Chemical Warfare Agents

What is a Chemical Warfare Agent?

A United Nations report from 1969 defines chemical warfare agents as "... chemical substances, whether gaseous, liquid or solid, which might be employed because of their direct toxic effects on man, animals and plants ... ".

The Chemical Weapons Convention defines chemical weapons as including not only toxic chemicals but also ammunition and equipment for their dispersal. Toxic chemicals are stated to be "... any chemical which, through its chemical effect on living processes, may cause death, temporary loss of performance, or permanent injury to people and animals". Plants are not mentioned in this context.

Toxins, i.e., poisons produced by living organisms and their synthetic equivalents, are classed as chemical warfare agents if they are used for military purposes. However, they have a special position since they are covered by the Biological and Toxin Weapons Convention of 1972. This convention bans the development, production and stockpiling of such substances not required for peaceful purposes.

About 70 different chemicals have been used or stockpiled as CW agents during the 20th century. Today, only a few of these are considered of interest owing to a number of demands that must be placed on a substance if it is to be of use as a CW agent.

* A presumptive agent must not only be highly toxic but also "suitably highly toxic" so that it is not too difficult to handle.

* The substance must be capable of being stored for long periods in containers without degradation and without corroding the packaging material.
* It must be relatively resistant to atmospheric water and oxygen so that it does not lose effect when dispersed.

* It must also withstand the heat developed when dispersed.

These Military Chemicals are Not Considered to be Chemical Weapons

* Incendiary agents such as napalm and phosphorus are not considered to be CW agents since they achieve their effect mainly through thermal energy.

* Certain types of smoke screen may be poisonous in extremely high concentrations but, nonetheless, smoke ammunition is not classed as a chemical weapon since the poisonous effect is not the reason for their use.

* Plants, microorganisms, algae, etc. which produce toxins are not classed as chemical weapons even if the produced toxins belong to that class. Pathogenic microorganisms, mainly viruses and bacteria, are classed as biological weapons.

1. **Purpose of using Chemical Weapons**
   a. Lethality.
   b. Delay effects-
       Mustard agents are a further example of efficacy arising from delayed effects. They are not readily detectable by smell or other quick-acting physiological responses or warning properties, so large numbers of personnel may be injured before the danger is recognized. The low lethality of such agents is not necessarily a disadvantage, since care of the disabled is demanding. In World War I, 2 percent of fatalities were mustard casualties
   c. Burden-
It is very difficult to rapidly detect all threats or to recognize all attacks in a complex military environment. Although modern protective equipment is highly effective, it poses very heavy burdens in many circumstances, e.g., heat stress; impaired vision, dexterity, communications, and control; and psychological stress. The aggregate of these burdens is such that there is an incentive to employ chemicals enough to force an opponent into protective posture, to degrade tactical performance quite independent of any casualties actually produced (Franke, 1967).

d. Fear-

Fear and confusion are prevalent in combat. Use or expected use of chemical weapons could further amplify that fear and confusion. During World War II, there were instances of U.S. units on Guadalcanal and in Normandy becoming disorganized at night when gas alarms sounded after troops had discarded their masks. More recently, it appears that fear of a chemical attack appears to have been a factor in flight from urban areas during the Iran-Iraq War, as both sides fired missiles at cities (Cordesman and Wagner, 1990). The high state of training and discipline in U.S. forces appears to have prevented panic during the tense periods of the Gulf War.

How to choose- The selection of an agent for use is more complex than a simple judgment of toxicity. Production, stability in storage, persistence, delivery, and dissemination are also important. It is not surprising that Iraq selected some agents that were known but not favored by other countries. For example, the Germans independently discovered lewisite during World War I but chose not to use it because they thought its prompt production of symptoms was a disadvantage. Other countries thought otherwise. It should be kept in mind that military agents often contain stabilizing chemicals that have their own toxicity, but most laboratory research on agent effects is done with chemicals purer than weapon-grade material and thus may not predict all effects of chemical weapons. The objectives of use can affect agent selection, from creating defensive barriers that
deny entry to territory and facilities using persistent agents, such as mustards or VX, to supporting attacks with highly toxic but volatile nonpersistent agents, such as sarin.

**Effects on Organism**

*lethal

*incapacitating A substance is classified as incapacitating if less than 1/100 of the lethal dose causes incapacitation, e.g., through nausea or visual problems. The limit between lethal and incapacitating substances is not absolute but refers to a statistical average. In comparison, it may be mentioned that the ratio for the nerve agents between the incapacitating and lethal dose is approximately 1/10.

**An overview of chemicals defined as chemical weapons**

**Main Groups**

1. **Casualty agents**

<table>
<thead>
<tr>
<th>a) Blood agents</th>
<th>b) Choking agents</th>
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<tr>
<td>* Arsine</td>
<td>* Chlorine</td>
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<tr>
<td>* Cyanogen chloride</td>
<td>* Diphosgene</td>
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<tr>
<td>* Hydrogen chloride</td>
<td>* PFIB</td>
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<td>* Phosgene</td>
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<tr>
<th>c) Nerve agents</th>
<th>d) Vesicants-(blistering)</th>
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<tbody>
<tr>
<td>* GA (Tabun)</td>
<td>* Distilled mustard</td>
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<tr>
<td>* GB (Sarin)</td>
<td>* Ethyldichloroarsine</td>
</tr>
<tr>
<td>* GD (Soman)</td>
<td>* Lewisite 1</td>
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<tr>
<td>* GE</td>
<td>* Lewisite 2</td>
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</tbody>
</table>
* GF
* VG
* VM
* VX

* Lewisite 3
* Methyldichloroarsine
* Mustard-Lewisite mixture
* Mustard-T mixture
* Nitrogen Mustard 1
* Nitrogen mustard 2
* Nitrogen mustard 3
* Phenyldichloroarsine
* Phosgene oxime
* Sesqui mustard

2. Harassing agents

Riot control agents

a) Lachrymators-(tearing)       b) Sternutators(sneezing) / Vomiting

* CA
* CN
* CNB
* CNC
* CNS
* CS
* DA
* DC
* DM (Adamsite)

3. Incapacitating agents

a) Depressants

* Morphine

b) Psychedelic drugs

* Agent-15
* BZ
* Lysergic acid-25
* Mescaline (cactus)
* Phenylcyclidine
c) **Stimulants**

* Amphetamine
* Cocaine
* Dexamphetamine
* Methamphetamine

4. **Toxins**

* Aflatoxin
* Botulinus toxin
* Ricin
* Saxitoxin
* Trichothecene mycotoxin

"**War Gases**" are Seldom Gases

CW agents are frequently called war gases and a war where CW agents are used is usually called a gas war. These incorrect terms are a result of history. During the First World War use was made of chlorine and phosgene which are gases at room temperature and normal atmospheric pressure.

*The CW agents used today are only exceptionally gases. Normally they are liquids or solids. However, a certain amount of the substance is always in volatile form (the amount depending on how rapidly the substance evaporates) and the gas concentration may become poisonous.

*Both solid substances and liquids can also be dispersed in the air in atomized form, so-called aerosols. An aerosol can penetrate the body through the respiratory organs in the same way as a gas.
Some CW agents can also penetrate the skin. This mainly concerns liquids but in some cases also gases and aerosols. Solid substances penetrate the skin slowly unless they happen to be mixed with a suitable solvent.

Classification

Physical Properties

* volatile substances, which mainly contaminate the air.

* persistent substances, which are involatile and therefore mainly cover surfaces. In order to achieve good ground coverage when dispersed from a high altitude with persistent CW agents the dispersed droplets must be sufficiently large to ensure that they fall within the target area and do not get transported elsewhere by the wind. This can be achieved by dissolving polymers (e.g., polystyrene or rubber products) in the CW agent to make the product highly-viscous or thickened. The result will be that the persistence time and adhesive ability increase which thus complicates decontamination. Although it may appear that a CW agent can be "custom-made" for a certain purpose, this is not the case. Instead, there is always some uncertainty about the persistence time, the dispersal and the effect.

1. History-
OVERVIEW OF CHEMICAL AND BIOLOGICAL WARFARE

1. WWI - Modern chemical warfare began with the extensive use of chemical agents during World War I, initially with German use of industrial chemicals, such as chlorine and phosgene, and later use of agents tailored for military use such as the mustards. Their effects were impressive but not decisive, although Russia suffered enormous casualties from chemicals. All combatants made some use
of chemicals. There was considerable research on both agents and protective equipment.

2. **WWII** - World War II combatants possessed chemical and biological weapons. Although the agents were little used, other than Japan’s use of such weapons against China early in the war. The Germans did, however, use chemicals in their extermination centers. The reasons for nonuse were complex and went beyond simple mutual deterrence. The views of national political leaders, equipment and training of troops, assimilation of doctrine, perceived tactical or strategic advantage or vulnerability, operational readiness, existence of alternative means, and technical preparedness all were important factors. In several situations during the war, use of chemical or biologicals was very seriously considered, e.g., in the defense of the United Kingdom (UK) against invasion and in dealing with Japanese island defenses (Utgoff, 1998). Research and development activities were intense during the war, with Germany developing nerve agents and with biological warfare programs and weapon development in several other countries.

3. **COLD War** - During the tense Cold War, there was extensive research and development, and both sides deployed weapon systems. Both sides also spent considerable effort on improving defensive systems. During this period, there were sporadic reports of chemical and biological employment in remote regional conflicts.

4. **Post Cold War** - In the declining days of the Cold War, some regional powers, such as Iraq, Iran, and Libya, developed and employed chemical and perhaps biological weapons. Chemical and biological weapons are capable of use across a wide spectrum of warfare, from acts of assassination and small-scale terrorism to various tactical and operational situations, both defensive and offensive, including strategic population attacks. The technical and economic barriers to development and weaponization have decreased. Although a few chemical agents, such as phosgene, chlorine, and phosgene oxime, may degrade materials (corroding metals, degrading...
rubber), chemical and biological agents are primarily directed at humans and other living organisms and, unlike nuclear weapons, spare equipment and facilities.

1. Nerve Agents

Lethal organo-phosphorus compounds inhibiting cholinesterase

a) Effect Among lethal CW agents, the nerve agents have had an entirely dominant role since the Second World War. Nerve agents acquired their name because they affect the transmission of nerve impulses in the nervous system. All nerve agents belong chemically to the group of organo-phosphorus compounds. They are stable and easily dispersed, highly toxic and have rapid effects both when absorbed through the skin and via respiration. Nerve agents can be manufactured by means of fairly simple chemical techniques. The raw materials are inexpensive and generally readily available.

b) History It was not until the early 1930's that German chemists observed that organo-phosphorus compounds could be poisonous. In 1934, Dr Gerhard Schrader, a chemist at IG Farben, was given the task of developing a pesticide. Two years later a phosphorus compound with extremely high toxicity was produced for the first time. According to contemporary regulations, discoveries with implications had to be reported to the concerned authorities, which was also done with Schrader's discovery. This phosphorus compound, given the name tabun, was the first of the substances later referred to as nerve agents.

A factory for production of the new CW agent was built and a total of 12 000 tonnes of tabun were produced during the years 1942-1945. At the end of the war the Allies seized
large quantities of this nerve agent. Up to the end of the war, Schrader and his co-workers synthesized about 2,000 new organo-phosphorus compounds, including sarin (1938). The third of the "classic" nerve agents, soman, was first produced in 1944. These three nerve agents are known as G agents in the American nomenclature. The manufacture of sarin never started properly and up to 1945 only about 0.5 tonne of this nerve agent was produced in a pilot plant. Immediately after the war, research was mainly concentrated on studies of the mechanisms of the nerve agents in order to discover more effective forms of protection against these new CW agents. The results of these efforts led, however, not only to better forms of protection but also to new types of agents closely related to the earlier ones.

By the mid-1950's a group of more stable nerve agents had been developed, known as the V-agents in the American nomenclature. They are approximately ten-fold more poisonous than sarin and are thus among the most toxic substances ever synthesized. The first publication of these substances appeared in 1955. The authors, R. Ghosh and J.F. Newman, described one of the substances, known as Amiton, as being particularly effective against mites. At this time, intensive research was being devoted to the organo-phosphorus insecticides both in Europe and in the United States. At least three chemical firms appear to have independently discovered the remarkable toxicity of these phosphorus compounds during the years 1952-53. Surprisingly enough, some of these substances were available on the market as pesticides. Nonetheless, they were soon withdrawn owing to their considerable toxicity also to mammals.

In the United States, the choice fell in 1958 on a substance known by its code name VX as suitable as a CW agent of persistent type. Full-scale production of VX started in April 1961 but its structure was not published until 1972. Tabun was the first nerve agent to be discovered. Dr Gerhard Schrader came across it in 1937 through his research into pesticides based on organophosphorus bondings. Tabun belongs to the G(erman)-class of nerve agent. The word 'tabun' has no particular meaning and was reportedly made up by Dr Schrader to disguise the discovery. The first time Tabun or any other nerve agent was ever used in war was by Iraq against Iran in 1984. Subsequently, its use was confirmed repeatedly until the end of the war in 1988.
Sarin, developed in 1938, is the most toxic of the three G-agents made by Germany. Its name is derived from the names of the chemists involved in its creation: Schrader, Ambrose, Rüdiger and van der Linde. NATO adopted it as a standard chemical warfare agent in the early 1950s. Iraq used sarin in the 1980-88 war with Iran and had large stocks available in the 1990-91 Gulf War. The Japanese Aum Shinrikyo religious sect released an impure form of sarin in Matsumoto in 1994 and in the Tokyo underground in 1995.

d) Mechanism of Action

1. Nerve agents are extremely toxic and that they have very rapid effect.

2. Nerve agent, either as a gas, aerosol or liquid, enters the body through inhalation or through the skin. Poisoning may also occur through consumption of liquids or foods contaminated with nerve agents.

3. Route for entering the body is of importance for the period required for the nerve agent to start having effect. It also influences the symptoms developed and, to some extent, the sequence of the different symptoms. Generally, the poisoning works faster when the agent is absorbed through the respiratory system than via other routes. This is because the lungs contain numerous blood vessels and the inhaled nerve agent can therefore rapidly diffuse into the blood circulation and thus reach the target organs. Among these organs, the respiratory system is one of the most important. If a person is exposed to a high concentration of nerve agent, e.g., 200 mg sarin/m3 (see table) death may occur within a couple of minutes.

4. Poisoning takes longer when the nerve agent enters the body through the skin. Nerve agents are more or less fat-soluble and can penetrate the outer layers of the skin. However, it takes some time before the poison reaches the deeper blood vessels. Consequently, the first symptoms do not occur until 20-30 minutes after
the initial exposure but subsequently the poisoning process may be rapid if the total dose of nerve agent is high. The toxic effect of nerve agents depends on them becoming bound to an enzyme, acetylcholinesterase, and thereby inhibit this vital enzyme's normal biological activity in the cholinergic nervous system.

5. Mechanism of action- Nerve agents in general attack the nervous system of the human body. When a nerve receives a stimulus acetylcholine is released in order to carry the impulse to muscles and organs. Once the impulse has passed, the enzyme cholinesterase acts to prevent the accumulation of acetylcholine after its release in the nervous system. Nerve agents inhibit the functioning of cholinesterase, as a consequence of which the acetylcholine continues to act so that nervous impulses continue to be transmitted. The first symptoms a victim will experience following exposure to nerve agents are a runny nose, tightness in the chest and constriction of the pupils (miosis). The victim will then encounter difficulties breathing, drooling from the mouth and nausea. Because of the loss of control over bodily functions, vomiting, defecation and urination occurs. This phase is followed by twitching and jerking. Ultimately the victim will become comatose and will suffocate as a consequence of convulsive spasms.

Tabun is essentially absorbed through the skin, although vapours can also be hazardous. If a person does not receive an immediate lethal dose, death will occur after approximately 20 minutes. People who did not accumulate a lethal dose but did not receive immediate appropriate medical treatment may suffer permanent neurological damage.

d) Symptoms-

1. Low Dose- minor poisoning, characteristic symptoms are increased production of saliva, a running nose and a feeling of pressure on the chest. The pupil of the eye becomes contracted (miosis) which impairs night-vision. The accommodation capacity of the eye is also reduced so that short-range vision deteriorates and the victim feels pain when he tries to focus on an object nearby. This is accompanied
by headache. More unspecific symptoms are tiredness, slurred speech, hallucinations and nausea.

2. Moderate dose- symptoms are more pronounced. Broncho constriction and secretion of mucous in the respiratory system leads to difficulty in breathing and to coughing. Discomfort in the gastrointestinal tract may develop into cramp and vomiting. Involuntary discharge of urine and defecation may also form part of the picture. The discharge of saliva is powerful and the victim may experience running eyes and sweating. Symptoms from the skeletal muscles are very typical. If the poisoning is moderate, this may express itself as muscular weakness, local tremors or convulsions.

3. High Dose- the muscular symptoms are more pronounced. The victim may suffer convulsions and lose consciousness. To some extent, the poisoning process may be so rapid that earlier mentioned symptoms may never have time to develop. Muscular paralysis caused by nerve agents also affects the respiratory muscles. Nerve agents also affect the respiratory centre of the central nervous system. The combination of these two effects is the direct cause of death. Consequently, death caused by nerve agents is a kind of death by suffocation.

The figure shows examples of poisoning results caused by different doses of sarin vapour. In similarity to other poisons, different individuals are more or less sensitive to nerve agents. The figure shows that the lethal dose for the most sensitive individuals is about 70 mg.min/m3 and about twice this level for more resistant people.

The toxic effect depends on both the concentration of nerve agent in the air inhaled (C) and the time of exposure (t). In extremely high concentrations there is a simple relationship, C t, which gives a certain toxic effect. Inhalation of sarin vapour with a concentration of 100 mg/m3 for one minute gives the same result as inhalation of 50 mg/m3 for two minutes. However, at low concentrations this relationship does not apply since the human body is capable of some degree of detoxification. In order to obtain a
corresponding effect, it is then necessary to have relatively longer periods of exposure. The values given in the table for toxicity of nerve agents apply to high concentrations.

d) **Specific Agents**

1. **Tabun GA**: \((\text{CH}_3)_2\text{N-P(=O)(-CN)(-OC}_2\text{H}_5), \text{O-ethyl dimethylamidophosphorylcyanide, with the American denomination GA. This nerve agent is the easiest to manufacture. Consequently, it is more likely that developing countries start their CW arsenal with this nerve agent whereas industrialized countries consider tabun to be out-of-date and of limited use. Tabun is essentially absorbed through the skin, although vapours can also be hazardous. If a person does not receive an immediate lethal dose, death will occur after approximately 20 minutes. People who did not accumulate a lethal dose but did not receive immediate appropriate medical treatment may suffer permanent neurological damage.**

2. **Sarin, GB**: \(\text{CH}_3\text{-P(=O)(-F)(-OCH(CH}_3)_2\text{isopropyl methylphosphonofluoridate, with the American denomination GB, a volatile substance mainly taken up through inhalation. Sarin is a highly volatile liquid, so that inhalation as well as absorption through the skin pose a great threat. Even vapour concentrations will immediately penetrate the skin. Death may follow in one minute after direct ingestion of extremely low concentrations (0.01 mg per kg of body weight or higher). People who did not accumulate a lethal dose but did not receive immediate appropriate medical treatment may suffer permanent neurological damage.**

3. **Soman, GD**: \(\text{CH}_3\text{-P(=O)(-F)(-CH(CH}_3)_3\text{pinacolyl methylphosphonofluoridate, with the American denomination GD, a moderately volatile substance which can be taken up by inhalation or skin contact. Colourless liquid, which gives off an odour of rotting fruit when vaporizing. The vapour is colourless. The lethal dose for soman through inhalation is about half that of sarin. It is also a far more persistent agent than sarin so that it can easily remain in a particular area for a day or longer, depending on the atmospheric conditions.**
4. GF: CH₃-P(=O)(-F)(cyklo-C₆H₁₁)Cyclohexyl methylphosphonofluoridate, with the American denomination GF, a substance with low volatility which is taken up through skin contact and inhalation of the substance either as a gas or aerosol.
5. VX: CH₃-P(=O)(-SCH₂CH₂N(CH(CH₃)₂)₂)(-OC₂H₅) -ethyl S-diisopropylaminomethyl methylphosphonothiolate, better known under the American denomination VX, a persistent substance which can remain on material, equipment and terrain for long periods. Uptake is mainly through the skin but also through inhalation of the substance as a gas or aerosol.

3. Toxicity-

**Toxicity of the most important nerve agents to man**

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<tr>
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<th>LC₅₀</th>
<th>LD₅₀</th>
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<tr>
<td>Inhalation</td>
<td>mg.min/m³</td>
<td>mg/individual</td>
</tr>
<tr>
<td>Skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabun</td>
<td>200</td>
<td>4 000</td>
</tr>
<tr>
<td>Sarin</td>
<td>100</td>
<td>1700</td>
</tr>
<tr>
<td>Soman</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>VX</td>
<td>50</td>
<td>10</td>
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The values are estimates of the doses which have lethal effects on man. LD₅₀ expresses the dose at which 50 per cent of the exposed population will die as a result of their injuries. A different measure is used for inhalation, the product of the concentration (C) and the length of exposure (t). Again, L stands for lethal and ₅₀ for 50 per cent effect.
The toxicity sequence is the same for the two routes of exposure but the differences are much greater in skin exposure. This is mainly caused by the more volatile nerve agents evaporating from naked skin. If the evaporation is prevented, e.g., by tightly fitting clothing, the difference will be less.

The same type of phosphorus compounds are used as, for example, insecticides. In the structure of insecticides P(=O) has generally been replaced by P(=S) and a less reactive group than (-F), (-CN) or (-SCH2CH2N[CH(CH3)2]2) is used. All nerve agents in pure state are colourless liquids. Their volatility varies widely. The consistency of VX may be likened to an involatile oil and is therefore classified as belonging to the group of persistent CW agents. Its effect is mainly through direct contact with the skin. Sarin is at the opposite extreme, being an easily volatile liquid (comparable with, e.g., water), and mainly taken up through the respiratory organs. The volatilities of soman, tabun and GF are between those of sarin and VX.

By addition of a thickener it is possible for, e.g., soman, to be transferred from the category of volatile CW agents to the persistent agents.

Sarin is very soluble in water whereas other nerve agents are more sparingly soluble. VX has the unexpected property of being soluble in cold water but sparingly soluble in warm water (>9.5 oC).

The most important chemical reactions of nerve agents take place directly at the phosphorus atom. The P-X bond is easily broken by nucleophilic reagents, such as water or hydroxyl ions (alkali). In aqueous solution at neutral pH the nerve agents decompose slowly, whereas the reaction is greatly accelerated following the addition of alkali. The result is a non-toxic phosphoric acid.

The formation of the non-toxic phosphoric acid is also accelerated by rise in temperature or by a catalyst (e.g., hypochlorite ions from bleaching powder). This hydrolysis forms the basis of most decontamination procedures utilizing decomposition. In general, we may assume that an area exposed to G-agents decontaminates itself within a few days. However, V-agents may remain on the ground for several weeks because of their greater stability with respect to water and their much lower volatility. At pH-levels between 7
and 10 large quantities of VX are transformed into an extremely non-volatile product of hydrolysis which is incapable of penetrating skin. Admittedly, this is less toxic than VX but still implies a risk during decontamination. The nucleophilic attack on the phosphorous atom (P) also forms the basis of different types of colour reaction used in detecting nerve agents.

Agents were once released from pressurized cylinders, but contemporary delivery systems make substantial use of modified conventional bomb and shell systems, although spray tanks and bomblets designed for agent delivery are also used.

Iraqi forces had a variety of delivery systems available: toxin loads for Scud missiles; aircraft using bombs or spray tanks, including unmanned aircraft; and artillery-delivered systems using shells and free rockets. Chemical mines were theorized at the beginning of the war (although no such mines were found after the war). Although Saddam Hussein spoke of binary weapons, no such binary delivery systems have been reported since the war. In general, Iraq’s delivery systems were not sophisticated, e.g., Iraq used simple bursters in shells to dis-
Until the actual moment of use, the ammunition contains only relatively non-toxic initial substances. It is therefore considered to be safer to manufacture, store, transport and, finally, destroy. However, some critics question whether this practically untested type of new ammunition is reliable. The technique for mixing substances in bombs and rockets is complicated and requires space. The reaction has to be controlled (e.g., the temperature) and the process should preferably take place without solvents.

In 1991 Iraq declared to the United Nations Special Commission (UNSCOM) a different binary munitions concept. According to this the munitions were stored containing one component. Shortly before use the munitions were opened and the second component was added. Thus the reaction began even before the munitions were launched.

**Antidotes and Methods of Treatment**

1. **Injection**- Nerve agents have an extremely rapid effect. If medical methods of treatment are to serve any purpose, they must be introduced immediately. In many countries, the armed forces have access to an auto-injector containing antidotes to nerve agents. It is so simple to use that a person can inject him(her)self or another person without any difficulty.

Ex. Swedish auto injector-

Contains two active components: HI-6 (500 mg) and atropine

a) **HI-6** (500 mg) HI-6 is an oxime which directly reacts with the cause of the injury, i.e., nerve agent-inhibited acetylcholinesterase. HI-6 functions as a reactivator which restores the enzyme to an operational condition. Oximes have a poor penetration capacity into the brain and thus mainly work in the peripheral nervous system.

The various nerve agents cause poisoning which are more or less easy to treat with oximes. From this standpoint, VX and sarin are the easiest to treat and all oximes used increase the chances of surviving poisoning with these nerve agents. Obidoxime is the most effective against tabun poisoning but also HI-6 has
a positive effect. Soman causes the most difficultly treated poisoning and can only be treated with HI-6.

Soman poisoning is complicated by the inhibited enzyme going through an "ageing" process. Following the ageing the enzyme cannot be reactivated by any oxime. It is possible that HI-6 has some further positive antidote effect in addition to its reactivating ability.

b) **Atropine** is the classical antidote in cases of poisoning by organo-phosphorus compounds. It is a medication which relieves the symptoms but does not attack the cause of the injury. Atropine becomes bound to the receptors for acetylcholine, which are present in the cholinergic synapse (see figure). When acetylcholine is bound, the signal is transmitted but if atropine has become bound to the receptor, then no such transmission takes place. Atropine thus gives protection against the excess of acetylcholine which results from inhibition of acetylcholinesterase. Atropine has effects only within certain parts of the cholinergic nervous system.

There are two types of acetylcholine receptors, the nicotinic which are found, e.g., in the skeletal muscles, and the muscarinic, which are found in, e.g., smooth muscles, glands and the central nervous system. Atropine blocks the muscarinic receptors. Atropine and oxime may therefore be considered to complement each other and the two antidotes also have a synergetic effect, i.e., they boost each other.

An additional auto-injector can be given to victims of nerve agents if their situation does not improve within ten minutes. Subsequently, the victim should be treated by qualified medical staff who should initially inject additional atropine and an anti-convulsant drug, diazepam. In cases of severe poisoning by nerve agents, large doses of atropine (grammes) may be required. The level of operational acetylcholinesterase is gradually restored by the body's own production but this process requires at least two weeks. During this period, and possibly also later, the victim may require medical care not only for mental disorders such as difficulty in sleeping, amnesia, difficulties in concentrating, and anxiety, but also for muscular weakness. Mental problems may also occur after long exposure to extremely low concentrations to nerve agents.
There are also medical antidotes which can be taken preventively. These antidotes are taken as tablets and used when ordered in connection with maximum C-preparedness. One of the tablets contains a carbamate, pyridostigmine, as active ingredient. Pyridostigmine inhibits acetylcholinesterase and protects the enzyme against inhibitory effects of nerve agents. The dose is low and leads to about 25 per cent inhibition. The pyridostigmine-inhibited enzyme is continuously released to active state and thereby can reasonably effectively maintain the transfer of nerve impulses despite injury caused by nerve agents. The effect is restricted to the peripheral cholinergic nervous system since the substance does not enter the brain.

Pyridostigmine does not cause any side effects since there is a large excess of enzyme in the cholinergic synapse. In actual fact, 1-2 per cent of functional enzyme is sufficient to have a functioning synapse. This explains why carbamate pretreatment has such good effect.

Pretreatment with carbamate should be combined with oxime therapy (the auto-injector) after the poisoning in order to provide maximum effect. This combination reduces the toxic effects of all nerve agents. A diazepam tablet is also generally given as a pretreatment, primarily affecting the central nervous system. Diazepam strengthens the effect of other nerve agent antidotes. There will be better prospects of survival and less injury. Diazepam also provides protection against permanent brain damage which may result from heavy exposure to nerve agents.

Pretreatment has best effect if a warning system is available and operative, since the tablets need about 30 min. to have effect after being swallowed. The best protective effect is achieved after about two hours, which is followed by decreasing efficacy. If the situation so requires, treatment can be repeated at eight-hourly intervals for some days. The tablets should not be taken once nerve agent injury has occurred. Admittedly, diazepam has a positive effect but pyridostigmine at that stage will aggravate the injury.

**Mustard Agents**
An overview of the sulfur and nitrogen mustard agents

Mustard Agents

Source: A FOA Briefing Book on Chemical Weapons

Mustard agents are usually classified as "blistering agents" owing to the similarity of the wounds caused by these substances resembling burns and blisters. However, since mustard agents also cause severe damage to the eyes, respiratory system and internal organs, they should preferably be described as "blistering and tissue-injuring agents". Normal mustard agent, bis-(2-chloroethyl)sulphide, reacts with a large number of biological molecules. The effect of mustard agent is delayed and the first symptoms do not occur until 2-24 hours after exposure.

Mustard agent was produced for the first time in 1822 but its harmful effects were not discovered until 1860. Mustard agent was first used as a CW agent during the latter part of the First World War and caused lung and eye injuries to a very large number of soldiers. Many of them still suffered pain 30-40 years after they had been exposed, mainly as a result of injuries to the eyes and chronic respiratory disorders.

During the war between Iran and Iraq in 1979-88, Iraq used large quantities of chemical agents. About 5 000 Iranian soldiers have been reported killed, 10-20 per cent by mustard agent. In addition, there were 40 000 to 50 000 injured. A typical result of warfare with mustard agent is that the medical system is overloaded with numerous victims who require long and demanding care.

One of the Iranian soldiers who were treated for mustard agent burns in a Swedish hospital. The photo, taken several weeks after exposure, shows extensive injury, which is now starting to heal.
Incidents are still occurring annually in the neighbourhood of Sweden where people risk injury from mustard agent. This largely involves fishermen who are exposed to mustard agent brought to the surface by fishing nets. The background is found in the dumping of chemical weapons after the Second World War in waters off the Danish and Swedish coasts. Many fishing ports in south Sweden and Denmark have resources to care for injured people and to decontaminate equipment contaminated by mustard agent. Certain resources are also available on the fishing vessels.

Mustard agent is very simple to manufacture and can therefore be a "first choice" when a country decides to build up a capacity for chemical warfare.

Apart from mustard agent, there are also several other closely related compounds which have been used as chemical weapons. During the 1930's, several reports were published on the synthesis of nitrogen mustard agent and its remarkable blistering effect. The mechanism of action and symptoms largely agree with those described for mustard agent. Germans and Americans started the military production of nitrogen mustard agent in 1941 and 1943, respectively, whereas the development in England was abandoned following an explosion. There is no verified use of nitrogen mustard agents as chemical weapons and their usefulness is restricted by these types of agents being unsuitable for storage.

**Physical and Chemical Properties**

In its pure state, mustard agent is colourless and almost odourless. The name was given to mustard agent as a result of an earlier production method which yielded an impure mustard-smelling product. Mustard agent is also claimed to have a characteristic smell similar to rotten onions. However, the sense of smell is dulled after only a few breaths so that the smell can no longer be distinguished. In addition, mustard agent can cause injury
to the respiratory system in concentrations which are so low that the human sense of smell cannot distinguish them.

At room temperature, mustard agent is a liquid with low volatility and is very stable during storage. The melting-point for pure mustard agent is 14.4 oC. In order to be able to effectively use mustard agent at lower temperatures, it has been mixed with lewisite in some types of ammunition in a ratio of 2:3. This mixture has a freezing-point of -26 oC.

During the Second World War, a form of mustard agent with high viscosity was manufactured by means of the addition of a polymer. This is the first known example of a thickened CW agent.

Mustard agent can easily be dissolved in most organic solvents but has poor solubility in water. In aqueous solutions, mustard agent decomposes into non-poisonous products by means of hydrolysis. This reaction is catalyzed by alkali. However, only dissolved mustard agent reacts, which means that the decomposition proceeds very slowly. Bleaching-powder and chloramines, however, react violently with mustard agent, whereupon non-poisonous oxidation products are formed. Consequently, these substances are used for the decontamination of mustard agent.

Mechanism of Action

The toxic effects of mustard agent depend on its ability to covalently bind to other substances. The chlorine atom is spiked off the ethyl group and the mustard agent is transferred to a reactive sulphonium ion. This ion can bind to a large number of different biological molecules. Most of all it binds to nucleophiles such as nitrogen in the base components of nucleic acids and sulphur in SH-groups in proteins and peptides. Since mustard agent contains two "reactive groups", it can also form a bridge between or within molecules. Mustard agent can destroy a large number of different substances in the cell by means of alkylation and thereby influence numerous processes in living tissue.

Symptoms
In the form of gas or liquid, mustard agent attacks the skin, eyes, lungs and gastrointestinal tract. Internal organs may also be injured, mainly blood-generating organs, as a result of mustard agent being taken up through the skin or lungs and transported into the body. The delayed effect is a characteristic of mustard agent. Mustard agent gives no immediate symptoms upon contact and consequently a delay of between two and twenty-four hours may occur before pain is felt and the victim becomes aware of what has happened. By then cell damage has already been caused.

Symptoms of mustard agent poisoning extend over a wide range. Mild injuries consist of aching eyes with abundant flow of tears, inflammation of the skin, irritation of the mucous membrane, hoarseness, coughing and sneezing. Normally, these injuries do not require medical treatment. Severe injuries which are incapacitating and require medical care may involve eye injuries with loss of sight, the formation of blisters on the skin, nausea, vomiting and diarrhoea together with severe respiration difficulty.

*A Baltic fisherman with a relatively fresh mustard agent injury. The photo was taken at Bornholm Hospital, Denmark, by Dr. Steen Christensen.*

Acute mortality arising from exposure to mustard agent is low. The dose needed to directly kill a person upon inhalation is, e.g., about 50 times larger than the dose giving acute mortality upon poisoning with the nerve agent soman. People who die after exposure to mustard agent usually do so after a few days up to one or more weeks.
Minor skin damage may be caused by mustard agent in the gaseous state whereas the most severe injuries are caused after contact with liquid mustard agent. Skin damage first appears as a painful inflammation. Depending on the level of exposure, the injury may develop into pigmentation, which flakes-off after a couple of weeks, small surface blisters or deep liquid-filled blisters with subsequent skin necrosis. In extreme cases, the skin necrosis may be so comprehensive that no blisters occur. Skin injuries are more severe in humid and warm climates. Similarly, the injuries will be more severe where the skin is moist and warm, e.g., in the groin and armpits.

Experience has shown that even extremely extensive skin damage, 80-90 %, can be cured if the patient is kept free of infection. However, injuries to the skin require a very long period of recuperation, much longer than thermal burns, and may require care and plastic surgery over a period of several months.

Injury to the eyes appear initially as irritation with eye inflammation and a strong flow of tears. Depending on exposure, the symptoms thereafter may successively develop to sensitivity to light, swollen eyelids, and injury to the cornea. Severe damage to the eye may lead to the total loss of vision. Victims suffering damage to the eyes may encounter problems persisting up to 30-40 years following exposure.

The most common cause of death as a result of mustard agent poisoning is complications after lung injury caused by inhalation of mustard agent. Lung injuries become apparent some hours after exposure and will first appear as a pressure across the chest, sneezing and hoarseness. Severe coughing and respiration difficulties caused by pulmonary oedema will gradually occur and after a couple of days, a "chemical pneumonia" may develop. Most of the chronic and late effects are also caused by lung injuries.

The effect on inner organs which is most pronounced is injury to the bone marrow, spleen and lymphatic tissue. This may cause a drastic reduction in the number of white blood cells 5-10 days after exposure, a condition very similar to that after exposure to radiation. This reduction of the immune defence will complicate the already large risk of infection in people with severe skin and lung injuries.

**Antidotes and Methods of Treatment**
There is no treatment or antidote which can affect the basic cause of mustard agent injury. Instead, efforts must be made to treat the symptoms. By far the most important measure is to rapidly and thoroughly decontaminate the patient and thereby prevent further exposure. This decontamination will also decrease the risk of exposure to staff. Clothes are removed, the skin is decontaminated with a suitable decontaminant and washed with soap and water. If hair is suspected to be contaminated then it must be shaved off. Eyes are rinsed with water or a physiological salt solution for at least five minutes.

In medical treatment, efforts are made to control infections by means of antibiotics. Pain can be eased by local anesthetics. After skin injuries have healed, it may be necessary to introduce plastic surgery. Lung injuries are treated with bronchiodilatory treatment. Medicine to relieve coughing and also cortisone preparations may be used. Eye injuries are treated locally with painkillers and with antibiotics if required. Despite treatment, inflammation and light sensitivity may remain for long periods.

Modern knowledge on the mechanisms behind mustard agent injuries may lead mainly to new ways of treatment. The first step, alkylation, takes place extremely rapidly and is probably very difficult to influence. Future treatment may concentrate on suppressing and alleviating the development of symptoms and thereby improve the opportunities for good recovery.

Types of Injury Caused by Mustard Agent

It is impossible to identify a single mechanism for the damage caused by mustard agent. However, two possible important mechanisms can be mentioned where the first step in both is the formation of a reactive sulphonium ion. One such mechanism is the bonding of mustard agent to the base compounds in DNA (alkylation). The bonding may induce breakages of strands and the formation of bridges between the two strands in the DNA molecule. Bridges of this kind prevent DNA from functioning normally during cell
division which may lead to severe injury and possibly cell mortality. Damage to the DNA may also lead to mutations and disturbance to the natural repair mechanisms of DNA. The influence on DNA can cause the increased frequency of cancer observed after exposure to mustard agent.

The other mechanism of action is interaction between mustard agent and intracellular glutathion. Glutathion is a small peptide molecule which, among other things, takes care of the free radicals formed during cell respiration. If too large an amount of glutathion is bound by mustard agent, then the regulation of these free radicals no longer functions. Since free radicals are extremely toxic, this may lead to a number of processes in the cell being severely disturbed.

Mustard agent can also bind to different proteins in the cell. However, it is not known how much this contributes to the injuries caused. The binding takes place at the functional groups, e.g., the sulphhydryl or amino groups. If the binding is made to, for example, the active site of enzymes, then their activity is inhibited which could lead to metabolic disorders. If, on the other hand, membrane proteins are bound, the result can be a modified uptake of substances and the inner environment of the cell will become disturbed.

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Physical Properties of Mustard Agent

Molecular weight, Dalton  159.1
Density, g/cm3  1.27
Boiling-point oC  217
Melting-point oC  14
Vapour pressure mm Hg at 25 oC  0.11
Volatility mg/m3 at 25 oC  900
Solubility in water % at 20 oC  0.06

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Toxicity of Mustard Agent

Inhalation: LC50 1 500 mg*min/m3
Skin exposure: LC50 10 000 mg*min/m3
Smallest blister-causing dose on skin: 0,02 mg

Psychotomimetic Chemical Weapons

An overview of chemical weapons acting on the mind

Source: A FOA Briefing Book on Chemical Weapons
This group of agents usually includes substances which, when administered in low doses (<10 mg) cause conditions similar to psychotic disorders or other symptoms emanating from the central nervous system (loss of feeling, paralysis, rigidity, etc.). The effects are transitory and cause inability to make decisions and incapacitation. Several such substances may be used to achieve these objectives and only a few examples are given here.
During the 1950's, studies were made of substances such as glycolic acid esters (glycolates). Particular interest was paid to 3-quinuclidinylbenzilate, BZ. The effects of this group of substances are similar to those caused by atropine. BZ causes poisoning at doses of 0.5-5 mg. Peripheral symptoms such as distended pupils, deteriorated short-distance vision, dry mouth and palpitations occur after about 30 minutes.
A serious effect of poisoning with BZ, as also with other atropine-like substances, is an increased body temperature. Deterioration in the level of consciousness, hallucinations and coma occur subsequently. Incapacitating after-effects may remain 1-3 weeks after the poisoning. Since the effect of glycolates was found to be difficult to predict, interest in continued research into this type of substance gradually decreased.
Phencyclidine is a substance with analgetic and anaesthetic properties. Symptoms such as disturbed body-awareness, disorientation and vivid dreams occur. These symptoms occur after some hours at doses of 5-20 mg. At very high doses (>100 mg) there is a major risk
for, e.g., respiratory depression and death. Phencyclidine is widely used by drug addicts who drench tobacco in this substance and then inhale it when smoking. Phencyclidine is easy to produce.

LSD is probably one of the most active of all known substances having psychotomimetic effects. However, its chemical stability is very low and it is probably of little use as a CW agent. Nonetheless, there are other chemical substances with effects similar to LSD. These substances are chemically similar to amphetamine and are also stable. Theoretically, this type of substance could be used as a CW agent in special circumstances and dispersed as an aerosol.

**Toxins**

**Potential chemical weapons from living organisms**

*Source: A FOA Briefing Book on Chemical Weapons.*

Toxins are effective and specific poisons produced by living organisms. They usually consist of an amino acid chain which can vary in molecular weight between a couple of hundred (peptides) and one hundred thousand (proteins). They may also be low-molecular organic compounds. Toxins are produced by numerous organisms, e.g., bacteria, fungi, algae and plants. Many of them are extremely poisonous, with a toxicity that is several orders of magnitude greater than the nerve agents.

Toxins started to attract military interest already during the first half of the present century. At that time, it was difficult to manufacture sufficiently large amounts of toxin which caused interest to decrease. Many of the toxins discussed at that time were sensitive to heat and light which made them unstable and unpractical to use. The U.S.A. ended its toxin programme in the late 1960's and destroyed its stockpile of, e.g., botulinum toxin.

The Biological and Toxin Weapons Convention of 1972 prohibits the development, production and stockpiling of toxins as weapons. The 1925 Geneva Protocol prohibition
of use of chemical and bacteriological weapons also covers the use of weapons based on
Toxins. Since the definition of chemical weapons includes toxins they are also covered by
the Chemical Weapons Convention.

Delivery-
Toxins are still considered to be less suitable for dispersal on a large scale.
Nonetheless, they could be used for sabotage or in especially designed inputs,
e.g., against key persons. Since toxins have low volatility, they are dispersed as
aerosols and then taken up foremost through inhalation. The new
microencapsulation technology, which is easy to use, makes it possible to protect
unstable toxins when dispersed.

Decontamination-
Most toxins are unstable in alkaline water solutions and are thus easily
destroyed by means of normal decontamination methods.

Emerging technology
In the late 1970's, there was a rapid development of gene technology together
with biotechnology. This led to the threat from toxins as CW agents again arising. Now it
became possible to produce greater amounts of many toxins more easily, in some cases
even synthetically. Gene technology can be used to modify the toxin genes so that the end
product obtains new properties and, for example, may become less sensitive to sunlight.
Together with increased research into toxins, the bioregulators have also been studied and
synthesized. Bioregulators are naturally-occurring substances, usually peptides, which
participate in the physiological and neurological activities of the body. These substances
can also be modified synthetically, whereupon they may obtain new properties.
The scientific and commercial development have together provided increased
opportunities to incorrectly utilize biotechnology for military purposes. Recent research,
for example, has made it possible to "target" toxins to different body organs or structures.
This new knowledge mainly emanates from civilian research into, e.g., the treatment of
cancer patients.

Examples-
A few examples of toxins which may be used as chemical warfare agents are listed below. The trichothecenes, mycotoxins obtained from, e.g., *Fusarium* genera, were alleged in the early 1980's to have been used as CW agents in Southeast Asia ("yellow rain"), but are of no military value today.

1. Bacterial Toxins

   Botulinum toxin, produced by the bacteria *Clostridium botulinum*, is the most poisonous substance known. The bacteria grows on, e.g., poorly preserved food and causes a severe form of food-poisoning (botulism). The incubation period is between one and three days after which the victim becomes ill with stomach pains, diarrhoea, disturbances to vision, giddiness and muscular weakness. The whole body including the respiratory musculature becomes paralyzed which leads to death by suffocation within a few days.

   The toxin is a protein available in seven different forms, where the most poisonous is type A (molecular weight = 150,000 D). The lethal dose to man has been estimated to about one microgram if ingested and even less if inhaled. It is possible to vaccinate against botulism but once the victim has become poisoned there is no antidote. Botulinum toxin is today commercially produced and is used in treating squinting and other muscular disorders.

2. *Staphylococcus enterotoxin type B* (SEB)

   Not all toxins have a lethal outcome. One of those classified in the incapacitating group is Staphylococcus enterotoxin type B (SEB), which is produced by *Staphylococcus aureus* bacteria. SEB is the toxin which is most commonly found to have caused food poisoning.

   SEB is a protein (molecular weight = 28,500 D), which is easily soluble in water and relatively stable. It can withstand boiling for a couple of minutes and when in freeze-dried state, it can be stored for more than one year. Persons exposed to SEB (20-25 g) fall ill after a few hours with typical food poisoning symptoms, such as stomach cramp, diarrhoea and vomiting. The sufferer frequently recovers without special treatment within 24 h.
Plant Toxins

1. ricin

The seeds of the castor oil plant can be used to extract a mixture of poisonous proteins, ricin. One of these has also been produced by *Escherichia coli* bacteria to which the ricin gene has been transferred.

Ricin became of interest as a CW agent at an early stage as it is relatively easy to produce in large quantities. In 1978, it was used in the "umbrella murder" in London where a ricin-treated bullet was used to shoot a Bulgarian defector who died within a day. Ricin is now included in Schedule 1 of the Chemical Weapons Convention.

Ricin poisoning occurs through blockages of the body's synthesis of proteins. The development is slow and includes decreased blood pressure. Death frequently occurs through heart failure.

Ricin has approximately the same toxicity as saxitoxin. Different forms of ricin bound to, e.g., monoclonal antibodies are being studied today in order to treat leukaemia and cancer of the liver.

2. saxitoxin - synthesized by a type of blue-green algae

Many toxins are produced by marine organisms. One such example is saxitoxin, which is synthesized by a type of blue-green algae (cyanobacteria). These algae provide food for different shellfish, e.g., mussels. The mussels themselves are not influenced by the poison, but human beings who later eat the mussels may become seriously ill.

Saxitoxin attacks the nervous system and has a paralyzing effect, but causes no symptoms in the gastro-intestinal tract. The development of the illness is extremely rapid and at high doses death may occur within less than 15 minutes. The LD50 for man is at about 1 mg. Saxitoxin is a small molecule with a molecular weight of 370 D. It is not sensitive to heat but is destroyed by oxygen.
Saxitoxin is included in Schedule 1 of the Chemical Weapons Convention.

**Bioregulators**

During recent years, discussions have started on the risk of bioregulators being used as CW agents. These types of substances do not belong to the group of toxins but are, nonetheless, grouped with them since their possible use is similar. They are closely related to substances normally found in the body and may be algogenic (causing pain), anaesthetic, or influencing blood pressure. A characteristic of them is that they are active in extremely low doses and frequently have rapid effect. One example of this group of substances is Substance P, a polypeptide (molecular weight = 1,350 D) which is active in doses of less than one microgramme. Substance P causes, for example, a rapid loss of blood pressure which may cause unconsciousness.