delivered, a very thorough and careful investigation will be required by the health authority. Such an investigation would combine clinical, epidemiological and laboratory investigations. The investigations would endeavour to determine whether an attack had been made, the causative agent or agents employed, what method of dissemination had been used, and the area and degree of contamination. This will require the organization of those presently engaged in the peacetime control of communicable disease since it will not be possible to allocate special groups for exclusive duty in connection with defence measures against biological warfare. The local laboratories in health departments, universities, hospitals and scientific institutions should be organized to function within the limits of their competence, and regional centres having specialized skills and equipment set up to enable complete identification to be carried out. The proper briefing of such personnel is an important part of the scheme.

The Department of National Health and Welfare, in its current planning for defence against biological warfare has, as one of its objectives, the training of key personnel with regard to general policy and the operational and technical responsibilities on a federal level. In turn, the provincial and local departments of health can arrange for the proper briefing and training of local personnel so that in the event of an attack a well-organized plan is in readiness. The old maxim, "Eternal vigilance is the price of safety", should be kept in mind.

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MEDICAL ASPECTS OF CHEMICAL WARFARE

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The modern history of the use of chemical warfare agents dates from the first World War when the Germans introduced chlorine gas in an attack in 1915. Before the termination of that conflict both groups of belligerents had employed a variety of chemical agents, the most effective of which was mustard gas. In the second World War both sides were prepared for the possibility of chemical attack and had stockpiled all the standard agents. Scientific teams sent into Germany by the Allies at the close of hostilities discovered that the Germans had developed a new and highly toxic series of agents which, because of their specific action on the nervous system, were named "nerve gases."† It is considered today that although any one of a number of toxic chemicals might be employed on a small scale in local sabotage attempts or in a harassing rôle, a generalized, full-scale chemical attack would see employment of *Nerve gases*, and possibly also of *Blistering gases* of the mustard gas type. The following discussion will, therefore, be confined to a consideration of the symptomatology and treatment of casualties resulting from exposure to agents of these two groups. However, teams of specialists familiar with the treatment of casualties resulting from all known types of chemical warfare agents will be available in the major centres across the country.

*Formerly Defence Research Board, now Industrial Health Laboratory, Ottawa.
†Not to be confused with HCN, CO and other gases which also have been referred to in earlier literature as "nerve gases".

The Nerve Gases

The nerve gases are a group of organic phosphorus compounds, liquid at room temperature and essentially colourless and odourless. They exhibit a high lipoid solubility and are also soluble in water in which they are hydrolyzed; the decomposition is particularly rapid in alkaline aqueous medium. These compounds are highly volatile and the vapours are extremely

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toxic when inhaled or when they come in contact with mucous surfaces. The liquid nerve gases in the form of fine droplets may be inhaled and coarser droplets are readily absorbed through the skin, and particularly so through burned or wounded areas. The most striking characteristic of this group of agents is the rapidity of action, a lethal dose killing in a few minutes.

Nerve gases possess the property of irreversibly inhibiting enzymes of the cholinesterase group and it is believed that the effects which they are capable of inducing can be attributed exclusively to this fundamental biochemical action. Cholinesterase activity is manifested normally at central synapses, at preganglionic endings of the sympathetic nervous system, at postganglionic junctions of the parasympathetic division and at myoneural junctions of skeletal muscle. The cholinesterases are responsible for the hydrolysis of acetylcholine, the chemical mediator of impulse transmission at these sites. In nerve gas poisoning, the inhibition of cholinesterases leads to an accumulation of acetylcholine and the development of acetylcholine intoxication. Thus, nerve gases have a physiological action similar to, but more prolonged than, physostigmine. Most of the classical symptoms of both muscarine and nicotine poisoning ensue, and the excessive accumulation of acetylcholine at myoneural junctions results in a curare-like flaccid paralysis in severe cases. Furthermore, repeated exposures tend to be cumulative unless sufficient time has elapsed to allow for at least partial recovery of cholinesterase activity.

Symptoms

The nerve gases act with extreme rapidity and the severity of the signs and symptoms which develop depends primarily upon the amount of the agent absorbed. Following a minimal exposure to trace concentrations of nerve gas, the effects are confined to local action on the eyes and upper respiratory tract. The subject may complain of difficulty in seeing in a dim light, the result of a pupillary constriction which could last from one to three days. A mild intermittent bronchoconstriction, as indicated by a recurrent sensation of tightness in the chest, will be experienced by some individuals for a few hours. There may also be a moderate watery nasal discharge.

With a somewhat larger exposure to the agent, the onset of intermittent bronchoconstriction is very rapid and the condition is likely to persist for several days. While the difficulty in breathing is harassing, the bronchoconstriction is not sufficient to produce hypoxæmia. A rhinorrhœa will also be seen in most cases. The meiosis will be severe and, in addition, spasm of the ciliary muscles of the eye will be marked. The resulting difficulty of accommodation is manifested by a moderate photophobia and pain when attempting to focus on near objects. The subject will probably complain of headache radiating frontally or to the occiput.

When the amount of nerve gas absorbed is approximately eight times the smallest dose capable of eliciting any detectable effects, the intensity of the symptoms may prove incapacitating in many cases. Bronchoconstriction becomes almost continuous and mild anoxæmia can be detected; the individual will be confused and panicky and will experience a sensation of suffocation.

Still larger exposures will be completely incapacitating and interference in respiration is further complicated by central and peripheral effects, a consequence of systemic absorption of the agent. Initially the bronchoconstriction is so severe that the respiratory tract may be nearly closed. Laryngeal spasm and bronchorrhœa add to the great difficulty in breathing, and the subject may be seized with panic in his struggle for air. In spite of vigorous muscular effort, little ventilation of the lungs will be accomplished and the resulting anoxæmia may cause collapse and unconsciousness. The efforts of the respiratory muscles then decline because of (a) fatigue, (b) the effects of the anoxia of both the muscles of respiration and inhibition of the respiratory centre and (c) from a developing paralysis which follows the accumulation of acetylcholine at the myoneural junctions. The airway will now relax slightly and, since the respiratory paralysis is not complete at the dosage under consideration, the subject will likely possess enough muscular function to survive the anoxia. In the early stages, while the subject is conscious, the heart rate will be somewhat accelerated and the blood pressure elevated. Subsequently, however, when systemic effects of the absorption of nerve gas become established, there is a definite bradycardia and the blood pressure falls. As a result of the anoxia and the direct action of nerve gas on the central nervous system, muscular tremors develop followed by fibrillary twitchings and occasional clonic-tonic convulsions. A variety

of muscarinic effects of the intoxication will also be manifest under these conditions of exposure; they include profuse salivation, intestinal hypermotility resulting in nausea, vomiting, cramps and diarrhœa. Urinary incontinence and premature labour may also be seen.

With lethal doses of the agent, the clinical picture is similar to that of a severe casualty but the sequence of events occurs more rapidly. The initial blocking of respiratory passages of the airway is essentially complete so that anoxia with collapse and unconsciousness develops quickly. Despite some relaxation which now supervenes, spontaneous respiration fails because of paralysis of the accessory muscles of respiration and central inhibition. Tonic-clonic convulsions will be followed by a generalized flaccid paralysis. The bradycardia is extreme, often resulting in a sudden and complete arrest of heart action; this may be the terminal event. Massive salivation and incontinence of urine and fæces are the rule.

The signs of poisoning which develop after contamination of the skin and exposed areas differ little from those seen following inhalation of nerve gas vapour. Localized muscular twitching may be seen at the site of contamination, and meiosis generally will not appear except in severely poisoned cases. However, if the eyes are contaminated with liquid nerve gas, there is an intense meiosis and ciliary spasm. It should be remembered that poisoning may occur by ingestion of contaminated food or water.

Behavioural manifestations of central effects of nerve gas may become apparent in subjects surviving the severe functional derangements. In milder cases, there may be giddiness, tension, anxiety, insomnia and excessive dreaming. With more severe exposure, withdrawal, depression, restlessness, tremor, emotional lability and irrational behaviour may be seen.

Treatment

The Civil Defence organization recognizes three levels at which treatment may be undertaken: self-help, first-aid, and hospital treatment; discussion of the treatment of nerve gas casualties will be considered from this point of view.

Self-Help

It is the responsibility of the individual to carry out personal decontamination and to fit and remove his respirator as indicated below. Since any high explosive attack may be combined with the use of chemical warfare agents, each person should fit his respirator as soon as he is aware that such an attack is in progress. It is especially important that the respirator be worn in the presence of any unidentified object emitting smoke or mist. If the individual is splashed with droplets or sees any gross liquid contamination on his person he should remove excess liquid by daubing and immediately carry out personal decontamination. All outer clothing except the respirator must be removed and discarded outdoors. The affected individual should proceed to a sheltered, uncontaminated area and remove the balance of his clothing, including the respirator. He should then wash thoroughly in running water but avoid rubbing the skin. The following materials should be applied to the contaminated areas in order of availability: bleach slurry or household equivalent such as chloride of lime solution, Javex, javel water, washing soda or baking soda. He should then sluice off with clear water, dry and dress in clean clothing. It must be emphasized that speed in carrying out the steps outlined above is most essential because of the rapidity of action of nerve gas.

First-Aid

While the procedures outlined above may be carried out by the individual if he is within a short distance of his home, he may be within range of a decontamination centre where not only the above steps but certain first-aid measures may be performed. Both non-medical and medical personnel will be available in first-aid stations to which the decontamination units are attached. The immediate administration of atropine intramuscularly will help relieve the central and muscarinic actions of nerve gas. The dosage employed will depend on the severity of the symptoms exhibited and will range from one injection of 2 mgm. to counteract paroxysmal bronchospasm up to three injections or more in the case of casualties exhibiting severe bronchospasm and cyanosis. A thorough atropinization of the patient is desired, and it must be remembered that the patient's tolerance for large doses of atropine is markedly elevated in nerve gas poisoning. The immediate use of atropine is only contra-indicated when the subject has undergone a profound and prolonged anoxia; under these circumstances, the administration of atropine

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may suddenly release the heart from vagal control and, in the presence of the severe anoxia, the attendant increase of the work of the cardiac muscle would almost certainly lead to ventricular fibrillation and death. Thus, in severely anoxic cases, artificial respiration should be undertaken until the lungs have been ventilated and the heart has made a partial recovery from its anoxia before atropine is administered. Holger-Nielson, or in applicable cases the Emerson method, is recommended because procedures such as the Schaefer prone pressure method, which depend upon the elastic recoil of the lungs, will be useless in patients suffering from flaccid paralysis of the respiratory musculature. A pulmotor and iron lung may be used if available.

Hospital Treatment

Additional treatment may be indicated in the case of patients exhibiting clonic and tonic convulsions and also in the case of those suffering intense pain and headache as a result of severe meiosis and ciliary muscle spasm.

In the case of the ocular effects, systemic atropinization may not be effective in producing relief and should be supplemented with local therapy. Mild cases will respond to the ophthalmic administration of homatropine; severer cases may require repeated instillations of atropine until good mydriasis is obtained. Convulsions may be controlled with thiopental, tridione or ether anæsthesia. If thiopental is used, overdosage must be avoided as it acts synergistically with nerve gas in depressing respiration. Tridione will depress cortical activity without depressing respiration if administered intravenously up to a maximum dosage of 5 grams. The use of these therapeutic measures is best undertaken in hospital under medical supervision. It must be remembered that convalescence in a severely poisoned patient may take several weeks.

Blister Gases

The blister gases or vesicants include the mustard gas of World War I and the newer nitrogen mustards. These substances are oily liquids ranging in colour from pale yellow to dark brown and they possess characteristic odours resembling garlic, horseradish, shoe polish or spoiling fish. The blister gases are very soluble in the usual fat solvents, but are only slightly soluble in water in which they are slowly decomposed. Blister gases are classified as persistent agents since it is possible to contaminate material and terrain for long periods with the liquids which slowly and continuously emit vapours.

Because of their high lipoid solubility, vesicants are readily absorbed by the skin and they exert a local cytotoxic action leading to the development of necrotizing lesions. The vapour rapidly attacks the eyes and the warm, moist skin of the perineum, axillæ, antecubital fossæ and neck. The inhalation of mustard gas vapour may result in damage to the respiratory tract. Damage to skin and eyes will be most severe after contamination with the vesicant in the form of liquid.

Symptoms

After contamination of the skin by either the liquid or vapour of blister gases, there is a latent period, ranging from 1 hour in the event of liquid contamination, to several days after mild vapour exposure. Erythema and œdema are followed by the development of vesicles due to liquefaction necrosis of the underlying epidermal layers. The typical mustard blister is large and domed, thin-walled, superficial, translucent, yellowish and surrounded by erythema. The blister tends to rupture but the fluid may be resorbed over the course of several days to a week. While there is no pain at the time of contamination with mustard, an itching or mild burning may accompany the development of erythema. If blisters do develop, the area may be painful.

The eyes are affected by even very low concentrations of mustard vapour. There is a latent period of 4 to 12 hours after a mild exposure, when the first symptoms of lachrymation and a sensation of grit in the eyes become evident. The conjunctivæ and lids become red and œdematous. If the exposure is more severe, the latent period is reduced and severe lesions of the eye may ensue. These include mild corneal involvement with superficial scarring and vascularization of the cornea. In very severe cases there will be necrosis of the conjunctivæ and the cornea will be deeply ulcerated with the formation of opacities. The inhalation of blister gas vapours causes damage primarily to the laryngeal and tracheobronchial mucosæ. The lesions develop slowly. The patient becomes hoarse and may become completely aphonic. A cough, particularly pronounced at night, is observed and in later stages becomes productive. Fever, dyspnœa and moist

râles are present and the incidence of bronchopneumonia is high. Moderate exposures produce hyperæmia of the respiratory mucous membrane with necrosis of the lung epithelium. In more severe cases there is pulmonary congestion, mild patchy œdema, moderate acute emphysema and focal atelectasis. Bacterial infection of the lungs complicates the situation and suppurative bronchitis and bronchopneumonia may follow.

Self-Help

The respirator provides complete protection for the eyes and respiratory tract and must be worn at all times when the presence of mustard vapour is suspected or reported. If the eyes become contaminated either with droplets of blister gas or their vapour immediate decontamination is essential. The eyes should be thoroughly irrigated immediately with copious quantities of water. Unless this is carried out within a few seconds of contamination the damage cannot be completely prevented although it may be somewhat mitigated. When available, 2% sodium bicarbonate which is a decontaminant followed by saturated boric acid solution or normal saline is indicated.

In the event of liquid contamination of the skin, the free liquid should be blotted off with absorbent cloth and the latter discarded in a safe place. The contaminated area should then be treated with a bleach cream or household equivalent and then sluiced off. Lacking any of these protective preparations, the skin would be washed with soap and water after first removing gross contamination with absorbent cloth.

First-Aid

Personnel in the first-aid stations are prepared to carry on with the subsequent treatment of mustard lesions. Mild conjunctivitis from blister gases may be treated by the instillation of tetracaine which will exert an analgesic action. Application of sterile petrolatum to the lid margins will prevent the eyes from adhering together. If the injuries are more severe so that œdema of the lids with photophobia and blepharospasm are present and the patient is in considerable pain, apply an eye dressing with systemic sedation with morphine and the instillation of atropine sulphate solution where indicated.

Erythema of the skin from mild contamination requires little care beyond the application of a soothing lotion. If blisters have developed, a sterile petrolatum gauze dressing should be applied, and in the case of vesicles which have burst, the lesions should be treated with the same sterile technique that is employed for thermal burns.

No treatment other than rest is required for the hoarseness and sore throat which follow mild respiratory tract injury. Cough may be relieved by codeine.

Hospital

Hospital care is directed to limiting the invalid period and preventing complications. In the event of corneal involvement, which may be detected by staining with fluorescein, the patient should be referred to an ophthalmologist. Should the skin lesions become infected, or entry into burns or wounds suspected, specific anti-bacterial therapy may be instituted. If clinical signs of severe respiratory tract injuries become manifest, treatment is best given in hospital where the prophylactic administration of penicillin or sulphadiazine is recommended. The accepted practices for the treatment of bronchopneumonia will be performed there.

Summary

1. Civil Defence authorities envisage the use of a variety of chemical warfare agents, but consider that nerve gases and blister gases of the mustard type constitute the greatest threat in any generalized chemical attack.

2. The properties of the latter two groups of agents have been described and an outline presented of the symptoms which develop in humans who have been contaminated either by the liquid or vapour forms of these agents.

3. The treatment of affected individuals has been considered at the three levels of self-aid, first-aid, and in hospital.

4. In the case of nerve gas casualties, personal decontamination has been stressed. The administration of atropine at first-aid stations constitutes the most important phase of the supportive therapy of such casualties.

5. Personal decontamination has also received stress as the first step in counteracting the effects of mustard gas exposure. The subsequent treatment of the lesions of the skin, eyes and respiratory tract follows established lines of procedure for the management of necrotizing lesions of these sites.