminated intravascular coagulopathy. Other complications include smallpox pneumonia, arthritis (may have permanent joint deformities) and keratitis (may cause blindness). Smallpox is less communicable than measles and influenza with about 30% of exposures subsequently developing the disease.

Like many viral diseases, the diagnosis is best made by clinical impression. Routine labs are not helpful, although leukopenia is frequent. Clotting factors may be depressed and thrombocytopenia may be found. Diagnosis may be made with immunofluorescence, electron microscopy, or culture (Table 23).

Therapy is entirely supportive. Contacts should be quarantined for 17 days and patients kept isolated until scabs heal over completely. Patients remain infectious until then. Objects in contact with a contaminated source must be decontaminated with steam or sodium hypochlorite solution.

Prophylaxis against smallpox is well documented. Since smallpox is presumed to have been eradicated worldwide, there is no recommendation or requirement for routine vaccination. However, adequate stocks of smallpox vaccine are probably not available for exposure of large populations.

Hemorrhagic Fever Viruses

Hemorrhagic fever viruses researched as potential biological weapons include Yellow Fever, and Congo-Crimean Hemorrhagic virus. Yellow fever and Congo-Crimean hemorrhagic virus are just two of the many viruses that cause viral Hemorrhagic fever (VHF). Virus that cause VHF are RNA viruses transmitted to humans by contact with infected animals (zoonotic spread). This includes viruses from the following families:

Arenaviridae: Lassa Fever (Lassa virus), Argentine Hemorrhagic fever (Junin virus), Bolivian Hemorrhagic Fever (Machupo virus), Venezuelan Hemorrhagic Fever (Guanarito virus), Brazilian Hemorrhagic Fever (Sabia virus)

Bunyaviridae: Rift Valley Fever virus, Congo-Crimean Hemorrhagic virus, Hantavirus

Filoviridae: Ebola virus, Marburg virus

Flaviviridae: Yellow Fever virus, Dengue Hemorrhagic Fever virus

VHF syndrome presents as an acute febrile illness with malaise, myalgia, prostration, increased vascular permeability and dysfunctional circulatory regulation. Hypotension and bleeding can occur along with hepatic failure and renal failure. Each of the virus has its distinctive clinical features. Diagnosis requires serological confirmation: ELISA, reverse transcriptase polymerase chain reaction (RT-PCR), viral cultures. There is a vaccine for yellow fever.

Congo-Crimean Hemorrhagic Virus

Congo-Crimean Hemorrhagic Virus (CCHF) virus is in the genus Nairovirus and is distributed over geographic areas where Hyalomma ticks can be found - South Africa, sub-saharan Africa, Eastern Europe, Middle East, Asia.

CCHF is endemic in cattle, hares and herbivores in South Africa. Transmission to humans is by tick bite and contact with infected animals. Besides zoonotic spread, person-to-person transmission can occur via respiratory droplets, blood and biological fluids.

For these reasons, the CCHF virus has been researched for biological warfare potential. Incubation period is 3-6 days followed by acute onset of febrile illness with influenza-like symptoms. Hemorrhagic clinical features occur several days later with petechial rash, ecchymoses, hematemesis, melena, thrombocytopenia and leukopenia. Jaundice, increased liver enzymes, renal failure and hepatomegaly may occur. Mortality varies from 10-50% (47).

Camelpox Virus

Camelpox virus is a member of chordopoxviridae family of orthopoxvirus genus. In addition to camelpox virus, the other orthopoxviruses are Cowpox virus, California vole poxvirus, Ectromelia virus, Monkeypox virus, Racoon poxvirus, Tatera poxvirus, Vasin Gishu poxvirus, Vaccinia virus, Variola virus. Poxviruses are the largest of all viruses.

Long recognized as a cause of generalized pox disease in camels. Camelpox virus is found in areas of distribution of Africa and Asia where dromedary camels are found (48). Research has shown that camelpox virus is not a significant problem for humans. Why the Iraqi government was developing this virus as a potential weapon is unknown.

Human Rotavirus

Rotaviruses are the most important etiologic agents of severe diarrheal illness in children worldwide (47). Rotaviruses contain RNA and are in the family Reoviridae. Infection produces clinical manifestations of mild to severe diarrheal illness with massive and sometimes fatal dehydration. Other clinical features include fever, irritability, lethargy, pharyngitis, rhinitis, wheezing. Vomiting and diarrhea may last days. Chronic symptomatic infection can occur in immunosuppressed individuals. Method of detection is by ELISA.

Enterovirus

The genus Enterovirus consists of several important human infectious agents: poliovirus, coxsackie viruses, echoviruses and enteroviruses. Poliovirus was the first enterovirus to be recognized (47). Human enteroviruses consist of four types, 68-71, and are RNA containing. But only three viruses cause diseases:

Type 68: Pneumonia and bronchitis

Type 70: Acute hemorrhagic, conjunctivitis, paralysis, meningoencephalitis

Type 71: Meningitis, hand-foot-mouth disease, meningoencephalitis

Different enteroviruses can produce the same syndrome. Clinical manifestations of infection can range from minor febrile illness to severe and permanent paralysis. The most common syndrome of enterovirus infection is minor malaise (47). However, a persistent infection can occur with myalgic encephalomyelitis (post viral fatigue) syndrome (47).

FEDERAL RESPONSE TO CHEMICAL AND BIOLOGICAL TERRORISM

Recent terrorist attacks using both chemicals and explosive devices have prompted the U.S. government to develop an overall organizational approach to respond to terrorist activities. Most local emergency responders are not sufficiently trained nor equipped to respond to toxic or biological warfare weapon use in a terrorist attack despite their training for general hazardous material responses. A terrorist attack would expose first responders to unknown and highly lethal agents. Also, such attacks would be more subtle than the usual hazardous material releases and spills. Both victims and emergency responders may have no indication that they are being exposed until it is too late. The generation of a large number of casualties would overwhelm local emergency response efforts and local health care facilities: There is a limited supply of antidotes such as atropine, 2-pam chloride and limited supplies of antibiotics and vaccines. Contamination of emergency EMS personnel and health care facilities would occur, extending injury from such agents.

Roles of Federal Agencies

The Federal Bureau of Investigation (FBI) is responsible for responding to any incident of domestic terrorism and is the lead agency in crisis management response. The Federal Emergency Management Agency (FEMA) is the lead agency for consequence management following an incident. FEMA coordinates federal management and assistance to states and local governments in disaster and terrorist situations. FEMA would marshall federal agencies such as the EPA, Department of Defense, Human Health and Services, Department of Agriculture and others as needed to support the FBI and local authorities as required.

The National Guard and U.S. Army Reserve have 43 chemical defense units in their makeup (49). But while the state's governors have the ability to call up the National Guard to provide medical, decontamination and other support services, this activation usually requires 12 to 24 hours.

Presidential Decision Directive 39 has provided the concept for overall federal response to terrorist attacks (49). The FBI is the lead crisis management responder in all cases of domestic terrorism. FEMA coordinates consequence management. Other federal agencies provide support to the FBI or FEMA as necessary. The FBI has a hazardous materials response unit within their scientific analysis section in Quantico, Virginia which maintains a forensic analysis laboratory. The FBI also has the necessary scientific technology tactical units to support chemical and biological responses to terrorist actions. The role of the FBI in crisis management includes assessment of threat, emergency consultation and availability of technical assistance in the chemical and biological area.

When the U.S. Congress enacted the Defense Against Weapons of Mass Destruction Act of 1997, it directed a domestic preparation program which enhances the capability of the federal government to prevent and to respond to terrorist activities involving biological and toxic weapons. The Department of Defense is directed to develop and implement a domestic preparation program to improve the ability of local and state federal agencies to cope with threats and to conduct preparation for such events. The Department of Defense has established a Chemical, Biological Quick Response Force to respond to and assess terrorist incidents and coordinate military support as necessary. This response force also includes military troops.

The Domestic Preparedness Program also trains local responders such as firefighters, police and EMS personnel for responding to chemical or biological terrorist attacks. Major U.S. cities are targeted by the Department of Defense for training of emergency medical responders to incidences in the event of a chemical or biological terrorist incident. Also, under this new legislation, the Department of Defense is funding the public health service to assist local governments in initial planning and development of these teams, procurement of antidotes and pharmaceuticals, and equipment and training of personnel. Appropriate detection equipment and protective gear for such biological and toxic agents is not readily available at the local level and part of this program will be the dissemination of such support items. The Department of Defense hopes to have at least 120 of the nation's largest cities prepared with these training programs by 1999.

THE PSYCHOLOGICAL IMPACT OF TERRORISM

The success of a terrorist act is measured by the psychological impact on the population and the number of casualties it causes. Terrorists select targets to maximize shock value and depend on the media to maximize its psychodrama. Psychological reactions include difficulty sleeping and eating, depression, social conflict, irritability, feelings of guilt, difficulty concentrating, anxiety and flashbacks. For many individuals, they find daily activities difficult to balance and coordinate (50). Victims of terrorism may meet the definition of post traumatic stress disorder.

Psychosocial reactions to terrorism include feelings of hostility, dependence and powerlessness along with the feeling of violation of a previously safe environment. Loss of control compounds this traumatic experience. The individual's ability to cope is a major factor in preventing such responses. Perceptions and beliefs about the terrorist's act also shape post-attack psychology of victims and the public (50).

Three psychological response phases are identified following a terrorist attack (50): (1) Within the first two to three weeks following the disaster or terrorist event survivors are preoccupied with thoughts about the event. They discuss their anxieties openly. (2) Three to six weeks after the event, an inhibition phase emerges, chronic stress occurs, and health problems begin. (3) In the third phase which occurs after six weeks, those who are able to cope experience an adaption with recession of symptoms and distress.

Many symptoms are similar to those induced by acute and chronic stress (51). Immediate stressors are the dead, dying and injured plus the fear generated by the chemical or biological agent. The crisis and panic created by dysfunctional and overwhelmed emergency medical system will further feelings of hopelessness, doom and anger. Some signs and symptoms of acute stress and fear (autonomic arousal) may be mistaken for symptoms of exposure.

Quarantine may be required of individuals with infections from agents. This creates feelings of isolation, impending doom, and further escalates stress. Decontamination facilities may be in short supply and contaminated patients may panic, flooding health care facilities. The site of emergency responders in full protective garb while potential victims remain exposed escalates anxiety and panic. Influx of cases to the emergency medical system and health care facilities will create massive triage problems. An organized and effective emergency response to any attack is important to assure victims and the public. A chaotic response that seems to fail will exacerbate feelings of despair and psychological trauma. Also, part of the terrorist's goal is to interfere with the capacity of emergency responders to react in an organized manner.

CONCLUSION

Biological and chemical weapons do not win wars, but they can start wars. Their obvious and perverse use appears to be as weapons for political violence and instilling fear and fervor in a society (52). Treaties are no guarantee that such weapons will be restricted from terrorist possession. Therefore, the burden falls on law enforcement prevention efforts, response to terrorist attacks, and preparation of local, state and federal agencies to mitigate health effects.

Biological weapons in particular are easy to disperse and difficult to detect. And genetic bioengineering provides a tool for production of novel biotoxins and infectious agents. Defensive and preemptive measures along with more sophisticated detection methods, vigilance, and treatment modalities appears to be the best response to the weapons of terror.

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Table 1

Notable Biological and Chemical Terrorist Events

Biological terrorist events

- 1972: Order of Rising Sun uses typhoid to poison Chicago and St. Louis water.
- 1984: Red Army Faction tries to use botulinum in Paris.
- 1986: Bhagwan Cult poisons Oregon salad bars with salmonella, 715 people ill.
- 1995: Aryan Nation order plague, and Minnesota Patriots Council plans ricin use.
- 2001: Anthrax delivered by envelope to U.S. Senator's office in Washington D.C. and to news media offices in New York City causes illness and deaths.

Chemical terrorist events

- 1985: Covenant Group found to possess 33 gal of cyanide.
- 1992: Police prevent Neo-Nazis from using cyanide in synagogue.
- 1994: Aum Shinrikyo uses sarin in Matsumoto, 7 dead and 280 injured.
- 1995: Aum Shinrikyo uses sarin in Tokyo subway, 12 dear and 5,500 injured.
- 1995: Copycat attacks in Japan using cyanide, phosgene, and pepper spray.
- 1997: Chlorine bombs in Sydney, Australia, shopping centers injure 14 and 500 were evacuated.

Table 2

The Centers for Disease Control (CDC) List of Restricted Agents

Viruses

Crimean-Congo hemorrhagic fever virus
Eastern equine encephalitis virus
Ebola viruses
Equine morbillivirus
Lassa fever virus
Marburg virus
Rift Valley fever virus
South American hemorrhagic fever viruses
Tick-borne encephalitis complex viruses
Variola major virus (smallpox virus)
Venezuelan equine encephalitis virus
Viruses causing hantavirus pulmonary syndrome
Yellow fever virus
Exemptions: Vaccine strains of viral agents
(Junin virus strain candid #1, Rift Valley fever virus strain MP-12, Venezuelan equine encephalitis virus strain TC-83, and yellow fever virus strain 17-D).

Bacteria

Bacillus anthracis
Brucella abortus, Brucella melitensis, Brucella suis
Burkholderia (Pseudomonas) mallei
Burkholderia (Pseudomonas) pseudomallei
Clostridium botulinum
Francisella tularensis
Yersinia pestis
Exemptions: vaccine strains as described in Title 9 CFR, 78.1.

Rickettsiae

Coxiella burnetii
Rickettsia prowazekii
Rickettsia rickettsii

Fungi

Coccidioides immitis

Toxins

Abrin
Aflatoxins
Botulinum toxins
Clostridium perfringens epsilon toxin
Conotoxins
Diacetoxyscirpenol
Ricin
Saxitoxin
Shigatoxin
Staphylococcal enterotoxins
Tetrodotoxin
T-2 toxin
Exemptions: Toxins for medical use, inactivated for use as vaccines, or toxin preparations for biomedical research use at a median lethal dose for vertebrates of more than 100 ng/kg; national standard toxins required for biologic potency testing as described in Title 9 CFR Part 113.

Reprinted with permission: Biological Weapons and US Law in JAMA, August 6, 1997, Volume 278, Number 5, Page 359.

Table 3

Nerve Agent Attack Suspicion

- Multiple casualties with cholinesterase inhibition signs and symptoms
- Casualties appearing in downwind and/or confined space
- Rapid onset of severe symptoms clustered near maximum concentration
- Variable signs and symptoms extending out from radius of exposure
- Time course of effects dependent on vapor or liquid contact and route of absorption

Table 4

Signs and Symptoms of Nerve Agent Poisoning

Site of Action	Signs and Symptoms
	Following Local Exposure
1. Muscarinic	Miosis, marked, usually maximal (pinpoint), sometimes unequal.
Pupils	Frontal headache, eye pain on focusing, blurring of vision.
Ciliary body	Rhinorrhea, hyperemia.
Nasal mucous membranes	Tightness in chest, bronchoconstriction, increased secretion, cough.
Bronchial tree	Occasional nausea and vomiting.
Gastrointestinal	
	Following Systemic Absorption (depending on dose)
Bronchial tree	Tightness in chest, with prolonged wheezing expiration suggestive of bronchoconstriction or increased secretion, dyspnea, pain in chest, increased bronchial secretion, cough, cyanosis, pulmonary edema.
Gastrointestinal	Anorexia, nausea, vomiting, abdominal cramps, epigastric and substernal tightness (cardiospasm) with "heartburn" and eructation, diarrhea, tenesmus, involuntary defecation.
Sweat glands	Increased sweating.
Salivary glands	Increased salivation.
Lacrimal glands	Increased lacrimation.
Heart	Bradycardia.
Pupils	Miosis, occasionally unequal, later maximal miosis (pinpoint).
Ciliary body	Blurring of vision, headache.
Bladder	Frequency, involuntary micturition.
2. Nicotinic	
Striated muscle	Easy fatigue, mild weakness, muscular twitching, fasciculations, cramps, generalized weakness/flaccid paralysis (including muscles of respiration) with dyspnea and cyanosis.
Sympathetic ganglia	Pallor, transitory elevation of blood pressure followed by hypotension.
3. Central Nervous System	Immediate (Acute) Effects: Generalized weakness, depression of respiratory and circulatory centers with dyspnea, cyanosis and hypotension; convulsions, loss of consciousness, and coma. Delayed (Chronic) Effects: Giddiness, tension, anxiety, jitteriness, restlessness, emotional lability, excessive dreaming, insomnia, nightmares, headaches, tremor, withdrawal and depression, bursts of slow waves of elevated voltage in EEG (especially on hyperventilation), drowsiness, difficulty concentrating, slowness of recall, confusion, slurred speech, ataxia.

Source: Treatment of Chemical Agent Casualties and Conventional Military Chemical Injuries, Field Manual, No.8-285, NAVMED P-5041, Air Force Manual No. 160-12, Headquarters, Departments of the Army, the Navy, and the Air Force, Washington DC, 28 February, 1990.

Table 5

Time Course of Effects of Nerve Agents

	Types of Effects	Route Absorption	Description of Effects	When Effects Appear After Exposure	Duration of Effects After Mild Exposure	Duration of Effects After Severe Exposure
Vapor	Local	Lungs	Rhinorrhea, nasal hyperemia, tightness in chest, wheezing	One to several minutes	A few hours	1 to 2 days
Vapor	Local	Eyes	Miosis, conjunctival hyperemia, eye pain, frontal headache	One to several minutes	Miosis - 24 hours	2 to 3 days
Vapor	Systemic	Lungs or eyes	Muscarinic, nicotinic, and central nervous system effects	Less than 1 minute to a few minutes after moderate or severe exposure; about 30 minutes after mild exposure	Several hours to a day.	Acute effects: 2 to 3 days. CNS effects: days to weeks.
Liquid agent	Local	Eyes	Same as vapor effects	Instantly	Similar to effects of vapor.	
Liquid agent	Local	Ingestion	Muscarinic, nicotinic, and central nervous system effects	About 30 minutes after mild exposure	Several hours to a day.	2 to 5 days.
Liquid agent	Local	Skin	Local sweating and muscular Twitching	3 minutes to 2 hours	3 days	5 days.
Liquid agent	Systemic	Lungs	Muscarinic, nicotinic, and central nervous system effects	Several minutes		1 to 5 days.
Liquid agent	Systemic	Eyes	Same as for vapor	Several minutes		2 to 5 days.
Liquid agent	Systemic	Skin	Generalized sweating	15 minutes to 2 hours		2 to 5 days.
Liquid agent	Systemic	Ingestion	Muscarinic, nicotinic, and central nervous system effects	15 minutes to 2 hours		3 to 5 days.

After lethal or near lethal exposures to nerve agents, the time to onset of symptoms and to maximal severity of symptoms is shorter; it may be extremely brief after overwhelming exposure. Following exposure to lethal concentrations, the time interval to death depends upon the degree, the route of exposure, and the agent. If untreated, exposure to lethal concentrations of nerve agents can result in death 5 minutes after appearance of symptoms.

Source: Treatment of Chemical Agent Casualties and Conventional Military Chemical Injuries, Field Manual, No.8-285, NAVMED P-5041, Air Force Manual No. 160-12, Headquarters, Departments of the Army, the Navy, and the Air Force, Washington DC, 28 February, 1990.

Table 6

The Effects of Chemical Nerve Agents on the Central Nervous System

Giddiness, floating sensations
Tinnitus, nystagmus, pyrexia
Tremor, ataxia
Paralyses, paraesthesiae, polyneuritis
Speech difficulties:
  slurring
  difficulty in forming words
  changes in speech
  repetition of syllables
  difficulty in saying what is intended
Memory defect - slowness of recall
Insomnia
Lassitude and weakness
Drowsiness
Concentration difficulty
Mental confusion
Uneasiness
Restlessness
Anxiety
Tremulousness
Emotional lability
Depression with weeping spells and insomnia
Schizophrenic reaction
Dissociation
Somnambulism and excessive dreaming
Fugue

Reprinted with permission: Delayed Toxic Effects of Chemical Warfare Agents, A Sipri Monograph, Stockholm International Peace Research Institute, Almqvist & Wiksell International, Stockholm, 1975.

Table 7

A psychiatric delayed-effect syndrome was found as a result of systematic investigations on former members of chemical warfare production and testing stations for the Wehrmacht . In terms of frequency, two groups of symptoms can be distinguished - each consisting of four separate symptoms or signs.

1 . The great majority of persons examined showed:

a. persistently lowered vitality

b. defective autonomic regulation leading to cephalalgia, gastrointestinal and cardiovascular symptoms, and premature decline in libido and potency;

c. intolerance symptoms (alcohol, nicotine, medicines);

d. impression of premature aging.

2 . Further, one or more symptoms of the second group were found;

a. depressive or subdepressive disorders of vital functions;

b. cerebral vegetative (syncopal) attacks;

c. slight or moderate amnestic and demential defects;

d. slight organoneurological defects (predominantly microsymptoms and singular signs of extrapyramidal character).

Reprinted with permission: Delayed Toxic Effects of Chemical Warfare Agents, A Sipri Monograph, Stockholm International Peace Research Institute, Almqvist & Wiksell International, Stockholm, 1975.

Table 8

Eye Lesions Caused by Organophosphorus Compounds

- reduction of vision 98%
- narrowing of peripheral visual fields 95%
- refraction anomaly with high astigmatism 88%
  (severe case shows keratoconus)
- neurological abnormalities with EEG abnormalities 71%
- disturbance of smooth pursuit motion of the eyes 57%
- insufficiency of the pupillary sphincter 52%
- optic neuritis and/or retinochoroid atrophy 65%
- dysfunction of liver
  - reduction of serum cholinesterase 33%
  - increment of serum phosphorus 30%
  - increment of acid phosphatase 62%
  - increment of alkali phosphatase 10%
  - abnormalities of cephalin-cholesterol-lecithin flocculation test 46%
- reduction of ocular tension 25%
- paresis of accommodative convergence 20%
- cycloplegia 12%
- nystagmus or fixation disability 6%

Reprinted with permission: Delayed Toxic Effects of Chemical Warfare Agents, A Sipri Monograph, Stockholm International Peace Research Institute, Almqvist & Wiksell International, Stockholm, 1975.

Table 9

Estimates of Casualties Produced by Hypothetical Biological Attack*

Agent	Downwind Reach, km	No. Dead	No. Incapacitated
Rift Valley fever	1	400	35,000
Tick-borne encephalitis	1	9500	35,000
Typhus	5	19,000	85,000
Brucellosis	10	500	125,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>20	95,000	125,000

* Release of 50 kg of agent by aircraft along a 2-km line upwind of a population center of 500,000.

Reprinted with permission: Christopher G, Cieslak T, Pavin J, Eitzen E. Biological warfare, Journal of the American Medical Association, August 6, 1997, Volume 278, Number 5.

Table 10

Biological Weapon Agent Attack Suspicions

- Location of casualties in a downwind pattern
- Affected animals in same area as people
- Unusual disease presentation
- High disease rates among exposed persons
- Respiratory clinical presentation
- Occurrence of a disease that is unusual in a geographic area
- A vector borne disease occurring in an area that lacks vectors
- More than one epidemic occurring at once
- Higher morbidity and mortality than expected for a disease
- Lower attack rate in unexposed individuals

Table 11
Biological Warfare Agents (continued on next page)

Agent	Infective Dose (Aerosol)	Incubation Period	Diagnostic Samples (BSL)	Diagnostic Assay	Patient Isolation Precautions
Anthrax	8000 to 50,000 spores	1-5 days	Blood (BSL-2)	Gram stain Ag-ELISA, Serology: ELISA	Standard precautions
Brucellosis	10-100 organisms	5-60 days (occasionally months)	Blood, bone marrow, acute and convalescent sera (BSL-3)	Serology: agglutination Culture	Standard precautions Contact isolation if draining lesions present
Plague	100-500 organisms	2-3 days	Blood, sputum, lymph node aspirate (BSL-2/3)	Gram or Wright-Giemsa Stain Ag-ELISA, Culture, Serology: ELISA, IFA	Pneumonic: droplet precautions until patient treated for 3 d
Q fever	1-10 organisms	10-40 days	Serum (BSL-2/3)	Serology: ELISA, IFA	Standard precautions
Tularemia	10-50 organisms	2-10 days	Blood, sputum, serum EM of tissue (BSL-2/3)	Culture Serology: agglutination	Standard precautions
Smallpox	Assumed low (10-100 organisms)	7-17 days	Pharyngeal swab, scab material (BSL-4)	ELISA, PCR, virus isolation	Airborne precautions
Viral encephalitides	10-100 organisms	VEE, 2-6 days EEE/WEE, 7-14 days	Serum VEE (BSL-3) EEE (BSL-2) WEE (BSL-2)	Viral isolation Serology: ELISA or hemagglutination inhibition	Standard precautions (mosquito control)
Viral hemorrhagic fevers	1-10 organisms	4-21 days	Serum, blood Most viral Hemorrhagic fevers (BSL-4) RVF, KHF, and YF (BSL-3)	Viral isolation Ag-ELISA RT-PCR Serology: Ab-ELISA	Contact precautions Consider additional precautions if massive hemorrhage
Botulinum	0.001 ug/kg (type A)	1-5 days	Nasal swab (possibly) (BSL-2)	Ag-ELISA, Mouse neutral	Standard precautions
Staphylococcal enterotoxin B	30 ng/person (incapacitating); 1.7 ug/person (lethal)	1-6 hours	Nasal swab, serum, urine (BSL-2)	Ag-ELISA Serology: Ab-ELISA	Standard precautions

*Information on diagnostics, medical management, and vaccines is available by contacting Commander, USAMRIID, at 301-619-2833 (phone) or 301-619-4625 (fax). Readers are advised to consult product literature before administering drugs or vaccines. BSL indicates biosafety level; Rx, chemotherapy; Px, chemoprophylaxis,; Ag, antigen; ELISA, enzyme-linked immunosorbent assay; IV, intravenously; q, every; IM, intramuscular; qd, each day; bid, twice a day; PO, my mouth; IFA, immunofluorescent assay; IND, Investigational New Drug; SC, subcutaneous; EM, electron microscopy; PCR, polymerase chain reaction; VIC, vaccinia immune globulin; DOD, Department of Defense; VEE, Venezuelan equine encephalitis; EEE, eastern equine encephalitis; WEE, western equine encephalitis; NA, not available; RVF, Rift Valley fever; KHF, Korean hemorrhagic fever; YF, yellow fever; RT-PCR, reverse transcriptase polymerase chain reaction; Ab, antibody; CCHF, Congo-Crimean hemorrhagic fever; AHF, Argentine hemorrhagic fever; BHF, Bolivian hemorrhagic fever; CDC, Centers for Disease Control and Prevention.

Franz et al. Exposure to Biological Warfare Agents, JAMA, August 6, 1997, Vol. 278, No. 5, pp. 400-401.

Agent	Chemotherapy (Rx)	Chemoprophylaxis (Px)	Vaccine Availability	Comments
Anthrax	Ciprofloxacin 400 mg IV q 8-12 h Doxycycline 200 mg IV, then 100 mg IV q 8-12 h Penicillin 2 million units IV q 2 h plus streptomycin 30 mg/kg IM qd (or gentamicin)	Ciprofloxacin 500 mg PO bidx4 wk If vaccinated, begin initial doses of vaccine Doxycycline 100 mg PO bidx4 wk plus vaccination	Michigan Biological Products Institute vaccine (licensed): 0.5 mL SC at 0, 2, 4 wk and 6, 12, 18 mo, then annual boosters	Vaccine: boost at-risk annually Alternates for Rx: gentamicin, erythromycin, and chloramphenicol
Brucellosis	Doxycycline 200 mg/d PO plus rifampin 600-900 mg/d POx6 wk	Doxycycline and rifampin for 3 wk in inadvertently inoculated persons	No vaccine available for human use	Trimethoprim-sulfamethoxazole may be substituted for rifampin; however, relapse rate with this drug may be up to 30%
Plague	Streptomycin 30 mg/kg IM qd in 2 divided doses x 10 d (or gentamicin) Doxycycline 200 mg IV then 100 mg IV q 12 hx10-14 d Chloramphenicol 1 g IV q 6 hx10-14 d	Tetracycline 500 mg PO qidx7 d Doxycycline 100 mg PO q 12 hx7 d	Greer inactivated vaccine (licensed): 1.0 mL, then 0.2 mL boost at 1-3 and 3-6 mo	Boost at-risk 12, 18 mo & yearly. Plague vaccine not protective against aerosol in animal studies Alternate Rx: chloramphenicol or trimetroprim-sulfamethoxazole Rx: chloramphenicol for plague meningitis
Q fever	Tetracycline 500 mg PO q 6 hx5-7 d Doxycycline 100 mg PO q 12 hx5-7 d	Tetracycline start 8-12 d postexposure x5 d Doxycycline start 8-12 d postexposure x5 d	IND 610-inactivated whole cell vaccine given as single 0.5 mL SC	Recommended skin test before vaccination
Tularemia	Streptomycin 30 mg/kg IM qd x10-14 d Gentamicin 3-5 mg/kg/dx10-14 d	Doxycycline 100 mg PO q 12 hx14 d Tetracycline 2 g/d POx14 d	Live attenuated vaccine (IND): scarification	Culture difficult and potentially dangerous
Smallpox	Cidofovir (effective in vitro)	Vaccinia immune globulin 0.6 mL/kg IM (within 3 d of exposure; best within 24 h	Wyeth calf lymph vaccinia vaccine (licensed) DOD cell-culture derived vaccinia vaccine (IND): scarification	Preexposure and postexposure vaccination recommended if >3 y since last vaccination
Viral encephalitides	Supportive therapy analgesics anticonvulsants as needed	NA	VEE DOD TC-83 live attenuated vaccine (IND): 0.5 m: SCx1 dose VEE DOD C-84 (formalin inactivated TC-83)(ND): 0.5 mL SC for up to 3 doses EEE inactivated (IND): 0.5 mL SC at 0 & 28 d WEE inactivated (IND): 0.5 mL SC at 0, 7, and 28 d	TC-83 reactogenic in 20% No seroconversion in 20% Only effective against subtypes 1A, 1B, and 1C Vaccine used for nonresponders to TC-83 EEE and WEE inactivated vaccines are poorly immunogenic, and multiple immunizations are required
Viral hemorrhagic fevers	Supportive therapy Ribavirin (CCHF/arenaviruses) 30 mg/kg IV initial dose, 15 mg/kg IV q 6 hx4 d, 7.5 mg/kg IV q 8 hx6 d Antibody passive for AHF, BHF, Lassa fever, and CCHF	NA	AHF Candid #1 vaccine (x-protection for BHF)(IND) RVF inactivated vaccine (IND)	Aggressive management of secondary infections and hypotension is important
Botulinum	DOD heptavalent antitoxin for (Serotypes A-G) (IND): equine despeciated 1 vial (10 mL) IV CDC Trivalen equine antitoxin for Serotypes A, B, E (licensed)	NA	DOD pentavalent Toxoid for serotypes Q-E (IND): SC at 0, 2, & 12 wk, then yearly boosters	Skin testing for hypersensitivity before equine antitoxin administration Ventilatory assistance
Staphylococcal enterotoxin B	Ventilatory support and supportive care	NA		Vomiting and diarrhea may occur if toxin is swallowed

Franz et al. Exposure to Biological Warfare Agents, JAMA, August 6, 1997, Vol. 278, No. 5, pp. 400-401.

Figure 1

Symptom Algorithm for Diagnosis of Biowarfare Agents

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