ultimately become both a public health and an economic disaster to the Islands. With only a limited supply of quinine or other anti-malarials, the further spread of *Anopheles* and malaria might well affect an entire campaign and even the final outcome of the war in the Pacific.

The problem of mosquito control, which is of the utmost importance, is, of course, beyond the scope of this series of studies on faunal distribution. It has, moreover, been dealt with at length by leading authorities such as Herms and Gray.

As part of this series, revised lists of mosquitoes and other vectors of disease in the Pacific and other islands are being completed for publication in the hope that the dissemination of such information may be of use in the present emergency.

MECHANISM OF ACTION OF ORDINARY WAR GASES

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CURRENT interest in war gases justifies pharmacological discussion of their mechanism of action. This may help to give a rational background for advice to civilians for reasonably effective protection against, and management of, possible war gas injury.

In general, the intensity of biological action of any chemical is determined by (1) the dosage, in terms of mass of chemical per mass of living material; (2) the ratio of the rate of absorption and distribution of the drug through the living tissue to its rate of excretion or destruction; (3) the physico-chemical properties of the drug, such as its differential solubility in different solvents, its polarity, its molecular configuration and energy organization, its dissociation characteristics and its optical properties, and (4) the peculiarities of the particular type of living tissue involved, such as its age, its metabolic and allergic states and its enzyme balance. These factors may be summarized in short-hand fashion in the following non-mathematical formula:

$$I = (f)\left[D\frac{rA}{rE}\right], \text{Ch}, \text{P}.$$

The concentration (C) of the chemical in the tissues at any given moment after administration is given by the product of D and the ratio of rA to rE.

Consistent appreciation of these factors may aid both in understanding the difference in action of various war gases and also the variation in intensity of effect of the same war gas in the same concentration on different individuals. An appropriate analogy to the latter situation is the difference in response of different people to the same intensity of sunlight or poison ivy.

For this discussion we may limit ourselves to a consideration of the ordinary war gases, such as the lung irritants, like phosgene or chloropicrin, or the vesicants, like mustard gas and lewisite. We may thus disregard such unusual possibilities as catalyzed cyanides or metallic carbonyls, and such gaseous associates of demolition bombs and incendiaries as carbon-monoxide, "nitrous fumes," "blast," hot oil smoke or phosphorus. However, the tissue aggressiveness of "nitrous fumes" suggests that these deserve attention in the same way as ordinary war gases.[1]

As indicated in Table 1, the ordinary war gases may be considered to be chemical relatives of such types of aliphatic hypnotic and inhalation anesthetic agents as alcohol, chloroform and ether. There is general knowledge of the locally irritating powers of these common compounds. Their war gas relatives may owe an increased irritative action to aggressive factors associated with altered halogenation and polarity. These war gases usually contain a rather labile halogen, like chlorine or bromine, which, with the hydrocarbon portion, may be considered to be relatively lipoproteophilic with respect to the rest of the molecule. On the other hand, the war gases also contain more potent polarizing radicles, like oxygen, sulfur, arsenic, a nitro group or oxime, which may be relatively hydrophilic or which may reduce the strength of the halogen bond. Differences in relative water-fat solubilities and in ease of hydrolysis may be important factors in the site of action or in the onset or duration of action, as exemplified in the contrast between lacrimators and vesicants.

TABLE 1

CHEMICAL RELATIONS BETWEEN COMMON IRRITANT DRUGS AND TYPICAL WAR GASES

Aliphatic irritant	Corresponding war gas
Alcohol $H{-}CH_2CH_2{-}OH$	Ethyl dichloroarsine $H{-}CH_2CH_2{-}AsCl_2$
Chloroform $Cl_3C{-}H$	Chloropicrin $Cl_3C{-}NO_2$
Ether $(H{-}CH_2CH_2)_2O$	Mustard gas $(Cl{-}CH_2CH_2)_2S$

One theory explaining the action of war gases is on

[1] Proceedings of a Board of the Chemical Warfare Service appointed for the purpose of investigating conditions incident to the disaster at the Cleveland Hospital Clinic, Cleveland, Ohio, on May 15, 1929. Edgewood Arsenal, Maryland, Lieutenant-Colonel Walter C. Baker, C.W.S., commanding. U. S. Government Printing Office, Washington, 1929, 104 pp.

the basis of splitting off halogen, with immediate irritant effect from the resulting halo-acid. This may occur promptly on the wet surfaces of eyes, and of mucous membranes of the nose, mouth, throat and lungs, with such agents as the lacrimators, phosgene and lewisite. On the other hand, as with mustard gas, the partition coefficient may favor absorption into the cells, after which the halogen may split off. The resulting halo-acid within the cell may alter enzyme systems, permeability of the surface membrane or protein equilibria, in such a way as to kill the cell. While such formation of acid may occur, it would have to exceed the buffering capacity of cells and tissues, and this might require relatively large amounts in order to pass the threshold. Neutralization by cellular buffers would be expected to produce the corresponding halide ion which would not markedly affect cellular function. At any rate, exhaustion of the buffer mechanism should reduce further hydrolysis. Direct experiment has shown that molecularly intact mustard gas may be isolated from deep skin layers many hours after absorption. Again, acid injury usually involves protein denaturation and precipitation, whereas war gas injury is characterized more by disturbances of cellular permeability, with swelling, protein hydrolysis and cellular disintegration.[2]

Another type of mechanism of action may operate. This relates to the relatively rigid molecular configuration of the war gas molecule as compared to the cell membrane. The latter is interpreted as a water-lipo-protein interface.[3] Portions of the war gas molecule seem to be relatively lipo-proteophilic, while other portions seem to be more hydrophilic. If enough war gas molecules are present at the cell surface, distortion of the interface may occur. This would result from orientation of the war gas molecule in accordance with the selective affinity of different parts of the molecule for water and lipo-protein, respectively. If this affinity and the interatomic angle forces in the war gas molecules are greater than the surface tension forces which maintain the normal cell surface, torsion may follow, with changes in permeability of the surface film, with resulting swelling and further distortion and strain of the surface membrane. This may comprise the initial inflammatory response to war gases, which may go on to cellular rupture, vascular breakdown, autolysis and necrosis, as so well described by Livingston and Walker.[2] Tight packing of cells, as may be accomplished by high ascorbic acid intake,[4] would tend to reduce the intensity of this reaction, as Livingston and Walker noted.[2]

Whichever mechanism occurs, the prolonged tissue response to war gases would subsequently include the slow removal of necrotic debris, to be followed by gradual repair. In the case of lung irritants, this sluggish process indicates the need for protracted oxygen administration as well as for prophylaxis against psychiatric pneumophobia.

In the biological effects of war gases, therefore, it seems that one or more of the following factors are concerned: (1) relative water, fat and protein solubility, both in transport and in relation to cell surface; (2) relative ease of hydrolysis, with relation to possible formation of halogen acid and the effects of the rest of the molecule; (3) distortion of cellular surfaces due to the molecular configuration of war gas molecules or to their secondary valence forces, and (4) effects of war gas molecules on pH, redox potential and colloid, interface and enzyme equilibria.

As in the case of sunburn or exposure to poison ivy, once the process of war gas injury is under way, one may hope for benefit only on the basis of symptomatic relief, of aiding the removal of necrotic tissue and of promoting repair. It would seem wise, therefore, to train civilians in "self-aid" in suspected contact with war gas, since first-aid or professional care is apt to be too late.

In order to reduce confusion of thought to a minimum and thus to help prevent panic in suspected attack with war gas, "self-aid" should be devised in as simple a manner as possible. Recommendations should be based on the least common denominator of effectiveness for whatever is likely to be used by a smart enemy. Since mixtures of war gases are certain to be employed, it seems unwise to worry about specific identification and specific management of potential injury, if such identification is based on such an indefinite procedure as smell.

Absorption of the ordinary war gases and their many obvious chemical relatives may be inhibited by neutralizing hydrolysis, oxidation or adsorption. For civilian use, these methods may be improvised from materials readily available in homes. Since the war gases in general are decomposed or poorly soluble in water, a wet cloth tied over the nose and mouth is a relatively effective barrier to the passage of such vapors, including oil smoke and "nitrous fumes," to the nose, throat and lungs.

The most readily available effective oxidants are the common kitchen bleach solutions, such as "Clorox." These are buffered 3 to 5 per cent. sodium hypochlorite solutions and are non-irritating for blotting the

[2] P. C. Livingston and H. M. Walker, *British Jour. Ophthal.*, 24: 76, 1940.

[3] J. F. Danielli and H. Davson, *Jour. Cell. Comp. Physiol.*, 5: 495, 1934; J. F. Danielli, *Proc. Roy. Soc.*, B, 121: 605, 1937; A. J. Clark, General Pharmacology, Hndb. Exper. Pharmakol., Erganzungswerk, 4: 14, 1937.

[4] S. B. Wohlbach, *Amer. Jour. Path.*, 9: 689, 1933; J. F. Rinehart, L. D. Greenberg, M. B. Olney and F. Choy, *Arch. Intern. Med.*, 61: 552, 1938.

skin, but should be diluted for application to mucous membranes, for washing the skin or for wetting cloths to breathe through. As is well known, such a solution reacts promptly with mustard gas, 2,2′-dichlorodiethyl sulfide (BP 217° C.), converting it quantitatively to the non-toxic crystalline 2,2′-dichlorodiethyl sulfoxide (MP 110° C.). The use of such sodium hypochlorite solutions for the prevention of mustard gas injury has been widely advertised in England.[5] Confirmation of their effectiveness against both mustard gas and lewisite has been obtained by Professor T. D. Stewart, of the University of California, Berkeley, on scores of human subjects, and by ourselves on humans and experimental animals. It is immaterial whether oxidation of mustard gas produces the sulfoxide or sulfone, or further decomposition, or what is produced on treating lewisite with hypochlorite. Direct experiment shows that such treatment of these compounds or their obvious chemical relatives results in non-toxic residues.

For alkaline hydrolysis, sodium bicarbonate solutions around 2 per cent. may be readily prepared in a black-out room by dissolving a teaspoonful of baking soda in a glass of water. Such a solution is helpful in washing out the eyes, nose and throat in suspected war gas irritation, or for wetting cloths to breathe through.

The most suitable and readily available detergent adsorbent is lather from ordinary soap and water or soap flakes or tincture of green soap. This is particularly useful, as are hypochlorite solutions, in preventing skin injury from suspected contact with blister gases. The data in Table 2 show the value of soap and hypochlorite in reducing skin injury (in a rather sensitive test object) from mustard gas application, in comparison with such a mustard gas solvent as kerosene.

The common blister gases are soluble in kerosene, gasoline, acetone, carbon tetrachloride and similar fat solvents. During World War I, it was naturally assumed that such solvents would be useful in removing liquid blister gas splashes from the skin. We have found no data to support this idea. However, current advice to civilians retains this recommendation. It is to be remembered that kerosene, gasoline and acetone may be absorbed through the skin, and that, like carbon tetrachloride, they are themselves skin irritants. They are also solvents of low viscosity and tend to spread easily. It is unlikely that they would be used carefully under the conditions of excitement existing in the crisis of suspected war gas contact. Our experiments show (Table 2) that even under controlled conditions they are much less satisfactory than lather or hypochlorite.[6]

Pharmacologists have the obligation of establishing and explaining the facts regarding the action of chemicals on living things. They have the privilege of applying such information to whatever practical problem may be appropriate. With respect to war gases, present pharmacological information suggests that the simplest and most effective advice for civilian protection against such gases might be: (1) obey air-raid rules, taking refuge during an alarm in an air-raid shelter or black-out room, with doors and windows shut and the windows screened or heavily curtained on the inside to prevent injury from flying glass, if bombing occurs; (2) if the shelter is broken open by bombing, and if war gases are suspected by fogs, peculiar odors, smarting or stinging in the eyes, nose or throat, or by coughing, sneezing or gasping, or by any other suspicions, tie a cloth soaked in baking-soda solution, or diluted kitchen bleach solution, over the nose and mouth to breathe through,

TABLE 2

AVERAGE CHARACTER OF SKIN RESPONSE IN RABBITS TO 0.05 CC 10 PER CENT. MUSTARD GAS (HS) IN ETHER, WITH TREATMENT CONSISTING OF THRICE BLOTTING AREA OF APPLICATION (ROUGH CIRCLE 10 MM IN DIAMETER) ONE MINUTE AFTER APPLYING HS WITH GAUZE SOAKED IN KEROSENE, SOAP AND WATER, OR 3 PER CENT. NaOCl (CLOROX), RESPECTIVELY*

Day	Untreated	Kerosene	Soap	3 Per Cent. NaOCl
1	Intense erythema and edema	Moderate erythema, slight edema	Diffuse erythema, slight edema	Diffuse erythema
2	Diffuse erythema and edema, central blanched area	Diffuse erythema and edema, central blanched area	Blanched area, 10 × 15 mm	Blanched area, 10 × 15 mm
5	Deep hemorrhagic necrotic area, 10 × 12 mm	Hemorrhagic necrotic area, 12 × 15 mm, with diffuse necrosis at edges	Thin scaley necrosis, 8 × 10 mm	Thin scaley necrosis, 8 × 10 mm
15	Heavy adherent scab, 10 × 12 mm	Broad adherent scab, 15 × 20 mm	Thin flakey scab, 8 × 10 mm	Thin flakey scab, 8 × 10 mm
22	Heavy adherent scab, 10 × 12 mm	Broad adherent scab, 15 × 20 mm	Light scar	Light scar

* No significant difference from untreated areas observed after application (as above) of either 3 per cent. H_2O_2, acetone or "bleach paste." Treatment with 5 per cent. NaOH in 30 per cent. glycerine seems to increase inflammatory reaction during first week, producing a deeper and slower healing necrotic area. Ten per cent. benzoyl peroxide in nona ethylene glycol seems to have little effect on HS reaction during first day or so, but seems to reduce necrotic reaction and time required for healing. However, 10 per cent. benzoyl peroxide in talc affords no protection when dusted on skin previous to exposure. Observations similar to the above have been obtained with lewisite; healing, however, is more rapid.

[5] Half-page advertisement *British Med. Jour.*, opposite page 445, April 4, 1942.

[6] D. F. Marsh and C. D. Leake, *Calif. West. Med.*, 57: 8, 1942. Acknowledged in spite of printer's many typographical errors!

keep it wet, shut one eye and squint through the other, and lie down with head in arms; (3) if eyes, nose or throat are irritated, wash them with a solution of a teaspoonful of baking soda in a glass of water; (4) if splashes of liquid are suspected on the skin or clothes, throw the outer clothing out the window, blot the skin splash promptly and repeatedly with a cloth wet with kitchen bleach solution, lather thoroughly and frequently with soap and rinse copiously with water. If subsequent injury results, the management is symptomatic at a casualty station or hospital.

These considerations were fully reviewed early in 1942 by the San Francisco and Alameda Committees on the Medical Aspects of War Gases. Special discussions along these lines have been widely published on the West Coast for civilian information.[7] Experience has shown that these suggestions for "self-aid" in handling suspected war gas exposure are appreciatively received by the public because they are simple and sensible. Recently these suggestions in substance have been included in "official" recommendations.[8]

OBITUARY

JACOB GOULD SCHURMAN
1854–1942

The death of Jacob Gould Schurman at the ripe age of eighty-eight years will remind present-day scientists of the versatility of their colleagues in an earlier generation. Dr. Schurman was trained as a philosopher in a day when to be such was to qualify both as a metaphysician and moralist and also as a mental scientist. When, in 1903, the first selection of distinguished men was made from those listed in the first edition of "American Men of Science," Dr. Schurman's name received a "star" among the fifty leading psychologists of that time. He had already served eleven years as president of Cornell University, but was still rated by his colleagues as an active scientist and member of the American Psychological Association.

Dr. Schurman's long career was marked with distinction as a scholar and teacher, as a university administrator and as a diplomat. As dean of the Susan Linn Sage School of Philosophy, which was established at Cornell by a trustee, Henry W. Sage, in memory of his wife, Dr. Schurman saw to it that one of the chairs in this school should be devoted to the new science of psychology. The first incumbents, Frank Angell, followed after one year by Edward Bradford Titchener, were brought to Cornell by President Schurman from the psychological laboratory of Wilhelm Wundt in Leipzig. Thus, from the beginning of the school, experimental research in psychology was fostered and developed by its dean and president.

Academic men of science also owe a debt of gratitude to this president of Cornell for his promotion of faculty participation in university administration. It was under Dr. Schurman's régime that faculty representatives were first elected to the board of trustees of Cornell University, and it was likewise with his support that the faculty of the College of Arts and Sciences was granted opportunity to elect its own dean. In all matters of university policy Dr. Schurman was well in advance of his time. If the elective deanship failed to perpetuate itself at Cornell, it was for lack of faculty enterprise and not for lack of support by the president.

The foundation and endowment of the Cornell Medical College owe much to Dr. Schurman, and the advancement of experimental science at Cornell was always of first importance to him. It was under his leadership that the university acquired three of its outstanding laboratories: Stimson Hall for the promotion of the medical sciences; Rockefeller Hall for the promotion of physics, and the well-planned and equipped Baker Laboratory of Chemistry.

After thirty-four years at Cornell, including twenty-eight as president of the university, Dr. Schurman retired to carry on a political and diplomatic career already initiated by his appointment in 1899 as president of the first United States Philippine Commission. Yet his interest in academic matters never lapsed. He was the leading spirit in raising an endowment of one-half million dollars for the University of Heidelberg—a university in which Dr. Schurman himself, like many other American scholars, had received training. He also lectured frequently before academic audiences, including appointments in 1931 and 1932 as honorary lecturer on international relations at the Institute of Technology in Pasadena, California.

Men of his breadth of view and depth of knowledge are rare to-day. To be a great educational leader and at the same time to be recognized as a participating member of several cognate fields of learning, is a distinction which can no longer be claimed by a specialist. Yet it is to men like Dr. Schurman that we owe the foundations and endowments which have made modern scientific progress possible, and our debt to them is greater than we are likely to remember.

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[7] Articles on war gases by J. F. Hildebrand (*The Commonwealth*, 1942; *San Francisco Chronicle*, Feb. 15, 1942), M. Silverman, *San Francisco Chronicle*, March 15, 22, 29, Apr. 5, 1942) and W. F. Mould, leading West Coast newspapers through June and July, 1942.

[8] *Jour. Am. Med. Assn.*, 119: 889, July 11, 1942.