# NATO HANDBOOK ON THE MEDICAL ASPECTS OF NBC DEFENSIVE OPERATIONS AMedP-6(B)

## PART III - CHEMICAL

**1 FEBRUARY 1996**

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# CHAPTER 1

# INTRODUCTION

## 101. Definition.

The NATO definition of a chemical agent is: A chemical substance which is intended for use in military operations to kill, seriously injure or incapacitate people because of its physiological effects. Excluded from this definition are riot control agents, herbicides, smoke and flame. Structural formulae and physical properties of some of the more important compounds are shown in figures and tables in the appropriate chapters. Brief consideration of riot control agents, herbicides and smoke and flame materials are also included in this text. It must be remembered that possible new agents are constantly being discovered, and also, that some chemical agents may be used together as a mixture. Toxins are discussed in AMedP-6(B), Part II. From the medical standpoint, toxins could pose similar problems to those produced by chemical agents. By constant vigilance on the part of all medical personnel in looking for new or unexpected syndromes, and by prompt reporting of any suspicious event, the use of new or mixed agents can be discovered.

## 102. Historical.

a. Chemical agents in the modem sense were first used in World War I, when chlorine gas was released, from large cylinders, in a favorable wind. This surprise operation caused massive casualties, demoralisation of the forces attacked and demonstrated the need for protection from this kind of warfare. The first improvised mask was a cotton pad soaked in sodium thiosulphate, glycerine and sodium carbonate. Subsequently in World War I, a great variety of chemical agents were used by both sides, the most damaging being the blister producing mustard gas. Military clothing, even with a respirator, gave little protection against this agent. Chemical agents were not used in World War II, but at the end of the war stockpiles of newer agents, called “nerve gases,” were discovered. These were found to be effective in much lower concentrations than those agents known up to that time. The standard of training and preparedness of the Services and the fear of retaliation were possible reasons why chemical agents were not used.

b. Between World Wars I and II, mustard gas was used with considerable effect against unprotected troops. Since World War II, there have been several confirmed reports that chemical agents have been used in armed conflicts including the Iran-Iraq conflict.

c. Riot control agents such as CS (tear agent) have been used repeatedly, for example, in South-East Asia to support tactical operations: in particular to flush out guerrillas from hiding and to render places of concealment untenable. These compounds and other tear agents are frequently used as riot control agents by police forces.

d. The advent of nuclear weapons and the fact that chemical agents were not used in World War II did not prevent their use in recent conflicts and do not exclude the possibility of their use in a future war. The effectiveness of chemical agents as tactical weapons was clearly demonstrated in World War I and in the Iran-Iraq conflict. They can equally affect both forward and rear areas. It seems probable that

the nature and severity of casualties may differ in future from those recorded in World War I.

## 103. General Factors Influencing the Employment and Choice of Chemical Agents.

a. The effective use of any chemical agent is dependent on its physical and chemical properties and on meteorological conditions.

(1) *Persistency*. Chemical agents may be divided into two main categories as follows: Non-persistent and persistent agents.

(a) Non-persistent agents disperse rapidly after release and present an immediate, short duration hazard. They are released as airborne particles, liquids and gases, and intoxication usually results from inhalation.

(b) Persistent agents continue to present a hazard for considerable periods after delivery by remaining as contact hazard or by vaporizing over a period to produce a hazard by inhalation. Non-persistent agents may be made persistent by thickening.

(2) *Effectiveness*. Effectiveness is the capacity of an agent to produce the maximum number of casualties or amount of disruption of operations with the least amount of agent, although other tactical criteria may be used to gauge this effectiveness. "Effectiveness" is a general term which takes in such criteria as suitability, toxicity, irritancy, etc. For instance, of two similar volatile toxic agents, the one which is toxic at a lower dose can be said to be more effective. Similarly, of two irritant compounds, the one which is irritant at a lower dose can be said to be the more effective. Effectiveness is also dependent on the ability of the population attacked to neutralise or counter the effects of agents once they have been delivered. The duration of effectiveness depends on the physical characteristics of the agent, the amount of agent delivered, the weapon system used and the terrain and weather in the target area at the time the agent is delivered and later.

b. The following meteorological factors will influence the duration of effectiveness of chemical agents:

(1) *Winds*. The effect of wind is to disperse agents rapidly in open country. However, dangerous concentrations may remain longer in woods, trenches, dug-outs and built-up areas.

(2) *Temperature*. High temperatures decrease the persistency of agents and cause higher vapour concentrations. Low temperatures increase the persistency of agents. Some agents may freeze thus reducing the immediate contact hazard. There is a danger of carrying such frozen agents on clothing and equipment into a warm building with the subsequent risk of toxic vapour being given off.

(3) *Rain*. Rain disposes, dilutes and promotes hydrolysis of agents. This reduces their effectiveness but does not make them impossible to use.

(4) *Atmospheric Stability*. When the air temperature is higher than that at ground level (a state of inversion), agents in the vapour state will persist for longer periods than when the air temperature is lower than that at ground level (a state of lapse).

## 104. Characteristics.

a. *Physical.* Known agents cover the whole range of physical properties. Under ambient conditions their physical state may be gaseous, liquid or solid. Their vapour pressures vary from high to negligible. Their vapour densities vary from slightly lighter to considerably heavier than air. The range of odours varies from none to highly pungent or characteristic. They may be soluble or insoluble in water. In the following chapters the physical properties of various agents are given in tables in the appropriate chapter. These may give an indication of the behaviour of the agents in the field with regard to vapour hazard, persistency and possible means of decontamination, etc. Agents with a low boiling point and high vapour pressure tend to be non-persistent. Agents with a high boiling point and low volatility tend to be more persistent.

b. *Chemical.* The only general characteristic of the known agents is that they are sufficiently stable to survive dissemination and transport to the site of their biological action. Their inherent reactivity and stability can vary widely. Some chemically reactive agents denature rapidly, whereas other less reactive agents require, for example, bleach solutions to inactivate them. Solid absorbents (e.g., fullers' earth) are very effective decontaminants but do not denature agents and the potential for off-gassing should be recognised.

c. *Toxicological.*

(1) It should be realised that not all individuals of a species react in the same way to a given amount of agent, some being more or less sensitive as a result of many factors, of which genetic background, race and age are examples. Also, toxicological studies estimate the biological effects of potential agents by different routes of exposure. The physical properties of such materials may affect the toxicological studies since the response of the biological system concerned may vary depending on the physical state of the material.

(2) Studies of the mode of action are related to the development of medical countermeasures and physical protection devices.

## 105. Terminology.

The terminology used in this manual is as follows:

a. *Dose.* The dose is the quantity of the compound received by the subject.

b. $LD_{50}$. The LD (lethal dose)$_{50}$ is the dose which kills 5070 of the exposed population.

c. $ID_{50}$. The ID (incapacitating dose)$_{50}$ is the dose which incapacitates 50% of the exposed population.

d. *Ct (Concentration time).* The Ct is a measure of exposure to a vapour or aerosol. The concentration in the air and the time of exposure govern the dose received, as does rate of respiration. It is assumed that, when the product of concentration and time is constant, so is the biological effect over a limited range of concentration and time. For very short or long exposures the biological effect may vary. Concentration is expressed as $mg.m^{-3}$ and time as minutes, so that the concentration time (Ct) is expressed as $mg.min.m^{-3}$.

e. $LCt_{50}$: The LCt (lethal concentration time)$_{50}$ is the Ct which will kill 50% of the exposed population.

f. $ICt_{50}$: The ICt (incapacitating concentration time)$_{50}$ is the Ct which will incapacitate 50% of the exposed population.

## 106. Routes of Absorption.

Chemical agents may enter the body by several routes and the nature and onset of signs and symptoms may vary accordingly. Gases, vapours and aerosols, when inhaled, may be absorbed through any part of the respiratory tract, from the mucosa of the nose and mouth to the alveoli of the lungs. They may also be directly absorbed by the eye. Aerosol particles larger than 5 µm tend to be retained in the upper respiratory tract, while those smaller than 1 µm tend to be breathed in and out again, although some of these smaller particles may be retained. Droplets of liquid and, less commonly, solid particles may be absorbed through the surface of the skin and mucous membranes. Toxic compounds with a characteristic action on the skin can produce their effects when deposited on the skin as solid or liquid particles. Agents which penetrate the skin may form temporary reservoirs so that delayed absorption may occur. Even the vapour of some volatile agents can penetrate the intact skin and intoxication may follow. Wounds or abrasions (even minor injuries caused by shaving or by chemical depilation) present areas which are more permeable than intact skin. Chemical agents may contaminate food and drink and so be absorbed by the gastrointestinal tract. The penetration of agents by these various routes may not be accompanied by irritation or damage to the surfaces concerned.

# CHAPTER 2

# NERVE AGENTS

## SECTION I - GENERAL

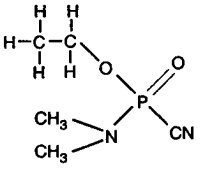
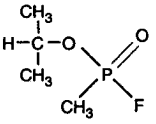
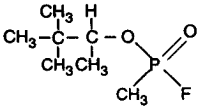
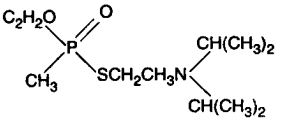
### 201. Introduction.

The nerve agents (NA) are a group of particularly toxic chemical warfare agents. They were developed just before and during World War II and are related chemically to the organophosphorus insecticides. The principle agents in this group are: GA (Tabun), GB (Sarin), GD (Soman), GF and VX (methylphosphonothioic acid). (In some countries the "V" agents are known as "A" agents.)

### 202. Physical and Chemical Properties.

a. Nerve agents are organophosphorus esters. The "G' agents tend to be non-persistent whereas the "V" agents are persistent. Some "G' agents may be thickened with various substances in order to increase their persistence, and therefore the total amount penetrating intact skin. The physical properties are given in Table 2-I.

*Table 2-I. Physical Properties of Nerve Agents*

| Property | Tabun (GA) | Sarin (GB) | Soman (GD) | VX |
|---|---|---|---|---|
| Appearance | Colourless to brown liquid giving off colourless vapour | Colourless liquid giving off a colorless vapour | Colourless liquid giving off a colourless vapour | Amber coloured liquid |
| Chemical formula |  |  |  |  |
| Molecular weight | 162.12 | 140.10 | 182.2 | 267.4 |
| Density ($g.cm^{-3}$ at 25°C) | 1.07 | 1.09 | 1.02 | 1.01 |
| Melting point | -50.0°C | -57.0°C | -42.0°C | -51.0°C |
| Boiling point | 240.0°C | 147.0°C | 198.0°C | 298.0°C |
| Vapour density | 5.63 | 4.86 | 6.33 | 9.2 |
| Vapour pressure (mmHg at 25°C) | 0.07 | 2.9 | 0.4 | 0.007 |
| Volatility ($mg.m^{-3}$) | 90 (0°C)<br>610 (25°C)<br>858 (30°C) | 4,100 (0°C)<br>22,000 (25°C)<br>29,800 (30°C) | 531 (0°C)<br>3,900 (25°C)<br>5,570 (30°C) | 10.5 (25°C) |

b. It may be seen that at room temperature GB is a comparatively volatile liquid and therefore non-persistent. GD is also significantly volatile, as is GA though to a lesser extent. VX is a relatively non-volatile liquid and therefore persistent. It is regarded as presenting little vapour hazard to people exposed to it. In the pure state nerve agents are colorless and mobile liquids. In an impure state nerve agents may be encountered as yellowish to brown liquids. Some nerve agents have a faint fruity odour.

c. In general, nerve agents are moderately soluble in water with slow hydrolysis, highly soluble in lipids, rapidly inactivated by strong alkalis and chlorinating compounds.

## 203. Detection.

Nerve agents may be detected by a variety of means. Single and three colour detector papers are available for individual issue to detect liquid nerve agent. Area detectors are also available as are monitoring devices for local contamination and water testing kits.

## 204. Protection.

a. To prevent inhalation of an incapacitating or lethal dose it is essential that the breath is held and the respirator put on at the first warning of the presence, or suspected presence, of a nerve agent.

b. Normal clothing is penetrated by these agents whether contact is with liquid or vapour and specialised clothing including a respirator, nuclear, biological, and chemical (NBC) suit, gloves and overboots are required for protection when liquid agent is present. The respirator protects the eyes, mouth and respiratory tract against nerve agent spray vapour and aerosol. Nerve agent vapour in field concentrations is absorbed through the skin very slowly, if at all, so that where a vapour hazard exists alone, the respirator may provide adequate protection without the use of an NBC suit.

## 205. Decontamination.

a. The importance of early decontamination can not be over emphasised. Decontamination of the skin should be accomplished quickly if it is to be fully effective. Liquid agent may be removed by fullers' earth or chemically inactivated by the use of reactive decontaminants. Decontamination personnel should use a respirator and full protective equipment whilst decontamination is performed.

b. Once a casualty has been decontaminated, or the agent fully absorbed, no further risk of contamination exists. The casualty's body fluids, urine or faeces do not present a chemical warfare (CW) hazard.

## 206. Mechanism of Action.

a. *Absorption*. Nerve agents may be absorbed through any body surface. When dispersed as a spray or an aerosol, droplets can be absorbed through the skin, eyes and respiratory tract. When dispersed as a vapour at expected field concentrations, the vapour is primarily absorbed through the respiratory tract. If enough agent is absorbed, local effects are followed by generalised systemic effects. The rapidity

with which effects occur is directly related to the amount of agent absorbed in a given period of time.

b. *Inhibition by Agents.*

(1) The effects of the nerve agents are mainly due to their ability to inhibit acetylcholinesterase throughout the body. Since the normal function of this enzyme is to hydrolyse acetylcholine wherever it is released, such inhibition results in the accumulation of excessive concentrations of acetylcholine at its various sites of action. These sites include the endings of the parasympathetic nerves to the smooth muscle of the iris, ciliary body, bronchial tree, gastrointestinal tract, bladder and blood vessels; to the salivary glands and secretory glands of the gastrointestinal tract and respiratory tract; and to the cardiac muscle and endings of sympathetic nerves to the sweat glands. The accumulation of acetylcholine at these sites results in characteristic muscarinic signs and symptoms.

(2) The accumulation of acetylcholine at the endings of motor nerves to voluntary muscles and in some autonomic ganglia results in nicotinic signs and symptoms.

(3) The accumulation of excessive acetylcholine in the brain and spinal cord results in characteristic central nervous system symptoms. (See Table 2-II.)

(4) The inhibition of cholinesterase enzymes throughout the body by nerve agents may be irreversible and its effects prolonged.

(5) Treatment with oximes should begin promptly.

(6) Until the tissue cholinesterase enzymes are restored to normal activity, there is a period of increased susceptibility to the effects of another exposure to any nerve agent. The period of increased susceptibility occurs during the enzyme regeneration phase which could last from weeks to months, depending on the severity of the initial exposure. During this period the effects of repeated exposures are cumulative.

c. *Location of Acetylcholinesterase.* Acetylcholinesterase is found associated with the post-junctional membrane at the neuromuscular junction and in the cell bodies and processes of cholinergic neurons. The concentration is particularly high in some central nervous system neurons. The location of acetylcholinesterase in autonomic ganglia is less well understood than that at the neuromuscular junction. Acetylcholinesterase is also found at sites where, as yet, no functional role has been identified: the musculotendinous junction, red blood cells, platelets and the placenta.

d. *Further Information.* Further information on the action of nerve agents on acetylcholinesterase is given in Annex A.

## 207. Pathology.

Aside from the decrease in the activity of cholinesterase enzymes throughout the body (which may be detected by chemical methods or by special staining), no specific lesions are detectable by ordinary gross examination. At post-mortem examination there is usually capillary dilation, hyperaemia and oedema of the lungs; there may be similar changes in the brain and the remaining organs. Neuropathological changes have been reported in animals following severe intoxication. During the acute phase these include damage within the central nervous system and

at the neuromuscular endplate. Later on, following severe exposure to some nerve agent, lesions to the peripheral motor nerves may be identified.

*Table 2-II. Likely Signs and Symptoms of GB Poisoning Shown in Terms of Vapour Exposure and Approximate Blood Acetylcholinesterase Depression*

| Short term Ct mg.min.m$^{-3}$ | Approximate AChE depression | Symptoms and signs* | |
|---|---|---|---|
| | | Vapour | Systemic exposure only eyes protected |
| <2 | <5% | Incipient miosis (miosis produced at Ct=2, t=30 min), slight headache. | Nil. |
| 5 | 20% ±10% | Increased miosis, headache, eye pain, rhinorrhoea, conjunctival injection, tightness in chest. | Tightness in chest. |
| 5-15 | 20-50% ±10% | Eye signs maximal. Bronchospasm in some subjects. | Symptoms beginning to appear. Bronchospasm. |
| 15 | 50%±10% | Bronchospasm and all the effects already described. | Wheezing, salivation, eye effects, nausea, vomiting. (Local sweating and fasciculation in liquid contamination of the skin.) |
| 40 | 80%±10% | Symptoms and signs as for systemic exposure. | Weakness, defecation, urination, paralysis, convulsions. |
| 100 | 100% | Respiratory Failure Death | Respiratory Failure Death |

* All symptoms and signs will be subject to very considerable inter-subject variation.

## SECTION II - EFFECTS OF NERVE AGENTS

### 208. Signs and Symptoms.

a. The order in which signs and symptoms appear and their relative severity depend on the route of exposure and whether the casualty has been exposed to liquid agent or vapour.
b. The signs and symptoms following exposure to nerve agents are given in Table 2-III.
c. The local effects of vapour and liquid exposure are described followed by a description of the systemic effects which occur after significant absorption of agent via any route.

### 209. Effects of Nerve Agent Vapour.

a. *Absorption.* The lungs and the eyes absorb nerve agents rapidly. Changes occur in the smooth muscle of the eye, resulting in miosis and in the smooth muscle and

secretory glands of the bronchi, producing bronchial constriction and excessive secretions in the upper and lower airways. In high vapour concentrations, the nerve agent is carried from the lungs throughout the circulatory system; widespread systemic effects may appear in less than 1 minute.

*Table 2-III. Signs and Symptoms of Nerve Agent Poisoning*

| Site of action | Signs and symptoms |
|---|---|
| a. Muscarinic. | |
| (1) Pupils. | Miosis, marked, usually maximal (pin-point), sometimes unequal. |
| (2) Ciliary body. | Frontal headache, eye pain on focusing, blurring of vision. |
| (3) Nasal mucous membranes. | Rhinorrhoea, hyperaemia. |
| (4) Bronchial tree. | Tightness in chest, bronchoconstriction, increased secretion, cough. |
| (5) Gastrointestinal. | Occasional nausea and vomiting. |
| b. Muscarinic following systemic absorption (depending on dose). | |
| (1) Bronchial tree. | Tightness in chest, with prolonged wheezing expiration suggestive of bronchoconstriction or increased secretion, dyspnoea, pain in chest, increased bronchial secretion, cough, cyanosis, pulmonary oedema. |
| (2) Gastrointestinal. | Anorexia, nausea, vomiting, abdominal cramps, epigastric and substernal tightness (cardiospasm) with "heartburn" and eructation, diarrhoea, tenesmus, involuntary defecation. |
| (3) Sweat glands. | Increased sweating. |
| (4) Salivary glands. | Increased salivation. |
| (5) Lachrymal glands. | Increased lachrymation. |
| (6) Heart. | Bradycardia. |
| (7) Pupils. | Miosis, occasionally unequal, later maximal miosis (pin-point). |
| (8) Ciliary body. | Blurring of vision, headache. |
| (9) Bladder. | Frequency, involuntary micturition. |
| c. Nicotinic. | |
| (1) Striated muscle. | Easy fatigue, mild weakness, muscular twitching, fasciculations, cramps, generalised weakness/flaccid paralysis (including muscles of respiration) with dyspnoea and cyanosis. |
| (2) Sympathetic ganglia. | Pallor, transitory elevation of blood pressure followed by hypotension. |
| d. Central nervous system. | Immediate (Acute) Effects: Generalised weakness, depression of respiratory and circulatory centres with dyspnoea, cyanosis and hypotension; convulsions, loss of consciousness and coma.<br><br>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. |

b. *Local Ocular Effects.*

(1) These effects begin within seconds or minutes after exposure, before there is any evidence of systemic absorption. The earliest ocular effect which follows minimal symptomatic exposure to vapour is miosis. This is an invariable sign of ocular exposure to enough vapour to produce symptoms. It is also the last ocular manifestation to disappear. The pupillary constriction may be different in each eye. Within a few minutes after the onset of exposure, there also occurs redness of the eyes due to conjunctival hyperaemia, and a sensation of pressure with heaviness in and behind the eyes. Usually vision is not grossly impaired, although there may be a slight dimness especially in the peripheral fields or when in dim or artificial light.

(2) Exposure to a level of a nerve agent vapour slightly above the minimal symptomatic dose results in miosis, pain in and behind the eyes attributable to ciliary spasm, especially on focusing, some difficulty of accommodation and frontal headache. The pain becomes worse when the casualty tries to focus the eyes or looks at a bright light. Some twitching of the eyelids may occur. Occasionally there is nausea and vomiting which, in the absence of systemic absorption, may be due to a reflex initiated by the ocular effects. These local effects may result in moderate discomfort and some loss of efficiency but may not necessarily produce casualties.

(3) Following minimal symptomatic exposure, the miosis lasts from 24 to 72 hours. After exposure to at least the minimal symptomatic dose, miosis is well established within half an hour. Miosis remains marked during the first day after exposure and then diminishes gradually over 2 to 3 days after moderate exposure but may persist for as long as 14 days after severe exposure. The conjunctival erythema, eye pain, and headache may last from 2 to 15 days depending on the dose.

c. *Local Respiratory Effects.* Following minimal exposure, the earliest effects on the respiratory tract are a watery nasal discharge, nasal hyperaemia, sensation of tightness in the chest and occasionally prolonged wheezing expiration suggestive of bronchoconstriction or increased bronchial secretion. The rhinorrhoea usually lasts for several hours after minimal exposure and for about 1 day after more severe exposure. The respiratory symptoms are usually intermittent for several hours duration after mild exposure and may last for 1 or 2 days after more severe exposure.

## 210. Effects of Liquid Nerve Agent.

a. *Local Ocular Effects.* The local ocular effects are similar to the effects of nerve agent vapour. If the concentration of the liquid nerve agent contaminating the eye is high, the effects will be instantaneous and marked; and, if the exposure of the two eyes is unequal, the local manifestations may be unequal. Hyperaemia may occur but there is no immediate local inflammatory reaction such as may occur following ocular exposure to more irritating substances (for example, Lewisite).

b. *Local Skin Effects.* Following cutaneous exposure, there is localised sweating at and near the site of exposure and localised muscular twitching and fasciculation.

However, these may not be noticed causing the skin absorption to go undetected until systemic symptoms begin.

c. *Local Gastrointestinal Effects.* Following the ingestion of substances containing a nerve agent, which is essentially tasteless, the initial symptoms include abdominal cramps, vomiting and diarrhoea.

## 211. Systemic Effects of Nerve Agent Poisoning.

a. The sequence of symptoms varies with the route of exposure. While respiratory symptoms are generally the first to appear after inhalation of nerve agent vapour, gastrointestinal symptoms are usually the first after ingestion. Following comparable degrees of exposure, respiratory manifestations are most severe after inhalation, and gastrointestinal symptoms may be most severe after ingestion. Otherwise, the systemic manifestations are, in general, similar after any exposure to nerve agent poisoning by any route. If local ocular exposure has not occurred, the ocular manifestations (including miosis) initially may be absent.

b. The time course of effects following exposure to nerve agents are given in Table 2-IV.

c. The systemic effects may be considered to be nicotinic, muscarinic or by an action at receptors within the central nervous system. The predominance of muscarinic, nicotinic or central nervous system effects will influence the amount of atropine, oxime or anticonvulsant which must be given as therapy. These effects will be considered separately.

## 212. Muscarinic Effects of Nerve Agent Poisoning.

a. Tightness in the chest is an early local symptom of respiratory exposure. This symptom progressively increases as the nerve agent is absorbed into the systemic circulation, whatever the route of exposure. After moderate or severe exposure, excessive bronchial and upper airway secretions occur and may become very profuse, causing coughing, airway obstruction and respiratory distress. Audible wheezing may occur, with prolonged expiration and difficulty in moving air into and out of the lungs, due to the increased bronchial secretion or to bronchoconstriction, or both. Some pain may occur in the lower thorax and salivation increases.

b. Bronchial secretion and salivation may be so profuse that watery secretions run out of the sides of the mouth. The secretions may be thick and tenacious. If postural drainage or suction is not employed, these secretions may add to the airway obstruction. Laryngeal spasm and collapse of the hypopharyngeal musculature may also obstruct the airway. The casualty may gasp for breath, froth at the mouth, and become cyanotic.

c. If the upper airway becomes obstructed by secretions, laryngeal spasm or hypopharyngeal musculature collapse, or if the bronchial tree becomes obstructed by secretions or bronchoconstriction, little ventilation may occur despite respiratory movements. As hypoxaemia and cyanosis increase, the casualty will fall exhausted and become unconscious.

*Table 2-IV. Time Course of Effects of Nerve Agents*

| Nerve agent | Types of effects | Route of absorption | Description of effects | When effects appear after exposure* | Duration of effects after: Mild exposure | Duration of effects after: Severe exposure |
|---|---|---|---|---|---|---|
| Vapour. | Local. | Lungs. | Rhinorrhoea, nasal hyperaemia, tightness in chest, wheezing. | One to several minutes. | A few hours. | 1 to 2 days. |
| Vapour. | Local. | Eyes. | Miosis, conjunctival hyperaemia, eye pain, frontal headache. | One to several minutes. | Miosis 24 hours. | 2 to 3 days. |
| Vapour. | Systemic. | Lungs or eyes. | Muscarinic, nicotinic, and central nervous system effects.(See Table 3-I). | Less than one minute to a few minutes after moderate or severe exposure. | Several hours to a day. | Acute effects: 2 to 3 days. CNS effects: days to weeks. |
| Liquid. | Local. | Eyes. | Same as vapour effects. | Instantly. | Similar to effects of vapour. | |
| Liquid. | Local. | Ingestion. | Gastrointestinal. (See Table 3-I). | About 30 minutes after ingestion. | Several hours to a day. | 2 to 5 days. |
| Liquid. | Local. | Skin. | Local sweating and muscular twitching. | 3 minutes to 2 hours. | 3 days. | 5 days. |
| Liquid. | Systemic. | Lungs. | See Table (3-I). | Several minutes. | | 1 to 5 days. |
| Liquid. | Systemic. | Eyes. | Same as for vapour. | Several minutes. | | 2 to 4 days. |
| Liquid. | Systemic. | Skin. | Generalised sweating. | 15 minutes to 2 hours. | | 2 to 5 days. |
| Liquid. | Systemic. | Ingestion. | Gastrointestinal. (See Table 3-I). | 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.

d. Following inhalation of nerve agent vapour, the respiratory manifestations predominate over the other muscarinic effects: they are likely to be most severe in older casualties and in those with a history of respiratory disease, particularly bronchial asthma. However, if the exposure is not so overwhelming as to cause death within a few minutes, other muscarinic effects appear. These include sweating, anorexia, nausea and epigastric and substernal tightness with heartburn and eructation. If absorption of nerve agent has been great enough (whether due to a single large exposure or to repeated smaller exposures), there may follow abdominal cramps, increased peristalsis, vomiting, diarrhoea, tenesmus, increased lachrymation and urinary frequency. Cardiovascular effects are a bradycardia, hypotension and cardiac arrhythmias. The casualty perspires profusely, may have involuntary defecation and urination and may go into cardiorespiratory arrest followed by death.

## 213. Nicotinic Effects.

a. With the appearance of moderate muscarinic systemic effects, the casualty begins to have increased fatiguability and mild generalised weakness which is increased by exertion.

b. This is followed by involuntary muscular twitching, scattered muscular fasciculations and occasional muscle cramps. The skin may be pale due to vasoconstriction and blood pressure moderately elevated (transitory) together with a tachycardia, resulting from cholinergic stimulation of sympathetic ganglia and possibly from the release of epinephrine. If the exposure has been severe, the muscarinic cardiovascular symptoms will dominate and the fascicular twitching (which usually appear first in the eyelids and in the facial and calf muscles) becomes generalised. Many rippling movements are seen under the skin and twitching movements appear in all parts of the body. This is followed by severe generalised muscular weakness, including the muscles of respiration. The respiratory movements become more laboured, shallow and rapid; then they become slow and finally intermittent. Later, respiratory muscle weakness may become profound and contribute to the respiratory depression. Central respiratory depression may be a major cause of respiratory failure.

## 214. Central Nervous System Effects.

a. In mild exposures, the systemic manifestations of nerve agent poisoning usually include tension, anxiety, jitteriness, restlessness, emotional lability, and giddiness. There may be insomnia or excessive dreaming, occasionally with nightmares.

b. If the exposure is more marked, the following symptoms may be evident: headache, tremor, drowsiness, difficulty in concentration, impairment of memory with slow recall of recent events, and slowing of reactions. In some casualties there is apathy, withdrawal and depression. With the appearance of moderate symptoms, abnormalities of the electroencephalogram occur, characterised by irregularities in rhythm, variations in potential, and intermittent bursts of abnormally slow waves of elevated voltage similar to those seen in patients with epilepsy. These abnormal waves become more marked after one or more minutes of hyperventilation which, if prolonged, may occasionally precipitate a generalised convulsion.

c. If absorption of nerve agent has been great enough, the casualty becomes confused and ataxic. The casualty may have changes in speech, consisting of slurring, difficulty in forming words, and multiple repetition of the last syllable. The casualty may then become comatose, reflexes may disappear and respiration may become Cheyne-Stokes in character. Finally, generalised convulsions may ensue.

d. With the appearance of severe central nervous system symptoms, central respiratory depression will occur (adding to the respiratory embarrassment that may already be present) and may progress to respiratory arrest. However, after severe exposure the casualty may lose consciousness and convulse within a minute without other obvious symptoms. Death is usually due to respiratory arrest and anoxia, and requires prompt initiation of assisted ventilation to prevent death. Depression of the

circulatory centres may also occur, resulting in a marked reduction in heart rate with a fall of blood pressure some time before death.

## 215. Cumulative Effects of Repeated Exposure.

a. Daily exposure to concentrations of a nerve agent insufficient to produce symptoms following a single exposure may result in the onset of symptoms after several days. Continued daily exposure may be followed by increasingly severe effects.

b. After symptoms subside, increased susceptibility may persist for up to 3 months. The degree of exposure required to produce recurrence of symptoms and the severity of these symptoms depend on the dose received and the time interval since the last exposure. Increased susceptibility is not limited to the particular nerve agent initially absorbed.

## 216. Cause of Death.

a. In the absence of treatment, death is caused by anoxia resulting from airway obstruction, weakness of the muscles of respiration and central depression of respiration.

b. Airway obstruction is due to pharyngeal muscular collapse, upper airway and bronchial secretions, bronchial constriction and occasionally laryngospasm and paralysis of the respiratory muscles.

c. Respiration is shallow, laboured, and rapid and the casualty may gasp and struggle for air. Cyanosis increases. Finally, respiration becomes slow and then ceases. Unconsciousness ensues. The blood pressure (which may have been transitorily elevated) falls. Cardiac rhythm may become irregular and death may ensue.

d. If assisted ventilation is initiated via cricothyroidotomy or endotracheal tube and airway secretions are removed by postural drainage and suction and diminished by the administration of atropine, the individual may survive several lethal doses of a nerve agent. However, if the exposure has been overwhelming, amounting to many times the lethal dose, death may occur despite treatment as a result of respiratory arrest and cardiac arrhythmia.

e. When overwhelming doses of the agent are absorbed quickly, death occurs rapidly without orderly progression of symptoms.

# SECTION III - TREATMENT OF NERVE AGENT POISONING

## 217. Diagnosis and Therapy of Nerve Agent Poisoning.

a. *Symptoms.* Nerve agent poisoning may be identified from the characteristic signs and symptoms. If exposure to vapour has occurred, the pupils will be very small, usually pin-pointed. If exposure has been cutaneous or has followed ingestion of a nerve agent in contaminated food or water, the pupils may be normal or, in the presence of severe systemic symptoms, slightly to moderately reduced in size. In this event, the other manifestations of nerve agent poisoning must be relied on to establish the diagnosis. No other known chemical agent produces muscular twitching and

fasciculations, rapidly developing pin-point pupils, or the characteristic train of muscarinic, nicotinic and central nervous system manifestations.

b. *Symptom Differentiation.* It is important that individual service members know the following MILD and SEVERE signs and symptoms of nerve agent poisoning. Service members who have most or all of the symptoms listed below must IMMEDIATELY receive first aid (self-aid or buddy aid respectively).

c. *MILD Poisoning (Self-Aid).* Casualties with MILD symptoms may experience most or all of the following:

(1) Unexplained runny nose.
(2) Unexplained sudden headache.
(3) Sudden drooling.
(4) Difficulty in seeing (dimness of vision and miosis).
(5) Tightness in the chest or difficulty in breathing.
(6) Localised sweating and muscular twitching in the area of the contaminated skin.
(7) Stomach cramps.
(8) Nausea.
(9) Bradycardia or tachycardia.

d. *MODERATE Poisoning.* Casualties with MODERATE poisoning will experience an increase in the severity of most or all of the MILD symptoms. Especially prominent will be an increase in fatigue, weakness and muscle fasciculations. The progress of symptoms from mild to moderate indicates either inadequate treatment or continuing exposure to agent.

e. *SEVERE Symptoms (Buddy Aid).* Casualties with SEVERE symptoms may experience most or all of the MILD symptoms, plus most or all of the following:

(1) Strange or confused behaviour.
(2) Wheezing, dyspnoea (severe difficulty in breathing), and coughing.
(3) Severely pin-pointed pupils.
(4) Red eyes with tearing.
(5) Vomiting.
(6) Severe muscular twitching and general weakness.
(7) Involuntary urination and defecation.
(8) Convulsions.
(9) Unconsciousness.
(10) Respiratory failure.
(11) Bradycardia.

f. *Aid for Severe Cases.* Casualties with severe symptoms will not be able to treat themselves and must receive prompt buddy aid and follow-on medical treatment if they are to survive.

## 218. Treatment.

The lethal effects of nerve agent poisoning may be combated by a combination of pretreatment and post exposure therapy.

## 219. Pretreatment.

a. Poisoning by nerve agents which form rapidly aging complexes (for example Soman) may be particularly difficult to treat. These difficulties have been solved, in part, by the use of carbamates as pretreatment. The terms pretreatment or prophylaxis should perhaps be defined as used in this context:

(1) Pretreatment: the administration of drugs in advance of poisoning designed to increase the efficacy of treatment administered post-poisoning.

(2) Prophylaxis: the administration of drugs in advance of the poisoning designed to make post-poisoning therapy unnecessary.

b. The terms are to an extent interchangeable and as, in cases of severe poisoning, post-poisoning therapy is nearly always needed, the term pretreatment will be used here.

c. Carbamate anticholinesterases, e.g., pyridostigmine, may be used as pretreatment against nerve agent poisoning by virtue of their capacity to bind acetylcholinesterase *reversibly*, preventing the organophosphate (OP) binding to the enzyme. The term reversible is here used comparatively: the carbamate-acetylcholinesterase complex breaks down fairly rapidly, while organophosphate-acetylcholinesterase complexes break down very slowly. The aged soman-acetylcholinesterase complex breaks down virtually not at all.

d. When carbamates are used as pretreatments, carbamoylation of acetylcholinesterase prevents phosphorylation, but later the carbamate-acetylcholinesterase complex dissociates, freeing active enzyme. Current pretreatment regimes bind 30-40% of available red blood cell acetylcholinesterase, thereby allowing the carbamate to protect some of the acetylcholinesterase against attack by nerve agent.

e. The carbamate pyridostigmine, given in a dose of 30 mg every 8 hours, is used as a pretreatment. In conjunction with post exposure therapy, good protection against lethality is obtained within 2 hours of the first dose, but is not optimal until the third dose.

f. Pyridostigmine pretreatment should be stopped upon developing symptoms of nerve agent poisoning following a chemical warfare attack and post exposure therapy started.

g. Pyridostigmine tablets were taken over a 4 to 5 day period by large numbers of troops during the Gulf War of 1991.

(1) The effects of pyridostigmine were examined in several studies including one uncontrolled study of 42,000 troops when, following the recommended dose regime, under the stress of combat conditions, gastrointestinal intestinal changes including increased flatus, loose stools, abdominal cramps and nausea were noted by approximately half the population. Other reported effects were urinary urgency, headache, rhinorrhoea, diaphoresis and tingling of the extremities. These effects were considered tolerable. They did not noticeably interfere with performance of the full range of demanding physical and mental tasks required of service personnel.

(2) Symptoms due to pyridostigmine may be ameliorated by taking the tablets with food.

(3) Pyridostigmine pretreatment was discontinued on medical advice in less than 0.1 % of individuals, generally because of intolerable nausea and diarrhoea.

h. When taken in excess of the recommended dosage, symptoms of carbamate poisoning will occur. These include diarrhoea, gastrointestinal cramps, tight chest, nausea, rhinorrhoea, headache and miosis.

i. Good compliance is required if optimal protection is to be obtained. The importance of pyridostigmine pretreatment should therefore be stressed during training.

## 220. Post-Exposure Therapy.

The main principles of therapy for nerve agent poisoning are early treatment, assisted ventilation, bronchial suction, muscarinic cholinergic blockade (atropine), enzyme reactivation (oximes) and anticonvulsants (benzodiazepines).

## 221. Emergency Field Therapy.

a. *Self Aid (or Buddy Aid).*

(1) This comprises first aid measures which the soldier can apply to help him or herself. The rapid action of nerve agents call for immediate self treatment. Unexplained nasal secretion, salivation, tightness of the chest, shortness of breath, constriction of pupils, muscular twitching, or nausea and abdominal cramps call for the immediate intramuscular injection of 2 mg of atropine, combined if possible with oxime. From 1 to 3 automatic injection devices, each containing 2 mg atropine or mixture of atropine, oxime and/or anticonvulsant, are carried by each individual.

(2) One device should be administered immediately when the symptoms and/or signs of nerve agent poisoning appear. This may be done by the casualty or by a buddy; the injection being given perpendicularly through the clothing into the lateral aspect of the middle of the thigh. Further devices, up to a total of 3, should be administered by the casualty or by his or her buddy during the following 30 minutes if the symptoms and/or signs of poisoning fail to resolve.

(3) The timing of these further injections and whether they are given at one time or separately may depend on the casualty's condition and on instructions promulgated by individual nations.

(4) NOTE: If automatic injectors are used in the absence of exposure to agent, the following signs and symptoms may be seen: Dry mouth, dry skin, fast pulse (>90 beats per minute), dilated pupils, retention of urine and central nervous system disturbance. Susceptibility to heat exhaustion or heat stroke is increased, particularly in closed spaces or while wearing protective clothing.

b. *First Aid by Trained Personnel.*

(1) This comprises the emergency actions undertaken to restore or maintain vital bodily functions in a casualty. Wherever the casualty is not masked the respirator must be adjusted for him or her by the nearest available person. Attention should be given to decontamination at the earliest possible moment

and any skin contamination must be removed with a personal decontamination kit.

(2) After nerve agent poisoning, the administration of atropine is repeated at intervals until signs of atropinization (dry mouth and skin and tachycardia >90 per minute) are achieved. Miosis from vapour exposure is not relieved by systemic atropine.

(3) Mild atropinization should be maintained for at least 24 hours by intramuscular injection of 1-2 mg of atropine at intervals of ½ to 4 hours, as required. The danger of ventricular arrhythmias arising from atropinization while the casualty is anoxic must be remembered.

(4) Assisted ventilation is required for severely poisoned individuals as they will have:

(a) Marked bronchoconstriction;

(b) Copious secretions in the trachea and bronchi;

(c) Paralysis of the respiratory muscles; and

(d) Central respiratory depression, hypoxia, and convulsions.

c. *Resuscitation*.

(1) Positive pressure resuscitation should be given but the pressure necessary to overcome the bronchoconstriction may be more than 65 cm of water so that incubation if possible is highly desirable. In an uncontaminated atmosphere assisted ventilation may be done by the standard mouth-to-mouth method after decontamination of the casualty's face and mouth. In a contaminated atmosphere ventilation may be given by a portable resuscitator with NBC filter attached. Both the casualty and the resuscitator should be decontaminated.

(2) In a well equipped medical facility, mechanical resuscitation of the positive pressure type may be used with endotracheal incubation or tracheostomy-artificial respiration must be continued until the casualty is breathing normally or the medical personnel have pronounced the casualty dead. Due to the production of copious secretions, regular suction will be required.

## 222. Pharmacological Treatment of Nerve Agent Poisoning.

a. The pharmacological treatment of nerve agent poisoning involves the use of

(1) Anticholinergics to antagonise the muscarinic effects (atropine).

(2) Oximes to reactivate inhibited enzyme.

(3) Anticonvulsants to prevent CNS damage.

b. The effects of drugs used in nerve agent poisoning are described below.

## 223. Atropine.

a. Atropine sulphate remains an essential drug in the treatment of nerve agent poisoning. It acts by blocking the effects of acetylcholine at muscarinic receptors and so produces relief from many of the symptoms previously listed. If given in large doses, some therapeutic effects are also produced within the central nervous system

although atropine does not readily penetrate the blood brain barrier and central muscarinic receptors are thought not to be identical with those in the periphery. It is thought to counteract the respiratory depression in the medulla oblongata.

b. Urgent treatment with atropine in cases of nerve agent poisoning is essential. After the emergency field treatment, atropinisation should be maintained for at least 24 hours by intramuscular injection or slow intravenous infusion of 1 to 2 mg of atropine per hour as required. The dose should be repeated at intervals until signs of successful atropinisation are noted. Intervals of 5 to 15 minutes seem reasonable, but severe poisoning may require higher doses (4 mg to 6 mg per hour or more). Signs of successful atropinisation include the drying up of bronchial, salivary and skin secretions and an increase in heart rate to greater than 90 beats per minute.

c. The effect of atropine in drying bronchial secretions may make the removal of mucus more difficult so suction is likely to be necessary. In excessive doses, atropine may render the ischaemic myocardium more liable to arrhythmias and electrocardiogram ( ECG) monitoring should be undertaken in all patients if possible.

d. Atropine overdosage may produce euphoria, hallucinations, anxiety, and delirium and close observation of patients is necessary. Bladder dysfunction may necessitate catheterisation.

e. By inhibition of sweat production, atropine increases heat stress and in warm or hot weather care must be taken to avoid hyperthermia.

f. Atropine given parenterally has comparatively little effect on nerve agent induced miosis. The local application of cycloplegics (atropine eye drops) to the eye reduces both the degree of rniosis, eye pain and headache. However, expert opinion on the value of atropine containing eye drops in the management of nerve agent induced miosis remains divided. It is believed by some that problems of accommodation may be made worse by the application of the drops and that, overall, little benefit may be produced.

g. If atropine is administered in the absence of nerve agent poisoning, the following effects may be noted: dryness of the mouth and pharynx, decreased sweating, slight flushing and tachycardia, some hesitancy of micturition, slightly dilated pupils, mild drowsiness, slowness of memory and recall and blurring of near vision. After 2mg these symptoms should not interfere with ordinary activity except in the occasional person, in hot environments or at high work rates. Higher doses, or repeated doses, will produce more marked symptoms which will usually not be totally incapacitating except in warm environments or high work rates. The effects of atropine are fairly prolonged, lasting 3 to 5 hours after one or two injections of 2mg and 12 to 24 hours after marked over-atropinisation.

## 224. Oximes.

a. *Oximes.*

(1) While atropine blocks the muscarinic effects of nerve agent poisoning it has little effect upon the nicotinic actions of the agent at the skeletal neuromuscular junction and at the autonomic ganglia.

(2) Amelioration of the effects of nerve agents at these sites and also at

muscarinic sites can, however, be obtained by reactivation of the inhibited acetylcholinesterase by means of oximes. Oximes, therefore, relieve the clinically important symptom of skeletal neuromuscular blockade. However, they penetrate into the central nervous system poorly, and the simultaneous administration of atropine is therefore still required.

b. *Enzyme Reactivation.*

(1) The relative potency of different oximes in reactivating acetylcholinesterase inhibited by some nerve agents is given in Table 2-V.

(2) Dosing schemes for the clinical intravenous use of currently available oximes, as applied in poisoning of humans by organophosphate insecticides, are shown in Table 2-VI. Under field conditions similar doses can be given intramuscularly, but care should be taken to avoid accidental intra-arterial injection. The dose rates given could form the base for the determination of national dosing procedures which should include emergency field treatment.

*Table 2-V. Effectiveness of Various Oximes in the Treatment of Nerve Agent Poisoning*

| Oxime | GA | GB | GD | GF |
|---|---|---|---|---|
| $P_2S$ | - | + | - | - |
| Obidoxime | + | + | - | +/- |
| HI6 | +/- | + | +/- | + |

+ = Effective - = Not effective
+/- = Sometimes effective

*Table 2-VI. Examples of Current Dosing Scheme for the Intravenous Administration of Oximes*

| Degree of poisoning | PAM Cl dose | $P_2S$ dose | Obidoxome dose |
|---|---|---|---|
| Mild | 1 g | 400 mg | 250 mg |
| Moderate | 1 g* | 400 mg** | 250 mg*** |
| Severe | 1 g* | 500 mg** | 250 mg*** |

* To be repeated every 8 to 12 hours.
** Second dose of 400 mg to 500 mg after 30 minutes. Further doses of 200 mg to 400 mg every 4 to12 hours.
*** Second dose after 2 hours. Further doses to be repeated every 6 to 12 hours.

(3) An alternative method of administering oxime is as a continuous infusion. On the basis of a theoretical therapeutic plasma concentration of 4mg.1-[1], the loading dose and maintenance dose for intravenous use can be calculated for different oximes using data obtained in healthy human volunteers (Table 2-VII). Data from human organophosphorus insecticide poisoning suggest that these dose rates are also applicable in patients.

(4) Clinical experience in human poisoning by organophosphorus insecticide shows that oxime treatment should be continued for some hours after reactivation has been obtained and the patient has recovered. If no enzyme reactivation has been obtained after a 24 to 48 hour period of treatment and the patient has not recovered, then it should be accepted that the enzyme inhibition is resistant to reactivation by the particular oxime and administration should be stopped. There is only limited experience with human poisoning with organophosphorus nerve agents, but animal data suggest that the clinically relevant persistence of nerve agent in the body will probably be shorter than for insecticides. It may be suggested therefore, that oxime treatment should be continued until the recovery of the patient, with a probable maximum duration of 24 to 48 hours.

c. *Oxime Induced Side Effects.* The rapid injection of pralidoxime 2 (PAM Cl or $P_2S$) can produce drowsiness, headache, disturbance of vision, nausea, dizziness, tachycardia and an increase in blood pressure, hyperventilation and muscular weakness. Obidoxime produces hypotension, a menthol-like sensation and a warm feeling in the face. On intramuscular injection, it can produce a dull pain at the site of injection; after multiple dosing, hepatic dysfunction can be observed. HI6 (a type of oximide) produces similar effects.

*Table 2-VII. Loading Doses and Infusion Rates for Oxime Administration to Obtain a Plasma Concentration of 4 mg.1$^{-1}$*

| Oxime | Loading dose** (mg.kg$^{-1}$) | Approximate dose for 70 kg person (mg) | Infusion rate*** (mg.kg$^{-1}$.h$^{-1}$) | Approximate rate for 70 kg person (mg.h$^{-1}$) |
|---|---|---|---|---|
| PAM Cl | 4.2 | 300 | 2.2 | 160 |
| $P_2S$ | 4.4 | 310 | 2.1 | 150 |
| Obidoxime | 0.8 | 56 | 0.5 | 34 |
| HI6* | 1.6 | 110 | 0.8 | 54 |

* Based on data from intramuscular administration.
** Loading dose = therapeutic plasma concentration x volume of distribution.
*** Infusion rate = therapeutic plasma concentration x clearance.

## 225. Anticonvulsants.

a. Atropine protects only partially against convulsions and the resulting brain damage in severe poisoning. Complementary treatment, including anticonvulsants, should be applied as necessary.

b. It has been shown in experimental soman poisoning that diazepam antagonises the convulsive action of soman and that addition of diazepam to the basic treatment regime greatly improves morbidity and mortality, independent of its anticonvulsive effect. Diazepam is the drug of choice and should be injected intramuscularly as a 10 mg dose initially and further doses should be given frequently enough to control convulsions. This may require injections at intervals ranging from a few minutes to several hours.

## 226. Supportive Care.

Although pre and post exposure therapy will protect against lethality, casualties may still be incapacitated. A patient severely poisoned by an anticholinesterase is a critical medical emergency and may require intensive care for days or weeks. Assisted ventilation may be needed for many hours or days and the patient may be comatose for hours or days and brain damage may result from periods of hypoxia. General supportive care such as IV feeding, restoring electrolyte balance, treatment of shock and control of convulsions is needed. Therapy to control infection, should this occur, should be on the usual lines. Special care should betaken using muscle relaxants in patients poisoned by nerve agents.

# CHAPTER 3

# VESICANTS (BLISTER AGENTS)

## SECTION I - MUSTARD AND NITROGEN MUSTARDS

### 301. Introduction.

a. Blister or vesicant agents are likely to be used both to produce casualties and to force opposing troops to wear full protective equipment thus degrading fighting efficiency, rather than to kill, although exposure to such agents can be fatal. Blister agents can be thickened in order to contaminate terrain, ships, aircraft, vehicles or equipment with a persistent hazard. The vesicant agents include sulphur mustard (HD), nitrogen mustard (HN), the arsenical vesicants such as lewisite (L) (this may well be used in a mixture with HD), and the halogenated oximes whose properties and effects are very different from those of the other vesicants.

b. Vesicants burn and blister the skin or any other part of the body they contact. They act on the eyes, mucous membranes, lungs, skin and blood-forming organs. They damage the respiratory tract when inhaled and cause vomiting and diarrhoea when ingested.

### 302. Mustard Agents.

a. Sulphur mustard was used extensively in World War I and has been used in more recent military campaigns. Protection against these agents can only be achieved by a full protective ensemble. The respirator alone protects against eye and lung damage and gives some protection against systemic effects. Extensive, slow healing skin lesions will place a heavy burden on the medical services.

b. Sulphur mustard is the best known of these agents. Synthesised in 1822, its vesicant properties were discovered in the middle of the nineteenth century. As a chemical agent it was used for the first time in 1917 near Ypres from which it derives its French name (Yperite). Mustard is 2,2' -di(chloro-ethyl)-sulphide. It is also known by the name "Lost" in German.

c. In the US the symbol HD has been given to the distilled product. In this chapter it will be indicated thus. In 1935 it was discovered that the vesicant properties remained when the sulphur atom was substituted by a nitrogen atom. Thus it became possible to synthesise the nitrogen mustards with similar properties, of which there are three, viz:

(1) N-ethyl-2,2'di(chloroethyl)amine, or HN1.
(2) N methyl-2,2'di(chloroethyl)amine, or HN2.
(3) 2,2',2''tri(chloroethyl)amine, or HN3.

d. From a military standpoint, HN3 is the principal representative of the group of nitrogen mustards and is the only nitrogen mustard likely to be used in war.

## 303. Physical and Chemical Properties.

a. The mustards are able to penetrate cell membranes in tissues and a great number of materials: woods, leather, rubber, plants, etc. Due to their physical properties, mustards are very persistent in cold and temperate climates. It is possible to increase the persistency by dissolving them in non-volatile solvents, e.g., chlorinated rubber. In this way thickened mustards are obtained that are very difficult to remove by decontaminating processes.

b. In warmer climates persistence of mustards is less but higher concentrations of vapour occur.

c. When dissolved in water, mustards are hydrolyses at an appreciable rate, yielding poly-alcohols and hydrochloric acid (HCI), so that the solution may still be damaging to the skin. In more concentrated solutions, interaction of products becomes more pronounced and several dimers are formed. In 2 hours 22% of the initial concentration is hydrolyses, in 6 hours 35% and in 24 hours 60%. However, as their volubility in water is very poor, two phases are generally formed and hydrolysis of the undissolved bulk is very slow. In running water the contact surfaces are frequently changed and persistency is only a few days, but in stagnant water, persistency can be several months. Mustard is denser than water, but small droplets remain on the water surface and present a special hazard in contaminated areas. Alkalinity and higher temperatures increase the rate of hydrolysis.

d. Owing to its bivalent sulphur atom, sulphur mustard has very good reducing properties. Depending on their strengths, oxidants oxidise mustard to a greater or lesser extent, e.g., to sulphoxide, sulfone or sulphate. Of these only the sulfone has appreciable vesicant properties.

e. Nitrogen mustards are much less easily oxidised than sulphur mustard.

## 304. Detection.

a. Mustards have the interesting property of forming, under certain conditions, coloured complexes with para-nitrobenzpyridine thus making it possible to detect minute amounts.

b. Mustard agents can be detected by a variety of means. Single and three colour detector papers will detect liquid agent and are available for individual issue. Monitoring devices for local contamination and water testing kits are also available.

## 305. Protection.

a. Ordinary clothing gives little or no protection against mustard agents. Special equipment including a respirator, NBC suit, gloves and overboots are required. Due to slow absorption of mustard by many materials, protective equipment must be changed regularly according to the appropriate national drills.

b. No drug is available for the prevention of the effects of mustard on the skin and the mucous membranes caused by mustards. It is possible to protect the skin against very low doses of mustard by covering it with a paste containing a chlorinating

agent, e.g., chloramine. The only practical prophylactic method is physical protection such as is given by the protective respirator and special clothing.

## 306. Decontamination.

a. *General.* The decontamination of clothing, equipment, arms, vehicles, materials, buildings and terrain does not come within the framework of this manual. Decontamination of food and drinking water is discussed in Chapter 12. Only the decontamination of the skin, mucous membranes, eyes and wounds is dealt with here. Exposure to mustard is not always noticed immediately because of the latent and sign-free period that may occur after skin exposure. This may result in delayed decontamination or failure to decontaminate at all.

b. *Decontamination of Mucous Membranes and Eyes.* The substances used for skin decontamination are generally too strongly irritant to be used on mucous membranes and the eyes. In this case the affected tissues should be flushed immediately with water from the water bottle (canteen). The eyes can be flushed with copious amounts of water, or, if available, isotonic sodium bicarbonate (1.26%) or saline (0.9%).

c. *Decontamination of the Skin.* Each soldier is given the means for a preliminary decontamination of the skin, the means being based on physical adsorption or on the combination of physical adsorption and chemical inactivation. Physical adsorption can be achieved by adsorbing powders. Chemical inactivation is often effected by chlorinating compounds incorporated into adsorbing powders, ointments, solutions or organic solvents. Mustards should not be decontaminated with water, except for the eyes, as this may spread the agent.

d. *Additional Procedures.* Whatever means is used has to be efficient and quick acting. Within 2 minutes contact time, a drop of mustard on the skin can cause serious damage. Chemical inactivation using chlorination is effective against mustard and Lewisite, less so against HN3, and is ineffective against phosgene oxime. In the case of thickened mustard, where the usual procedure is inadequate, the agent may be scraped off with a knife or similar hard object. This maybe followed by wetting the surface with a cloth drenched in an organic solvent, e.g., petrol (unleaded gasoline) and subsequent application of the usual decontaminating procedure. If water is available in abundant amounts these procedures should be followed by copious washing.

e. *Decontamination of Wounds.*

(1) Mustard may be carried into wounds on fragments of cloth. These wounds should be carefully explored using a no-touch technique. Fragments of cloth should be removed and placed in a bleach solution. This removes the hazard from mustard vapour off-gassing.

(2) Wounds should be irrigated using a solution containing 3000-5000 ppm (parts per million) free chlorine (dilute “milton” solution) with a dwell time of approximately 2 minutes. The wound should then be irrigated with saline. Irrigation of the contaminated wound should not be used in the abdominal, or thoracic cavities, nor with intracranial head injuries.

## 307. Mechanism of Action.

a. Sulphur and nitrogen mustards are bifunctional alkylating agents, containing two reactive chloroethyl functions. Interaction products with cellular components can occur via formation of ethylenesulfonium (sulphur mustards) or ethylenimonium ions (nitrogen mustards) through cyclisation and subsequent binding. (See Figure 3-1.) In deoxyribonucleic acid (DNA), monofunctional adducts are formed predominantly (the second chloroethyl function is converted into hydroxyethyl), but bifunctional binding, leading to formation of cross-links, does occur. (See Figure 3-1.) Also alkylation of ribonucleic acid (RNA), proteins, cellular membrane components and cross-links between DNA and proteins can be the cause of cellular damage. Among the DNA- and RNA-bases guanine is affected most.

b. The formation of reactive species of sulphur mustard and the interaction with guanine residues in DNA are shown in Figure 3-I.

c. The binding of reactive sulphur or nitrogen mustard species to DNA produces a range of effects.

(1) Due to their relative instability, N7-alkylated guanine residues may be released from the DNA. Upon DNA replication, the remaining apurinic sites do not provide a proper template of information, which results in erroneous incorporation of nucleotides. This may lead to mutations and synthesis of non-functional proteins.

(2) In general, the presence of damage to DNA can include cellular repair mechanisms, which are not error-free. These processes thus may also give rise to erroneous DNA replication.

(3) Crosslinks, in particular interstrand crosslinks, for example between two guanines (as shown in Figure 3-I), may play an important role in the cytotoxicity of the sulphur and nitrogen mustards. They inhibit the DNA replication process when they are not properly repaired.

## 308. Toxicity.

a. HD and HN3 are the most feared vesicants historically, because of their chemical stability, their persistency in the field, the insidious character of their effects by attacking skin as well as eyes and respiratory tract, and because no effective therapy is yet available for countering their effects. Since 1917, mustard has continued to worry military personnel with the many problems it poses in the fields of protection, decontamination and treatment. It should be noted that the ease with which mustard can be manufactured and its great possibilities for acting as a vapour would suggest that in a possible future chemical war HD will be preferred to HN3.

b. Three distinct levels of biological action can be discerned following exposure to mustards: cytostatic, mutagenic and cytotoxic effects. In the present state of knowledge one cannot rule out the possibility that some effects might be due to reactions with cellular membranes or critical enzymes. The actions of mustards resembling those produced by ionising radiations and mustards have been called radiomimetic compounds.

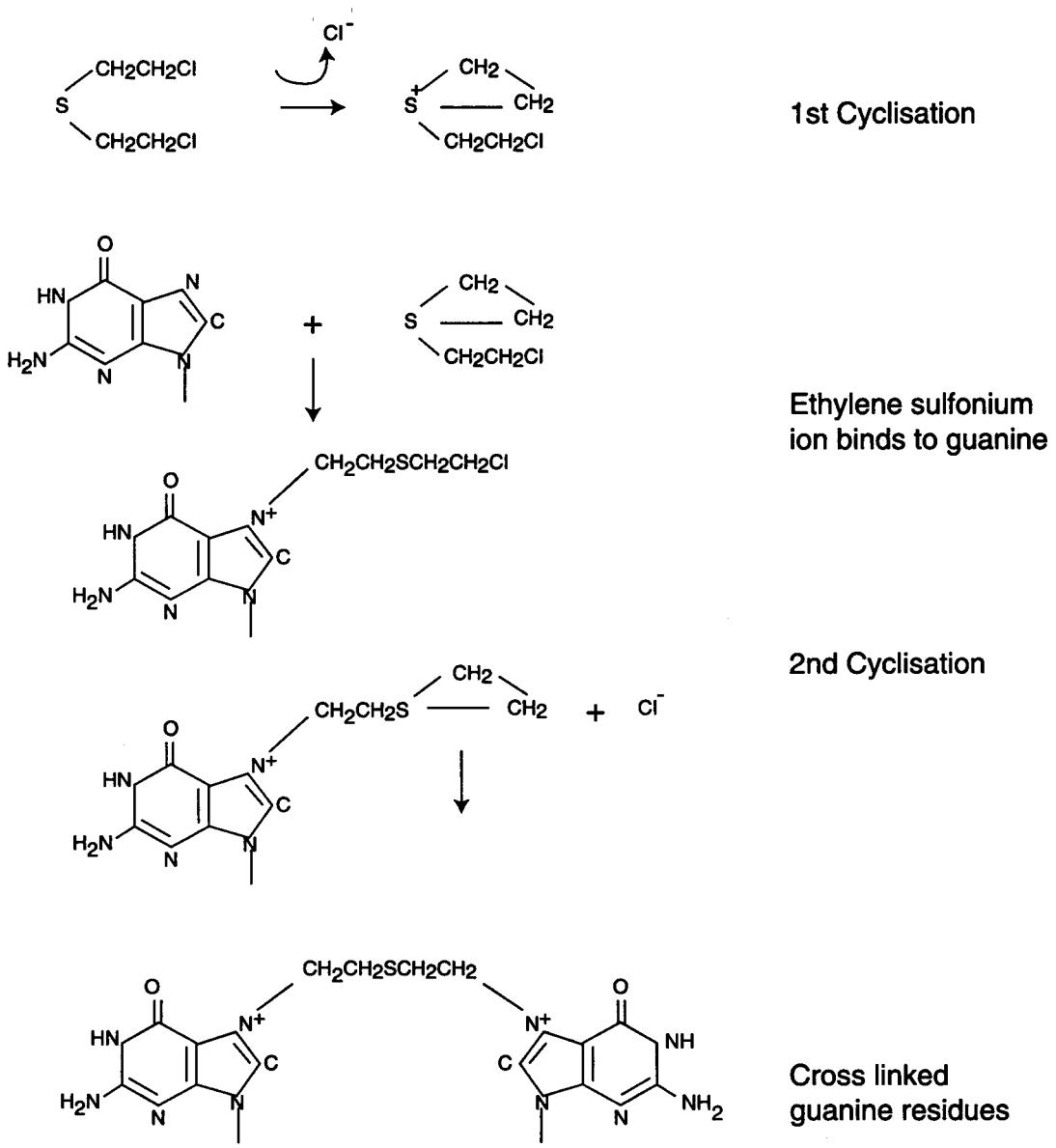



*Figure 3-I. Formation of Reactive Sulphur Mustard and Interaction with Guanine in DNA*

c. Actively proliferating cells are affected most; thus basal epidermal cells, the haemopoietic system and the mucosal lining of the intestine are particularly vulnerable.

## SECTION II - CLINICAL-PATHOLOGICAL EFFECTS

### 309. Eyes.

a. In a single exposure the eyes are more susceptible to mustard than either the respiratory tract or the skin. Conjunctivitis follows exposure of about 1 hour to

concentrations barely perceptible by odour. This exposure does not effect the respiratory tract significantly. A latent period of 4 to 12 hours follows mild exposure, after which there is lachrymation and a sensation of grit in the eyes. The conjunctival and the lids become red and oedematous. Heavy exposure irritates the eyes after 1 to 3 hours and produces severe lesions. Mustard burns of the eyes may be divided as follows:

(1) Mild conjunctivitis (75% of cases in World War 1). Recovery takes 1 to 2 weeks.

(2) Severe conjunctivitis with minimal corneal involvement (15% of cases in World War 1). Blepharospasm, oedema of the lids and conjunctival occur, as may orange-peel roughening of the cornea. Recovery takes 2 to 5 weeks.

(3) Mild corneal involvement (10% of cases in World War 1). Areas of corneal erosion stain green with fluorescein dyes. Superficial corneal scarring and vascularisation occurs as does iritis. Temporary relapses occur and convalescence may take 2 to 3 months. Hospital care is indicated for casualties of this type.

(4) Severe corneal involvement (about 0.1% of World War 1 mustard casualties). Ischaemic necrosis of the conjunctival may be seen. Dense corneal opacification with deep ulceration and vascularisation occurs. Convalescence may take several months and patients are predisposed to late relapses.

b. Although temporary blindness may occur, permanent blindness is very rare. Casualties should therefore be reassured and a positive attitude taken.

c. Care must be exercised to avoid transferring liquid agent from the hands to the eyes.

## 310. Skin.

a. The hallmark of sulphur mustard exposure is the occurrence of a latent symptom and sign free period of some hours post exposure. The duration of this period and the severity of the lesions is dependent upon the mode of exposure, environmental temperature and probably on the individual himself. High temperature and wet skin are associated with more severe lesions and shorter latent periods. Some people are markedly more sensitive to mustard than others. Burns may be the result of either vapour or liquid exposure.

b. The sequence of skin changes normally seen is as follows:

(1) *Erythema (2-48 hour post exposure).* This may be very striking and reminiscent of scarlet fever. Slight oedema of the skin may occur. Itching is common and may be intense. As the erythema fades areas of increased pigmentation are left. (This sequence is reminiscent of that seen in sun burn.)

(2) *Blistering.* Blisters are not, per se, painful, though they may be uncomfortable and feel tense. Blisters at points of flexure, anterior aspects of elbows and posterior aspects of knees, can seriously impede movement. Mustard blisters are delicate and may be easily ruptured by contact with bed linen, bandages or during transport of casualties. Crops of new blisters may appear as late as the second week post exposure. Blister fluid is not dangerous and does not produce secondary blistering if applied to skin.

(3) *Deep burning leading to full thickness skin loss.* This is particularly likely to occur on the penis and scrotum.

c. Lesions tend to be painful and some patients complain of very severe pain. Healing of skin lesions is slow. The areas which were markedly erythematous darken and may become very hyperpigmented. Brownish-purple to black discoloration of some areas may occur. These changes tend to disappear over a period of several weeks with desquamation leading to the appearance of areas of hypopigmentation. The appearance of such areas alongside those of hyperpigmentation may be striking.

d. The sensitivity of the skin depends on its thickness and upon the density of sweat and sebaceous glands. Apart from mucous membranes the most sensitive areas are the face, armpits, genitalia, neck, skin between the fingers and the nail beds. The palm of the hand, sole of the foot and the skin of the scalp are very resistant. If only a small dose is applied to the skin the effect is limited to erythema and after several days the colour changes from red to brown. The itch diminishes progressively and the epidermis desquamates. At higher doses blister formation starts, generally between 4 and 24 hours after contact, and this blistering can go on for several days before reaching its maximum. They are often more than 1 $cm^2$ and maybe very large and pendulous. Their domes, which are thin and yellowish, contain a relatively clear or slightly yellow liquid. The blisters are fragile and usually rupture spontaneously giving way to a suppurating and necrotic wound. The necrosis of the epidermal cells is extended to the underlying tissues, especially to the dermis. The damaged tissues are covered with slough and are extremely susceptible to infection. The regeneration of these tissues is very slow, taking from several weeks to several months, much longer than the time required for the restoration of skin destroyed by physical means or by caustic compounds. Healing may result in contractures, scarring and fragile skin which may be easily damaged by trauma.

## 311. Respiratory Tract.

Mustard attacks all the mucous membranes of the respiratory tract. After a latent period of 4 to 6 hours, it irritates and congests the mucous membranes of the nasal cavity and the throat, as well as the epitheliums of the trachea and large bronchi. Symptoms start with rhinorrhoea, burning pain in the throat and hoarseness of the voice. This pain may make the patient reluctant to cough. A dry cough gives way to copious expectoration. The vocal cords often become damaged, resulting in aphonia. Airway secretions and fragments of necrotic epitheliums may obstruct the lungs; rales and reduced air entry can be detected by auscultation. There is pronounced dyspnoea. The damaged lower airways become infected easily, predisposing to bronchopneumonia after approximately 48 hours. If the inhaled dose has been sufficiently high the victim dies in a few days, either from pulmonary oedema or mechanical asphyxia due to fragments of necrotic tissue obstructing the trachea or bronchi, or from superimposed bacterial infection, facilitated by an impaired immune response.

## 312. Bone Marrow.

Mustard agents may cause a general depletion of all elements of the bone marrow. The cells of the granulocyte series and megacaryocytes appear more susceptible to damage than those of the erythropoietic system. A reactive leukocytosis may occur during the first three days, followed by a decrease in the peripheral white cell count. The development of a severe leukopoenia or an aplastic anaemia indicates a poor prognosis.

## 313. Gastrointestinal Tract.

Ingestion of contaminated food or water may cause destruction of mucous membranes. Symptoms include nausea, vomiting, pain, diarrhoea and prostration. These features may make casualties reluctant to eat. Vomit and faeces may be bloodstained. Shock may occur.

## 314. Systemic Action.

Systemically absorbed mustards by any route, including severe skin exposure, may cause signs similar to those of irradiation, such as headache, nausea, vomiting, leucopenia and anaemia. Gastrointestinal pain commonly occurs. Absorption of high doses may result in CNS excitation leading to convulsions, followed by CNS depression. Cardiac irregularities may occur with atrio-ventricular block and cardiac arrest may follow.

# SECTION III -TREATMENT OF MUSTARD LESIONS

## 315. Prophylaxis.

There is no practical drug treatment available for preventing the effects of mustard.

## 316. Therapy.

a. There is no specific treatment available for the treatment of mustard lesions.
b. The aim of therapy is to:
   (1) Relieve symptoms.
   (2) Prevent infections.
   (3) Promote healing.

## 317. Eye Lesions.

a. The effects of mustard on the eyes are very painful. Use of local analgesics may increase corneal damage and are not recommended. Systemic analgesics (narcotics) should therefore be used as required. Secondary infection is a serious complication and increases the amount of corneal scarring. To prevent infection treat with appropriate anti-bacterial preparations. When the lesion proves more serious (blistering of the eyelids, blepharospasm, etc.), continue application of the anti-

bacterial preparation at more frequent intervals. Patients with corneal lesion should receive mydriatics to prevent adhesions between the iris and cornea. In case of troublesome secretions accumulating, the eyes may be carefully irrigated with a 0.9% sterile saline solution and sterile petroleum jelly (Vaseline™) may be applied to the eyelids to prevent sticking. Do not cover the eyes with a bandage, but, if necessary, protect them with dark or opaque goggles. When the eyelids can be separated without too much pain examine the cornea for possible lesions with fluorescein solution followed by lavage: a green spot indicates a lesion, which, when severe should be treated by an ophthalmologist as soon as possible. In some countries ophthalmologists have recommended controversial treatments including the use of citrate and ascorbate eye drops and regular topical steroids.

b. More severe injuries will cause enough oedema of the lids, photophobia and blepharospasm to obstruct vision. This alarms the patients. To allay their fears, the lids may be gently forced open to assure them that they are not blind.

c. Although temporary blindness may occur, permanent blindness is very rare. Casualties should therefore be reassured and a positive attitude taken.

## 318. Skin Lesions.

a. It is important to ensure that no remaining contamination is present before commencing treatment.

b. The skin turns red and itches intensely. This itching can be diminished by local applications of cooling preparations, e.g., calamine lotion, corticosteroids in solution, or even water. Ointments and creams are not advised for microbiological reasons. Severe erythema around the genitalia may become quite painful and associated weeping and maceration may ensure. Often, treatment with exposure of the area is desirable and care must be taken so that secondary infection of tissue does not occur.

c. Infection is the most important complicating factor in the healing of mustard burns. There is no consensus on the need to de-roof blisters or on the optimum form of treatment (open or covered, dry or wet). Once blisters have broken, it is best to remove its ragged roof to decrease the possibility of secondary infection. Routine wound inspection aids in the early detection and institution of appropriate therapy for any complicating bacterial infections. Analgesics should be given as required. Skin grafting is rarely required and when it has been attempted, grafts have not taken well. The use of cytokines is undergoing further research.

d. In a recent review on the casualties from the Iran-Iraq conflict, it appeared that the healing process and the final outcome were more dependent on the severity of the initial lesion than on the treatment applied.

## 319. Respiratory Tract Lesions.

Mild respiratory tract injury, with hoarseness and sore throat only, usually requires no treatment. Cough may be relieved by codeine. Laryngitis and tracheitis may be treated symptomatically with steam or sterile cool mist inhalations. If more severe respiratory tract

injury is suspected, hospitalisation may be advisable. If a bacterial pneumonia occurs, isolation of the specific organisms with their antibiotic sensitivities should be performed, then antibiotic therapy can be limited to the specific agents.

## 320. Systemic Effects.

a. Every effort should be made to maintain adequate metabolic status and to replace loss of fluids and electrolytes. Infection should be treated promptly and vigorously. The use of growth factors is the subject of ongoing research.

b. It has been suggested by some authorities that sodium thiosulphate will prevent or reduce systemic damage from mustard, provided that it can be given intravenously within 20 minutes of exposure. Its efficacy is very doubtful if given later.

## 321. Burns Caused by High Doses of Vapour.

After exposure to a high dose of mustard vapour, especially under tropical conditions, nausea, vomiting and symptoms of collapse are usually evident before erythema develops completely. It is important to note that this occurs also among personnel who are masked during exposure. Constitutional symptoms may persist several days, during which burns will increase in severity. Cases of this type should be classed as casualties. Severe vapour burns of the trunk produce a generalised erythema but include pale grey areas that eventually vesicate or become necrotic. It is common to see patches of unaffected skin as a result of protection by overlying equipment.

## 322. Burns Caused by Low Doses of Vapour.

Mild vapour burns cause erythema, itching, and irritation but do not produce casualties. The medical officer should always consider the interval after exposure in relation to the severity of the burn. Mild lesions may represent early phases of severe exposure to vapour. When the period since exposure is uncertain, rapidity of development and the presence of constitutional symptoms may help to determine the severity.

## 323. Sensitisation Due to Multiple Exposures to Mustard.

a. Attention should be paid to the characteristic appearance of “re-exposure” burns. This manifestation may occur in individuals as a result of exposure to mustard 1 to 3 weeks (or more) previously. A small percentage of men and women will become sensitised to the agent and will react differently, both qualitatively and quantitatively, upon re-exposure. Sensitisation will be followed by a more rapid onset of symptoms upon re-exposure. Erythema, with or without oedema, and pronounced itching and burning usually appear within 1 hour. Lower concentrations of mustard may produce effects in a sensitised person than in a non-sensitised person. When erythema and oedema result from exposure to a low dose, they generally develop rapidly and subside within 2 to 3 days. Also, vesication resolves

more rapidly in the sensitised individual.

b. One of the most frequent manifestations of re-exposure in sensitised individuals is the development of a morbilliform rash. Another characteristic reaction is the appearance of eczematoid dermatitis surrounding old lesions, whether or not they are healed. This may last for several days and resembles dermatitis venenata (from poison ivy). Similar phenomena due to sensitisation have been known to occur with the nitrogen mustards.

## 324. Disposition of Casualties.

a. Evaluation of lesions that have most generally led to disability of personnel exposed to blister agents during field trials and who subsequently participated in simulated combat exercises, obstacle course tests and marches, resulted in the following observations:

(1) Widespread vesication of the trunk produced casualties.

(2) Vesication localised in particular areas of the body produced casualties.

(3) Burns caused by high doses of the vapour to masked personnel, especially in tropical climates, are of casualty severity partly due to oedema and vesication of the skin and partly to constitutional reactions such as nausea, vomiting and prostration.

(4) Burns produced by doses of vapour low enough to cause only such skin reactions as mild erythema, oedema, burning and itching usually do not produce casualties.

(5) The stage of development of the lesion must be considered when classifying an individual as a casualty or non-casualty.

b. The effects of mustard on particular areas of the body are explained below.

## 325. Trunk and Neck.

*a. Extensive Vesication of the Trunk.*

(1) All the patients considered under this heading should be evacuated promptly. Extensive vesication may occur over a large part of the trunk. Intervening areas of skin may be erythematous with pin-point vesication. These burns are more likely to occur on the back than anteriorly.

(2) Some protection is afforded anteriorly by equipment such as webbing and ammunition pouches. The front of the uniform also gives some anterior protection because it does not cling to the body.

(3) Extensive vesication may be followed by fever, nausea and vomiting.

(4) These effects tend to occur more readily in tropical climates.

(5) Secondary bacterial infection may complicate the clinical course. The medical officer in a forward position is not likely to see infection of vesicated areas because such cases will have been evacuated before secondary infection develops.

*b. Localised Vesication of the Trunk.*

(1) Vesication occurring within the natal cleft (between the buttocks) usually requires evacuation of the casualty. Walking becomes difficult, defecation is

painful and dressings require frequent changing. The lesion is usually most intense at the upper end of the cleft. Vesication of the buttocks usually results from sitting on contaminated ground or in contaminated trousers for prolonged periods. The vesicated area may extend forward across the perineum to involve the scrotum and the penis.

(2) Trivial burns, such as mild erythema affecting the natal cleft, are not of casualty severity. However, these burns require careful attention because walking or running aggravates the lesions and may break down injured skin.

(3) Single discrete blisters on the buttocks away from the natal cleft do not produce casualties.

(4) Blisters on the trunk generally require protective dressings to prevent friction due to clothing. The medical officer must decide whether dressings should remain in position during regular duty.

## 326. Arms.

a. Most individuals with blister agent injuries of the arms, when suitably treated, are permitted to continue with their duties. Vesication, when localised produces little or no disability.

b. Extensive vesication involving the axillae and the elbows, volar or dorsal aspects, partially impairs the movement of the limbs at those joints. Oedema of the surrounding tissue tends further to immobilise the extremities. The dorsal aspects of the elbow and forearm are common sites of severe burns because these parts touch contaminated ground when men and women are firing in the prone position. Casualties of this type should be evacuated.

c. Widespread vesication of the arms results in partial disability. Casualties of this type should be evacuated.

## 327. Hands.

a. Blister agent burns of the hands are often encountered. These burns tend to cause a degree of disability out of proportion to the size of the lesions. Considerable care and judgement are required in correct disposition.

b. Experience in tropical experimental installations indicates that protective gloves and protective ointment provide adequate protection against high doses of vapour. Yet it is hard to avoid burns of the hands in a heavily contaminated jungle. The palms are more resistant to vesication but blisters affecting the palms are characteristically painful and slow to heal.

c. A solitary lesion of limited extent may result in little or no disability if treated properly.

d. Burns from liquid vesicant on the dorsum of the hand result in severe local reactions characterised by intense oedema of the backs of the hands and fingers. Pain is characteristic and is intensified by movement of the fingers or wrist. These patients should be regarded as casualties. An individual exposed within the previous 24 hours and reporting for treatment with apparently trivial blisters may be totally incapacitated the following day. Sharp erythema of the dorsum of the hand, with

vesication beginning 12 to 24 hours after exposure, indicates a lesion that will progress to extensive vesication and oedema. Under such circumstances the individual should be evacuated when first seen.

e. More commonly, the lesions consist of scattered small vesicles and limited areas of erythema. These lesions can be protected satisfactorily and the individuals returned to duty.

f. Exposure to vesicant vapour produces diffuse erythema of the dorsum of the hand and wrist. Higher doses cause oedema and vesication as well; patients of this type require evacuation.

## 328. Lower Extremities.

a. When the lower extremities are involved, the knees are the most common sites of burns from liquid vesicant. These lesions and those of the ankles often result in incapacitation by interfering with locomotion. Movement of joints tends to aggravate existing lesions by increasing oedema. A further disabling factor is introduced by the wearing of firm dressings applied to mobile joints.

b. Vesication often spreads over the kneecaps, upward onto the thighs, and down toward the feet. These burns tend to be extensive and are associated with oedema often extending halfway up the thigh and down the leg. Medical officers should evacuate casualties with such lesions.

c. In general, burns of the leg are more incapacitating than burns of the thigh.

d. It has been shown that the presence of many superficial blisters on the legs and thighs alone is not enough to make an individual incapable of carrying out routine military duties. Individuals with such lesions, having suitable dressings, were able to take part in daily marches and routine gun drills. In disposing of these cases, the medical officer will consider the mental and physical status of the individual, his or her willingness to carry on, and the tactical situation at the time. Such patients are in the category of partial disability. After suitable dressings have been applied, individuals with high morale and robust physiques may be returned to duty.

e. A relatively small blister or group of blisters situated in the popliteal area may reduce the efficiency of a man or woman so much that he or she may require evacuation. This is due to aggravation of the lesions by movement of the limbs and interference with ambulation. However, blisters affecting this area are not necessarily casualty-producing. (Inflammation, oedema, infection and lesions on other parts of the body should be considered when deciding upon the disposition of an individual). Available evidence indicates that the mustard blister, size for size, is potentially more incapacitating than a blister from lewisite. This results from the tendency of mustard blisters to be associated with erythema and oedema, while the lewisite blister usually causes little local reaction.

f. Vesicant lesions also develop near the ankles at the tops of the shoes. Blistered areas occurring at such unprotected points are associated with severe pain due to circulatory impairment and tense oedema of the leg. These patients should be evacuated.

g. Vapour burns of the legs tend to be most aggravated in the popliteal spaces. Pin-point

vesication is often found here. Higher doses cause intense erythema with scattered areas of vesication over the entire surface of the leg. Such lesions are invariably casualty producing and are generally accompanied by severe burns elsewhere, frequently with severe systemic effects.

h. Mild vapour burns of the legs produce irritation and itching common to all widespread vapours burns. While these effects are troublesome, they are not casualty producing, and men or women so affected maybe returned to duty.

i. Extensive vesication of the feet is uncommon. The soles are protected by shoes and are comparatively resistant to vesication. Burns on the dorsal aspect of the foot are often associated with local reactions like those seen on the backs of hands. Individuals with these burns, especially if widespread over the foot, find it difficult or impossible to wear shoes and will require evacuation. Small discrete blisters may be of non-casualty significance. These blisters may be effectively protected so as to allow wearing of shoes and walking with little discomfort.

## 329. Genitalia.

a. The genital region, in addition to the eyes and the respiratory tract, is highly sensitive to blister agent burns. In World War I such burns produced many casualties. The majority of these burns were caused by vapour. Despite present methods of protection against blister agents, including impregnated garments designed to protect the genitalia, medical officers (especially in tropical areas) may be confronted with many casualties with such burns.

b. Vapour is a more common cause of burns affecting the male genitalia than liquid agent. Erythema may not be conspicuous. The most prominent feature of the burn is the oedema involving the penis and scrotum. Fluid accumulates most readily in the prepuce, distending its entire circumference and forming a characteristic semitranslucent ring around the cornea. In more severe cases the entire body of the penis becomes oedematous.

c. The lesions cause apprehension as well as physical discomfort. Occasionally vesication is superimposed on the oedema. Ulceration is not infrequent at the tip of the prepuce where it may become secondarily infected. In severe cases associated with marked oedema, retention of urine may result from both mechanical and reflex effects.

d. In mild cases, objective changes of the scrotum often tend to pass undetected due to the normal pigmentation, elasticity, and looseness of the skin. Even considerable oedema may not be enough to reveal its presence. In severe cases the scrotum may become grossly enlarged. The rugae may be partly or completely obliterated. Pin-point vesication may occur, usually after a lapse of a few days. The scrotal skin tends to breakdown resulting in small painful ulcers and fissures.

e. Burning is the most prominent subjective symptom in involvement of the genitalia. Apprehension and anxiety are distressing during the presence of the objective changes described above. As oedema decreases, itching starts and may persist long after the acute effects have subsided. Sometimes this itching is intolerable. The scrotum may continue to crack and ulcerate for a considerable period, causing pain and irritation.

f. Mild exposure of the genital region characteristically is followed by a delay in tie development of symptoms, often for as long as 4 to 10 days.

g. Patients with mild burns without oedema or vesication, but who complain of irritation and burning, may be safely returned to duty following treatment. In disposing of mild burns of the genitalia, the medical officer must assure himself that the symptoms are not too early to be judged with finality. Severely affected individuals should be evacuated on the basis of the apprehension that may be suffered as well as the physical discomfort involved.

## 330. Systemic Effects of Cutaneous Burns.

a. Systemic effects due to blister agents probably may be encountered with disabling skin lesions and lesions of the respiratory tract. The medical officer should be familiar with the signs and symptoms. These include anorexia, nausea, vomiting, depression and fever and are far more prone to occur in hot than in temperate climates. Malaise and nausea generally are the first reactions and may then progress either to mild, transient vomiting or to severe, persistent vomiting and retching. Anorexia may be the only complaint in mild reactions. The actual time of onset of symptoms is 4 to 12 hours after exposure and symptoms often occur before skin injury is manifest. No rule can be given for the duration of systemic symptoms, although men or women usually have recovered from severe vomiting within 24 to 26 hours. Anorexia and nausea may persist for a longer time.

b. The temperature may remain elevated for several days. Mental depression may follow mustard burns and persist for several days.

c. People with systemic reactions will generally be casualties, particularly in view of the probability of associated extensive skin burns. Such casualties should be evacuated quickly.

## 331. Secondary Bacterial Infection in Blister Agent Burns.

a. This paragraph considers the problem of secondary bacterial infection after blister agent injuries only as it influences the disposition of affected personnel in forward positions.

b. Secondary bacterial infection has often been cited as a common complication of mustard burns of the skin. Compared with the incidence of infection in thermal and traumatic wounds, indications are that the incidence of sepsis in mustard lesions is remarkably low according to observations made at experimental installations.

c. Secondary infection becomes manifest several days after injury. Medical officers are not likely to see secondary infection with extensive blister agent burns in the front lines because severely affected patients should have been evacuated early.

d. Infection of small lesions does not require evacuation. Infection of multiple lesions is likely to be an indication for evacuation, particularly if constitutional effects are associated. Infection is particularly disabling when it involves the feet, the hands, the genitalia or tissues overlying the joints of the limbs.

e. Secondary infection is more likely to occur in severe, rather than mild, vapour injury

to the respiratory tract. Severe respiratory symptoms will almost invariably be associated with severe eye effects. Respiratory lesions may not develop for several days, and by then the individual should have been evacuated as an eye casualty.

f. Secondary infection is uncommon as a sequel to mild degrees of mustard conjunctivitis and ordinarily would not prevent an individual from continuing duty.

g. Mild conjunctival burns maybe associated with pharyngitis, laryngitis, and tracheitis, increasing in severity for several days. Occasionally more extensive respiratory infection may ensue.

## 332. Course and Prognosis.

As has already been stated, the great majority of mustard gas casualties survive. Resolution of specific problems can be difficult to predict but the following may provide a guide.

a. *Eye lesions:* Most are resolved within 14 days of exposure.

b. *Skin lesions:* Deep skin lesions maybe expected to heal in up to 60 days. Superficial lesions heal in 14-21 days.

c. *Upper respiratory tract lesions:* It is very difficult to define a time course for complete recovery. Recent experience with patients from the Iran-Iraq conflict during 1984-86 was that they were often discharged whilst still coughing and complaining of expectoration. Lung function tests on patients with purely upper respiratory tract lesions were usually normal on discharge. Patients with parenchymal damage often showed an abnormal pattern on lung function testing.

## 333. Long Term Effects of Mustard Gas Poisoning.

The long term effects of mustard maybe divided into three groups:

a. Personnel exposed to mustard agents may experience prolonged psychological manifestations including chronic depression, loss of libido and anxiety.

b. Local effects of mustard exposure may include:

(1) Visual impairment (permanent blindness is extremely rare).

(2) Scarring of the skin.

(3) Chronic bronchitis.

(4) Bronchial stenosis.

(5) Increased sensitivity to mustard gas.

c. Sulphur mustard is a known carcinogen. A follow up study of American soldiers exposed to sulphur mustard during World War I revealed an increased incidence of lung cancer (and chronic bronchitis) as compared with soldiers who had sustained other injuries. A study of British workers involved in the production of sulphur mustard during World War II revealed no increase in deaths due to cancer amongst those who had died since 1945, but an increase in the prevalence of laryngeal carcinoma amongst those still alive.

## SECTION IV - ARSENICAL VESICANTS - LEWISITE

### 334. Introduction.

The arsines possessing the $-AsCl_2$ group are endowed with vesicant properties. Of these lewisite is the best known and the most characteristic. Initially preparations contained considerable impurities, but at the end of World War I it was purified in the US, without having been used on the battlefield. Lewisite is 2-chlorovinyl-dichloroarsine, $ClCH=CH-AsCl_2$.

### 335. Physical and Chemical Properties.

a. *Physical Properties.* In a pure form lewisite is a colorless and odourless liquid, but usually contains small amounts of impurities that give it a brownish colour and an odour resembling geranium oil. It is heavier than mustard, poorly soluble in water but soluble in organic solvents. The physical properties are shown in Table 3-I.

b. *Chemical Properties.* In contact with water lewisite is hydrolyses at an appreciable rate, forming an oxide that is equally vesicant, according to the reaction: $ClCH=CH-AsCl_2 + H_2O \rightarrow ClCH=CH-AsO + 2HCl$. In contact with strong alkalis lewisite is totally decomposed to non-vesicant products. Lewisite is very sensitive to oxidants due to the trivalent arsenic atom.

### 336. Detection.

The detection of lewisite is facilitated by the fact that it forms coloured products with many reagents. Draeger™ tubes are available which react with organic arsenical. However, no automatic detectors are available for use in the field.

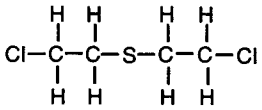
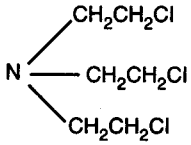
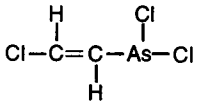
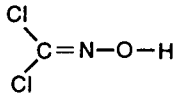
### 337. Protection.

Ordinary clothing gives little or no protection against lewisite. Special equipment including a respirator, NBC suit, gloves and overboots are required.

### 338. Decontamination.

Decontamination is the same as for mustard.

*Table 3-I. Physical Properties of Vesicants*

| Property | Sulphur mustard | Nitrogen mustard | Lewisite | Mustard/ lewisite mix | Phosgene oxime |
|---|---|---|---|---|---|
| Appearance | Colourless to light yellow liquid, giving off a colourless vapour | Dark coloured liquid giving off a colourless vapour | Dark oily liquid giving off a colourless vapour | Dark oily liquid giving off a colourless vapour | White solid or yellow-brown liquid |
| Chemical formula |  |  |  | |  |
| Molecular weight | 159.1 | 204.5 | 207.35 | Not applicable | 113.9 |
| Density ($g.cm^{-3}$) | 1.27 (25°C) | 1.24 (25°C) | 1.89 (20°C) | 1.66 (20°C) | |
| Melting point | 14.5 °C | -3.7°C | -8 to 0.1°C (diff. purity) | -24.4°C | 39 to 43°C |
| Boiling point | 217.0 °C | 256.0°C | 190.0°C | 190.0°C | 129.0°C |
| Vapour density | 5.4 | 7.1 | 7.1 | 6.5 | 3.94 |
| Vapour pressure (mmHg) | 0.072 (°20C) | 0.011 | 0.087 (0°C)<br>0.394 (20°C) | 0.02 (-10°C)<br>0.248 (20°C)<br>1.03 (40°C) | 3.6 (20°C) |
| Volatility ($mg.m^{-3}$) | 75 (0°C)<br>610 (20°C)<br>2860 (40°C) | 13 (0°C)<br>121 (25°C)<br>390 (40°C) | 1060 (0°C)<br>4480 (20°C)<br>8260 (30°C) | 240 (-11°C)<br>2730 (20°C)<br>10270 (40°C) | 20,000 (20°C)<br>60,000 (35°C) |





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## 339. Mechanism of Action.

a. Due to its physical and chemical properties, lewisite can easily penetrate the skin, where it exerts its vesicant action. It can spread through the whole body and act as an arsenical poison. It has been shown that lewisite inhibits a great number of SH (percentage saturation of hemoglobin) group containing enzymes. Inhibition of the pyruvate dehydrogenase system is a property common to all trivalent arsenic compounds.

b. Lipoic acid is an essential part of the pyruvate dehydrogenase system, acting as a co-enzyme in the formation of acetyl-Co-A from pyruvate. Lewisite is thought to combine with lipoic acid to form a cyclic compound, thereby interfering with energy production within the cell (Figure 3-II).

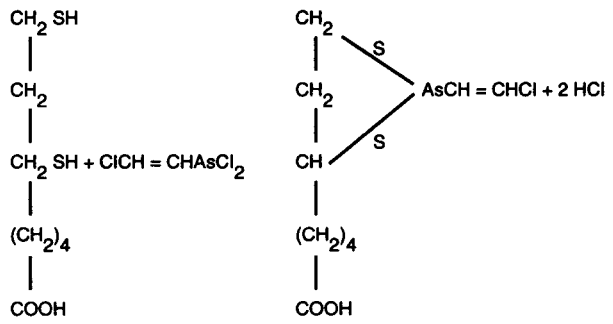


*Figure 3-II. Formulation of Cyclic Compound From Lewisite*

## SECTION V - CLINICAL-PATHOLOGICAL EFFECTS

## 340. Eyes.

Liquid arsenical vesicants cause severe damage to the eye. On contact, pain and blepharospasm occur instantly. Oedema of the conjunctival and lids follow rapidly and close the eye within an hour. Inflammation of the iris usually is evident by this time. After a few hours, the oedema of the lids begins to subside, while haziness of the cornea develops and iritis increases. The corneal injury, which varies with the severity of the exposure, may heal without residual effects, induce pannus formation, or progress to massive necrosis. The iritis may subside without permanent impairment of vision, if the exposure was mild. After heavy exposure, hypopyon may ensue, terminating in necrosis, depigmentation of the iris and synechia formation. Liquid arsenical vesicants instantly produce a grey scarring of the cornea, like an acid burn, at the point of contact. Necrosis and sloughing of both bulbar and palpebral conjunctival may follow very heavy exposure. All injured eyes are susceptible to secondary infection. Mild conjunctivitis due to arsenical vesicants heals in a few days without specific treatment. Severe exposure may cause permanent injury or blindness.

## 341. Skin.

a. *Pathology*. Liquid arsenical vesicants produce more severe lesions of the skin than liquid mustard. Contamination of the skin is followed shortly by erythema, then by vesication which tends to cover the entire area of erythema. The surrounding halo of erythema is less noticeable than with mustard blisters, although the two are often indistinguishable. Microscopically, the blister roof is slightly thicker than the mustard blister roof, consisting of almost the complete thickness of the epidermis and showing more complete coagulation necrosis and less disintegrative necrosis than that of the mustard blister. The yellowish blister fluid is slightly more opaque than that of the mustard blister and microscopically, contains more inflammatory cells. It contains a trace of arsenic but is non-toxic and non-vesicant. There is deeper injury to the connective tissue and muscle, greater vascular damage, and more severe inflammatory reaction than is exhibited in mustard burns. In large, deep, arsenical vesicant burns, there may be considerable necrosis of tissue, gangrene and slough.

b. *Symptoms*. Stinging pain is felt usually in 10 to 20 seconds after contact with liquid arsenical vesicants. The pain increases in severity with penetration and in a few minutes becomes a deep, aching pain. Pain on contact with liquid arsenical vesicants usually gives sufficient warning so that decontamination may be begun promptly and deep burns thus avoided in conscious victims. After about 5 minutes of contact, there appears a grey area of dead epitheliums resembling that seen in corrosive burns. Erythema is like that caused by mustard but is accompanied by more pain. Itching and irritation persist for only about 24 hours whether or not a blister develops. Blisters are often well developed in 12 hours and are painful at first, in contrast to the relatively painless mustard blister. After 48 to 72 hours, the pain lessens.

## 342. Respiratory Tract.

The vapours of arsenical vesicants are so irritating to the respiratory tract that conscious casualties will immediately put on a mask to avoid the vapour. No severe respiratory injuries are likely to occur except among the wounded who cannot put on masks and the careless, who are caught without masks. The respiratory lesions are similar to those produced by mustard except that in the most severe cases, pulmonary oedema may be accompanied by pleural effusion.

## 343. Systemic Effects.

Liquid arsenical vesicants on the skin, as well as inhaled vapour, are absorbed and may cause systemic poisoning. A manifestation of this is a change in capillary permeability, which permits loss of suficient fluid from the bloodstream to cause haemoconcentration, shock and death. In non-fatal cases, haemolysis of erythrocytes has occurred with a resultant haemolytic anaemia. The excretion of oxidised products into the bile by the liver produces focal necrosis of that organ, necrosis of the mucosa of the biliary passages with peribiliary hemorrhages and some

injury of the intestinal mucosa. Acute systemic poisoning from large skin burns causes pulmonary oedema, diarrhoea, restlessness, weakness, subnormal temperature and low blood pressure.

## SECTION VI - TREATMENT OF LEWISITE LESIONS

### 344. General.

An antidote for lewisite is dimercaprol (2, 3-dimercapto-propanol, $CH_2SH$ - CHSH - $CH_20H$, BAL (British Anti Lewisite)). Purified dimercaprol is a colorless liquid, soluble 1 part in 15 parts of water and more soluble in peanut oil or in ethanol. It can combine with arsenic forming a water soluble complex that can be excreted. With arsenical, the complex formed possesses a pentagon with two carbon atoms, two sulphur atoms and one arsenic atom at the comers. This is the same mechanism by which lewisite blocks two adjacent SH groups of pyruvate dehydrogenase system. The therapeutic action of dimercaprol can thus be explained by the law of mass action: dimercaprol provides the organism with a great number of adjacent SH groups that displaces the arsenic bound to enzymes. The enzymes are reactivated and can resume their normal biological activity. However, the toxicity of dimercaprol itself must be considered. It sometimes provokes local irritation.

### 345. Eyes.

a. Dimercaprol eye ointment may diminish the effects of lewisite if applied within 2 minutes of exposure. Its value is questionable if applied later than this.

b. In severe cases, the systemic use of morphine may be necessary for control of pain. When the conjunctival oedema subsides enough to permit ophthalmic examination, the cornea should be stained with fluorescein to detect erosions and the iris should be examined for iritis. Atropine sulphate ointment should be instilled to obtain and maintain good mydriasis in all cases with corneal erosions, iritis cyclitis or with marked photophobia or miosis. Antibiotics may be used to combat infection. Sterile petroleum jelly (Vaseline™) applied to the lid margins will help prevent their sticking together. Irrigations of the eye should be sparing, employing isotonic solutions. Occlusive dressings or pressure on the globe must be avoided.

### 346. Skin.

a. Dimercaprol (British Anti-Lewisite (BAL)) ointment may be applied to skin exposed to lewisite before actual vesication has begun. Any protective ointment already on the skin must be removed before application of BAL ointment because it may destroy the latter. BAL ointment is spread on the skin in a thin film and allowed to remain at least 5 minutes. Occasionally, BAL ointment causes stinging, itching or urticarial weals. This condition lasts only an hour or so and should not cause alarm. Mild dermatitis may occur if BAL ointment is frequently applied on the same area of skin; hence, this property precludes its use as a protective ointment. Dimercaprol is chemically incompatible with silver sulphadiazine and the two should not be used together.

b. Some blistering is inevitable in most arsenical vesicant cases which come to the

Medical Services. The treatment of the erythema, blisters and denuded areas is identical with that for similar mustard lesions. A severe third degree burn involving a large surface area is similar to a thermal injury and must be managed by intravenous resuscitation to correct potential hypovolaemic shock. Morphine and splinting of the affected parts may be necessary to relieve pain. When the involved area is greater than 20% of the body surface area, hospitalisation is indicated. Hospitalisation may be indicated when the involved area is less than 20% when the depth of the skin involvement appears to be significant.

## 347. Systemic.

burns severe enough to cause shock and systemic poisoning are life-threatening. Even if the patient survives the acute effects, the prognosis must be guarded for several weeks.

## 348. Indication for Systemic Treatment.

The indications for systemic treatment, following exposure to arsenical blister agents by any route are:

a. Cough with dyspnoea and frothy sputum, which may be blood tinged and other signs of pulmonary oedema.

b. A skin burn the size of the palm of the hand or larger, caused by a liquid arsenical blister agent which was not decontaminated within the first 15 minutes.

c. Skin contamination by a liquid arsenical vesicant covering 5% or more of the body surface, in which there is evidence of immediate skin damage (grey or dead-white blanching of the skin), or in which erythema develops over the area within 30 minutes.

## 349. Types of Treatment.

a. The following two types of treatment may be used:

(1) Local neutralisation on and within the skin by a liberal application of dimercaprol (BAL) ointment. The affected skin is to be left covered with a layer of ointment. Remove any other protective ointment before treatment with BAL ointment.

(2) Intramuscular injection of BAL in oil (10%).

b. The maximum dosage of BAL is as follows. 3 $mg.kg^{-1}$(200 mg for an average person) intramuscularly repeated every 4 hours for 2 days, every 6 hours on the third day and every 12 hours for up to 10 days. The injection must be by deep intramuscular injection; subcutaneous leakage must be avoided.

c. Dimercaprol when given by injection often produces alarming reactions including:

(1) Increased systolic and diastolic pressure.

(2) Tachycardia.

(3) Nausea and vomiting.

(4) Headache.

(5) Burning sensation of lips.

(6) Feeling of constriction of the chest.

(7) Conjunctivitis.
(8) Lachrymation.
(9) Rhinorrhoea.
(10) Sweating.
(11) Anxiety and unrest.

d. Despite these effects "the cure is not worse than the disease" and they pass in a few hours. About 50% of patients will experience such adverse reactions if 5 $mg.kg^{-1}$ doses of dimercaprol are given.

e. Unless unduly severe or prolonged they do not contra-indicate the full course of treatment.

## 350. Therapy.

a. Dimercaprol is the current therapy for lewisite poisoning. Newer chelating agents, however, have been developed and some look promising for systemic use.

b. The abbreviations used in this paragraph are as follows:

(1) DMSA (meso-dimercaptosuccinic acid).
(2) DMPS (2,3-dimercapto-l-propanesulfonic acid).
(3) Na (salt).
(4) DMPA (N-(2,3-dimercaptopropyl)-phthalamidic acid).

c. Their formulae and that of dimercaprol are shown in Figure 3-III.

d. The advantages of these compounds include:

(1) They are water soluble, active when given orally and relatively non-toxic.
(2) They are substantially more effective systemically, using the therapeutic index as a measure.
(3) BAL produces mobilisation of arsenic from most tissues (for brain see (4)) but is less effective in so doing than DMSA, DMPS and DMPA.
(4) BAL given to rabbits poisoned with sodium arsenite produced an increase in brain arsenic levels. DMPA and DMPS on the other hand produced a marked fall in brain arsenic levels.
(5) DMSA and DMPS have been identified as having an anti-lewisite action.
(6) Of the series DMPS, DMSA and BAL when tested for capacity to reverse or prevent pyruvate dehydrogenase inhibition by sodium arsenite, DMPS proved the most potent and BAL the least potent drug.

e. The evidence then appears to support the contention that the more recently developed chelating agents should be considered as alternatives to dimercaprol in the treatment of systemic lewisite poisoning. Detailed metabolic studies have not yet been performed on DMSA and DMPS and there is an urgent need for such work.

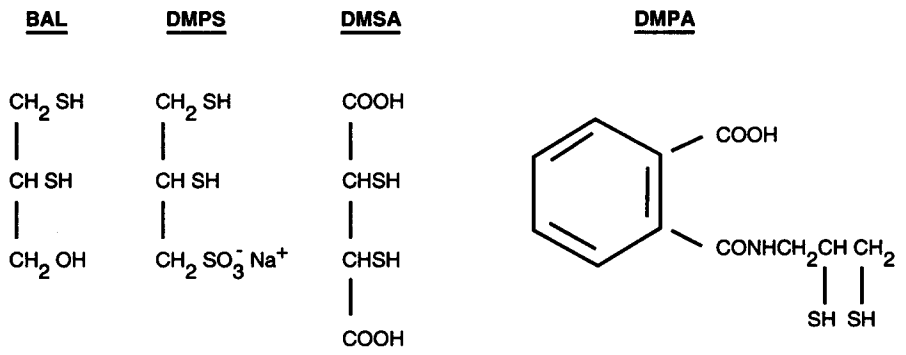


*Figure 3-III. Formulae for Lewisite Antidotes*

## 351. Course and Prognosis.

The long term effects of exposure to lewisite are unknown.

## SECTION VII - HALOGENATED OXIMES

## 352. Introduction.

The urticant properties of the halogenated oximes were discovered long before World War II. To this group belong diiodofomoxime, dibromoformoxime, monochloroformoxime and dichloroformoxime. The last mentioned oxime is the most irritant of the series; it is commonly known as phosgene oxime, symbolised by CX. Its chemical formula is $CCl_2 = NOH$.

## 353. Physical and Chemical Properties of Phosgene Oxime.

Phosgene oxime is a white crystalline powder. It melts between 39 - 40°C, and boils at 129°C. By the addition of certain compounds it is possible to liquify phosgene oxime at room temperature. It is fairly soluble in water and in organic solvents. In aqueous solution phosgene oxime is hydrolyses fairly rapidly, especially in the presence of alkali. It has a high vapour pressure, its odour is very unpleasant and irritating. Even as a dry solid, phosgene oxime decomposes spontaneously and has to be stored at low temperatures.

## 354. Detection.

The characteristic signs and symptoms of phosgene oxime exposure may suggest its use. There are no automatic detectors available for use in the field.

## 355. Protection.

Ordinary clothing gives little or no protection against phosgene oxime. Special equipment including a respirator, NBC suit, gloves and overboot are required.

## 356. Decontamination.

Chemical inactivation using alkalis is effective, whereas chlorination is ineffective against phosgene oxime. The eyes should be flushed immediately using water or isotonic sodium bicarbonate solution if available. Physical decontamination of the skin using adsorbent powders, e.g., fullers' earth, is advised.

## 357. Mechanism of Action.

In low concentrations, phosgene oxime severely irritates the eyes and respiratory organs. In high concentrations, it also attacks the skin. A few milligrams applied to the skin cause severe irritation, intense pain, and subsequently a necrotising wound. Very few compounds are as painful and destructive to the tissues. Systemic toxicity has been described from parenteral absorption. The exact mode of action is not known. The effects are said to be caused by phosgene oxime reacting with SH and $H_2N$ groups.

## 358. Clinical-Pathological Effects.

Phosgene oxime also affects the eyes, causing corneal lesions and blindness and may affect the respiratory tract causing pulmonary oedema. The action on the skin is immediate: phosgene oxime provokes irritation resembling that caused by a stinging nettle. A few milligrams cause intense pain which radiates from the point of application, within a minute the affected area turns white and is surrounded by a zone of erythema which resembles a wagon wheel in appearance. In 1 hour the area becomes swollen and within 24 hours the lesion turns yellow and blisters appear. Some days later the area shows desquamation with necrosis of the skin followed by crust formation and a purulent discharge.

## 359. Treatment.

Treat as any other ulcerated necrotic skin lesion (e.g., thermal burn) with due consideration of other supportive measures. Pulmonary oedema should be treated appropriately.

## 360. Course and Prognosis.

Recovery takes 1 to 3 months.

# CHAPTER 4

# LUNG DAMAGING AGENTS (CHOKING AGENTS)

## SECTION I - GENERAL

### 401. Introduction.

a. *Definition.*

(1) Chemical agents which attack lung tissue, primarily causing pulmonary oedema, are classed as lung damaging agents. To this group belong phosgene (CG), diphosgene (DP), chlorine (Cl) and chloropicrin (PS). Certain other substances, while, not likely to be used as agents, are still likely to be met with on the battlefield (e.g., nitrous fumes and zinc chloride smoke in an undeliquesced state) and may have a similar action.

(2) Similar substances encountered in fires, e.g., perfluoroisobutylene (PFIB) and HCl may also induce lung damage.

b. *Phosgene.* The toxic action of phosgene is typical of a certain group of lung damaging agents. Phosgene is the most dangerous member of this group and the only one considered likely to be used in the future. Phosgene was used for the first time in 1915, and it accounted for 80% of all chemical fatalities during World War I.

## SECTION II - PHOSGENE

### 402. Physical and Chemical Properties.

Phosgene is a colorless gas under ordinary conditions of temperature and pressure. Its boiling point is 8.2°C, making it an extremely volatile and non-persistent agent. Its vapour density is 3.4 times that of air. It may therefore remain for long periods of time in trenches and other low lying areas. In low concentrations it has a smell resembling new mown hay. Phosgene is readily soluble in organic solvents and fatty oils. In water, phosgene is rapidly hydrolyses with the formation of hydrochloric acid and carbon dioxide. Its physical properties are shown in Table 4-I.

### 403. Detection.

There are no automatic detectors available for use in the field.

### 404. Protection.

The respirator gives adequate protection against this agent.

*Table 4-I. Physical Properties of Lung Damaging Agents*

| Property | Phosgene (CG) | | Diphosgene (DP) | |
|---|---|---|---|---|
| Appearance | Colourless gas | | Colourless gas | |
| Chemical formula | COCl2 | | $ClCOOCCl_3$ | |
| Molecular weight | 98.2 | | 197.9 | |
| Density ($g.cm^{-3}$) | 1.38 | (20°C) | 1.65 | (20°C) |
| Melting point | -128.0°C | | -57°C | |
| Boiling point | 7.6°C | | 127°C | |
| Vapour density | 3.4 | | 6.8 | |
| Vapour pressure (mmhg) | 365<br>555<br>1173 | (-10°C)<br>( 0°C)<br>(20°C) | 1.0<br>4.2 | ( 0°C)<br>(20°C) |
| Volatility ($mg.m^{-3}$) | 528,000<br>2,200,000<br>4,300,000 | (-40°C)<br>(-10°C)<br>( 7.6°C) | 12,000<br>45,000<br>270,000 | ( 0°C)<br>(20°C)<br>(52°C) |

## 405. Decontamination.

Because of its physical and chemical properties, the agent will not remain in its liquid form for long, and decontamination is not required except when it is used in very cold climates.

## 406. Mechanism of Action.

a. The mode of action is still not fully understood. It has been suggested that phosgene may act by inhibiting enzymes, or by producing HCl in the alveoli. It has more recently been suggested that phosgene, which is itself a highly reactive molecule, may react directly and instantaneously at the alveolar and capillary wall, permitting plasma to flood the alveoli. Its effects usually reach a maximum 12-24 hours after exposure.

b. Whatever the mechanism of action, phosgene increases the permeability of the alveolar capillaries with resultant pulmonary oedema. This interferes with pulmonary gaseous exchange, leading to hypoxia. The loss of fluid into the alveoli also results in haemoconcentration which, together with hypoxia, causes cardiac embarrassment which may proceed to cardiac failure.

## 407. Clinical-Pathological Effects.

The outstanding feature of phosgene poisoning is massive pulmonary oedema. This is preceded by damage to the bronchiolar epitheliums, development of patchy areas of emphysema, partial atelectasis, and oedema of the perivascular connective tissue. The trachea and bronchi are usually normal in appearance. This contrasts with the findings in chlorine and chloropicrin poisoning in which both structures may show serious damage to the epithelial lining with desquamation. The lungs are large, oedematous and darkly congested. Oedema fluid, usually frothy, pours from the bronchi and may be seen escaping from the mouth and nostrils. With exposure to very high concentrations death may occur within several hours; in most fatal cases pulmonary oedema reaches a maximum in 12 hours followed by death in 24-48 hours. If the casualty survives, resolution commences within 48 hours and, in the absence of complicating infection, there may be little or no residual damage.

## 408. Signs and Symptoms.

During and immediately after exposure, there is likely to be coughing, choking, a feeling of tightness in the chest, nausea, and occasionally vomiting, headache and lachrymation. The presence or absence of these symptoms is of little value in immediate prognosis. Some patients with severe coughs fail to develop serious lung injury, while others with little sign of early respiratory tract irritation develop fatal pulmonary oedema. There maybe an initial slowing of the pulse, followed by an increase in rate. A period follows during which abnormal chest signs are absent and the patient may be symptom-free. This interval commonly lasts 2 to 24 hours but may be shorter. It is terminated by the signs and symptoms of pulmonary oedema. These begin with cough (occasionally substernally painful), dyspnoea, rapid shallow breathing and cyanosis. Nausea and vomiting may appear. As the oedema progresses, discomfort, apprehension and dyspnoea increase and frothy sputum develops. Rales and rhonchi are audible over the chest, and breath sounds are diminished. The patient may develop shock-like symptoms, with pale, clammy skin, low blood pressure and feeble, rapid heartbeat.

## 409. Treatment.

a. *Rest and Warmth.* It is desirable that a casualty exposed to a lung-damaging agent be kept at rest until the danger of pulmonary oedema is past, but the operational situation may prevent this. Tightness of the chest and coughing should be treated with immediate rest and comfortable warmth. The casualty should be evacuated in a semi-seated position if dyspnoea or orthopnoea make a supine posture impractical. Mandatory evacuation by litter in cases of significant respiratory involvement has been advocated.

b. *Sedation.* Sedation should be used sparingly. Codeine in doses of 30 to 60 mg may be effective for cough. Restlessness may be a manifestation of hypoxia; therefore, only cautious use of sedatives is advised. Use of sedatives should be withheld until adequate oxygenation is assured and facilities for possible respiratory assistance are available. Barbiturates, atropine, analeptics and antihistamines are all contraindicated.

c. *Oxygen*. Hypoxaemia may be controlled by oxygen supplementation. Early administration of positive airway pressure intermittent positive pressure breathing (IPPB), positive end-expiratory pressure (PEEP) mask ("PEEP mask") or, if necessary, incubation with or without a ventilator) may delay and/or minimise the pulmonary oedema and reduce the degree of hypoxaemia.

d. Antibiotics. Antimicrobial therapy should be reserved for acquired bacterial bronchitis/pneumonitis. Prophylactic therapy is not indicated.

e. *Steroids*. After exposure to a sufficiently high dose of phosgene or similar agent, pulmonary oedema will follow. Administration of corticosteroids has been recommended, but proof of their beneficial effects is lacking. It has been suggested that, when steroid treatment is initiated within a very short time of the exposure, this therapy may lessen the severity of the oedema. Two inhalational regimes are in use: one using dexamethasone and the other using betamethasone or beclomethasone. In either case, treatment should be started as soon as possible, ideally within 15 minutes of exposure. Doses of steroids used are much greater than those prescribed in asthma and when steroids are used they should be given in high doses by inhalation and in severe cases by injection.

f. *Other*. Rest, warmth, sedation and oxygen are of great importance, as indicated above. Treatment for exposure to a lung-damaging agent, or similar compound, except for zinc chloride smoke, for which an extended regimen is essential, should be judged on the basis of:

(1) Precautionary treatment for what seems a mild but possibly dangerous exposure; and

(2) Definitive treatment for an exposure which is definitely expected to endanger life.

## 410. Course and Prognosis.

During the acute phase, casualties may have minimal signs and symptoms and the prognosis should be guarded. Casualties may very rapidly develop severe pulmonary oedema. If casualties survive more than 48 hours they usually recover without sequelae.

# CHAPTER 5

# CYANOGEN AGENTS (BLOOD AGENTS)

## SECTION I - GENERAL

### 501. Introduction.

a. Cyanogen agents produce their effects by interfering with oxygen utilisation at the cellular level. Inhalation is the usual route of entry.

b. The term "blood agents" has, in the past, been used to describe "cyanogen agents." It should be noted however, that not all "blood agents" are cyanogens (e.g., carbon monoxide) and that cyanogens are not necessarily "blood agents."

c. In this chapter only hydrogen cyanide, (HCN, (AC)) and those agents that derive their toxicity primarily from the liberation of the CN-group in the organism will be discussed, but it should be noted that hydrogen sulphide, $H_2S$ has a toxicity comparable with HCN and appears to act by a similar mechanism. Only HCN itself and the four cyanogen halides are likely to be of military interest. The cyanogen halides owe their toxicity to the CN-group, but the halogen moiety supplies them with their irritant properties. The most important of the cyanogen halides is cyanogen chloride (CK). During World War I hydrogen cyanide and cyanogen chloride were used and cyanogen bromide to a limited extent.

## SECTION II - HYDROGEN CYANIDE

### 502. Properties.

a. *Physical Properties.* Hydrogen cyanide is a colorless, highly volatile liquid and represents a non-persistent hazard. The vapour is less dense than air and has a faint odour, somewhat like bitter almonds, although about 25% of people are unable to smell this. It is highly soluble and stable in water. (See Table 5-I.)

b. *Chemical Properties.*

(1) The CN compounds hydrolyse slowly in water with subsequent gradual loss of toxicity. They are neadily oxidised by strong oxidants, e.g., potassium permanganate.

*(2)* Hydrogen cyanide has an affinity for oxygen and is flammable; hence it is less efficient when dispersed by artillery shells. Compounds which contain labile sulphur atoms ($R\text{-}S{=}S^{2-}$) react with HCN even in vivo, for example:

$$HCN + Na_2S_20_3 \longrightarrow HSCN + Na_2S0_3$$

and metal ions easily form complex compounds, for example:

$$CoCl_2 + 4CN \longrightarrow Co(CN)d + 2Cl.$$

c. *Usage*. Use is made of this property in some forms of therapy. Hydrogen cyanide, because of its volatility and low molecular weight, is poorly absorbed by the charcoal in the canister of the respirator. This charcoal is therefore impregnated with metal salts in order to improve the performance of the canister, but the protection provided against HCN is not unlimited.

## 503. Detection.

Automatic detectors are available which detect attack concentrations of cyanide vapour. Draeger™ tubes are also available, as are water testing kits.

## 504. Protection.

Specialist equipment including a respirator, NBC suit, gloves and overboots give good protection. Modem NBC filters are effective against attack with hydrogen cyanide, but should be changed immediately afterwards.

## 505. Decontamination.

Because of its physical properties the agent will not remain for long in its liquid state. Decontamination should not, therefore, be necessary.

## 506. Mechanism of Action.

The cyanide ion forms a reversible complex with the respiratory cytochrome oxidase enzyme system, an enzyme system essential for oxidative processes within cells. This results in impairment of cellular oxygen utilisation. The central nervous system, particularly the respiratory centre, is especially susceptible to this effect and respiratory failure is the usual cause of death.

## 507. Signs and Symptoms.

a. The more rapidly the tissue cyanide levels build up, the more acute are the signs and symptoms of poisoning and the smaller is the total absorbed dose required to produce a given effect.

b. In high concentrations there is an increase in the depth of respiration within a few seconds. This stimulation may be so powerful that a casualty cannot voluntarily hold his or her breath. Violent convulsions occur after 20 to 30 seconds with cessation of respiration within 1 minute. Cardiac failure follows within a few minutes.

c. With lower concentrations, the early symptoms are weakness of the legs, vertigo, nausea and headache. These may be followed by convulsions and coma which may last for hours or days depending on the duration of exposure to the agent. If coma is prolonged, recovery may disclose residual damage to the central nervous system manifested by irrationality, altered reflexes and unsteady gait which may last for several weeks or longer; temporary or permanent nerve deafness has also been

described. In mild cases there may be headache, vertigo and nausea for several hours before complete recovery.

## 508. Treatment.

a. Successful treatment for acute cyanide poisoning depends upon rapid fixation of the cyanide ion, either by methaemoglobin (metHB) formation or by fixation with cobalt compounds.

b. Any casualty who is fully conscious and breathing normally more than 5 minutes after presumed exposure to cyanide agents has ceased will recover spontaneously and does not require treatment, cyanide being very rapidly detoxified in the body.

c. Artificial resuscitation, though possible, is not likely to be helpful in the absence of drug treatment.

## 509. Case Management.

Management of cases of hydrogen cyanide poisoning divides into two parts:

a. *First Aid Measures.* The casualty should be removed from the source of hydrogen cyanide. Rescue workers should wear adequate individual protective equipment (IPE).

b. *Therapy*. The key to treatment of patients poisoned with hydrogen cyanide is speed. Though disagreement regarding the ideal drugs for use in the treatment still occurs there is none regarding the need for urgent action.

## 510. Treatment Approaches.

a. Two major approaches are involved in the treatment of cyanide poisoning:

(1) Provision of binding sites for the cyanide ions. These sites provide alternatives to those of cytochrome oxidase and essentially reactivate that enzyme. Binding sites may be provided by drugs such as dicobalt edetate and by hydroxocobalamin or by the production of methaemoglobin in the blood. Methaemoglobin binds avidly to cyanide ions and may be produced by compounds such as sodium nitrite and amyl nitrite and dimethylarninophenol. Methaemoglobin forming compounds should be used cautiously in patients suffering from concurrent carbon monoxide poisoning or hypoxia.

(2) Provision of additional sulphur groups to enhance the detoxification of cyanide and thiocyanate by endogenous rhodanese. This is accomplished by giving sodium thiosulphate.

b. It is generally agreed that binding the cyanide ions is the first priority of treatment but that thiosulphate must be provided to permit conversion of the cyanide ions to thiocyanate.

## 511. Drugs That Bind Cyanide Ions.

a. *Compounds Producing Methaemoglobin*.

(1) *Amyl Nitrite.* Amyl nitrite is useful only in a closed positive pressure

respiratory system. Crushing the ampoule around the face or even inside the facepiece of the respirator is inadequate. It should not be used with concurrent oxygen administration due to the risk of explosion. Treatment with amyl nitrite should be followed by sodium thiosulphate.

(2) *Sodium Nitrite.*

(a) Sodium nitrite should be administered intravenously. Ten millilitres of a 3% solution (300 mg) of sodium nitrite should be injected intravenously over a period of 3 minutes. The therapeutic index of sodium nitrate is very low; the above dose, indicated for adults has caused death in children. The sodium nitrite is given to produce methaemoglobin, thus sequestering the cyanide on the methaemoglobin. The cyanide is then removed from the body as thiocyanate after administration of sodium thiosulphate.

(b) The decrease in blood pressure following sodium nitrite injections is negligible unless the patient is allowed to get into an upright position. The development of a slight degree of cyanosis is evidence of a desirable degree of methaemoglobin formation (methaemoglobinaemia). It is not anticipated that at the above dosages an extreme or injurious degree of methaemoglobinaemia will develop. If it does, however, it should be treated by oxygen administration.

(3) *4-Dimethylaminophenol-hydrochloride (DMAP).*

(a) 4-Dimethylaminophenol-hydrochloride (DMAP) has proved very effective in the treatment of cyanide poisoning owing to rapid formation of methaemoglobin. DMAP can be life saving, but not curative; intravenous thiosulphate is required for definitive cure. DMAP should be slowly injected intravenously in a dose of 250 mg. Muscular necrosis may follow intramuscular injection and the intramuscular route should be avoided.

(b) If sodium thiosulphate is not immediately available 250 mg of DMAP should be given every hour until thiosulphate can be given; this latter completes the treatment.

(c) It should be remembered that DMAP will cause cyanosis due to methaemoglobin formation. This indicates effective treatment and does not call for resuscitation. Where too much methaemoglobin has been formed, methylene blue may be given to convert methaemoglobin to hemoglobin (Hb).

b. *Hydroxocobalamin.* Hydroxyocobalamin (vitamin B12a) binds cyanide to form cyanocobalamin (vitamin B12). It must be given intravenously in large doses and it is not feasible to give it via any other route.

c. *Dicobalt Edetate.* Dicobalt edetate given intravenously in doses of 600 mg (40 ml of a 1.5% solution in glucose/water solution) has proved successful. The injection should be followed by an intravenous injection of sodium thiosulphate. It should be noted that cobalt edetate is toxic to the kidney and causes hypotension.

## 512. Provision of Sulphur Groups.

Sodium thiosulphate provides additional thiosulphate ions and these combine with cyanide ions under the influence of rhodanese to produce thiocyanate. It should be given to

supplement any other form of treatment for cyanide poisoning. The dose is 12.5 grams intravenously (50 millilitres of a 50% solution) over a 10 minute period.

### 513. Additional Therapy.

Oxygen should be given if available.

### 514. Course and Prognosis.

a. Death may occur within minutes without treatment, but a casualty who is fully conscious and breathing normally 5 minutes after presumed exposure has ceased does not require treatment.
b. Occasionally, where tissue hypoxia has been prolonged, residual injury of the CNS may persist for weeks and some damage may be permanent.

## SECTION III - CYANOGEN HALIDES

### 515. Introduction.

Cyanogen chloride and cyanogen bromide after absorption react in such a way that hydrogen cyanide is eventually released. Their effects on the body are essentially similar to those of hydrogen cyanide, but, in addition, they also have local irritant effects.

### 516. Physical and Chemical Properties.

a. Cyanogen chloride is a colorless, highly volatile liquid. Although only slightly soluble in water, it dissolves readily in organic solvents. Its vapour, heavier than air, is very irritating to the eyes and mucus membranes. Cyanogen chlorides pungent, biting odour is marked by its irritating lachrymatory properties. Normally cyanogen chloride is non persistent. (See Table 5-I.)
b. Cyanogen halides are rather poorly absorbed onto charcoal, especially if the charcoal is damp. The cyanide group, not being ionised, does not react well with the metal salts found in respirator charcoals.

### 517. Detection.

Automatic detectors are available which detect attack concentrations of vapour. Draeger™ tubes are also available, as are water testing kits.

### 518. Decontamination.

See hydrogen cyanide.

*Table 5-I. Physical Properties of Cyanogen Agents*

| Property | Hydrogen Cyanide (AC) | | Cyanogen Chloride (CK) | |
|---|---|---|---|---|
| Appearance | Colourless liquid giving off a colourless vapour | | Strongly irritating colourless gas | |
| Chemical formula | HCN | | CNCl | |
| Molecular weight | 27.02 | | 61.48 | |
| Density ($g.cm^{-3}$) | 0.687 | (10°C) | 1.18 | (20°C) |
| Melting point | -13.3°C | | -6.9°C | |
| Boiling point | 25.7°C | | 12.8°C | |
| Vapour density | 0.93 | | 2.1 | |
| Vapour pressure | 165<br>256<br>600<br>742 | (-10°C)<br>( 0°C)<br>(20°C)<br>(25°C) | 1,010 | (20°C) |
| Volatility ($mg.m^{-3}$) | 37,000<br>1,080,000 | (-40°C)<br>(25°C) | 6,132,000 | (25°C) |

## 519. Mechanism of Action.

Cyanogen chloride acts in two ways. It systemic effects are similar to those of hydrogen cyanide but it also has local irritant effects on the eyes, upper respiratory tract and lungs.

## 520. Pathology.

Cyanogen chloride injures the respiratory tract, resulting in severe inflammatory changes in the bronchioles and congestion and oedema in the lungs. Very low concentrations (e.g., 10-20 $mg.min.m^{-3}$) produce eye irritation and lachrymation.

## 521. Signs and Symptoms.

The signs and symptoms caused by cyanogen chloride are a combination of those produced by hydrogen cyanide and a lung irritant. Initially, cyanogen chloride stimulates the respiratory centre and then rapidly paralyses it. In high concentrations, however, its local irritant action may be so great that dyspnoea is produced. Exposure is followed by an immediate intense

irritation of the nose, throat and eyes, with coughing, tightness in the chest and lachrymation. Afterwards the exposed person may become dizzy and increasingly dyspnoeic. Unconsciousness is followed by failing respiration and death within a few minutes. Convulsions, retching and involuntary defecation may occur. If these effects are not fatal, the signs and symptoms of pulmonary oedema may develop. There may be persistent cough with much frothy sputum, rales in the chest, severe dyspnoea and marked cyanosis.

## 522. Treatment.

Cyanogen halide poisoning should be treated in the same way as hydrogen cyanide poisoning as regards its cyanide-like effects. Pulmonary irritation should be treated in the same way as phosgene poisoning.

## 523. Course and Prognosis.

Recovery from the systemic effects of cyanogen halide poisoning is usually as prompt as in hydrogen cyanide poisoning. However, a higher incidence of residual damage to the central nervous system is to be expected. Depending on the concentration of cyanogen halide to which the casualty has been exposed, the pulmonary effects may develop immediately or may be delayed until the systemic effects have subsided. Early prognosis must, therefore, be guarded.

# CHAPTER 6

# INCAPACITANTS

## SECTION I-GENERAL

### 601. Introduction.

a. An incapacitant is a chemical agent which produces a temporary disabling condition that persists for hours to days after exposure to the agent has occurred (unlike that produced by riot control agents). Medical treatment while not essential may in some cases facilitate more rapid recovery. In the narrower sense the term has come to mean those agents that are:

(1) Highly potent (an extremely low dose is effective) and logistically feasible.
(2) Able to produce their effects by altering the higher regulatory activity of the central nervous system.
(3) Of a duration of action lasting hours or days, rather than of a momentary or fleeting action.
(4) Not seriously dangerous to life except at doses many times the effective dose.
(5) Not likely to produce permanent injury in concentrations which are militarily effective.

b. These criteria eliminate many drugs that might otherwise be considered as incapacitants. Opiates and strong sedatives are too dangerous on account of their low margin of safety and milder tranquilizers cause little actual loss of performance capability. Many compounds have been considered as incapacitants and medical staffs must be on the alert to detect and report any unusual clinical appearances. All lethal agents in low doses may produce incapacitating effects and it is possible that new agents for incapacitation may be developed. Agents which produce unconsciousness or induce vomiting may well be developed in the future.

c. In this chapter, consideration will be given to two categories which are well known: CNS depressants (anticholinergics) and CNS stimulants (LSD). Although cannabinols and psylocibin, for instance, have been considered in the past, their effective dose is too high for these to be regarded as likely agents for use in the field.

### 602. CNS Depressants.

CNS depressants produce their effects by interfering with transmission of information across central synapses. An example of this type of agent is 3-quinuclidinyl benzilate (BZ), which blocks the muscarinic action of acetylcholine both peripherally and centrally. In the central nervous system anticholinergic compounds disrupt the high integrative functions of memory, problem solving, attention and comprehension. Relatively high doses produce toxic delirium which destroys the ability to perform any military task.

## 603. CNS Stimulants.

CNS stimulants cause excessive nervous activity by facilitating transmission of impulses. The effect is to flood the cortex and other higher regulatory centres with too much information, making concentration difficult and causing indecisiveness and inability to act in a sustained purposeful manner. A well known drug which acts in this way is D-lysergic acid diethylamide; similar effects are sometimes produced by large doses of amphetamines.

## 604. Detection.

a. Field laboratory methods are not yet sufficiently developed to permit isolation and identification of specific agents in the environment and in samples of body fluid (for example, blood, urine, cerebrospinal fluid). Therefore, diagnosis rests almost entirely upon chemical acumen, combined with whatever field intelligence or detector system data may be available. Following the occurrence of a suspected chemical attack with incapacitating agents, the medical officer should be prepared to take the steps listed below.

b. Instruct field evacuation teams to transport casualties to an uncontaminated area. Resistant or disoriented individuals should be restrained in the triage area after they have been given the necessary first aid.

c. Once the diagnosis of a nerve agent or other lethal substance has been ruled out, the principal signs and symptoms to consider are those shown in Table 6-I.

d. In a large-scale attack, the diagnosis will be simplified by the epidemiological distribution of the casualties. It is better to look for characteristics common to all or most casualties, then to be overly impressed with atypical features. For example, some anticholinergics are capable of causing marked disorientation, incoherence, hallucinations and confusion (the pathognomonic features of delirium) with very little, if any, evidence of peripheral autonomic effect (such as tachycardia and dilated pupils). This should not dissuade the medical officer from considering the likelihood of a centrally predominant anticholinergic being the causative agent, since very few other pharmaceutical classes can produce delirium in militarily effective doses. The disturbance produced in indoles (such as LSD) or the cannabinols (such as marihuana extracts) is not really delirium, because the casualties remain receptive to their environment and can comprehend quite well, even though they may have great difficulty reacting appropriately.

## 605. Protection.

It is likely that such agents will be dispersed by smoke-producing munitions or aerosols, using the respiratory tract as a portal of entry. The use of the protective mask, therefore, is essential. With some agents the percutaneous route may be used and full individual protective equipment will be required.

*Table 6-I. Signs and Symptoms Produced by Incapacitating Agents*

| Signs and symptoms | Possible aetiology |
|---|---|
| Restlessness, dizziness, or giddiness; failure to obey orders, confusion, erratic behaviour; stumbling or staggering; vomiting. | Anticholinergics (e.g., BZ), indoles (e.g., LSD), cannabinols (e.g., marihuana), anxiety reaction, other intoxications (e.g., alcohol, bromides, barbiturates, lead). |
| Dryness of mouth, tachycardia at rest, elevated temperature, flushing of face; blurred vision, pupillary dilation; slurred or nonsensical speech, hallucinatory behaviour, disrobing, mumbling and picking behaviour, stupor and coma. | Anticholinergics. |
| Inappropriate smiling or laughter, irrational fear, distractability, difficulty expressing self, perceptual distortions; labile increase in pupil size, heart rate, blood pressure. Stomach cramps and vomiting may occur. | Indoles. (Schizophrenic psychosis may mimic in some respects.) |
| Euphoric relaxed, unconcerned daydreaming attitude, easy laughter; hypotension and dizziness on sudden standing. | Cannabinols. |
| Tremor, clinging or pleading, crying; clear answers, decrease in disturbance with reassurance; history of nervousness or immaturity, phobias. | Anxiety reaction. |

## 606. Decontamination.

Complete cleansing of the skin with soap and water should be accomplished at the earliest opportunity. Symptoms may appear as late as 36 hours after percutaneous exposure, even if the skin is washed within an hour. In fact, a delay in onset of several hours is typical. This time should be used to prepare for the possibility of an epidemic outbreak 6 to 24 hours after the attack.

## SECTION II - CNS DEPRESSANTS - BZ (3-QUINOCLINIDINYL BENZILATE) AND SIMILAR COMPOUNDS

## 607. Detection.

There is no device available at present for detecting this agent.

## 608. Protection.

Protection is given by the respirator, NBC suit, overboots and gloves.

## 609. Properties.

a. BZ and its analogues are glycollic acid esters. Some members of the group are liquid at ambient temperatures but BZ is a stable white crystalline powder that is only slightly soluble in water.

b. These agents are metabolised primarily in the liver and excreted by the kidneys.

## 610. Mechanism of Action.

a. BZ (3-quinuclidinyl benzilate) is a cholinergic blocking agent that at single doses of less than 1 mg produces delirium lasting several days. In this respect it resembles the well known belladonna alkaloids, atropine and scopolamine, except that it is more potent and its effects last longer. The safety margin (ratio of lethal to incapacitating dose) in people is estimated to be at least 30. No permanent adverse effects have been reported from clinical studies.

b. BZ is effective by all routes of administration, but its effectiveness percutaneously (when mixed with a suitable solvent) is limited, so that route is not likely to be used. However there are other related compounds which are effective percutaneously.

c. It readily crosses the blood-brain barrier and is distributed to all areas of the brain and spinal cord.

d. After administration of an effective dose by inhalation by mouth or by injection mild peripheral effects of BZ occur within 1 hour and maximal central effects occur after about 4 hours lasting 24 to 48 hours, with a peak at 8 to 10 hours. Some other compounds in this group may take longer for their effects to develop and to disappear. Doubling the dose prolongs the duration of severe central effects by about 40 hours and shortens the onset time of severe effects to about 1 hour.

e. BZ and other glycollates produce their effects within the nervous system in the same way as atropine and scopolamine, that is by interfering with cholinergic transmission at muscarinic sites, both in the peripheral autonomic nervous system and in the brain and spinal cord. Because of the wide distribution of these sites measurable effects upon almost every phase of neural regulation may be observed.

## 611. Signs and Symptoms.

Small doses of BZ cause sleepiness and diminished alertness. Diagnosis can be made by noting increased heart rate, dry skin and lips, drowsiness and a progressive intoxication in the untreated individual as follows:

a. *1-4 hours:* Tachycardia, dizziness, ataxia, vomiting, dry mouth, blurred vision, confusion, sedation progressing to stupor.

b. *4-12 hours:* Inability to respond to the environment effectively or to move about.

c. *12-96 hours:* Increasing activity, random unpredictable behaviour with delusions and hallucination; gradual return to normal 48 to 96 hours after exposure.

## 612. Treatment.

a. For most casualties, symptomatic treatment is all that will be necessary. Firm restraint when necessary and a friendly attitude are called for especially in dealing with these subjects who are capable of walking. All dangerous objects must be removed and anything likely to be swallowed should be kept away from the subject as bizarre delusions may occur.

b. The most important single medical consideration is the possibility of heat stroke. Clothing should be removed if the temperature is greater than 25°C. If the body temperature is greater than 39°C vigorous cooling is indicated. The casualty should be placed in the shade and air allowed to circulate. Water may be sprayed on the casualty to aid cooling, ice should *not* be applied to the skin.

c. Physostigmine, which is used as an antidote to BZ, should be reserved for casualties who appear to be in danger. Where this treatment is deemed to be necessary an injection of 2-3 mg will be required to alleviate the condition. Repeated injections at intervals of approximately 15 minutes to 1 hour may be required to build up a sufficient level. Once a desirable effect is achieved it should be maintained by slow intravenous injection or infusion. Doses of 2-4 mg every 1 or 2 hours may be required. The dose should be titrated against symptoms with gradual tapering of the dose as the effect of the poisoning runs its course. This may vary from a few hours to several days. Oral dosing should replace intravenous therapy as soon as possible (2 to 5 mg every 1 to 2 hours).

d. Peripherally acting drugs, which do not cross the blood-brain barrier, such as pyridostigmine, neostigrnine and pilocarpine are ineffective antagonists of the central effects of BZ and should not be used in place of physostigmine.

# SECTION III - CNS STIMULANTS-LSD (D-LYSERGIC ACID DIETHYLAMIDE)

## 613. Properties.

LSD is solid at normal temperatures and is soluble in water. It is a very difficult agent to disseminate and consequently is likely to be used by an enemy only in a clandestine manner.

## 614. Detection.

There is no device available for detecting this agent in the field.

## 615. Protection.

No personal protection is available against clandestine attack, but it seems probable that only small quantities of food or water could be contaminated. Good security of the food and water supply are therefore required.

## 616. Mechanism of Action.

a. Very small doses (for example 50 micrograms per person) are capable of inducing a psychotic state in people, but the precise mechanism of action is not yet known.

b. LSD has been shown to facilitate neural activity in the reticular activating system of the brain stem. It appears to interfere with the normal filtering action of this system, permitting sensory input to reach higher integrative centres without regard to its importance or relevance. The result is a decrease in the ability of the brain to process information selectively and in logical sequence.

## 617. Pathophysiology.

a. D-lysergic acid diethylamide is the most potent of the biologically active indole compounds, as little as 50 µg being required to produce dramatic psychological changes. Doses of 2 to 5 mg have been taken without permanent sequelae, and animal studies suggest that much higher doses may be tolerated. Convulsions may occur at doses above 2 mg.

b. LSD may be inhaled or ingested. Initial effects appear within a few minutes of inhalation or within 30 to 60 minutes of ingestion. Maximum effects are reached within 2 to 3 hours and gradually subside over the next 4 to 8 hours. The half-life in human plasma is about 3 hours. Tolerance is acquired rapidly on repeated exposures at daily intervals, but is shortlived.

c. LSD appears to interact with endogenous neurotransmitters such as serotonin with which it shares the common feature of an indole nucleus. It is metabolised by the liver and excreted through the kidneys.

## 618. Signs and Symptoms.

a. The clinical manifestations of LSD intoxication often include an early stage of nausea followed 45-60 minutes after dosage by a confused state in which delusions and hallucinations are common but not always experienced. There is some evidence that the effects may be held off, at least for a time, by determination to continue duty and that the presence of non-intoxicated comrades enables affected subjects to maintain contact with reality.

b. Subjects intoxicated with LSD show evidence of sympathetic stimulation (rapid heart rate, sweating palms, pupillary enlargement, cold extremities) and mental excitation (nervousness, trembling or spasms, anxiety, euphoria and inability to relax or sleep). Hyperthermia has been reported. Subjectively, feelings of tension, heightened awareness, exhilaration, kaleidoscopic imagery, emotions of every type, hilarity and exultation are characteristic. Paranoid ideas and more profound states of terror and ecstasy may also occur, especially in highly suggestible individuals. True hallucinations are rare, as is homicidal or suicidal behaviour.

## 619. Treatment.

No true antagonist to the indoles is as yet known. The best treatment known at present for LSD intoxication is the administration of diazepam 10-20 mg intravenously or intramuscularly or sodium amytal 200-400 mg intravenously to sedate the patient until spontaneous recovery occurs. Chlorpromazine has also been suggested but does not appear to have any advantage over these drugs.

## 620. Course and Prognosis.

The question of long term effects is still unresolved, but single exposures to doses in the clinical range (0.1 to 1.0 mg total dose) appear unlikely to cause any permanent biological damage.

## 621. Other Agents.

Unfamiliar agents or mixtures of agents may be encountered in future battlefield situations. In such instances, the general principles of restraint, close observation and supportive medical care apply. No medication should be given until an aetiological diagnosis can be made with reasonable certainty unless circumstances require it (for example, concomitant wounds, burns or fractures requiring major surgical intervention). The judgement of the medical officer remains the only useful guide to action in these complex and unforeseeable circumstances.

# CHAPTER 7

# RIOT CONTROL AGENTS

## SECTION I - GENERAL

### 701. Introduction.

Riot control agents are irritants characterised by a very low toxicity (chronic or acute) and a short duration of action. Little or no latent period occurs after exposure. Orthochlorobenzylidene malononitrile (CS) is the most commonly used irritant for riot control purposes. Chloracetophenone (CN) is also used in some countries for this purpose in spite of its higher toxicity. A newer agent is dibenzoxazepine (CR) with which there is little experience. Arsenical smokes (sternutators) have in the past been used on the battlefield. Apart from their lachrymatory action they also provoke other effects, e.g., bronchoconstriction and emesis and are some times referred to as vomiting agents. For historical reasons some older, more toxic compounds are briefly mentioned.

## SECTION II - LACHRYMATORS

### 702. CS (Orthochlorobenzylidene Malononitrile).

CS is used as a riot control agent in many countries. It is also commonly used as a training agent for simulation of chemical warfare conditions and for testing of respirators. The limit of perception by taste ranges from 0.25-0.5 $mg.m^{-3}$. The minimal irritant concentration ranges from 0.1- 1.0 $mg.m^{-3}$, the $ICt_{50}$ from 5-10 $mg.m^{-3}$, and the $LCt_{50}$ for persons very much larger, estimated as 60,000 $mg.min.m^{-3}$. This provides a high margin of safety in its use.

### 703. Properties.

CS is the code name for orthochlorobenzylidene malononitrile. On account of its stronger irritant effects and its lower toxicity it has superseded CN. It is a white crystalline solid substance. Volubility is very poor in water, moderate in alcohol and good in acetone, chloroform, methylene dichloride, ethylacetate and benzene. CS is unstable in aqueous solution. If enough CS can be dissolved in water (e.g., by adding propylene glycol or other organic co-solvent) spraying fluids with an irritant action of short duration result. Although the smoke is non-persistent, CS may stick to rough surfaces (e.g., clothes) from which it is released only slowly. At least 1 hour of aeration is necessary to cleanse such materials from CS after exposure. CS is usually dispersed as an aerosol generated pyrotechnically, or by spraying a solution of CS in a suitable solvent.

### 704. Detection.

The CS cloud is white at the point of release and for several seconds after release. Exposure is associated with a pepper-like odour, the presence of intense eye effects, dyspnoea, coughing and rhinorrhoea.

## 705. Protection.

Full individual protective equipment will provide complete protection. Protection against field concentrations of irritant agents is provided by the respirator and ordinary field clothing secured at the neck, wrists and ankles. Individuals who handle CS should wear rubber gloves, hood, rubber boots, rubber apron and respirator and secure their field clothing at the neck, wrists and ankles.

## 706. Decontamination.

a. Exposed persons should if possible move to fresh air, separate from fellow sufferers, face into the wind with eyes open and breathe deeply.
b. Following exposure, clothing and individual equipment should be inspected for residue. If a residue is found, individuals should change and wash their clothing to protect themselves and other unmasked persons.

## 707. Mechanism of Action.

a. Lachrymators act on the nerve endings, the cornea, mucous membranes and the skin. The reaction is very rapid.
b. The toxicity of CS is very low, the estimated lethal concentration over 1 hour for people being 1000 $mg.m^{-3}$, whereas a concentration of 1 $mg.m^{-3}$ is intolerable to most people.

## 708. Pathology.

Pathological examination of rabbits exposed to CS revealed an increase in number of goblet cells in the respiratory tract. Pulmonary oedema occurred after inhalation at very high concentrations, in excess of 20000 $mg.min.m^{-3}$. Experiments in dogs showed that the animals dying as a result of exposure to very high concentrations died from obstruction of the upper respiratory tract; inhalation of CS through an intratracheal cannula, on the other hand, caused pulmonary oedema.

## 709. Signs and Symptoms.

During exposure an individual is incapable of effective concerted action.

## 710. CS Exposure Symptoms.

Exposure to CS causes the following symptoms:
a. *Eyes.* Symptoms include a violent burning sensation, conjunctivitis (lasting up to 30 minutes), erythema of the eyelids (lasting about an hour) blepharospasm, violent lachrymation (over 10-15 minutes) and photophobia.
b. *Respiratory Tract.* The first symptom is a burning sensation in the throat, developing into pain and extending to the trachea and bronchi. At a later stage a sensation of

suffocation may occur, often accompanied by fear. In addition a burning sensation in the nose, rhinorrhoea, erythema of the nasal mucous membranes and sometimes mild epistaxis occurs. The sense of taste is often distorted for some hours after exposure. Nausea, diarrhoea and headache have been observed. Sneezing occurs after mild exposure and may be persistent. Many exposed people have reported fatigue for some hours afterwards. Coughing, choking, retching and (rarely) vomiting occur after exposure.

c. *Skin.* A burning sensation occurs especially in moist areas, but soon disappears. This burning sensation may recur some hours later, often while washing the area. Prolonged exposure to large amounts (e.g., when handling CS in bulk) can cause erythema and vesicle formation. Prolonged exposure, continuous or intermittent, to high concentrations, combined with high temperatures and humidity in the field may result in a cumulative effect. Sensitivity to CS may be provoked. It has been shown that the particle size affects the clinical result. Small particles (1-5 µm affect the eyes and respiratory tract more rapidly than larger ones (20-30 µm but recovery after exposure to small particles is more rapid. Very large particles (50 µm affect the eyes more than the respiratory tract, while recovery is slower.

## 711. First Aid.

a. In practically all cases it is sufficient to take the patient into fresh air where the symptoms will soon disappear. Clothing should be changed. If symptoms persist the eyes, mouth and skin may be washed with water (and with soap in the case of the skin). Oil based lotions should *not* be used. Skin decontarninants containing bleach should *not* be used, but should be reserved for more dangerous contamination (e.g., vesicants or nerve agents); bleach reacts with CS to form a combination which is more irritant to the skin than CS alone. Chest discomfort can usually be relieved by reassurance.

b. CS hydrolyses more rapidly in alkaline solutions and an acceptable skin decontamination solution is 6.7% sodium bicarbonate, 3.3% sodium carbonate and 0.1% benzalkonium chloride.

## 712. Therapy.

a. *Eyes.* Ordinarily the eye effects are self limiting and require no treatment. If large particles or droplets of agent have entered the eye, treatment as for corrosive materials may be required. Prompt irrigation with copious amounts of water is the best treatment for solid CS in the eye. After complete decontamination corticosteroid eye preparations may be used. Patients who have been heavily exposed must be observed for possible development of corneal opacity and iritis.

b. *Skin.* Early erythema and stinging sensation (up to 1 hour), especially in warm moist skin areas, are usually transient and require no treatment. Inflammation and blistering similar to sunburn may occur after heavy or prolonged exposure, especially in fair skin. Acute contact dermatitis should be managed initially in the same way as any other acute dermatitis. Corticosteroid cream or calamine lotion

may be applied to treat existing dermatitis or to limit delayed erythema. Oozing may be treated with wet dressings of 1 in 40 aluminium acetate solution for 30 minutes three times daily. A topical steroid should follow the wet dressing immediately. Secondary infection is treated with appropriate antibiotics. Significant pruritus can be treated with calamine lotion or corticosteroid preparations. If blisters develop these should be treated as any other second degree burn.

c. *Respiratory Tract*. In the rare event of pulmonary effects from massive exposure, evacuation is required. Management is the same as that for lung damaging agents (Chapter 4).

## 713. Course and Prognosis.

Most personnel affected by riot control agents require no medical attention and casualties are rare.

## 714. CR (Dibenzoxazepine).

a. CR is similar in its effects to CS, but the minimum effective concentration is lower and the $LCt_{50}$ is higher. Symptomatology and treatment are similar to those of CS.

b. It is a pale yellow crystalline solid which melts at 163°F (73°C) and is stable in organic solutions. It has limited volubility in water and is not hydrolyses in aqueous solutions. It has a pepper-like odour. The agent is currently used only in solution for dissemination in liquid dispensers. The solution in the dispensers contains 0.1% CR in 80 parts propylene glycol and 20 parts water. In organic solutions, CR is an eye irritant at concentrations down to 0.0025% or even lower. CR differs from CS in being less toxic when inhaled but CR skin effects are more pronounced. It is more persistent in the environment and on clothing.

## 715. CN (Chloracetophenone).

CN is a riot control agent and as a training agent is now superseded by CS, the latter being much less toxic. However, it is still in use by police in some countries.

## 716. Properties.

CN is a clear yellowish brown solid, with a melting point of 54 ºC. It is poorly soluble in water, but dissolves in organic solvents. The white smoke smells like apple blossom. The minimal irritant concentration is 0.3 $mg.m^{-3}$. It has been estimated from experimental data that the $LCt_{50}$ for people is 7000 to 14000 $mg.min.m^{-3}$, but inhalation of 350 $mg.m^{-3}$ for 5 minutes may be dangerous. The $ICt_{50}$ is 20 to 40 $mg.min.m^{-3}$. CN is more toxic than CS.

## 717. Mode of Action and Toxic Effects.

The mode of action is similar to that of CS; CN causes stimulation of sensory nerve endings.

## 718. Signs and Symptoms.

Exposure to CN primarily affects the eyes, producing a burning sensation, lachrymation, inflammation and oedema of the eyelids, blepharospasm, photophobia and, at high concentrations, temporary blindness. The severest of these symptoms is reached in a few minutes and then gradually decreases. After about 1 or 2 hours all symptoms disappear. High concentrations can cause irritation of the upper respiratory tract, inflammation of the skin with vesicle formation, visual impairment and pulmonary oedema. Drops or splashes in the eye may cause corrosive burns, corneal opacity and even permanent visual impairment. Drops or splashes on the skin may cause papulovesicular dermatitis and superficial skin burns. Ingestion of food or water contaminated with CN causes nausea, vomiting and diarrhoea.

## 719. First Aid.

After limited operational exposure ill effects will be adequately neutralised by letting fresh air blow into the open eyes. If necessary the eyes maybe washed with water from the water bottle (canteen). The eyes should never be rubbed as mechanical injury may complicate the chemical effect. Patients suffering from temporary blindness should be reassured; permanent blindness from exposure to *vapour* has never been observed even at very high concentrations.

## 720. CA (Bromobenzyl Cyanide) and BA (Bromoacetone).

Bromobenzyl cyanide (CA) and bromoacetone (BA) are older lachrymators. They are too toxic for use as riot control agents and must be considered obsolete. Their properties are listed in Table 7-I.

*Table 7-I. Properties of CA and BA*

| Property | CA | BA |
|---|---|---|
| Appearance | Yellow, solid | Colourless liquid |
| Melting point | 25°C | -54°C |
| Boiling point | 227-242°C | 136°C |
| Specific gravity | 1.52 | 1.63 |
| Solubility in water | Poor | Poor |
| Solubility in organic solvents | Good | Good |
| Volatility ($mg.m^{-3}$) | 130 (30°C) | 75000 (30°C) |
| Smoke vapour odour | Rotting fruit | Stinging |
| Smoke vapour colour | White | Colourless |
| Minimal irritant concentration | 0.3 $mg.m^{-3}$ | 1.0 $mg.m^{-3}$ |

## SECTION III - VOMITING AGENTS

### 721. Introduction.

Vomiting agents produce strong pepper-like irritation in the upper respiratory tract with irritation of the eyes and lachrymation. They cause violent uncontrollable sneezing, cough, nausea, vomiting and a general feeling of bodily discomfort. The principal agents in this group are diphenylchlorarsine (DA), diphenylaminearsine chloride (Adamsite (DM)) and diphenylcyanarsine (DC). DA, DM, and DC are also classed as sternutators. They are dispersed as aerosols and produce their effects by inhalation or by direct action on the eyes.

### 722. Properties.

a. *Characteristics.* They are non-persistent agents. The particles fall to the ground after dispersion and are virtually ineffective unless resuspended. Di-phenyl-cyanoarsine (DC) is the most irritating of the group. The principal characteristics of these agents are summarised in Table 7-II.

b. *Visual Detection.* It should be remembered that the colour of the solid agent depends on the degree of purity (technically raw products are often coloured) but the colour and odour of the smoke after dispersion may no longer be noticeable in concentrations which are nevertheless still highly irritant, so that odour and colour cannot be relied upon for detection.

c. *Toxicity.* The following data are applicable to DM. The $LCt_{50}$ estimated for people is 13000 to 44000 $mg.min.m^{-3}$ depending on the means of dissemination of the agent. The $ICt_{50}$ for man ranges from 22 to 150 $mg.min.m^{-3}$. The maximum concentration which is stated to cause no permanent damage after inhalation for 5 minutes is 100 $mg.m^{-3}$.[0]

*Table 7-II. Properties of Vomiting Agents*

| Property | DM | DA | DC |
|---|---|---|---|
| Appearance | Yellow or green solid | Colourless, crystalline | Colourless, solid |
| Melting point | 195°C | 38°C | 38°C |
| Boiling point | 410°C | 330°C | 346-337°C |
| Specific gravity | 1.68 | 1.4 | |
| Solubility in water | Poor | Poor | Poor |
| Solubility in organic solvents | Poor | Good | Good |
| Volatility ($mg.m^{-3}$) | 0.02 (20°C) | 0.68 (20°C) | 1.5 (20°C) |
| Smoke vapour odour | Coal fire | Shoe polish | Garlic |
| Smoke vapour colour | Yellow | White or grey | White |
| Minimal irritant concentration | 0.1 $mg.m^{-3}$ | 0.1 $mg.m^{-3}$ | 0.25 $mg.m^{-3}$ |

## 723. Detection.

The use of these agents may be suspected by the clinical symptoms and signs.

## 724. Protection.

Full individual protective equipment will provide complete protection. The standard protective respirator and ordinary field clothing gives adequate protection against field concentrations of vomiting agents.

## 725. Mechanism of Action.

This consists of inhibition of the SH containing enzymes, especially those of the pyruvate dehydrogenase system. These enzymes play a part in the energy producing processes in the cell. The integrity of the cell structure depends on the proper functioning of the metabolic processes and inhibition of the enzyme mentioned interferes with cell respiration resulting in the destruction of cell structure.

## 726. Pathology.

Vomiting agents produce local inflammation of the upper respiratory tract, the nasal accessory sinuses and the eyes.

## 727. Signs and Symptoms.

a. The onset of symptoms may be delayed for several minutes after initial exposure (especially with DM); effective exposure may, therefore, occur before the presence of the smoke is suspected. If the mask is put on then, symptoms will increase for several minutes despite adequate protection. As a consequence, the casualties may believe their mask is ineffective and by removing it expose themselves further.

b. Inhalation is followed by a burning sensation in the nose and throat, hypersalivation, rhinorrhea, coughing, sneezing, nausea and vomiting. Mental depression may occur during the progression of symptoms. The paranasal sinuses are irritated and fill with secretions and severe frontal headache results. Prolonged exposure may cause retrosternal pain, dyspnoea and asthma-like symptoms. Symptoms reach their climax after 5 to 10 minutes and disappear 1 to 2 hours after cessation of exposure. Effects on the eyes are slight and are restricted to a burning sensation and lachrymation. Exposure of the skin to high concentrations will cause erythema and itching, proceeding to a burning sensation and vesicle formation. On the battlefield, high concentrations are not likely to occur so that affection of the eyes and skin is unlikely. Ingestion of food and water contaminated by sternutators may cause nausea, vomiting, diarrhoea (sometimes bloodstained) and weakness and dizziness have been reported.

c. High concentrations are not expected in the open owing to movement of air, but may be met within enclosed spaces (shelters, tents, etc.), and under these circumstance the skin may show vesicle formation, capillary damage and localised swelling, while corneal necrosis and pulmonary oedema are possible results. Unsteady gait and a positive Romberg sign have been reported. Other neurological results of severe exposure include hyperaesthesia, anesthesia and paraesthesiae, especially in the legs. Loss of consciousness has been reported.

## 728. Treatment.

a. Put on the protective mask and wear it in spite of coughing, sneezing, salivation and nausea. Lift the mask from the face briefly if necessary to permit vomiting or to drain saliva from the facepiece. Carry on with duties as vigorously as possible - this will help to lessen and shorten the symptoms. Combat duties usually can be performed despite the effects of vomiting agents.

b. In spite of the dramatic appearance of the syndrome, the only treatment necessary is first aid. The patient should not smoke for some hours. If necessary the mouth may be rinsed with water, but the water should not be swallowed. The eyes and skin may be washed with water. Clothing should be well brushed. In cases of severe exposure treatment as for lung damaging agent poisoning may be required. A mild analgesic may be given to relieve headache and general discomfort.

## 729. Course and Prognosis.

Symptoms of exposure to field concentration of vomiting agents usually disappear in 20 minutes to 2 hours, leaving no residual injury. However, a few instances of severe pulmonary injury and death have occurred due to accidental exposure to high concentrations in confined spaces.

# CHAPTER 8

# SMOKES, FUELS, AND INCENDIARY MATERIALS

## SECTION I - SMOKES

### 801. Introduction.

a. Smokes are used to hide troops, equipment and areas from detection by obscuring vision. The smokes consist of small solid or liquid particles which become hydrated in contact with air and intercept or diffuse the light.

b. Most smokes are not hazardous in concentrations which are useful for obscuring purposes. However, exposure to heavy smoke concentrations for extended periods, particularly if near the source of emission, may cause illness or even death. Medical personnel should, therefore, be prepared to treat potential reactions to military smokes once such smokes have been introduced to the battlefield. Except with oil smoke, high concentrations of smoke generated in closed spaces are extremely dangerous. High concentrations of zinc chloride smoke generated under these conditions have caused fatalities. Under no circumstances should zinc chloride munitions be used indoors or in closed compartments.

c. In the open air, the air passages should be protected by a respirator if the smoke irritates the airway, if it is very thick or if a stay of longer than 5 minutes in a diluted cloud is necessary. The standard respirator gives the respiratory tract and eyes adequate protection against all smokes and should always be worn when smokes are used in confined spaces. It will not, however, protect against carbon monoxide.

### 802. Zinc Chloride Smokes.

Several methods of producing smoke by dispersing fine particles of zinc chloride have been developed. The mixture in common use is zinc chloride smoke mixture (HC), which contains hexachloroethane, grained aluminium and zinc oxide. Upon burning, the mixture produces zinc chloride, zinc oxychlorides and HC1 vapour which rapidly absorb moisture from the air to form a greyish white smoke. HC mixtures can be dispersed by several methods, including grenades, candles, smoke pots, cartridges, and air bombs.

### 803. Protection.

Some countries require the use of a respirator to protect the respiratory tract whenever zinc chloride smokes are used.

### 804. Clinical-Pathological Effects.

a. *Toxicity*. The toxicity of zinc chloride is mainly due to the formation of the strongly acidic HC1, but is also to a lesser extent due to thermal lesions. These are caused by

the exothermic reaction of zinc chloride with water. The acidic HC1 vapour causes lesions of the mucous membranes of the upper airways. The damage and clinical symptoms following zinc chloride exposure therefore appear immediately after the start of the exposure. However, damage to the lower airways also occurs and may result in delayed effects. These have been attributed to the presence of fine zinc chloride particles and phosgene.

b. *Acute Effects.* In high concentrations or with prolonged exposure HC smoke is highly irritating and may be very dangerous when inhaled. Symptoms following inhalation of high concentration of zinc chloride smoke include dyspnoea, retrosternal pain, hoarseness, strider, lachrymation, cough, expectoration and occasionally haemoptysis. Cyanosis and bronchopneumonia may develop. Due to the irritant and astringent nature of the compound, delayed pulmonary oedema may occur even in the presence of distinct and short-lasting initial symptoms. It is caustic to mucous membranes and can also cause subacute interstitial fibrosis.

c. *Chronic Effects.* Recent studies of the HC canister and of HC smoke reaction by-product gases indicate the presence of suspected carcinogens. Metal analysis of HC canisters showed, besides zinc, small amounts of cadmium and trace amounts of lead, arsenic and mercury. The by-product gases include chlorinated compounds, phosgene, HCl, carbon monoxide and chlorine. Although zinc chloride, the main constituent, is not felt to be a carcinogenic hazard, certain of the other by-products are known carcinogens in laboratory animals or in humans.

## 805. Treatment.

The casualty should don his or her respirator or be removed from the source of exposure. Oxygen should be administered in cases of hypoxia. Bronchospasm should be treated appropriately as should secondary bacterial infection. Early steroid therapy has been considered efficacious by some and, when used, steroids should be given in high doses similar to those used in the treatment of phosgene exposure and exposure to other lung damaging agents. Adequate analgesia is recommended.

## 806. Prognosis.

The prognosis is related entirely to the extent of the pulmonary damage. All exposed individuals should be kept under observation for 8 hours. Most individuals recover in a few days. At moderate exposures, some symptoms may persist for 1 to 2 weeks. In severe exposures, survivors may have reduced pulmonary function for some months after exposure. The severely exposed patient may progressively develop marked dyspnoea, cyanosis and die.

## 807. Chlorosulphonic Acid (CSA).

a. Chlorosulphonic acid (CSA) is a heavy, strongly acidic liquid which, when dispersed in air, absorbs moisture to form a dense white fog consisting of small droplets of hydrochloric and sulphuric acids. In moderate concentrations it is highly irritating to the eyes, nose and skin. The respirator should be worn in all concentrations which

are sufficient to cause any cough, irritation of the eyes or prickling of the skin.

b. A risk exists when chlorosulphonic acid comes in contact with water due to the generation of intense heat and the scattering of acid in all directions. Owing to its highly corrosive nature careful handling is required.

## 808. Symptoms.

The symptoms are usually limited to a prickling sensation of the skin, but exposure to high concentrations or long exposures to lower concentrations as found in the field, may result in severe irritation of the eyes, skin and respiratory tract. Conjunctival irritation and oedema, lachrymation and mild photophobia may occur. Mild cough and soreness in the chest and moderate chemical dermatitis of the exposed skin are occasionally seen. Splashes of liquid in the eye are extremely painful and cause mineral acid burns with corneal erosions. Liquid chlorosulphonic acid solution on the skin may cause painful acid burns.

## 809. Treatment.

a. *Eye.* Irrigate the contaminated eye with water or saline as soon as possible. Examine the cornea for erosion by staining it with fluorescein. If corneal erosion is present, the casualty should be transferred to the care of an ophthalmologist. If this is not practicable, mydriasis should be induced by the use of atropine sulphate eye drops or ointment. Conjunctival lesions should heal readily, but corneal erosions may lead to residual scarring.

b. *Skin.* Irritated skin or skin burns should be washed with water and then with sodium bicarbonate solution. The burns are then treated as for thermal burns of like severity.

## 810. Prognosis.

The skin burns, conjunctival lesions and respiratory irritation heal readily. Corneal erosions are more serious and may lead to residual scarring.

## 811. Titanium Tetrachloride (FM).

This is a yellow non-inflammable and corrosive fluid which on contact with damp air gives off a heavy dense white cloud. It is disseminated by aircraft for the production of vertical smoke curtains extending down to ground and sea level. The smoke consists of fine particles of free hydrochloric acid and titanium oxychloride. The smoke is unpleasant to breathe. Goggles or a respirator should be worn when the spray is falling due to the risk of droplets entering the eyes. Full protective clothing should be worn when handling the liquid to avoid contamination of eyes and skin.

## 812. Mode of Action.

Liquid FM produces acid burns of the skin or eyes.

## SECTION II - FLAME MATERIALS

### 813. General.

a. Incendiary agents are used to burn supplies, equipment and structures. The main agents in this group are thermite (TH), magnesium, white phosphorus (WP) and combustible hydrocarbons (including oils and thickened gasoline).

b. Chemical fire extinguishers containing carbon dioxide should not be used in confined spaces to extinguish thermite or magnesium types of incendiaries. When carbon tetrachloride is in contact with flame or hot metal, it produces a mixture of phosgene, chlorine, carbon monoxide and hydrochloric acid. The standard respirator with normal canister does not protect against some agents such as carbon monoxide.

### 814. Red and White Phosphorus.

a. At ordinary temperatures, white phosphorus (WP) is a solid which can be handled safely under water. When dry, it burns fiercely in air, producing a dense white smoke. Fragments of melted particles of the burning substance may become embedded in the skin of persons close to a bursting projectile, producing burns which are multiple, deep and variable in size. The fragments continue to burn unless oxygen is excluded by flooding or smothering.

b. WP may be used to produce a hot dense white smoke composed of particles of phosphorus pentoxide which are converted by moist air to droplets of phosphoric acid. The smoke irritates the eyes and nose in moderate concentrations. Field concentrations of the smoke are usually harmless although they may cause temporary irritation to the eyes, nose or throat. The respirator provides adequate protection against white phosphorus smoke.

c. In an artillery projectile white phosphorus is contained in felt wedges which ignite immediately upon exposure to air and fall to the ground. Up to 15% of the white phosphorus remains within the charred wedge and can re-ignite if the felt is crushed and the unburned white phosphorus exposed to the atmosphere.

d. Red phosphorus (RP) is not nearly as reactive as white phosphorus. It reacts slowly with atmospheric moisture and the smoke does not produce thermal injury, hence the smoke is less toxic.

### 815. Self Aid.

a. If burning particles of phosphorus strike and stick to the clothing, contaminated clothing should be removed quickly before the phosphorus burns through to the skin.

b. If burning phosphorus strikes the skin, smother the flame with water, a wet cloth, or mud. Keep the phosphorus covered with the wet material to exclude air until the phosphorus particles can be removed.

c. Try to remove the phosphorus particles with a knife, bayonet, stick or other available object. It may be possible to remove some particles by rubbing with a wet cloth.

## 816. Medical Aid.

a. At the earliest opportunity all phosphorus should be removed from the skin and placed in a container so as to prevent further contamination and secondary injuries. The affected part should be bathed in a bicarbonate solution to neutralise phosphoric acid, which then allows removal of visible phosphorus. Remaining fragments will be observed in dark surroundings as luminescent spots.

b. Some nations recommend washing the skin with a 0.5-2.0% copper sulphate solution or a copper sulphate impregnated pad. Wounds may be rinsed with a 0.1%-0.2% copper sulphate solution, if available. Dark coloured deposits may be removed with forceps. Prevent prolonged contact of any copper sulphate preparations with the tissues by prompt, copious flushing with water or saline, as there is a definite danger of copper poisoning. It may be necessary to repeat the first aid measures to completely remove all phosphorus.

c. The burn should be debrided promptly, if the patient's condition will permit, to remove bits of phosphorus which might be absorbed later and possibly produce systemic poisoning. An ointment with an oily base should not be applied until it is certain that all phosphorus has been removed. Further treatment should be carried out as for thermal burn.

d. If the eyes are affected, treatment should initially be commenced by irrigation with a 1% solution of copper sulphate or sodium bicarbonate 5%, followed by repeated lavage using water or saline. The lids must be separated and a local anesthetic instilled to aid in the removal of all embedded particles. In eyes with severe ulceration once all particles have been removed, atropine should be instilled. The patient should be transferred to the care of an ophthalmologist as soon as possible.

## 817. Thermite.

Thermite incendiaries are a mixture of powdered aluminium metal and ferric oxide and are used in bombs for attacks on armoured fighting vehicles. Thermite burns at about 2000°C and scatters molten metal, which may lodge in the skin producing small multiple deep burns.

## 818. Treatment.

The wound should be cooled immediately with water and the particles removed. Afterwards the treatment is that used for other thermal burns.

## 819. Magnesium.

Magnesium (Mg) burns at about 2000ºC with a scattering effect similar to that of thermite. Its particles produce deep burns. Healing is slow unless these particles are removed quickly. Removal is usually possible under local anesthesia. When explosive charges have been added to a magnesium bomb, the fragments may be embedded deep in the tissues, causing the localised formation of hydrogen gas and tissue necrosis.

## SECTION III - HYDROCARBON FUMES

### 820. General.

a. Fuels consist largely of hydrocarbons which may have a narcotic effect. In this respect, because of their lower volatility, diesel and paraffin (kerosene) fuels are less dangerous than petrol (gasoline).

b. Fumes from the combustion of these fuels in internal combustion or jet engines contain a proportion of carbon monoxide, nitrous fumes, etc., which varies with the characteristics of the engine and the rate at which it is being run. The overheating of lubricant oils may result in the production of acrolein which is an aldehyde with intense irritant properties. A concentration of 5 $mg.m^{-3}$ is immediately detectable by odour but a concentration of 50 $mg.m^{-3}$ causes death in a short time from pulmonary oedema.

### 821. Physical and Chemical Properties.

Petrol, diesel and paraffin vapours are heavier than air and as a result of this may be encountered in fuel tanks, in vehicles or in spaces where fuels have been stored. As far as their chemical properties are concerned, the hydrocarbons are inert, except when in an oxidising atmosphere, which is capable of supporting combustion.

### 822. Protection.

Although respirators provide full protection against these hydrocarbon fumes, there is a significant hazard from combustion products in confined spaces due to the presence of asphyxiant gases, e.g., carbon monoxide. In this case, self contained breathing apparatus is required.

### 823. Mechanism of Action.

Hydrocarbon fumes are preferentially absorbed into lipid rich tissue, for instance, the central nervous system. Their action is narcotic and they produce unconsciousness and death in concentrations over 1% (10,000 ppm) in the case of petrol fumes. The exact dangerous concentrations depend on the volatility of the hydrocarbons in question, and on their aromatic content. Swallowed fuels produce unconsciousness, and permanent brain damage has been reported. Aspiration pneumonia may follow as a complication.

### 824. Signs and Symptoms.

a. Drowsiness and unconsciousness proceeding to death are encountered in severe poisoning. Less severe exposures may cause dizziness, headache, nausea, vomiting and muscular incoordination. Acute emotional disturbances following hydrocarbon poisoning have been reported.

b. Lead poisoning from tetraethyl lead additives is very rare except among those who manufacture blended fuels. The risk of leucopenia has also been reported, in particular from workers using the aromatic hydrocarbon benzene.

## 825. Treatment.

Removal to fresh air is the only treatment necessary in cases of mild exposure. When severe poisoning has occurred, oxygen should be administered and positive pressure ventilation may be required.

## SECTION IV - INCENDIARY DEVICES - COMBUSTIBLE HYDROCARBON INCENDIARIES

## 826. Introduction.

Burns may be produced by flame-throwers, oil incendiary bombs which may also contain phosphorus and sodium, and fire bombs containing thickened gasoline. Lung damage from heat and irritating gases may be a complication added to the injuries from incendiaries, especially in confined spaces.

## 827. Flame-Thrower Attack.

As flame and burning fuel fills an enclosed fortification, the oxygen content of the air is reduced and a hot toxic atmosphere containing large amounts of carbon monoxide, unburned hydrocarbons and smoke is produced. The coolest and least contaminated air is found at floor level.

## 828. Casualties.

Deaths may occur during or shortly after a flame attack due to the heat, the toxic atmosphere or suffocation caused by laryngeal or glottic oedema. Survivors may have thermal burns of the skin and upper respiratory tract, as well as pulmonary damage from the hot gases.

## 829. Protection.

The floor level is the safest area during a flame attack. Any kind of cover affords some protection from heat. A wool blanket is excellent. The mask may give partial protection against smoke.

## 830. Treatment.

Casualties should be removed to fresh air as soon as possible. Assisted ventilation (using oxygen, if available) should be administered if breathing has ceased. burns of the skin are treated as thermal burns. If there are burns about the face, laryngeal burning with subsequent oedema-producing respiratory obstruction may occur, so that incubation, tracheotomy or cricothyroid cannulation can be performed in an emergency. The general treatment of the casualty produced by flame attack does not differ from the treatment of one with extensive thermal burns.

## 831. Fire-Bomb Attack.

A fire-bomb is a large tank containing thickened (gelled) gasoline that is air dropped. When it strikes the ground, the fuel is ignited by phosphorus igniters and a large fireball of intense heat is produced, lasting about 4 to 6 seconds. Also, a wide area of ground is covered with burning thickened gasoline, which may continue to burn for as long as 10 to 12 minutes.

## 832. Casualties.

Deaths may be caused by the intense heat or by suffocation from oedema of the larynx or glottis. Thermal burns of the skin and upper respiratory tract may occur in the survivors. Danger from a toxic atmosphere is small in fire-bomb attacks in an open or in a well-ventilated enclosure.

## 833. Treatment.

Burning clothing should be removed or the flames smothered. In general, treatment is similar to that used after flame-thrower attacks.

# CHAPTER 9

# HERBICIDES

## SECTION I - GENERAL

### 901. Introduction.

a. A herbicide is any preparation used to kill or inhibit the growth of plants. The term includes defoliants, desiccants, plant growth regulators and soil sterilants. Militarily, herbicides have been used against forest croplands and brush along roads and rivers and around military establishments.

b. A wide variety of chemical substances have been used as herbicides. This chapter will deal with those substances that have been used in admixtures. See Table 9-I.

c. There is very little likelihood of human beings or animals being poisoned as a result of dioxin-free non-cropland vegetation control. In spraying operations from aircraft, flag-men and women on the ground probably receive relatively high doses, yet a serious case of acute herbicide poisoning has never been confirmed. Poisoning may, however, result from accidental or suicidal ingestion of large quantities of undiluted herbicides. Also important is the fact that toxic residues of these herbicides will not accumulate sufficiently in meat animals to pose a hazard in humans.

*Table 9-I. Composition of Herbicides*

| Name | Composition |
|---|---|
| Compound one | 27.7% sodium cacodylate<br>4.8% cacodylic acid<br>67.5% water and sodium chloride |
| Compound two | 10.2% tri-isopropanolamine salt of 4-amino-3,5,6-tri-chloropicolinic acid<br>39.6% tri-isopropanolamine salt of 2,4-dichlorophenoxyacetic acid (2,4,D)*<br>50.2% unidentified by manufacturer other than for the presence of water and a surfactant |
| Compound three | 50% n-butyl ester of 2,4-D*<br>30% n-butyl ester of 2,4,5-tri-chlorophenoxyacetic acid (2,4,5-T*)<br>20% isobutyl ester of 2,4,5-T* |
| Compound four | 50% n-butyl ester of 2,4-D*<br>50% n-butyl ester of 2,4,5-T* |

* 2,4,-D and 2,4,5,-T may be contaminated with dioxins, some of which are very toxic. Dioxins have been incriminated as a cause of severe choracne in man.

## SECTION II - 2,4-D AND 2,4,5-T

### 902. Toxicity.

a. The risk of human and animal toxicity from the use of 2,4-D (2-4-dichlorophenoxyacetic acid) and its various esters and salts is low. A useful generalisation for this compound is that the toxicity of its derivatives is about the same as that of the acid equivalent.

b. 2,4,5-T(2,4,5-trichlorophenoxyaceticacid)is an impotant chlorophenoxy herbicide widely used as its ester in combination with an ethanolamine salt. From animal studies, it is generally considered to be slightly more toxic than 2,4-D. The biochemistry of 2,4,5-T is probably similar to that of 2,4-D.

### 903. Biochemistry.

Since 2,4-D and its salts, esters, and amides are used for the control of broad leaf plants, its dietary and accumulative effects in the body are important. Long term feeding studies in animals have revealed no evidence that 2,4-D accumulates in the body. The biochemistry of 2,4,5-T is probably similar to that of 2,4-D.

### 904. Mechanism of Action.

The mode of action of 2,4-D is not known. Animals killed quickly by large doses of 2,4-D are thought to die of ventricular fibrillation. Animals poisoned less severely develop a characteristic myotonia which, however, has not been observed in humans. The mode of action of 2,4,5-T is also not known.

### 905. Signs and Symptoms.

a. Ingestion of a toxic dose of 2,4-D causes gastroenteric distress, diarrhoea, mild CNS depression, dysphagia, and possibly transient liver and kidney damage. Some people have developed neuropathy as a result of skin contact with the compound. Some hours after exposure to the 2,4-D ester or the dimethylamine salt, pain, paraesthesia, and paralysis may develop. The disability may be protracted and recovery incomplete. However, the number of people who have developed neuropathy after exposure to 2,4-D is extremely small compared to the number of exposures that have occurred.

b. The signs and symptoms of 2,4,5-T poisoning are probably similar to those of 2,4-D poisoning.

### 906. Treatment.

If a toxic dose of 2,4-D or 2,4,5-T has been ingested, further absorption should be prevented by gastric lavage or inducing emesis and administration of activated charcoal. Supportive therapy should be given.

## SECTION III - CACODYLIC ACID

### 907. Toxicity.

The toxicity of cacodylic acid, or dimethylarsenic acid, in humans is not known. However, the experience of workers in a chemical company who have had repeated exposures over long periods of time confirms the observation on rats that the toxicity of these compounds is relatively low.

### 908. Biochemistry.

a. Cacodylic acid is a desiccant that causes leaf drop and death in certain hardwood species. Like 2,4-D and 2,4,5-T, its dietary and cumulative effects are important.

b. The military herbicide "Compound 1" contains 4.8% cacodylic acid with a trivalent arsenic content of less than 0.1 %. Cacodylic acid has medicinal properties similar to those of inorganic arsenic to which it is partially reduced in the body. However, no reduction to trivalent arsenic occurs.

### 909. Mechanism of Action.

The pharmacologic action of cacodylic acid is intimately related to its biochemistry. The effects of cacodylic acid are essentially those of inorganic arsenic. However, because conversion to arsenic is very slow, its action is more prolonged and considerably less toxic. The local irritant effects of cacodylic acid are minimal compared to those of arsenic. Cacodylic acid is judged as essentially non-irritating to both skin and eyes.

### 910. Signs and Symptoms.

Ingestion of a toxic dose of cacodylic acid by humans may cause slight burning of the mouth and throat, gastroenteric pain, vomiting, diarrhoea, haematuria, albuminuria, dehydration, jaundice, oliguria, and collapse. CNS symptoms (headache, dizziness, and hyperexcitability) may be present, obscuring gastroenteric complaints. Shock may develop as a consequence of paralysis and increased permeability of the capillaries.

### 911. Treatment.

Following ingestion of a toxic dose of cacodylic and further absorption should be prevented by gastric lavage, emesis or activated charcoal. Fluids should be given to combat dehydration.

## SECTION IV - PICLORAM

### 912. Toxicity.

Picloram (4-amino 3,5,6-trichloropicolinic acid) is one of the constituents of Compound 2. The major constituent is 2,4-D. Based on the criterion that an acute oral toxicity of 5000

$mg.kg^{-1}$ or greater in warm-blooded animals is non-toxic, picloram would be rated accordingly, and Compound 2 would be rated as mildly toxic. The data from extensive animal studies on the acute and chronic toxicity of picloram and Compound 2 suggest there would be little direct hazard of these formulations to humans.

## 913. Mechanism of Action.

The fate of picloram following ingestion has not been studied extensively and the pharmacology of picloram is unknown.

## 914. Signs and Symptoms.

As Compound 2 contains 2,4-D isopropyl amine salt, ingestion of a toxic dose would probably produce the same signs and symptoms as are produced by 2,4-D herbicide. Prolonged contact of Compound 2 with human skin will cause mild to moderate erythema. Contact with the eyes can also be irritating.

## 915. Treatment.

Should ingestion of a toxic dose of picloram occur, further absorption should be prevented by gastric lavage or emesis and by administration of activated charcoal, together with supportive therapy. Washing with soap and water in the event of accidental exposure is recommended. The eyes should be washed thoroughly with water in the event of contamination.

# CHAPTER 10

# RECOGNITION OF A CHEMICAL CASUALTY

## 1001. Introduction.

a. It is essential that medical personnel are familiar with the signs and symptoms of chemical agent poisoning to avoid repetition of the experience of World War I in which "medical officers frankly admitted that they were so handicapped by their lack of experience of cases of gas poisoning that they were often in doubt whether they were dealing with persons suffering from gas poisoning or not."

b. Medical and tactical intelligence channels should communicate with each other as early as possible. Threat information on potential use of CW weapons by enemy forces is important for the planning and execution of medical operations. Once CW weapons have been used, identification of agents will be important to medical intelligence channels for operational purposes.

## 1002. General.

Medical units should rely on information not only from detectors and intelligence sources but also from the casualties themselves. This applies particularly to agents for which at present there is no satisfactory detector, such as incapacitating agents. Some of the problems in the recognition and diagnosis of casualties suffering from the effects of chemical operations are discussed here. Medical personnel must bear in mind that with nerve agents, for example, symptoms and signs may range from mild, such as miosis, headache, and tightness of the chest to signs and symptoms associated with severe poisoning such as convulsions and respiratory failure. The nature and timing of symptoms will vary with the route of exposure. Although choking agents are less likely to be employed, the possibility of their use should not be forgotten, and here the danger is that the quiescent period which follows the initial poisoning might be mistaken for recovery and men or women sent back to duty even after a lethal dose. Battle casualties whose behavioral changes are not compatible with the physical signs of disability must be examined carefully to exclude the possibility of a psychomimetic agent having been used. When chemical agents have been used by the enemy, it is important that the fullest and earliest information be given to medical units to facilitate the diagnosis of individual cases and to permit the arrangements for the reception of casualties.

## 1003. Recognition of a Casualty of Chemical Operations.

Any individual who suddenly becomes a casualty without being wounded or who is suffering a greater degree of incapacitation than is compatible with his or her wound should be considered a possible chemical casualty. The differential diagnosis will include the possibility of psychiatric casualties. It is unlikely that chemical agents would produce single casualties under field conditions and a chemical attack should be suspected with any sudden increase in numbers

of unexplained casualties. If chemical operations are unlikely, and if only a few people are affected, another toxic hazard may be more probable (for example, carbon monoxide).

## 1004. Questioning Casualties.

Under operational conditions the medical situation may be complicated by the psychological effects. The medical officer's questions should be along the following lines:

a. Determine whether the casualty has been caused by a chemical agent:
- (1) Was the casualty wearing full protective equipment at the time of the attack?
- (2) Were there any aircraft or artillery bombardments in the area at the time of the attack?
- (3) Was there any evidence of spray, liquid droplets or smoke?
- (4) Was anybody else affected and if so, how was he or she affected?
- (5) Did the casualty notice any unusual smell? (This is not a very reliable symptom under battle conditions, but it should be considered.)
- (6) Did the available detection equipment respond positively?

b. Determine the identity of the agent:
- (1) What subjective effects were noticed and how soon?
  - (a) An unexplained sudden runny nose.
  - (b) A feeling of choking or tightness in the chest or throat.
  - (c) Blurring of vision and difficulty in focusing the eyes on close objects.
  - (d) Irritation of the eyes.
  - (e) Unexplained difficulty in breathing or increased rate of breathing.
  - (f) Sudden feeling of depression.
  - (g) Anxiety or restlessness.
  - (h) Dizziness or light-headedness.
  - (i) Slurred speech.
  - (j) Nausea.
  - (k) Muscular weakness.
- (2) Was there any delay between exposure or contamination and the onset of effects, and if so, for how long?
- (3) Did the effects persist after adjustment of the respirator?
- (4) Has the casualty used any self-injection device? If so, did the symptoms improve or deteriorate?
- (5) Is the casualty's behaviour normal?

c. Assess the dose of agent received:
- (1) Was the casualty exercising or at rest?
- (2) Was the casualty in the open or under cover?
- (3) For how long was the agent inhaled? How long was the interval between suspected contamination and decontamination?

## 1005. Types of Casualties.

On the chemical battlefield, the following types of casualties maybe seen:

a. *Conventional Casualties.*

(1) The conventional casualties with no chemical injury and with no contamination of their clothing and equipment.

(2) The conventional casualties with no chemical injury but with contamination of their clothing and equipment.

b. *Direct Chemical Casualties.*

(1) The chemical casualty with no other injury.

(2) The mixed casualty who has a conventional and chemical injury. Since chemical munitions often include explosive burst charges, such injuries may occur as part of a chemical agent attack. They may also occur when the chemical injury and conventional injury occur at different times. Other types of mixed casualties may occur if nuclear or biological weapons are used, and chemical injuries may occur combined with natural illness as well. (Infectious disease still accounts for the majority of casualties in contemporary warfare.)

c. *Indirect Chemical Casualties.*

(1) *Casualties suffering combat stress reaction (CSR).* Combat stress reaction occurs often in warfare, but maybe more frequent where the chemical warfare threat exists. The soldier will have additional stresses of isolation from wearing the chemical protective ensemble, additional fatigue from wearing the garments and fear of chemical agents. As in World War I, the differential diagnosis between the CSR casualties and chemical casualties may sometimes be difficult.

(2) *Casualties with side effects from chemical agent antidotes.* Some of the available antidotes may have undesirable side effects when taken inappropriately, or in large enough quantities. Atropine, for instance, causes decreased heat tolerance at a dose of 1 mg. Higher doses may cause tachycardia, dryness of the mouth, and decreased sweating. Medical personnel must be aware of the side effects of the available antidotes and be alert for their appearance.

(3) *Heat casualty.* Wearing the protective ensemble makes dissipation of excess body heat more difficult. Wearing the mask also makes water intake very difficult. Both will increase the probability of heat exhaustion or heat stroke.

# CHAPTER 11

# MEDICAL SUPPORT IN CHEMICAL OPERATIONS

## SECTION I - INTRODUCTION

### 1101. General.

a. Medical operations in a chemical warfare environment will be complex. In addition to providing care in protected environments or while dressed in protective clothing, medical personnel will have to treat chemically injured and contaminated casualties, sometimes in large numbers.

b. A mass casualty situation occurs whenever the numbers or type of casualty exceeds the capabilities of the unit to treat and manage them in a normal fashion. An erroneous reaction to such a possibility is to assume that the problem is too great to cope with and preparations would be futile. Rather, the success of the medical department to function effectively in a chemical war and to treat, successfully, the maximum number of casualties will directly relate to the efforts made in advance to prepare for the possibility.

c. The doctrine, organisation and equipment available to handle chemical casualties will vary between countries and most particularly between Services, because of differences in military operational requirements. However, whatever the system there will be a common set of problems that must be addressed in the management of chemical casualties because the clinical condition of the casualty will be the same or similar regardless of which Service he or she is a member, and because of similarities in the environment in which the casualty must be treated.

### 1102. Objectives of Medical Support in Chemical Operations.

The objectives are:

a. To conserve the fighting strength.

b. To continue to provide medical services and support to the maximum extent possible.

c. To protect medical personnel from chemical injuries while handling contaminated casualties, or while working in contaminated areas.

d. To minimise morbidity and mortality from conventional and chemical injuries.

e. To avoid the spread of contamination into medical vehicles and facilities.

### 1103. Characteristics of Chemical Agents.

a. The physical characteristics of chemical agents have been described in the individual chapters for each class of chemical agent. These characteristics, the method of employment, and the meteorological environment in which they are used will have a major impact on the type and number of casualties produced.

b. Some agents, such as nerve agents, cyanide, and phosgene are highly lethal, and a

large proportion of casualties may die unless care is given immediately after an attack. Other agents, such as mustard and Lewisite may be more incapacitating than lethal. The onset of symptoms will differ by type of agent and by route of exposure. Nerve agents and cyanide, especially by the inhalation route of exposure, are characteristically very rapid in onset of effects, whereas mustard and phosgene may have a latent period of several hours between exposure and onset of symptoms. During the latent phase the prognosis and future clinical course will not be apparent and the decision on whether to treat or evacuate will be difficult.

## 1104. Contamination Control.

a. One of the most difficult aspects of chemical warfare is that the chemical agents may persist in the environment for extended periods of time. This is especially true of agents such as VX, the mustards, thickened GB, or GD, which may remain as contact hazards for hours or days.

b. On the chemical battlefield, three types of environments may exist:

(1) An uncontaminated area where there are no chemical agents present.

(2) A contaminated area where chemical agents are present in a liquid state (and probably in a vapour state as well) presenting a surface contact hazard.

(3) A vapour-only environment, for example, in a downwind hazard area.

c. Complete decontamination of a contaminated environment may be difficult or impossible. However it may be possible to achieve sufficient decontamination, particularly in small areas, to create a vapour only hazard area. Thus it may be possible to decontaminate equipment so that no further surface contact hazard exists, even though chemical agent vapours may continue to be off-gassed from agent adsorbed onto or absorbed into the surface. In such environments, it may be possible to work without the full protective clothing ensemble, although respiratory and eye protection would still be required. This is because most agents in a vapour state penetrate through the skin very slowly. However, mustard at high vapour concentrations may still cause skin injury, particularly if the skin surface is wet or moist as may be the case in a warm environment.

d. Where a liquid hazard exists, decontamination of skin and eyes must be accomplished quickly if it is to be effective. Chemical agents may penetrate or react with the skin and eyes within minutes, so successful decontamination must be carried out immediately after exposure. Once agent is decontaminated, or has been absorbed, no further risk of contamination exists. The casualty's body fluids, urine, or faeces do not constitute a CW hazard.

e. Individual and collective protection are the first line of defence against chemical agent contamination. Individual protection comprises the respirator and protective clothing including gloves and boots. Full protective clothing is particularly important for persistent agents and agents that pose significant skin injury or skin penetration effects. For agents posing a respiratory or eye injury threat exclusively, the respirator would suffice. Individual protection imposes physiological and psychological stress on the individual, impairs communication, and reduces performance to a certain degree, depending on the individual's job performance requirements.

f. Collective protection is desirable, particularly for medical care. Adequate collective protection may not be possible, or may be difficult to achieve and will require personnel and equipment resources. In some instances, it may be feasible to establish a vapour only hazard area, and work within that area at less than full individual protection, such as using respiratory and eye protection. Limited medical care can be achieved in this manner, but full examination and definitive surgical treatment is impossible without full collective protection.

g. Collective protection provides the capability to medically manage severely toxic or injured decontaminated casualties in an environment where medical personnel are unencumbered by wearing individual protective equipment. Likewise, the casualties benefit from the capability of the medical unit to make full use of available medical equipment and procedures. A significant percentage of casualties (15-30%) can not be adequately treated in a contaminated environment without collective protection as their treatment requires the removal of their respirator.

h. In the presence of a CW threat, equipment and supplies should be kept in unopened, sealed or covered containers until required for use. The use of chemical agent resistant material (CARM) will provide good protection against liquid contamination, but even the use of conventional tentage will significantly reduce contamination by a liquid agent for a limited period.

## 1105. Mass Casualties.

a. Chemical weapons may cause large numbers of casualties in poorly protected or untrained personnel. World War I experience showed that large numbers of casualties most frequently occurred with units that were surprised or inexperienced in chemical warfare. Such casualty surges will require careful preplanning and training for medical units if they are to continue to operate efficiently.

b. All medical units must be prepared to receive mass casualties caused by or contaminated with chemical agents. Mass casualties are considered to be those who are produced within a relatively short period of time and who because of their number and type exceed the medical support capabilities for their care.

c. Casualty sorting must take into account the possibility that some casualties may be contaminated. Some provision for emergency treatment of contaminated casualties needs to be made, since some critical care may be required before decontamination can be accomplished. Proper triage procedures are an essential element in handling large surges of casualties. (See Paragraph 1107.) With adequate advance planning and training, mass casualty situations can be managed and excessive morbidity and mortality reduced. Lack of such preparation, or a mistaken belief that such preparations are futile, are sure ingredients for disaster.

## 1106. Medical Decision Making.

a. Differential diagnosis is one of the first and most difficult aspects of managing chemical casualties. Unless it is known to which agent the casualty was exposed, it may be difficult to establish a diagnosis with certainty. Further, the casualty may

still be partially or fully encapsulated in a protective ensemble, precluding elucidation of any but the most simple signs and symptoms. Knowledge of the principal signs and symptoms is necessary to determine the clinical diagnosis. The rapidity of the onset of symptoms may be an important clue, for example in nerve agent poisoning or cyanide poisoning. In some instances, it is better to act rather than try to obtain a certain diagnosis, particularly if the condition of the casualty is serious and rapidly deteriorating. In forward treatment areas, the diagnosis should be kept as simple as possible, and be keyed to making decisions that will lead to some specific action or actions.

b. When chemical casualties are received at a medical unit, they may also have traumatic wounds or illnesses due to other causes. These patients must be managed so as to minimise the injuries resulting from chemical exposure without aggravating their traumatic wounds or illnesses.

## 1107. Triage.

a. Triage is one of the most important tools for handling combat casualties, particularly in mass casualty situations. Basically, it is a medical decision process used to arrange casualties in priority order to ensure the most effective use of limited medical resources and minimise morbidity and mortality. Triage is a continuous, ongoing process through the casualty care chain and should be utilised whenever casualties must be assigned priority for treatment, evacuation or decontamination. Triage decisions should be made by highly experienced personnel familiar with chemical and conventional injuries. Triage criteria should be determined in advance and practised. They must be relevant to the medical capabilities of the medical unit. The four standard NATO mass casualty triage categories, adapted for chemical casualties, are as follows:

(1) *Immediate treatment (TI).*This includes those requiring emergency life saving treatment. Treatment should not be time consuming or require numerous, highly trained personnel, and the casualty should have a high chance of survival with therapy.

(2) *Delayed treatment (T2). The* general condition permits some delay in therapy although some continuing care and relief of pain may be required before definitive care is given.

(3) *Minimal treatment (T3).* This includes those with relatively minor signs and symptoms who can care for themselves or who can be helped by untrained personnel.

(4) *Expectant treatment (T4).* This group is comprised of patients whose treatment would be time consuming, require numerous highly trained people, who have life threatening conditions beyond the treatment capabilities of the medical unit, and would have a low chance of survival. It must be noted that the decision to place a casualty in the expectant category is not necessarily a decision to render no therapy. Rather, the triage categories determine the priority in which casualties are treated.

b. Chemical poisoning, besides being difficult to treat in itself, will complicate the therapy for other conditions. The addition of antidote therapy may further complicate management of other conditions requiring drug therapy, e.g., use of muscle relaxants for surgery or the use of analgesics. Some of these drug interactions are currently unknown, and the medical staff must remain alert for unusual reactions to otherwise common therapy on the battlefield.

## SECTION II - CASUALTY MANAGEMENT PHASES

### 1108. General.

a. *Field Medical Operations.* Field medical operations are conducted with several echelons of care, with increasing capabilities, and more sophisticated equipment towards the rear. The most forward medical support is usually provided by enlisted medical personnel with limited equipment, drugs, and medical capabilities.

b. *Far Forward Treatment.* Major advances have been made in casualty survival by advances in medical and surgical capability, and most importantly by advances in rapid evacuation and early stabilisation of casualties. On the chemical battlefield, early treatment and stabilisation will be particularly critical, since the lethal agents have very rapid onset of severe, life threatening effects. This means that far forward treatment, often by non-medical personnel, will be of even greater importance than in conventional warfare.

c. *Casualty Care Systems.*

(1) A specific example of a casualty care system is described in AMedP-7(A), Concept of Operations of Medical Support in a Nuclear, Biological and Chemical Environment. Because the mission requirements of each Service differ markedly, the organisation of medical support, the types and amount of medical resources at the echelons, and the evacuation distances between echelons will differ greatly. Further, there will be other national differences, such that the description of a particular system will not coincide with other national or Service systems.

(2) However, when the necessity of certain functional capabilities to handle different systems is considered, important similarities between the different systems can be identified. Nine functional phases of casualty care have been identified. Not every casualty will pass through all phases. Further, some phases such as evacuation, may be performed several times. Although the phases are arranged in order, the exact temporal order may vary from system to system, or be modified by force of circumstances. The first three phases, pre-attack, self aid and buddy aid will be carried out by non-medical personnel in the units themselves. The remainder of the phases will generally be carried out by medical personnel and units.

## 1109. Phase I - Pre-Attack.

a. The steps taken before an attack occurs will be the most important in determining how many and how severe the casualties will be. The protective mask and clothing are the first line of defence. Some nations have pre-treatments available for protection against certain chemical agents. Training will be essential to maximise protection of personnel and equipment. With multiple dose pre-treatments, strict discipline to ensure proper use will be necessary. The immediate commander exercises primary responsibility for ensuring that all necessary steps are taken. Medical personnel have a staff advisory role to the commanders in assisting them on matters of medical importance. For instance, commanders need to be advised of the physiological stress characteristics of the protective ensembles and how performance capabilities may be altered. The relation between environmental temperature and heat stress needs to be emphasised, especially in training situations, to avoid unnecessary heat casualties. Medical units will generally follow the same training and procedures for protecting themselves as do the non-medical units.

b. An example of possible guidance given for the prevention of heat casualties is given in Paragraph 1127. Each country may wish to issue its own specific guidelines.

## 1110. Phase II - Immediate Post-Attack/Self Aid.

a. The goal in this phase is to protect oneself from agent exposure during and immediately after an attack, to stop any further exposure, or to initiate immediate therapy if a significant exposure has occurred.

b. Since it is by definition “self care,” it is carried out only by personnel still capable of functioning. For agents with rapid onset, some personnel may not have time to take any steps before they are severely incapacitated and will by definition not pass through this phase. Since personnel in this phase will still be able to function to a certain degree, it is important that any treatment that they take not be incapacitating in itself. Some individuals will take such self aid mistakenly when they have not had a significant exposure, or even deliberately. Since the preservation of the unit effectiveness is most important at this point, additional casualties from the antidotes must be avoided.

c. The specific antidotes available for self care are discussed in the chapters for the different classes of agents, and are further prescribed in national and service doctrines. The specific steps in self-administration of the antidotes are likewise part of national and service doctrine and training. A critical factor in use of self aid antidotes is clearly defining the specific conditions under which they will be taken. Most commonly, they are taken when the individual notices a specific set of symptoms, characteristic for the agent. Additionally, self decontamination kits and their use are described in national and service doctrine.

## 1111. Phase III - Buddy Aid.

a. Buddy aid is the care given by non-medical personnel to personnel who are not able to care for themselves. Incapacition of various degrees is the marker differentiating between self care and buddy care.

b. Many units do not have medical personnel assigned or attached, or the medical personnel themselves may be casualties. Since immediate care is often so important in treating chemical casualties, buddy care will be the determining factor in the success of treatment. Unit commanders must take considerable care to ensure that all personnel have a adequate training to perform buddy care for chemical agent casualties. Such training is essential since the normal instinct of soldiers to help one another may be hampered by the inability in protective clothing to recognise that help is needed. Medical personnel may assist commanders in providing training.

c. Since the numbers of medical personnel are limited, particularly in forward units, commanders may wish to have a few non-medical personnel trained to a higher level of medical proficiency than would be feasible for all personnel. This could be valuable in resuscitation of nerve agent casualties for example, where the procedures are more complex. Such trained personnel would also provide back-up for medical personnel who may become casualties.

d. The antidotes available for buddy care will usually be the same as those provided for self aid. Since the casualty will be already incapacitated, the concern for further incapacitation from antidotes no longer applies, and further or higher doses of antidotes may be given if available. The individuals providing buddy care should not use their own antidotes to treat a casualty since they may need it themselves, but should use those belonging to the casualty, or any others available.

e. Commanders will have to exercise some control on buddy care, so as not to compromise mission accomplishment, but must also recognise their exclusive responsibility for the welfare of the casualties while they are still in the commanders' units. Manpower intensive procedures such as resuscitation must be applied judiciously, and only to those likely to benefit in order to avoid tying up too many personnel. Similarly, casualty evacuation out of the unit often requires the unit's own personnel initially and must be tightly controlled to retain personnel within the unit. Again, unit survival must be the overriding consideration.

## 1112. Phase IV - Initial Medical Care.

a. Initial medical care is the first care given by medical personnel. Although for administrative reasons medical care is sometimes defined as beginning when a casualty is treated by medical personnel, from a functional consideration medical care should be a continuous process, and this phase is a continuation of care given in preceding phases.

b. The goals of the initial medical care are to return to duty promptly all personnel still effective, and to stabilise and prepare for evacuation those casualties who require further medical care. Even though the medications, equipment, and medical personnel resources available far forward are limited, this phase will still be highly

critical for successful outcome. As a result of certain agents, casualties reaching this point may be severely incapacitated. Triage will be important in determining priorities of care and evacuation. The specific therapy available in this phase will depend on the unit, national and Service doctrines, and policies.

## 1113. Phase V - Life Support/Stabilisation.

Given the rapid onset and severe course of poisoning by some of the chemical warfare agents, nerve agents in particular, consideration for life support of vital, cardiovascular and respiratory function will often be required. Other conditions such as hemorrhage or shock from conventional wounds will also require immediate care. The ability to successfully manage these conditions will depend on the resources available at the various echelons. Triage criteria may dictate that some of these casualties will have a low priority of care. However, it is vital to make some effort to stabilise a casualty before evacuation to higher echelons and some effort at stabilisation should precede time consuming efforts such as full casualty decontamination. Therefore, some means of handling severe casualties should be incorporated early on in the system of managing casualties at each echelon. Hemorrhage, severe respiratory distress, cardiovascular collapse, shock, and seizures are among the conditions requiring prompt attention.

## 1114. Phase VI - Evacuation.

Evacuation of chemically injured casualties entails more than transportation. Monitoring is important to ensure that the casualty's condition is not deteriorating. Some provision for in transit care will also be critical. Since some casualties may be contaminated, the casualty evacuation system must be organised in a way as to minimise the spread of contamination. Since mass casualties may occur, and the number of medical vehicles may be inadequate to meet the increased load, unit commanders need to have contingency plans to supplement medical vehicles for casualty evacuation, or be prepared to retain casualties within their units for longer periods of time. Aeromedical evacuation is desirable when feasible, but the combat situation, the chemical environment and the possibility of contaminating helicopters may preclude their use far forward, in the initial stages of evacuation.

## 1115. Phase VII - Casualty Decontamination.

a. The goal of casualty decontamination differs from personal and unit decontamination. In addition to preventing exposure of the agent, casualty decontamination also has the goal of preventing exposure of medical care personnel and facilities to contaminated casualties. The requirement for casualty decontamination will be a function of the agent used, environmental factors, and particularly time. Liquid chemical agents on the skin may react with, or penetrate it rapidly. Some method of monitoring contamination would be valuable in determining the degree of decontamination required.

b. It is imperative that at least limited decontamination is performed as soon as possible. This will diminish the chance of recontamination of the casualty, or contamination of medical personnel and facilities from any agent left on the clothing or equipment.

Given the time it takes to evacuate casualties, the quantity of liquid agent on the skin or clothing will have diminished or even disappeared due to evaporation. Often careful removal of the clothing and equipment, with spot decontamination of skin areas that may be at risk of recontamination when the clothing is removed, will be just as effective as full decontamination, and can be accomplished more quickly and with fewer personnel. Protecting the wound from any further contamination with protective dressings is desirable. Further management of wounds should follow normal treatment procedures.

c. The hazard of off-gassing and further contamination from clothing and equipment removed from contaminated casualties requires that these items be disposed of properly. Several methods may be utilised for this purpose, such as impermeable bags or containers, or bleaching powders.

d. Disposal sites for these items must be marked in accordance with the standard NATO markings.

### 1116. Phase VIII - Definitive Care.

Specific therapy of the chemical casualty should be initiated as far forward as possible. It may occur across several echelons of care, involving increasingly sophisticated medical treatment as the casualty is evacuated to the rear.

### 1117. Phase IX - Disposition.

Following successful medical intervention, it must be decided whether a casualty should be returned to duty, held, or evacuated further to the rear for further treatment and convalescence. For casualties with minor exposures, it is desirable to return them to duty as soon as possible, and as far forward as possible, although this is not always operationally feasible. For casualties with severe poisoning, the course may be prolonged, and a long convalescence may be expected. The disposition of mustard injuries is dependent not only on the extent of injury, but also on the site of injury, as is described in Chapter 3. Care must be exercised in early mustard or phosgene injuries not to confuse the latent period with absence of injury. Nerve agent casualties with depleted cholinesterase levels are likely to be more susceptible to subsequent poisoning from nerve agents until their cholinesterase levels return to normal.

## SECTION III - COMBINED INJURIES

### 1118. Introduction.

a. Combined injuries occur when a casualty is affected by conventional weaponry and also by the use of nuclear, chemical or biological weapons. The situation in which a casualty is contaminated with a chemical agent, but not suffering from such an agent's effects is dealt with in AMedP-7(B).

b. Wounds which are not contaminated should be dressed in the usual way. They should then be covered with agent proof material (either impervious material or material similar to that of the protective suit) and any pressure bandage considered necessary

may then be applied over the protective covering. These precautions may prevent the casualty becoming a mixed chemical and conventional casualty.

c. The object of this section is to consider the effect of poisoning by chemical agents, and the effect of drugs used in the treatment of such poisoning upon the handling and treatment of casualties who are suffering from conventional wounding. A summary of possible interactions is listed in Table 11-I.

*Table 11-I. Potential Interactions of Chemical/Conventional Injuries*

| Chemical agent group | Potential interaction |
|---|---|
| Nerve agents<br>(carbamate pre-treatment)<br>(atropine) | Relaxants in anaesthesia.<br>Resuscitation. Narcotic analgesics.<br>Blood loss.<br>Shock. |
| Vesicants<br>(mustard and arsenicals) | Slow healing of wounds.<br>Haematopoietic depression.<br>Infection more likely. |
| Lung damaging agents | Resuscitation.<br>Blood loss.<br>Shock (latent period may be shorter). |
| Cyanogen agents | Resuscitation. Narcotic analgesics.<br>Blood loss.<br>Shock. |

## SECTION IV - NON PERSISTENT AGENTS

### 1119. Injury Complicated by Exposure to a Non Persistent Nerve Agent.

a. The dangers presented by this form of combined injury are those of the nerve agent itself, those of the interaction of respiratory depression with the conventional injury and those of the reduced cholinesterase activity upon drugs used in anesthesia during subsequent surgery; even carbamate pre-treatment may affect muscle relaxants to a limited extent.

b. Signs of nerve agent intoxication will call for treatment as described in Chapter 3.

c. Loss of blood will complicate respiratory failure, so that the administration of oxygen, if available, and positive pressure resuscitation if necessary, should be applied at the earliest indication of need. The need for replacement of blood lost through conventional injury will be correspondingly greater if respiratory depression is present. Reduced cholinesterase activity will affect the use of relaxant drugs used during anesthesia. On basic principles the action of anticholinesterases (including

to a lesser extent pyridostigmine pre-treatment) may be expected to potentate the action of depolarizing relaxants (e.g., succinylcholine) prolonging their action, but to oppose the action of non-depolarising relaxants of the curare type increasing the necessary dose. Drugs, such as opiates and other drugs, which reduce respiratory drive should be used with caution in cases of nerve agent intoxication.

## 1120. Injury Complicated by Exposure to Lung Damaging Agents.

a. This form of combined injury increases the stress element involved in the induction of pulmonary oedema. The latent period between exposure and the development of pulmonary oedema may possibly be shortened and the pulmonary oedema itself may be more severe.

b. The casualty should be kept at rest as far as possible during evacuation and steroid treatment if used should be applied at the earliest moment. There is no contra-indication to the use of opiates or other systemic analgesics in order to treat pain or shock from the conventional injury. Oxygen therapy may be required, but fluid replacement should be used with caution. The final decision on the necessity for fluid replacement must be made on the basis of the casualty's condition, bearing in mind the danger of precipitating or increasing pulmonary oedema.

## 1121. Injury Complicated by Exposure to Cyanogen Agents.

a. Combined injuries of this type will present especial danger from respiratory depression and from the therapeutic reduction of the oxygen carrying power of the blood, owing to the formation of methaemoglobinaemia in treatment.

b. The need for treatment of cyanide poisoning is urgent and must be started in accordance with Chapter 5. Oxygen therapy together with positive pressure resuscitation may be required all the more urgently in the presence of marked hemorrhage.

c. Opiates and other drugs which reduce respiratory drive must be used with caution in these combined injuries as the respiratory centre is depressed in cyanide poisoning.

# SECTION V - PERSISTENT AGENTS

## 1122. Injury Complicated by Persistent Nerve Agents.

a. Where the conventional injury is itself contaminated by a persistent nerve agent the danger of the casualty absorbing a lethal dose of nerve agent through the wound is very great and the prognosis is correspondingly bad. Although the wound track resulting from a conventional weapon injury in surrounded by devitalised tissue, there is rapid penetration of the tissues by nerve agent and a lethal dose may be quickly absorbed especially if a persistent agent contaminates the wound.

b. Decontamination of the skin surfaces around the wound should be carried out and then a surface dressing applied. The wound itself should be protected from further contamination and the integrity of the suit restored. Wounds may be irrigated using

a solution of hypochlorite and then flushed with normal saline. Hypochlorite should not be used, however, within the abdominal or thoracic cavities, nor with intracranial wounds. Early surgical excision of the contaminated wound may offer the best chance of success but autoinjector treatment should be started immediately the wound contamination is diagnosed and repeated as necessary.

c. Surgery of the contaminated wound offers minimal danger to medical and nursing staff if gloves made of butyl rubber are worn. If these are not available then two pairs of latex rubber gloves should suffice if washed at short intervals in hypochlorite solution and changed frequently. The evacuation of casualties with combined injuries requires careful observation while on route to a surgical unit and autoinjector treatment continued if signs of poisoning persist or worsen.

d. For conventional wounds not directly contaminated but with the surrounding skin affected by a chemical agent, decontamination of the skin should be carried out and any poisoning treated as appropriate for the particular agent involved.

e. Where the conventional injury is not directly contaminated, but skin absorption is thought to have occurred, skin decontamination should be carried out in the recommended way. Any signs of nerve agent intoxication should be treated. The casualty should be kept under as close observation as circumstances allow in case signs of delayed absorption of agent appear. If it is necessary to evacuate without medical supervision, consideration may be given to the use of one injection from the automatic injection device as a precaution against delayed absorption of nerve agent.

**1123. Injury Complicated by Contamination with Vesicant Agent.**

a. Vesicant agents will debilitate the casualty and may seriously delay the healing of any wound due to systemic effects, even if the wound itself is not directly contaminated. A contaminated wound will be very slow to heal and may also lead to rapid systemic absorption of the agent.

b. If the contamination of a wound with Lewisite occurs (immediate pain, disproportionate to the severity of the wound is suggestive of this) therapy with dimercaprol (BAL) will be required at an early stage.

c. The area around the wound should be decontaminated and the wound dressed. The dressed wound should be protected from further contamination with material similar to that of the protective suit.

d. Thickened mustard may be carried into wounds on fragments of cloth. These wounds should be carefully explored using a no-touch technique. Fragments of cloth should be removed and placed in a bleach solution. This removes the hazard from mustard vapour off-gassing. Wounds should be irrigated using a solution containing 3000-5000 ppm free chlorine (dilute “milton” solution) with a dwell time of approximately 2 minutes. The wound should then be irrigated with saline. This technique should not be used in the abdominal, or thoracic cavities, nor with intracranial head injuries.

e. Opiates should not be withheld if the condition of the casualty calls for their use.

## SECTION VI - OTHER CONSIDERATIONS

### 1124. Collective Protection.

Collective protection greatly enhances the treatment of casualties in a contaminated environment as 15-30% of casualties can not be adequately treated without removal of their respirator.

### 1125. Head Wounds.

Head wounds, after being attended to and dressed will necessitate the casualty being evacuated in a casualty bag or half bag or hood. In emergency the casualty's head may be protected in a pervious blouse from a spare protective suit.

### 1126. Heat Stress.

a. The use of individual protective equipment and casualty bags imposes a significantly greater heat stress upon the individual. In warm environments and at moderate work rates personnel are susceptible to heat injury.

b. The medical officer's responsibilities may include providing advice to commanders about work/rest cycles and of the need for increased fluid intake.

c. Medical attendants need to be especially aware of the need to replace fluids in casualties wearing individual protective equipment.

d. Protective equipment makes monitoring casualties difficult and a high index of suspicion for heat stress must be maintained at all times.

e. Table 11-II may be applied as guidance for the prevention of heat casualties in acclimatised individuals. In situations where work is heavy or prolonged, the risk of heat injury exists at wet bulb gradient temperatures (WBGT) below 78°F (25.5°C).

*Table 11-II. Heat Casualty Prevention Guide*

| Heat condition (category) | WBGT index* (°C) | Water intake (liters per hour) | Work/rest cycle (minutes) | WBGT index* (°F) | Water intake (US pints per hour) |
|---|---|---|---|---|---|
| 1 | 25.5 to 27.6 | At least 0.45 | Continuous | 78.0 to 81.9 | 1 |
| 2 | 27.7 to 29.3 | At least 0.45 | 50 / 10 | 82.0 to 84.9 | 1 |
| 3 | 29.4 to 31.0 | At least 0.9 | 45 / 15 | 85.0 to 87.0 | 2 |
| 4 | 31.1 to 32.1 | At least 1.4 | 30 / 30 | 88.0 to 89.9 | 3 |
| 5** | 32.2 and above | More than 1.8 | 20 / 40 | 90.0 and above | More than 4 |

* Individual protective gear or body armour adds at least 6°C (10°F) to the WBGT index.
** Suspend physical training and strenuous activity. If operational mission (non-training) mission requires strenuous activity, enforce water intake to minimise expected heat injuries.

# CHAPTER 12

# DISPOSITION OF CONTAMINATED FOOD AND WATER

## SECTION I - GENERAL

### 1201. Introduction.

a. Although it is expected that chemical agents will be used mainly against personnel, food and water supplies may easily become contaminated and may be contaminated deliberately. This may occur from contact with chemical agents in the form of vapour, aerosol, drops or splashes of liquid or particulate smokes. This may render food both unpalatable and toxic, but on the other hand, dangerously contaminated food may appear normal.

b. Decontamination of food is difficult and often impossible, so that all food not packed in agent proof containers must be stored under protection. When decontamination of food is possible, the decision to undertake decontamination must depend on local factors, for example, the availability of new food.

c. Food supplies in storage are not likely to be seriously contaminated if precautions are taken to protect them against chemical attack. For this reason, large supplies of food should not be condemned as a whole, simply because they have been exposed to possible chemical contamination. A prompt and careful survey of the supplies may reveal only a few items have been so contaminated and require special treatment. Prompt segregation of the heavily contaminated portions will prevent or minimise contamination of the remainder. Generally, foods not packed in protective packages constitute the major difficulty. The type and extent of contamination, the availability of replacement supplies, and the available means of decontamination will dictate whether or not reclamation of contaminated items is worthwhile.

d. Water is liable to contamination and may be contaminated deliberately. There are several methods of decontamination. Water is likely to be in short supply, and is more immediately important to the body than food, so that methods of protection, control and decontamination of water must be considered.

## SECTION II - EFFECTS OF CHEMICAL AGENTS ON FOOD AND WATER FOOD

### 1202. General.

The effects of chemical agents on food depend on the properties of both the agent and the food. Contamination of water may lead to a toxic hazard when it is used for food preparation.

### 1203. Penetration.

Nerve and mustard agents readily penetrate fatty foods and will also penetrate granular foods (e.g., grain and sugar). Arsenical penetrate proteins less readily owing to their coagulating

action. Fruit may be penetrated by nerve agents. Three groups of foods may be considered on the basis of their composition.

a. Foods with high water content, but low fat and a crystalline structure (e.g., fresh vegetables, fruit, sugar and salt). These absorb mustard and nerve agents in vapour and in liquid form.

b. Foods with low fat content and amorphous structure (flour, bread, grain, rice cereals, dried fruit and vegetables, tea, coffee, peas and beans). These absorb liquid nerve and mustard agents; some absorption of vapour may occur.

c. Foods with high fat and low water content (butter, fat, oil, ham, fat meat, cheese, milk, eggs and fish). These absorb nerve agents and mustard so readily that decontamination is impossible.

## 1204. Effect on Food.

a. *Food may become highly toxic without any change in its appearance.*

b. The expected effect of some chemical agents on the appearance of food are summarised in Table 12-I. The absence of these signs must *not* be relied upon in deciding that exposed food is fit for consumption. (See Table 12-II.)

*Table 12-I. Effect Of Certain Agents On The Appearance of Food*

| Agent | Taste | Smell | Colour | Residual toxicity |
|---|---|---|---|---|
| Mustard | Affected | Garlic | Meat discoloured | + |
| N-Mustards | Affected | Fishy | No discolouration | + |
| Arsenicals | Acid | Unpleasant | Meat & vegetables discoloured | + |
| Nerve agents | None | None | No effect | + |
| White phosphorus | Acid | Garlic | Glows in dark | + |

## 1205. Effect on Crops.

Heavy contamination of plants with mustard or arsenical will destroy crops. Lighter contamination may cause partial defoliation. Arsenical agents will leave sufficient arsenic to render the plant toxic, and nerve agents may penetrate plants so as to make them toxic.

## 1206. Effect on Livestock.

The effects of chemical agents on livestock will be the same as those upon human casualties apart from species specific variations. Mustard does not cause blistering in animals. The presence of large numbers of dead animals may indicate contamination in the area and these animals should not be eaten.

*Table 12-II. Effect of Chemical Agents on Food*

| Type of agent | High fat content (butter, fats, cheese, meat, bacon and shell eggs, etc.) | Low fat, high moisture content (fruit, vegetables, sugar, salt, etc.) | Low fat, low moisture content (cereal, tea, coffee, flour, bread, rice, etc.) |
|---|---|---|---|
| Nerve agents (liquid) | Condemn. | Condemn. | Condemn. |
| Nerve agents (vapour) | Condemn. | Expose dry food to the air for 48 hours. Wash other foods with 2% sodium bicarbonate solution, peel where applicable, and cook by boiling. | Expose dry food to the air for 48 hours. Wash other foods with 2% sodium bicarbonate solution, peel where applicable, and cook by boiling. |
| Blister agents (liquid) | Condemn. | Condemn. | Condemn. |
| Blister agents (vapour) | Condemn. | Expose dry food to the air for 48 hours. Wash other foods with 2% sodium bicarbonate solution, peel where applicable, and cook by boiling. | Expose dry food to the air for 48 hours. Wash other foods with 2% sodium bicarbonate solution, peel where applicable, and cook by boiling. |
| Choking agents* | Wash food with water where possible and expose to the air for 24 hours. Food may be unpalatable due to the acid product of hydrolysis. | Wash food with water where possible and expose to the air for 24 hours. Food may be unpalatable due to the acid product of hydrolysis. | Wash food with water where possible and expose to the air for 24 hours. Food may be unpalatable due to the acid product of hydrolysis. |
| Cyanide type agents | Unlikely to produce dangerous contamination of foodstuffs. | Unlikely to produce dangerous contamination of foodstuffs. | Unlikely to produce dangerous contamination of foodstuffs. |
| Riot control agents | Food may be unpalatable to the extent of being inedible. | Food may be unpalatable to the extent of being inedible. | Food may be unpalatable to the extent of being inedible. |

*Agents decompose rapidly on contact with water.

## SECTION III - PROTECTION OF FOOD AND WATER AGAINST CONTAMINATION WITH CHEMICAL AGENTS

## 1207. Packaging Materials.

*Decontamination of food is difficult and not likely to be satisfactory, so that the protection of food and drink is of the first importance.* Food supplies should therefore always be covered when transported or stored. Even the thinnest covering is better than no covering at all, but good protection can be given by suitable methods of packing and storing.

## 1208. Disposition of Packaged and Stored Supplies.

In determining the disposition of packaged and stored supplies which have been contaminated, consideration must be given to the nature of the contaminant, as well as to the type of foodstuffs and the security afforded by the packaging material. Some of these factors are outlined below:

a. Airtight glass bottles, sealed aluminium laminated packages, and sealed metal cans give complete protection against vapour and liquid.

b. Wooden boxes not sealed for the exclusion of air give almost no protection against vapour and liquid.

c. Waxed paper boxes sealed for the exclusion of air give good protection against vapour and fair protection against liquid.

d. Untreated wrapping papers give poor protection against vapour and very little against liquid.

e. Ordinary textiles in a single layer packaging give almost no protection against vapour and liquid.

f. Coverings of sod and earth give good protection against vapour and liquid.

g. Overhead shelters give protection against liquid sprays and splashes. Closed buildings give protection against liquids but often not against vapours, unless overpressured with filtered air.

h. Generally, double layers greatly increase the protective efficiency of packaging materials.

i. Field rations are packaged to protect the enclosed foods for hours even when the outside of the package is heavily contaminated with a liquid agent.

### SECTION IV - MONITORING FOR CONTAMINATION

## 1209. Monitoring Food.

a. *All food exposed to chemical attack which has not been protected by agent-proof containers or in fully protected stores must be considered contaminated.*

b. Monitoring for *volatile agents* only may be undertaken by putting the food into a clean plastic bag and sampling the air in the bag with suitable detection equipment.

c. Where arsenical contamination is suspected, the food may be suspended in water and the water tested with a water testing kit. Liquid contamination on the surface of containers may be tested for using detector papers, but this method will only be reliable whilst liquid agent remains.

d. *Mental incapacitants, biological agents and nuclear fallout will not be detected by these means.*

## SECTION V - DECONTAMINATION OF FOOD AND WATER

### 1210. Classification of Supplies.

Before any decontamination is done, a careful survey should be made to determine the extent of the contamination. From information gained in this survey, the exposed items should be divided into three groups for separate treatment as described below.

a. Group I will consist of canned and unopened packaged items which have been exposed only to the vapours of a chemical agent. Generally, the items in this group will be safe to issue to personnel after a brief period of outdoor airing to remove clinging vapours.

b. Group II will consist of canned and unopened packaged items, the outsides of which have been contaminated with a liquid chemical agent. The best procedure is to allow self decontamination of the packaging material by ageing and airing. If a shortage of food does not permit the necessary time for self decontamination, then a decontamination procedure is to strip off the outer contaminated coverings and examine the inner layer to see if agent penetration has occurred. If it has, continue stripping off layers until an uncontaminated layer is reached.

c. Group III will consist of unpackaged or poorly packaged items which have been exposed to an agent in either vapour or liquid form. Decontamination of food itself will be attempted only in emergency situations when there is no alternative supply of food. The general decontamination procedure to be followed in sequence is:

(1) Trimming of surface fat and/or grossly contaminated areas.

(2) Washing with water of 2% sodium bicarbonate solution or 1% chlorine solution.

(3) Boiling in water. Frying, roasting or boiling will not remove traces of nerve or blister agents from meats. In general, salvage of foods contaminated with droplets of the blister agents, especially the arsenical blister agents, is not practical.

### 1211. Water.

a. Contamination of water may lead to a toxic hazard when it is used for drinking, washing, and food preparation.

b. Although many agents hydrolyse in water, this is not satisfactory as a method of decontamination. Arsenical agents leave degradation products which are toxic even when hydrolysis is complete. The appearance of water does not indicate contamination, and any water exposed to high concentrations of vapour, or any liquid contamination must be regarded as toxic until tests have been made.

c. Open water sources subjected to chemical attack should be considered contaminated until tested. Water from deep wells will be safe provided that the well mouth is covered. Water in closed metal tanks will be safe provided that the tap and air inlet are decontaminated. Table 12-III gives the maximum allowable concentrations for certain agents in accordance with Stanag 2136.

*Table 12-III. Maximum Allowable Concentrations of Agents in Drinking Water*

| Agent | Maximum Allowable Concentration ($mg.l^{-1}$) consumed at 5 litres per day for not more than 7 days |
|---|---|
| Mustard | 0.2 |
| Nerve agents | 0.02* |
| Arsenic | 0.3 |
| Cyanogens | 6.0 |

* Many water testing kits are not sufficiently sensitive to detect nerve agent at this concentration.

## 1212. Monitoring Water.

a. Water testing kits will detect the following agents: mustard, nerve agents (0.05 ppm only), arsenic, antimony, cyanogen agents, other heavy metals (lead, copper, mercury). Water with a pH less than 3 is condemned since this high acidity may be due to contamination with mustard, but if free chlorine is present throughout 30 minutes mustard will be destroyed. Chlorine in excess of 5 ppm will, however, interfere with the testing and should be reduced (e.g., with thiosulphate).

b. The water testing kits will not detect mental incapacitants, biological agents or nuclear fallout.

## 1213. Decontamination of Water.

*Simple boiling is not a reliable method of decontamination.* The following methods are available for decontaminating water and may be used in combination:

a. *Filtration.*

(1) In a small scale emergency, water may be decontaminated by running it through a spare unused respirator canister, provided that the flow rate is such that the water emerges drop by drop; any water coming through at first faster than this should be discarded. No more than 5 litres should be filtered with one canister. *The canister cannot be used on a respirator after being used for this purpose.*

(2) On a larger scale, a modified water purification unit in which the kieselguhr filter is supplemented by a bed of activated charcoal is under development.

b. *Superchlorination.* Small amounts of water, in units of one litre, may be superchlorinated. Simple chlorination, as is used to disinfect water from naturally occurring bacterial contaminants, is not sufficient to decontaminate water suspected of being contaminated with chemical agents.

c. *Flocculation*. Larger quantities of water may be treated by flocculation with metal salts, after which the water is treated with chlorine.

d. *Reverse Osmosis*. Reverse osmosis is an effective method of removing contamination, including heavy metals.

# NATO HANDBOOK ON THE MEDICAL ASPECTS OF NBC DEFENSIVE OPERATIONS
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## PART III- CHEMICAL

## ANNEX A

## BIOCHEMICAL ACTION OF NERVE AGENTS

**1 FEBRUARY 1996**

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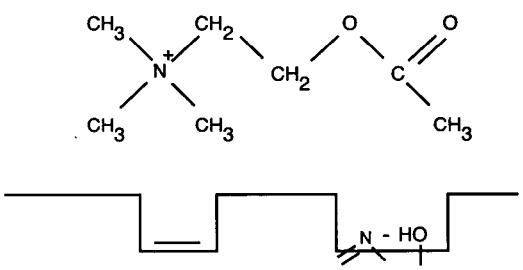
# ANNEX A

## BIOCHEMICAL ACTION OF NERVE AGENTS

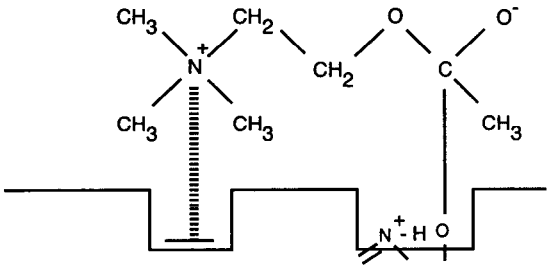
### A.01. Acetylcholinesterase.

a. Acetylcholinesterase exists as a large, complex molecule. The active centre has been suggested to comprise:
   (1) A negatively charged or anionic sub-site.
   (2) An esteratic sub-site.

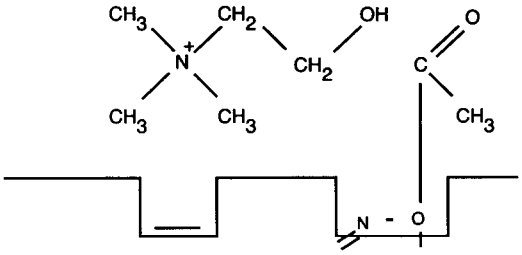
b. The current model for the binding group at the esteratic site is an hydroxyl group of a serine molecule of the enzyme. This group binds to the acyl carbon atom of acetylcholine. The sequence of reactions taking place during the hydrolysis of ACh is shown in Figure A-I.



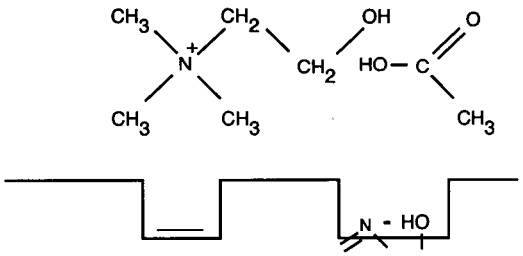

1. Acetylcholine molecule and active site of enzyme shown together but not having undergone any interaction.




2. Acetylcholine combined with enzyme to form a substrate-enzyme intermediate (short lived).




3. The ester link in the acetylcholine has been broken and free choline has been formed.




4. The acyl group has become detached from the enzyme leaving: choline, acetic acid, and the enzyme returned to its original state.

*Figure A-I. Hydrolysis of Acetylcholine*

c. The overall reaction could be represented by Figure A-II.

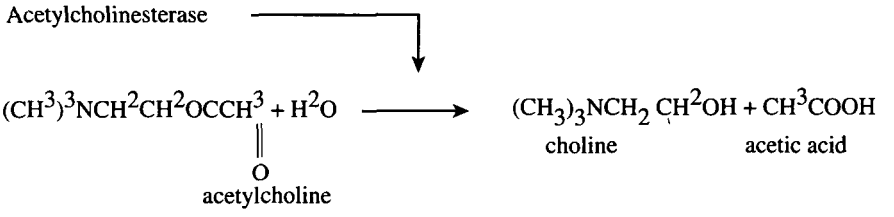



*Figure A-II. Overall Reaction Occurring During Hydrolysis of Acetylcholine*

d. The choline is taken up by the pre-synaptic or pre-junctional nerve terminals and recycled by combination with acetyl COA catalysed by the enzyme choline acetyltransferase to form more acetylcholine.

e. The destruction of acetylcholine by Ache is a very rapid reaction. Organophosphorus compounds (including the nerve agents) act by combining essentially irreversibly with acetylcholinesterase molecules and preventing their activity. The combination of GB with AChE is shown in the series of reactions in Figure A-III.

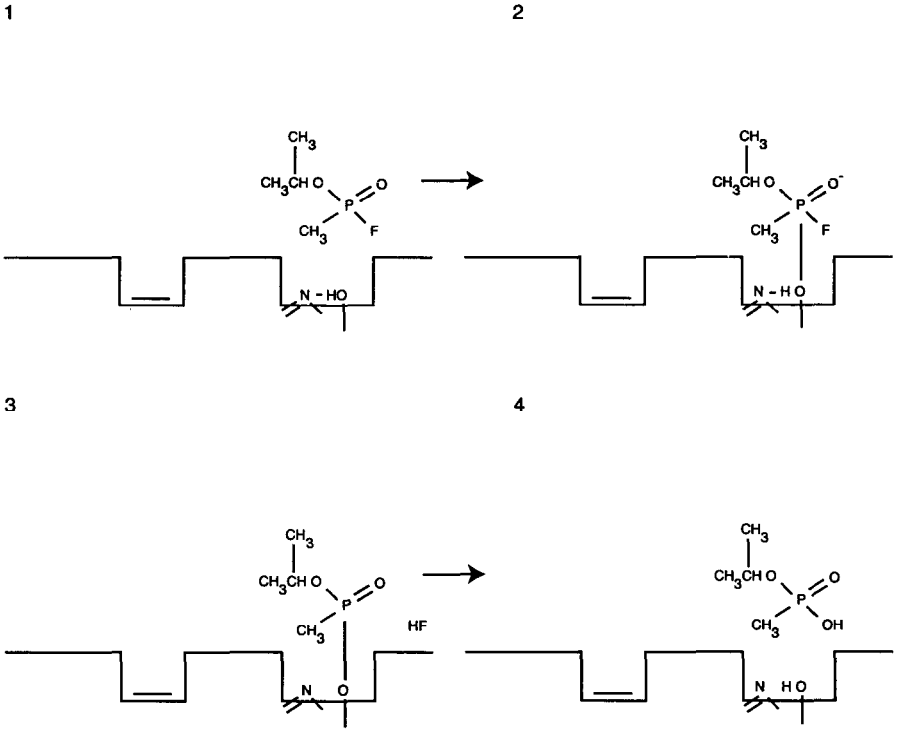



*Figure A-III. GB and AChE Reactions*

f. Unlike the hydrolysis of acetylcholine, however, this series of reactions is slow as a result of the very slow, and rate limiting, final step (3-4) in Figure A-II. This stage takes place so slowly that in practical terms no regeneration of enzyme takes place and if the dose of organophosphate is sufficiently large the patient dies.

g. Another reaction may be added to the above series: the reaction describing the process of AGING 11:

$$R.R'O.PO\ enzyme + H_2O \longrightarrow R.(OH)PO\ enzyme + R'OH.$$

h. This loss of an alkyl group produces a very stable agent-enzyme complex which is then resistant to spontaneous hydrolysis and reactivation by oximes. The rate of aging is dependent on the nature of the alkyl group and is fairly slow (hours) in the case of GB or VX but is very rapid (minutes) in the case of GD.

i. Aging is the main cause of failure of compounds designed to speed reactivation of the enzyme to be of as much value in GD poisoning as they are in the treatment of GB or VX poisoning.

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## PART III - CHEMICAL

## ANNEX B

## PHARMACOLOGY OF OXIMES

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# ANNEX B

## PHARMACOLOGY OF OXIMES

### B.01. Composition of Oximes.

a. The oximes comprise a group of compounds possessing one or more pyridinium rings and bearing one or more aldoxime groups. A large number of such compounds has been synthesised and are divided into:

(1) Mono pyridinium oximes such as pralidoxime (pyridine-2-aldoxime methyl chloride, PAM Cl, pralidoxime methylsulphonate) (Figure B-I).

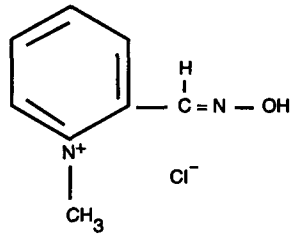


*Figure B-I. Formula of Pralidoxime*

(2) Bispyridinium oxides including obidoxime (Toxogonin ®) with the formula as shown in Figure B-II.

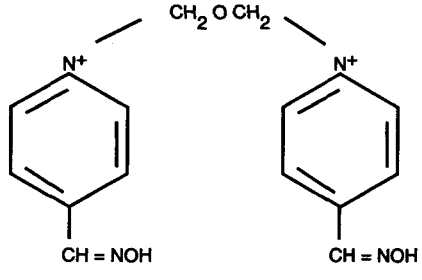


*Figure B-II. Formula of Obidoxime*

b. Recently the new Hagedorn (H) oximes have been synthesised and these include the compounds H16 and HS6 as shown in Figure B-III.

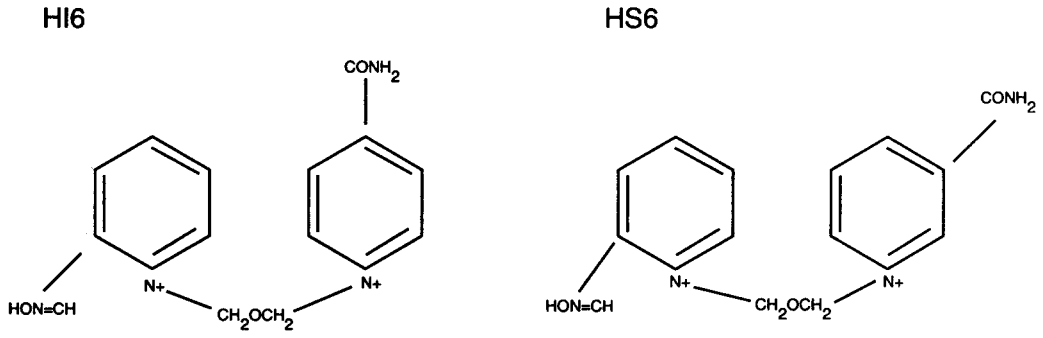


*Figure B-III. Formula of Hagedorn Oximes*

c. The oximes are thought to act by combining with the modified nerve agent molecule and removing it from the acetylcholinesterase enzyme. They also have other pharmacological effects which may contribute to their efficacy.

d. The sequence of reactions shown in Figure B-IV represents the reactivation of GB inhibited enzyme by pralidoxime.

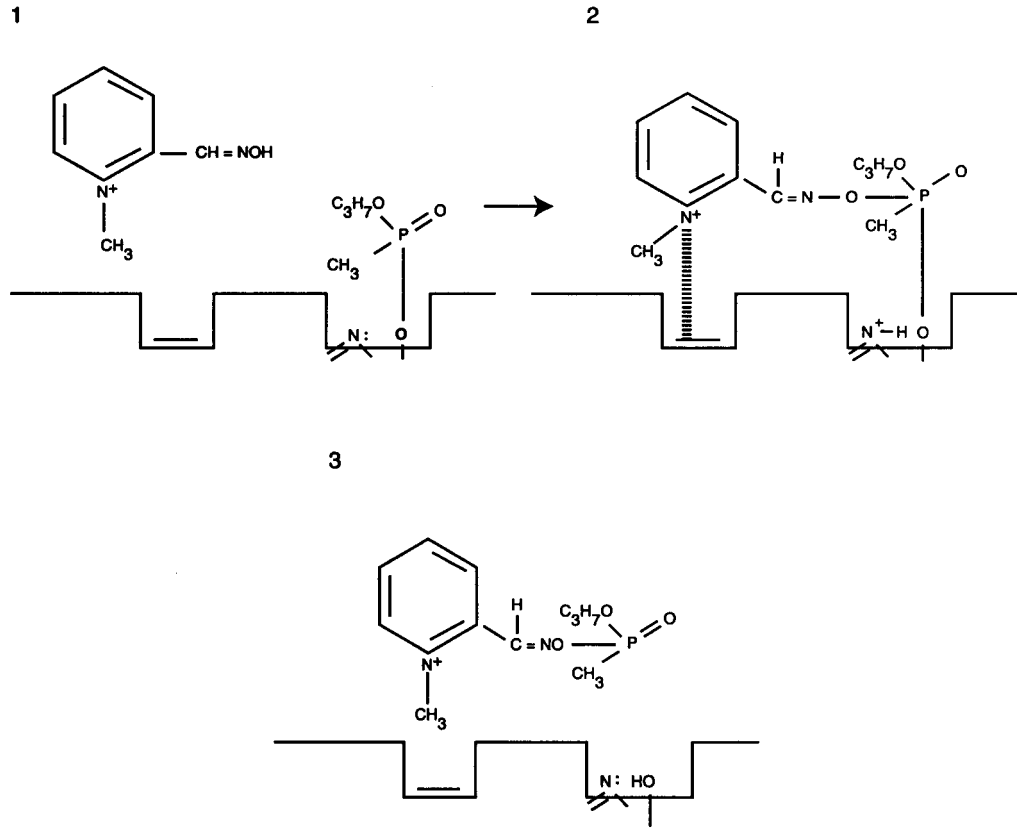


*Figure B-IV. Reactivation of GB Inhibited Enzyme by Pralidoxime*

# NATO HANDBOOK ON THE MEDICAL ASPECTS OF NBC DEFENSIVE OPERATIONS
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## PART III - CHEMICAL

## ANNEX C

## SUMMARY OF THE EFFECTS OF CHEMICAL AGENTS

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# ANNEX C
# SUMMARY OF THE EFFECTS OF CHEMICAL AGENTS
*Table C-I. Effects of Chemical Agents*

| Agent | Symbol | Odour | Mechanism of action | Eyes (pupils) | Eyes (conjunctivae) | Rest of eye |
|---|---|---|---|---|---|---|
| Tabun; Sarin; Soman; GF. | GA GB GD GF | None or faint sweetishness, fruity or paint-like. | Anticholinesterase agents. | Miosis. | Redness. | Pain, especially on focusing, dimness of vision, headache, lachrymation. |
| VX | VX | None. | | | | |
| Mustard | H HD | Garlic or horseradish, irritating. | Vesicants. Bone marrow depressant. Alkylating agents, damages DNA. | Mydriasis. | Redness, oedema, irritation, gritty pain. | Oedema of lids, pain, blepharospasm, photophobia, lachrymation, corneal ulceration and possibly scarring. |
| and nitrogen mustard. | HN | None or fishy, irritating. | | | | |
| Lewisite and other arsenical vesicants. | L | Fruity to geranium-like. Irritating. | Vesicants. Arsenical poisons. | | Prompt redness, oedma, irritation. | Immediate burning sensation, iritis, corneal injury. |
| Mustard/lewisite mixture. | HL | Garlic-like. | Like lewisite and mustard. | Like HD, HN and L | Like HD, HN and L. | Like HD, HN and L. |
| Phosgene oxime. | CX | Unpleasant and irritating. | Powerful vesicant. | | Violently irritating, redness, oedema. | Corneal injury with blindness, lachrymation. |
| Phosgene. | CG | Green corn, grass or new-mown hay. | Lung damaging agent. | | Irritation. | Lachrymation (after respiratory symptoms). |
| Hydrogen cyanide. | AC | Faint bitter almonds. | Interferes with oxygen utilisation at cellular level. | | | |
| Cyanogen chloride. | CK | Very irritating. | Like hydrogen cyanide, lung irritant. | | Irritation. | Lachrymation. |
| Vomiting agents. | DM DA DC | Burning fireworks, very irritating. | Local irritant, induces vomiting. | | Irritation. | Lachrymation. |
| Irritant agents. | CN CA | Irritating. | Local irritant. | | Redness, irritation. | Pain, blepharospasm, profuse lachrymation, photophobia. |
| | CS CR | Very irritating, pungent, pepper-like. | Local irritant. | | Intense irritation. | Pain, blepharospasm, lachrymation, photophobia. |
| Incapacitiating agents. | BZ | None. | Anticholinergic. | Mydriasis. | | Blurred vision. |
| | LSD | None. | Psychomimetic. | Mydriasis. | | |

*Table C-I. Effects of Chemical Agents (continued)*

| Symbol | Nose and throat | Respiratory tract | Skin | GI tract | Cardiovascular system |
|---|---|---|---|---|---|
| GA<br>GB<br>GD<br>GF<br><br>VX | Increased salivation. Rhinorrhoea. | Tightness in the chest, bronchoconstriction, occasional wheezing, increased bronchial secretion, cough, dyspnoea, substernal tightness. | Sweating, pallor then cyanosis. | Salivation, anorexia, nausea, vomiting, abdominal cramps, epigastic tightness, heartburn, eruction, diarrhorea, tenesmus, involuntary defecation. | Occasional early transient tachycardia and/or hypotension followed by bradycardia and hypotension. |
| H<br>HD<br><br>HN | Swelling, irritation, ulceration, discharge, occasional oedema of larnyx. | Slowly developing irritation, hoarseness, aphonia, cough, tightness, dyspnoea, rales. Pneumonia, fever, pulmonary oedema, in severe cases. Risk of secondary infection. | No immediate signs. After minutes to hours, redness and burning. Several hours later blisters surrounded by redness and itching. Several days later necrosis, generally limited to epidermis. Delayed hyper- and hypo-pigmentation. Moist areas affected most. Risk of secondary infection. | Pain, nausea, vomiting, diarrhoea. | Shock after severe exposure. |
| L | Prompt irritation. | Rapid irritation, hoarseness, aphonia, cough, pneumonia, fever, pulmonary oedema, pleural effusion in severe cases. | Prompt burning. Red within 30 minutes. Blisters on 1st or 2nd day. Pain worse and necrosis deeper than H. | Diarrhoea, nausea, vomiting, hepatic failure. | Shock after severe exposure. Haemolytic anaemia, haemo-concentration. |
| HL | | | | | |
| CX | Very irritating to mucous membranes. | Rapid irritation and coughing. Later pulmonary oedema. | Immediate severe irritation and intense pain. Within I minute the affected area turns white, surrounded by erythema. Swollen within 1 hour; blistered after 24 hours. Necrosis may occur. Long recovery (1-3 months). | | |
| CG | Irritation. | Coughing, choking, chest tightness on exposure. Latent period, then pulmonary oedema, dyspnoea, frothy sputum, rales, pneumonia and fever. | Possible cyanosis following pulmonary oedema. | Nausea, occasional vomiting after respiratory symptoms. | Shock after severe exposure, hypotension and tachycardia. |
| AC | | Deep respiration followed rapidly by dyspnoea, gasping then cessation of respiration. | Initially pinker that usual; may change to cyanosis. | Nausea. | Profound hypotension. |
| CK | Irritation. | Irritation, cough, choking, dyspnoea; pulmonary oedema can be rapid. | | Like hydrogen cyanide. | |
| DM<br>DA<br>DC | Pain, rhinorrhoea, tightness, sneezing. | Tightness and pain, uncontrollable coughing. | Stinging, (especially of face), occasional dermatitis. | Salivation, nausea vomiting. | |
| CN<br>CA | Irritation, burning. | Tightness and irritation if concentration is high. | Stinging, (especially of face) occasional dermatitis, may blister. | Occasional vomiting. | |
| CS<br>CR | Irritation, burning, tightness. | Tightness in chest and difficulty breathing. | Stinging, occasional dermatitis, may blister. | Nausea and vomiting. | |
| BZ | Extreme dryness. | | Dry, flushed. | Constipation. | Tachycardia, elevated blood pressure. |
| LSD | | | Sweaty palms, cold extremities. | | Tachycardia. |

*Table C-I. Effects of Chemical Agents (continued)*

| Symbol | Genito-urinary system | Central nervous system | Other | Treatment |
|---|---|---|---|---|
| GA<br>GB<br>GD<br>GF<br><br>VX | Frequent micturition, urinary incontinence. | Apprehension, giddiness, insomnia, headache, drowsiness, difficulty concentrating, poor memory, confusion, slurred speech, ataxia, weakness, coma with areflexia, Cheyne-Stokes respiration, convulsions. | Fasciculations, easy fatigue, cramps, weakness (including respiratory muscles), paralysis. | Pre-treatment with pyridostigmine.<br>Post-exposure therapy:<br>a. Cholinergic blockage - atropine.<br>b. Enzyme reactivation - oximes.<br>c. Anticonvulsant - diazepam.<br>d. Assisted ventilation.<br>e. Suction for respiratory secretions. |
| H<br>HD<br><br>HN | | Anxiety, depression. | Late depression of bone marrow, malaise and prostration. | Eyes: antibiotics, cyclopegics and systemic analgesia. Skin: local dressings and antibiotics for infection. Antibiotics for respiratory infection. IV fluids. |
| L | Renal failure. | Anxiety, depression. | Systemic arsenic poisoning. | Like sulphur and nitrogen, mustards. BAL in oil IM for systemic chelation. BAL ointment for eyes and skin. |
| HL | | Anxiety, depression. | | Like sulphur mustard, nitrogen mustard and lewisite. |
| CX | | Anxiety, depression. | | Apply dressings of sodium bicarbonate. Systemic analgesics. Treat as any other necrotic skin lesion. |
| CG | | Anxiety, depression. | | Corticosteroids IV and by inhalation promptly may be life-saving. Rest, oxygen, antibiotics. |
| AC | | May have initial excitation; then depression, giddiness, headache, irrational behaviour, ataxia, convulsions or coma. | | Drugs binding cyanide:<br>a. Methaemoglobin formers; nitrites or DMAP.<br>b. Scavengers; dicobalt edetate and hydroxocobalamin.<br>Provision of S-groups; thiosulphate.<br>Assisted ventilation. Oxygen. |
| CK | | | | Like hydrogen cyanide and phosgene. |
| DM<br>DA<br>DC | | Severe headache, mental depression. | May cause desire to remove respirator. | Wear mask in spite of symptoms. Spontaneous improvement. |
| CN<br>CA | | Headache. | | Spontaneous improvement. Analgesic eye and nose drops if necessary. |
| CS<br>CR | | Headache. | | Symptoms disappear rapidly in fresh air. |
| BZ | Urgency, urinary retention. | Headache, giddiness, drowsiness, disorientation, hallucinations and occasional maniacal behavior. Ataxia and/or lack of coordination. | | Restraint, cool environment. Physostigmine. Treatment may be required over several days. |
| LSD | | Mental excitation, poor concentration, tremor indecisiveness, inability to act in a sustained or purposeful manner. Hallucinations. | Pyrexia. | Reassurance, restraint, prompt evacuation, diazepam. |

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# GLOSSARY

| | |
|---|---|
| 2,4,5-T | 2,4,5-trichlorophenoxyacetic acid |
| 2,4,-D | 2-4-dichlorophenoxyacetic acid |
| AC | hydrogen cyanide |
| ACh | acetylcholine |
| AChE | acetylcholinesterase |
| BA | bromoacetone |
| BAL | British anti lewisite |
| BZ | 3-quinuclidinyl benzilate (an incapacitating agent) |
| C | celsius |
| CA | bromobenzyl cyanide (irritant agent) |
| CARM | chemical agent resistant material |
| CG | phosgene |
| CK | cyanogen chloride |
| cl | chlorine |
| cm | centimeter |
| CN | chloracetophenone (irritant agent) |
| CNS | central nervous system |
| Co-A | coenzyme-A |
| CR | dibenzoxazepine |
| CS | orthochlorobenzylidine malononitrile |
| CSA | chlorosulphonic acid |
| CSR | combat stress reaction |
| Ct | concentration time |
| CW | chemical warfare |
| CX | phosgene oxime |
| DA | diphenylchlorarsine |
| DC | diphenylcyanarsine |
| DM | diphenylaminearsine chloride (adamsite) |
| DMSA | meso-dimercaptosuccinic acid |
| DMAP | 4-dimethylaminophenol-hydrochloride |
| DMPA | N-(2,3-dimercaptopropyl)-phthalamidic acid |
| DMPS | 2,3-dimercapto-1-propanesulfonic acid |
| DNA | deoxyribonucleic acid |
| DP | diphosgene |
| ECG | electrocardiogram |
| F | Fahrenheit |
| FM | titanium tetrachloride |
| GA | tabun |
| G-agent | a non-persistent nerve agent |
| GB | sarin |
| GD | soman |

| | |
|---|---|
| H | sulphur mustard |
| Hb | hemoglobin |
| HC | zinc chloride smoke mixture |
| HCl | hydrochloric acid |
| HCN | hydrogen cyanide |
| HD | distilled sulphur mustard |
| HI6 | type of oximide |
| HN | nitrogen mustard |
| HN1 | N-ethy1-2,2'di(chloroethyl)amine (type of nitrogen mustard) |
| HN2 | N methyl-2,2'di(chloroethyl)amine (type of nitrogen mustard) |
| HN3 | 2,2',2''tri(chloroethyl)amine (type of nitrogen mustard) |
| ICt | incapacitating concentration time |
| ID | incapacitating dose |
| IPE | individual protective equipment |
| IPPB | intermittent positive pressure breathing |
| IPPV | intermittent positive pressure ventilation |
| kg | kilogram |
| $kg^{-1}$ | per kilogram |
| L | lewisite |
| LCt | lethal concentration time |
| LD | lethal dose |
| LSD | lysergic acid diethylamide |
| $m^{-3}$ | cubic meter |
| metHb | methaemoglobin |
| ug | microgram |
| mg | milligram |
| Mg | magnesium |
| mm | millimeter |
| mmHg | millimeters of mercury |
| Na | sodium |
| NA | nerve agent |
| NATO | North Atlantic Treaty Organisation |
| NBC | nuclear, biological and chemical |
| OP | organophosphate |
| $P_2S$ | pralidoxime |
| PEEP | positive end-expiratory pressure |
| PFIB | perfluoroisobutylene |
| ppm | parts per million |
| PS | chloropicrin |
| RNA | ribonucleic acid |
| RP | red phosphorus |
| SH | (percentage) saturation of hemoglobin |
| STANAG | standardization agreement |
| TH | thermite |

| | |
|---|---|
| V-agent | a persistent nerve agent |
| VX | methylphosphonothioic acid |
| WBGT | wet bulb gradient temperature |
| WP | white phosphorus |

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