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	165 256 600 742	(-10°C) (0°C) (20°C) (25°C)	1,010	(20°C)
Volatility ($mg.m^{-3}$)	37,000 1,080,000	(-40°C) (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.