DIMITRI IVANOWITCH MENDELEEFF was born in Tobolsk, Siberia, February 7, 1834.

He earned his master’s degree at the University of St. Petersburg (now Leningrad) in 1856 and his Doctor of Science degree some five years later, at which time he was appointed Professor of Chemistry at the Technological Institute. In 1866 he became Professor at the University. He resigned in 1890, and in 1893 was Director of the Bureau of Weights and Measures.

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The Biological Actions and Therapeutic Applications of the B-Chloroethyl Amines and Sulfides

Alfred Gilman, Major, and Frederick S. Philips, 1st Lieutenant, SnC, AUS
Pharmacology Section, Medical Division, CWS, Edgewood Arsenal, Maryland

At the conclusion of World War I the theory was generally accepted that mustard gas exerted its vesicant action by releasing hydrochloric acid intracellularly. A few isolated reports appeared describing remote systemic effects of mustard gas on hematopoietic tissues (1–3), the gastrointestinal tract (3–5), and electrolyte and fluid balance (3). Although in the interim between wars the adverse effects of mustard gas on leuкоpoietic tissues (6–8) and on the growth of experimental tumors (9) received some attention, biological research on chemical warfare agents remained relatively quiescent. With the advent of World War II research on war gases was resumed, and the newer knowledge and technics of a quarter of a century of scientific progress utilized. New compounds were proposed as potential offensive agents. Mustard, bis(β-chloroethyl) sulfide, shared interest with a series of nitrogenous analogues, bis- and tris(β-chloroethyl)amines. It was appreciated early that the sulfur and nitrogen mustards were not only contact vesicants but, following absorption, could exert cytotoxic actions on a variety of tissues. Furthermore, cellular susceptibility to these compounds appeared to be related in a general way to the degree of proliferative activity.

With the conviction that only with an understanding of the basic mechanisms of cellular action could significant advances be made in the treatment of vesicant war-gas casualties, the study of the actions of the sulfur and nitrogen mustards on fundamental cell processes was pursued. These studies have revealed a type of action on cells which can be likened to that of no other chemical agent but which resembles in many ways that of X-rays. Cautious preliminary trials have also been made of the possible value of the nitrogen mustards in the treatment of neoplasms, in particular those of lymphoid tissue.

The fact that agents classified as “confidential” were involved in the above studies has heretofore precluded the possibility of presenting the results in the open literature. This report reviews briefly the contributions which have focused attention on the cellular actions of the mustard compounds and gives a general description of their systemic effects as well as a preliminary statement of their possible clinical applications. Because of space limitations important contributions of many investigators will have to go unmentioned.

Chemical Transformations and Reactions of the Nitrogen and Sulfur Mustards

The nitrogen and sulfur mustards owe their physiological activity to a basic chemical reaction which they share in common, namely, intramolecular cyclization in a polar solvent to form a cycliconium cation with liberation of Cl−. The reaction may be depicted as follows, Z representing the sulfur or nitrogen atom:

\[ R-Z-CH_2CH_2Cl \rightarrow R-Z-CH_2CH_2+ + Cl^- \]

Theonium cation—ethylenimonium in the case of the β-chloroethyl amines, ethylensulfonium in the case of β-chloroethyl sulfide—reacts readily with anions and various uncharged nucleophilic molecules. It is the great reactivity of the cycliconium cation which imparts to this group of vesicants their varied actions.

The property of halogenated alkylamines to form cycliconium cations was known before the war (10–12). With the introduction of bis- and tris(β-chloro-
rogen mustards have been observed for a period of 28 months, the evaluation of the clinical status of this group of compounds will require many more years of careful study. At present there is no basis for assuming that the therapeutic efficacy of the nitrogen mustards is any greater than that of X-ray.

It is possible that the potential value of the nitrogen mustards in the treatment of neoplastic diseases will be fully realized only when the opportunity to explore the relationship between chemical constitution and pharmacodynamic action has been exhausted. At present only two of the nitrogen mustards have been investigated clinically, namely, tris(β-chloroethyl)amine and methyl-bis(β-chloroethyl)amine. These have been the product of a screening program designed for the evaluation of toxic chemical warfare agents rather than of compounds of therapeutic interest. Literally hundreds of congeners remain to be synthesized and evaluated. Thus, a series of compounds which can reproduce in many ways the cellular effects of X-rays is available for chemical and biological investigation. It may be hoped that the previous successes which have characterized the evolution of chemotherapeutic agents by chemical alteration of a parent compound may be duplicated in the case of the β-chloroethyl amines. The result would be a compound having a sufficiently specific toxic action for certain types of proliferative cells to possess therapeutic value.

(See p. 436 for list of references.)

Science and Our Future

E. U. Condon, Director

National Bureau of Standards, Washington, D. C.

The war’s destruction far exceeds that of any catastrophe yet known. The war ended with the application of a new weapon that is a thousand times more frightful than the weapons which produced most of the war’s frightfulness. And already we have responsible statements from scientists who effected this development that bombs a thousand times more powerful than those already used are capable of being made in the near future. There are men living who know how to make a single bomb whose destructiveness is equal to a million ten-ton blockbusters. One such bomb, dropped on Washington or any other major city, may be expected to wipe out its population, to destroy its buildings utterly, and to render the site uninhabitable due to poisoning by radioactive materials.

In the face of this situation, people react essentially in one of two ways. One group says: “It’s just another weapon. Mankind learned to adapt to the long bow, and the cross bow, and the B-29. We have always had wars.” An extreme expression of this kind is found in a speech delivered in Philadelphia last December by Prof. Leslie A. White, of the Anthropology Department of the University of Michigan, who said: “As for the extermination of the human race as a consequence of hurling atomic thunderbolts, this too may be admitted as a possibility, and all we can say is that if it is to come, it will come.” This is indeed a rather coldly hopeless, fatalistic expression. Prof. White further says: “Extravagant expressions of horror will not alter the course of events.”

There is a certain rhetorical trick here in that, in our language, “extravagant” connotes exaggeratedly inaccurate, and thus emotionally detracts from the serious warnings which responsible physicists are trying to give us. I would agree that expressions of horror alone will not alter the course of events. But I insist that if we look at what civilization has suffered in World War II, even before the atom bomb, and couple it with the picture of a war with plentiful use of the old-fashioned “one-hoss shay” atom bombs, and further with the picture of a war with both sides equipped with the really potent 1950 models—then no expression of horror of which our hearts are capable can be exaggerated or extravagant. We need not, and should not, fatalistically await death, reading papers to an academic society meeting in a museum in Philadelphia.

The second kind of people react differently. We say: “This is the end.” Mankind has brought down suffering and death on its head, spiritual values have been destroyed, hatreds have been nourished and developed into great social cancers by war, war fears, and war suspicions and divisions among men.

From an address delivered 5 March 1946 in Washington, D. C., at the conclusion of the Fifth Annual Science Talent Search (Science, 1946, 103, 336). The guests for the evening were the 40 winners from the Science Clubs of America who received the Westinghouse Scholarships and scientists from the Washington area. The event was arranged by Science Service, whose director, Watson Davis, served as toastmaster.
tary procedure for the conduct of scientific research, neither would I want our safety to depend on the outcome of a battle in which the scientific method of free discussion, independent thinking, and mutual criticism was followed by all the captains and lieutenants on the battlefield. Military operations and scientific research are two quite different kinds of human activity, and neither should be subordinated to the other.

Of course, my reason for stressing this point is that right now we are confronted in America with a situation in which scientists are being held very strictly under military domination, to the severe detriment of our scientific development and the development of wholesome international relations.

What is going on? Prominent scientists are denied the privilege of traveling abroad. Physicists are not allowed to discuss certain areas of their science with each other, even as between individuals working on closely related phases of the same subject. They can communicate only through official channels involving censorship of their communications by army officers without knowledge and so without competence. Information essential to understanding is being denied to students in our universities, so that, if this situation were to continue, the young students we honor here tonight will get from their professors only a watered-down army-approved version of the laws of nature.

In this connection one is reminded of the eighteenth verse of the eighth chapter of Ecclesiastes, where we read: "Wisdom is better than weapons of war; but one sinner destroyeth much good."

Some seem to think that the laws of nature are ours exclusively, and that we can keep others from learning by locking up what we have learned in the laboratory and not telling it to our allies. Later they will learn what we know—and more which, because of our unfriendly behavior, we cannot expect them to tell us. In the course of time, because of such provocations, we are allies no more—we start as friends and end as snarling, suspicious neighbors.

It is sinister, indeed, how one evil step leads to another. Having created an air of suspicion and mistrust, there will be persons among us who think other nations can know nothing except what is learned by espionage. So, when other countries make atom bombs, perhaps much better than those we have, these persons will cry "Treason!" at our scientists, for they will find it inconceivable that another country could make a bomb in any other way except by aid from Americans.

Let us cast this isolationist, chauvinist poison from our minds before we corrode our hearts and arouse suspicions of our motives in the minds of the decent peoples of the world. Let us cooperate wholeheartedly with the other nations of the world to agree to use atomic energy only for peaceful purposes and to set up an inspection system to enforce such agreement. The United Nations Assembly has voted unanimously to establish an Atomic Energy Commission to draw up such a plan. In the face of the frightfulness of atomic warfare, it is inconceivable to me that any nation will refuse to participate in a program of international cooperation and inspection. Yet, much public discussion, and even more private conversation, is based upon the assumption of such a refusal. We must push forward with all possible speed in order to find out where we stand in the world today so that it is no longer possible for different groups and different nations to base their thinking and their planning upon different hypotheses. I am confident that if we do this, the outcome will be world friendship and cooperation and not atomic war and the destruction of civilization.

Scanning Science—

Nature states that the Toronto Local Committee are assiduously engaged in preliminary work for the meeting of the British Association for the Advancement of Science in 1897. Meetings of the executive committee are held every fortnight. Besides the executive committee, a number of sub-committees are at work, including those on finance, conveyances, publication and printing, rooms for offices, meetings of the association and committees, hotels and lodgings, press, hospitality, reception and for securing cooperation of other institutes, associations and corporations, postal, telegraph and telephone facilities.

—27 March 1896
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Yes, survival is at stake—not merely personal and individual survival but the survival of our nation, of other nations, and of civilization itself.

The facts assembled in this book provide a vision of what atomic energy can do in a world which uses it for constructive and peaceful purposes. But these same facts point to the inescapable conclusion that while "the nations of the world can have atomic energy and much more, they cannot have it in a world where war may come."

MORRIS C. LEIKIND
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As the late Sir Henry Lyons has stated in his Introduction, this is not the complete history of the Royal Society: "This account of the way in which the Society carried on its business at different periods will provide the groundwork for a fuller discussion of its influence on the advancement of science; it also records the conditions under which the more eminent of its Fellows carried out their researches and discoveries. The complete history of the Society has not yet been undertaken, and it may well require the united efforts of several workers to deal with so wide a field of activity."

Nevertheless, this book contains a surprising amount of information about the origin of the Society and the 280 years of science in England since its establishment. Many interesting sidelights of scientific history are interspersed between the discussions of the financial problems and administrative organization of the Society which are its principal concern. It is amusing to learn, for example, that the Royal Society was accused of taking sides with the American colonists during the Revolution because it advocated the use of Benjamin Franklin's pointed lightning rods, and that the King himself tried to persuade the Society to rescind its resolution.

Although the original founders of the Royal Society were mostly scientists who met for the purpose of critically examining new discoveries and theories, the scientific purpose of the Society was often lost sight of, and scientists were actually in the minority until 1860. Even Samuel Pepys was president (a good one, to be sure) during the two years when Newton's Principia was being published. Incidentally, it was Sir Isaac Newton, first man of science to be knighted, who was responsible for the fact that the Royal Society now meets on Thursdays, since he was occupied at the mint on Wednesdays (the Society's original meeting day) during the first years of his presidency. Despite the presidencies of such well-known men of science as Newton and Sir Joseph Banks, the Royal Society was more of a cultural than a scientific institution until the middle of the Nineteenth Century. Since 1860, however, the Society has become the leader of scientific thought in Great Britain and a unique institution in the world of science. Like all venerable institutions, it is sometimes slow to