# Chemical Agent Terrorism

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## INTRODUCTION

On March 20, 1995, terrorism changed. For the first time, terrorists used a chemical warfare agent against a civilian population. The nerve agent sarin (GB) was released in the Tokyo subway system causing over 5500 people to seek medical attention. Although terrorists had released sarin previously outside an apartment building in the city of Matsomoto in June 1994, this earlier use was felt to be directed at a few people living in the building and not an attack on the general population.

The Aum Shinrikyo cult is accused of both these attacks and also of several other less successful efforts in the Tokyo subway system. This cult, with a large membership and assets of over a billion dollars, had a large facility for the manufacture of chemical warfare agents and of biological agents. This organization has a following in several European countries, including Germany and Russia, and in the United States. Whether or not one believes that this cult will strike in this country the point has been made: chemical warfare agents are now terrorist weapons.

Chemical warfare agents can readily be synthesized by a skilled chemist if the precursors are available. The processes for synthesis are readily available and are even on the Internet. Although these has been an international embargo on many of the precursors, this ban does not apply to intracountry shipment.

Can terrorist groups in this country obtain or manufacture these agents? One would like to think not, but this would be wishful thinking. To date, the intelligence and law enforcement agencies have been quite vigilant, and these agents have not been used. Any threat, such as the threat of sarin use at Disneyland last Easter, is taken very seriously.

How and where might such agents be used? Most chemical warfare agents are liquids. They evaporate at different rates to produce vapor ; cyanide is very volatile and the blister agent mustard and nerve agent VX have a volatility similar to that of light motor oil. It is unlikely that the liquid form would be effective in contaminating large numbers of people. It would have to be spread over an area in places that people will contact the droplets. To be effective liquid must be dispersed. This can be done by aerosolizing it by an aerial spray (such is done with pesticides) or by an explosion. Or the liquid agent can be allowed to evaporate and the vapor dispersed by some means. In the Tokyo the liquid sarin was placed on the floors of subway cars and allowed to evaporate without dissemination, which is why there were only 1000 casualties (most of whom had mild effects) out of the 5500 people who sought medical attention. Even a small fan would have spread the vapor causing more casualties. When used outside a vapor will not remain in place because even a small wind will dilute it and carry it away. However, when dispersed inside there would be no wind, and the agent vapor would remain and the concentration would build, at least until the ventilation system removed it. On the other hand, the ventilation system could well be the means of dissemination.

The site of agent use would depend on the objectives of the user. For maximal publicity one might chose a major event, such as the Olympics (parts of which are held inside), the political conventions (inside events), or even a major sporting event (most of which are outside). For the maximal number of casualties a busy subway system (an inside area) would be a good target. To make a statement and as a warning of attacks to come, a site in a smaller community might be the target. Terrorist attacks are unpredictable. Did anyone predict bombings in the World Trade Center and Oklahoma City or a train derailing in the southwest? We do not know where an attack might be.

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## CHEMICAL WARFARE AGENTS

### Nerve agents

Nerve agents are extremely potent organophosphorus compounds that cause biological effects by inhibiting the enzyme acetylcholinesterase. The more widely known nerve agents are tabun (GA), sarin (GB), soman (GD), GF, and VX. They are similar in structure and biological activity to some commonly used insecticides, such as Malathion7, and are similar in biological activity to carbamates used as insecticides, such as Sevin7, and used in medicine, such as Mestinon7, Neostigmine7, and Antilirium7.

When the enzyme acetylcholinesterase is inhibited the neurotransmitter acetylcholine accumulates to cause overstimulation of those structures innervated by the cholinergic nervous system, namely skeletal muscles, smooth muscles, exocrine glands, and certain nerves both in the central nervous system and at ganglia. The resulting effects, which are dependent on route and amount of exposure, are shown in Table I.

| Table I<br>Effects of Nerve Agents |
|---|
| **Eyes**: Miosis, tearing, conjunctival injection (pain, dim vision, blurred vision)<br>**Nose**: Rhinorrhea<br>**Airways**: Bronchoconstriction, bronchosecretions (dyspnea, cough)<br>**Gastrointestinal**: Hypermotility, secretions (nausea, vomiting, diarrhea, cramps)<br>**Skeletal muscles**: Fasciculations, twitching, paralysis (weakness)<br>**Central nervous system**: Immediate--loss of consciousness, seizures, apnea. Later--possible difficulty in thinking, impaired judgement, and other minor effects.<br>**Other**: Salivation, sweating |

Nerve agents are clear, colorless liquids with no perceivable odor (although two are said to have a slight odor, this is not a reliable detection method). The four "G-agents" are volatile to some degree, but the most volatile, sarin, evaporates at about the rate that water does. They all penetrate the skin and normal clothing well so exposure might be by skin penetration or from vapor. Most exposures to sarin have been from vapor.

All of these effects do not appear in every casualty; for example, miosis is uncommon in someone exposed to a droplet of agent on the skin unless the droplet is large enough to cause severe effects. After exposure to a small amount of vapor, the triad of miosis, rhinorrhea, and airway effects sometimes occurs, but often only one or two of these effects occur.

The more common effects from each route of exposure are shown in Tables II and III. The onset of effects from vapor is within seconds or a minute of exposure, whereas the onset of effects from a liquid droplet is from several minutes to 18 hours after contact. The rapidity with which the droplet penetrates depends on the size of the droplet; the larger the droplet the sooner the onset and the more severe the effects.

| Table II<br>Vapor exposure |
|---|
| **Mild**:<br>Miosis<br>Rhinorrhea<br>Dyspnea<br>Nausea<br>Weakness<br>**Severe**:<br>Above plus<br>Loss of consciousness<br>Seizures<br>Apnea<br>**Onset**:<br>Seconds to minutes |

| Table III<br>Liquid exposure |
|---|
| **Mild**: Local sweating and fasciculations<br>**Moderate**: Nausea, vomiting, diarrhea, weakness<br>**Severe**:<br>Above plus<br>Loss of consciousness<br>Seizures<br>Apnea<br>**Onset**: 5 min to 18 hours |

Blood cholinesterase is generally inhibited, or depressed, after exposure to a nerve agent, except that a small amount of vapor affecting the eyes, nose, and airways may or may not be absorbed to cause this inhibition. The erythrocyte (or red cell) cholinesterase is more sensitive to nerve agent inhibition and measure of this--rather than the plasma (or serum) enzyme--is preferred.

Antidotes for nerve agent poisoning are atropine and pralidoxime chloride. Atropine blocks the effects of the excess acetylcholine

at muscarinic sites (drying secretions, reducing muscular contraction in the airways and gastrointestinal tract), and pralidoxime chloride removes the agent from the enzyme allowing the enzyme to once again function (this drug is ineffective in soman poisoning). Clinically, pralidoxime chloride reverses effects in organs with nicotinic receptor sites (skeletal muscles).

Generally, in casualties with mild or moderate effects (Tables II and III) 2 mg of atropine should be used initially and will usually be sufficient. In a severe casualty, 6 mg of atropine (im) and 1 gram of pralidoxime chloride (infused slowly over 20-30 minutes) should be given initially. Miosis does not respond to the usual amounts of im or iv atropine and should be treated with a topical preparation only if the pain is severe. Atropine, 2 mg every 5-10 minutes, should be continued until (a) secretions are drying and (b) ventilation is adequate. Diazepam should be administered to every severe casualty whether seizing or not, and ventilation and suction of the copious secretions may also be necessary.

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**Vesicants**

Vesicant agents are so named because they cause blisters. Sulfur mustard is the most widely known of this class; others are Lewisite and phosgene oxime. Nitrogen mustard (Mustargen7), used in cancer chemotherapy for over 50 years, is a by-product of research on sulfur mustard. In World War I, mustard caused large numbers of casualties, but fewer than 5% of the casualties died.

In addition to causing blisters, mustard also damages the eyes and airways by topical contact and the gastrointestinal tract and bone marrow after absorption. Mustard evaporates at about the same rate as thin motor oil, but despite this low volatility most battlefield casualties have been from vapor.

Mustard crosses the skin or mucous membrane barrier and within a minute or two after contact it attaches to cellular or tissue components where it will later cause damage. Decontamination later than a minute or two after contact will reduce but not prevent tissue damage. Mustard causes no clinical effects (including pain) on contact, and it is only hours later that the damage becomes apparent. Sometime between 2 and 24 hours later (usually 4 to 8 hours) the skin will redden, and this erythema will be followed by blister formation sometime later. The initial effect in the eye is irritation and reddening, and depending on the amount of exposure there may later be inflammation and edema of the lids (to force the eyes closed causing "blindness") and corneal damage. Airway damage, which begins with destruction of the mucosa, starts in the nose and sinuses and descends down the airways in a dose-dependent manner to produce hoarseness and a non-productive cough. Once the agent is in the lower airways, a productive cough is accompanied by increasing dyspnea. In severe instances, the necrotic mucous membranes form pseudomembranes.

Gastrointestinal disturbances are common in the first day after mustard poisoning and are due to non-specific factors. Days later, if the mustard was ingested or large amounts were absorbed, the mucosa of the gut is destroyed leading to massive fluid loss. Mustard is considered a radiomimetic agent because of this and other tissue damage. When absorbed in large amounts mustard destroys the precursor cells in the bone marrow leading to leukocytopenia; this is followed by a decrease in red cells and platlets. Sepsis is not uncommon in severe poisoning.

There is no antidote to mustard poisoning. Management consists of keeping the skin lesions clean by frequent irrigation and application of topical antibiotics, good pulmonary care including intubation and assisted ventilation, and irrigation of the eyes followed by frequent application of topical antibiotics. Fluid loss from mustard burns is not of the magnitude seen after thermal burns, and one should resist the temptation to overload with fluids.

Lewisite and phosgene oxime cause pain on contact with agent vapor or with liquid agent. Because of this the casualty is more likely to leave the area and decontaminate than he is after mustard poisoning in which he has no sign of agent contact. Signs appear much earlier after these two agents than after mustard exposure. Both cause skin, eye, and airway damage, but neither causes bone marrow depression. The antidote for Lewisite, British-Anti-Lewisite (BAL), is useful if applied early.

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**Cyanide**

A lethal amount of cyanide causes death within minutes, but lower amounts produce few effects. There are two forms of cyanide, the solid salts (sodium, potassium, and calcium) and the volatile liquids (hydrogen cyanide and cyanogen chloride). The addition of an acid, such as sulfuric acid, to a salt produces the vapor or gas of cyanide. This was used in executions (the "gas chamber"), and these components were found unmixed in Tokyo subways. Large amounts of cyanide are required to cause death, compared to the amounts needed for nerve agents. Smaller than lethal amounts produce few serious effects.

Cyanide inhibits the cellular enzyme cytochrome oxidase to inhibit oxygen metabolism and energy generation by the cell. Most

signs and symptoms are of central nervous system origin and after inhalation of a large amount include a brief period of hyperpnea, seizures, a decrease in breathing rate until apnea occurs, and cardiac arrhythmias leading to death. After ingestion, with slower absorption, other effects include vertigo, nausea, and a feeling of weakness.

First aid therapy consists of amyl nitrite by inhalation. If apnea is present this drug must be given in a ventilator. Sodium nitrite and sodium thiosulfate, both of which must be given intravenously, are more definitive antidotes. Assisted ventilation with oxygen should also be used.

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### Pulmonary Agents

Pulmonary agents cause pulmonary edema, but very few other effects. These agents include phosgene (carbonyl chloride), a World War I chemical warfare agent now widely used in industry, and perfluroroisobutylene, a pyrolysis product of Teflon7. After inhalation these compounds breakdown the alveolar-capillary membrane which allows plasma to leak into the alveoli.

Potentially lethal pulmonary edema begins hours after exposure, with symptoms of dyspnea and a productive cough.

Because the effects do not begin until hours after exposure (usually four to 24 hours) the initial responder will see an asymptomatic patient. A person with a history of possible exposure to one of these compounds should be removed from the contaminated area and should be kept at complete rest without even walking. Exertion will increase the subsequent illness.

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### Incapacitating agents

Incapacitating agents are usually defined as chemical agents that produce reversible disturbances in the central nervous system that disrupt cognitive ability. The former military agent BZ (now used in pharmacology where it is known as QNB) is a cholinergic blocking compound and produces many effects similar to those of atropine, such as mydriasis, drying of secretions, heart rate changes, and decreased intestinal motility. BZ, after an onset time of an hour or more, will--like high doses of atropine--produce confusion, disorientation, and disturbances in perception (delusions, hallucinations) and expressive function (slurred speech). The antidote, physostigmine (Antilirium7), reverses these effects for about an hour, and because the effects of BZ last for hours to days repeated doses must be given.

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## MEDICAL RESPONSE

What can we as medical responders do about a terrorist attack? Prevention and prophylaxis are commonly used in medicine to prevent illness. However, these do not apply in this instance. Prevention is what intelligence and law enforcement agencies do. Medical personnel have neither the training nor resources to prevent a terrorist attack. Prophylaxis, in the form of immunization, is a common way to prevent disease, but there is no known prophylaxis for chemical agents, and even if there were it would be impractical to immunize a population at risk because we do not know what population is at risk.

Medical personnel have the task of taking care of casualties after the event has occurred. This includes diagnosis, management, and triage of casualties while preventing spread of the disease or agent.

Preparation for this includes knowledge and equipment. The responder must have knowledge of the agent, its effects, and countermeasures and knowledge of how to protect self and others, which includes decontamination of self and others. Equipment includes material for countermeasures, such as antidotes if known, and material for protection, such as protective clothing and masks.

How is all of this to be approached? Protective equipment should be already in place in most hospitals and responder units because it is a requirement under HAZMAT regulations, and the responder suits and self-contained breathing apparatus used for HAZMAT operations is generally quite adequate for chemical warfare agents. Knowledge of casualty decontamination is also a requirement under HAZMAT regulations, and the same techniques apply to chemical warfare agent casualties.

In rural areas medical facilities there may be supplies of atropine and 2-PAMCl for use in insecticide poisoning, but in cities these supplies are small at best. The antidotes for cyanide poisoning, sodium nitrite and sodium thiosulfate, are generally not available in large amounts. Is it cost effective to stock these antidotes in amounts adequate to treat the number of casualties that might be expected in our larger cities or for that matter in any town or city that might be a terrorist target? This question must be

addressed if we are to take terrorism with chemical agents seriously.

Finally, there is knowledge of these agents, their effects, and methods of counteracting these effects in casualties. Do civilian medical responders have this knowledge? Generally not. Most know that the nerve agents are similar to organophosphorous insecticides, and some may have an idea of what to do for a cyanide casualty. But poisoning by these compounds is uncommon in most parts of the country. In the past, military chemical warfare agents have been considered a military matter, not a concern for civilian medical personnel. The Tokyo subway attack changed that. These agents might very quickly and unexpectedly become a civilian concern, and civilians will have to respond quickly.

Is there training on the medical aspects of these agents in the civilian medical community? Currently not, except within the limited areas surrounding military depots. Whether initiated on the federal, state, or local level, this must be undertaken if one takes this threat seriously. Is there readily available information on these agents? Is there a single source of information to which a medical responder can turn in the event of a terrorist attack with a chemical warfare agent? Generally not unless the response unit is close to a military depot. There should be such a reference source in each medical response unit.

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## SUMMARY

Terrorists have used chemical warfare agents and may use them again. These agents range from those that cause death quickly, such as the nerve agents and cyanide, to those with effects beginning hours after exposure, such as mustard and the pulmonary agents. Although prevention of such an attack would be the best strategy, this may not be possible. Medical personnel must be prepared to diagnose, manage, and triage casualties. To do this, they must have equipment and knowledge.

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