When death takes place quickly, the symptoms are chiefly those of an action upon the central nervous system, such as hyperexcitability, rapid respirations, general convulsions, opisthotonos, gradual failure of respiration and circulation, coma and death. When the animal lives longer after small intravenous injections, or after subcutaneous injection, there develops a characteristic symptomatology of salivation, marked diarrhea, and fall of temperature, with marked anorexia, emaciation and depression. With subcutaneous injection of .015 to .06 c.c., death usually takes place from the fourth to the tenth day.

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The pathology of dichlorethylsulphide (" mustard gas ") poisoning.

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The specific microscopic pathology of the local lesions of dichlorethylsulphide poisoning consists in degeneration and necrosis of the cells with which it comes in contact. The earliest microscopic change is pyknosis of the nucleus and cell body, followed by hydropic degeneration, liquefaction or coagulation necrosis. In the skin, hyperemia, with regeneration of the damaged cells, pigmentation, vesicle formation, desquamation of the dead epidermis or eschar formation mark varying stages of severity of the lesion. The degenerative changes extend deepest in the hair follicles and sweat glands. In mild burns without vesication the papillary layer of the corium may show a greater degree of necrosis than the epidermis itself, thus explaining the frequent occurrence of Nikolsky's sign. Large pigmented chromatophores may be the only living cells left in the papillary layer. In severe burns the necrosis may extend entirely through the corium. In the cornea, pyknosis and simple or coagulation necrosis of the corneal epithelium and interstitial substance, even to the endothelial layer, in extent varying with the degree of

exposure, constitute the microscopic features. On the conjunctivæ the epithelium shows pyknosis, hydropic degeneration, liquefaction necrosis, or there may be a deeper necrosis extending into the subconjunctival tissues. The conjunctival surface suffers to a less degree proportionately than the epidermis. On the mucous membranes the epithelium shows pyknosis, hydropic or mucoid degeneration, desquamation, liquefaction or coagulation necrosis. The necrosis may extend into the submucosa, but the depth of the lesions on the conjunctivæ and the mucous membranes of the respiratory tract is never so great from identical exposures, as it is in the skin. Following the necrosis there is marked hyperemia, and the development of an edema, more marked in the subcutaneous and subconjunctival tissues in animals, but less marked in man. Human skin, however, shows a much greater tendency to vesication. The blood vessels in the necrotic area are killed, the blood cells hemolyzed to some extent without thrombus formation or much extravasation, except minute hemorrhages by diapedesis. Following the lesion there is a demarcating inflammation, with slow regeneration, repair or cicatrization. The regeneration of the epidermis proceeds from the epithelium of the sweat and sebaceous glands. On the mucous membranes there results in the severe cases a localized eschar or ulcer, or a more diffuse diphtheritis. With secondary infection the inflammatory process becomes purulent or suppurative. The influence of secondary trauma and infection is well shown in the early development of deep areas of decubitus in the injured regions of the skin. Multiple furuncles may develop, or large cutaneous areas become gangrenous. In the eye purulent involvement of the anterior chamber, iris and ciliary body may occur, or even a suppurative panophthalmitis. In the respiratory tract secondary infection of the injured mucosa may lead to a purulent bronchopneumonia.

The internal organs in animals with mustard gas lesions of the skin, eyes, respiratory or gastrointestinal tract offer nothing of a specific pathologic nature. There is general congestion, marked splanchnic congestion, acute catarrh of the intestines and, in infected cases, some cloudy swelling of the kidneys.

In fatal cases the cause of death is to be found in shock,

secondary infection with toxemia, or local conditions as laryngitis, tracheitis, bronchitis and bronchopneumonia. It is also possible that the entrance into the body of shell fragments carrying liquid dichlorethylsulphide might cause a relatively speedy death through absorption.

At the site of subcutaneous injections there is found a local eschar with demarcating hemorrhage, edema and inflammatory infiltration; in the large veins into which injections have been made, no changes have been found except occasional thrombosis.

The general pathology of the injected cases presents a specific pathologic picture in the intestinal tract in the form of a severe mucoid, desquamative or necrotic enteritis, the intestinal epithelium showing the most marked hydropic or mucoid degeneration, even to liquefaction necrosis. Similar changes may be found in the epithelium of the bile ducts. In a certain number of cases the spleen, lymph nodes and hemal nodes show a marked hemosiderosis, the hemosiderin being contained in large hemophages. It is most probable that these evidences of increased hemolysis are explainable by the extravasations and blood destruction occurring at the site of the injection. No specific changes were observed in the blood-forming organs. In the other organs no pathologic changes but congestion have been found, with the rare exception of emboli or thrombi.

Mode of Action.—The cause of death in intravenous and subcutaneous injections would appear to be the direct action of minute quantities of free dichlorethylsulphide or some poisonous product resulting from its decomposition, upon the cells of the central nervous system. It has been assumed that the pathologic action of dichlorethylsulphide is due to its hydrolysis within the tissue cells. The products of this hydrolysis, hydrochloric acid and dihydroxyethylsulphide, when injected into the blood, do not produce the same effects. Dihydroxyethylsulphide and hydrochloric acid, when injected into the circulation in much larger doses than would result from the hydrolysis of the fatal doses of mustard gas, are harmless. The effect upon the cells of the central nervous system may, however, depend upon hydrolysis, with the liberation of hydrochloric acid (*Marshall*), in these cells of minute quantities of mustard gas in the circulation, or these

cells may be injured without such hydrolysis occurring. It is probable that the gastrointestinal catarrh resulting from the injections of dichlorethylsulphide is secondary to the nervous injury, rather than to an excretion of the poison or poisonous products through this tract, although this point remains unsettled. No positive tests for dichlorethylsulphide or dihydroxyethylsulphide have been obtained in the bile, intestinal contents, or urine. Incidentally, it has been shown that the platinic chloride-sodium iodide color test for dichlorethylsulphide is not applicable to the body fluids or extracts of various organs and tissues, as similar color changes are produced by some of these.

Treatment.—The principles of treatment to be applied to mustard gas injuries are primarily those that will remove any of the gas remaining, lessen necrosis, prevent infection and promote healing. Our experience leads us to recommend the use of Dakin's solution in irrigation or full baths for the skin lesions, and a 0.5 per cent. solution of dichloramine-T for the eye lesions, and also as a mouth wash. The fluid intake should be forced when the urine is concentrated. Pressure must be removed from all injured areas. Air-excluding and infection-including protections, such as oily dressings, paraffin sprays and coatings, zinc stearate, olive oil, vaseline, etc., should not be used, unless there is an active and persistent germicidal agent present as in the case of sodium stearate impregnated with chloramine-T, or the chlorcosane solution of dichloramine-T.

Sequelæ.—Among the most important sequelæ of mustard gassing is the apparent increased susceptibility to influenza, bronchitis, pneumonia and tuberculosis following lesions of the respiratory tract cicatricial contractions, pulmonary fibrosis. The respiratory infections may become chronic and death from these may take place months after the gassing. Persistent aphonia, due to local lesions or as one expression of a traumatic neurosis, is not a rare sequel. Chronic disturbances of vision are also in part the result of local changes and in part psychical. In the skin conditions of chronic eczema, itching and desquamative dermatitis, and pigmentation occur as sequelæ. Leucotrichia has also been observed. It is safe to predict that a development of squamous cell carcinoma in the extensive cicatrices, following mustard gas

lesions will take place fifteen to twenty-five years later as in the case of extensive thermal burns. Finally, the psychical disturbances following mustard gassing should not be minimized.

As to its use in warfare, mustard gas is a disabling rather than a killing agent. Under the actual conditions of the field the great majority of mustard gas casualties are likely to be of a nature tending to incapacitate the injured for service for a number of days or weeks, or even for months. Added to this, the insidious character of this invisible fire, painless and often unrecognized in its action, makes mustard gas a potent factor in undermining the morale of the troops exposed to it.

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The optimum H-ion concentration for the growth of B. typhosus, and the effect of changes in H-ion concentration on the generation time.

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1. *B. typhosus* has a range of growth from P_{H^+} 5.0 — P_{H^+} 8.6, with an optimum growth at P_{H^+} 6.8 — P_{H^+} 7.0.

2. Stock cultures isolated from stools, blood, and urine have a more decided optimum than recently isolated cultures. In such cultures, the plateau is much more pronounced and extends over a wider range than in stock cultures. The latter is suggestive of microbic adaptation to changes in H-ion concentration in body fluids, particularly urine and bile.

3. The growth curve is influenced by changes in H-ion concentration.