Penicillin Aerosol: Contribution of the Chemical Warfare Service to Medicine

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IN A SUMMARY OF CERTAIN CONTRIBUTIONS of the Chemical Warfare Service to medicine, which appeared in *Science* (*4*), the role played by the Chemical Warfare Service in developing penicillin aerosol therapy of the lungs is not mentioned. For the sake of historical interest which penicillin aerosol therapy now merits, it seems desirable at this time to mention certain facts connected with this subject. It is not generally known that the investigations leading to the use of penicillin aerosols in the therapy of lung infections were initiated, organized, and developed in both preclinical and clinical phases by the Technical Division, Office of the Chief, Chemical Warfare Service. Since this type of therapy is perhaps the one medical procedure used most widely in everyday peacetime medicine as a result of the impetus given the subject by the Chemical Warfare Service, the historical aspects warrant recording in some detail.

Preliminary Phase

In the fall of 1942 it seemed desirable to me to take advantage of the experiences of a member of my staff, Lt. Col. H. A. Abramson (then Major), in the field of aerosol stabilization and therapy (*1*). He was instructed to carry forward his early work in the field and apply his experiences with low-pressure generation of aerosols to certain phases of the general problem, only two of which concern us in this presentation. These two phases were: (1) development of suitable nebulizers for use in the field for the aerosol therapy of chemical warfare casualties of the lungs, with particular reference to relief of bronchial obstruction; and (2) development of methods for the treatment of secondary infections of the lungs following exposure to chemical warfare agents of all types.

At a meeting held in Washington in August 1942, in the Office of the Chief, Chemical Warfare Service, this program was discussed in detail and was shortly implemented (September 1942) by a direct contract from the Technical Division to the Long Island Biological Association, Cold Spring Harbor, New York. Support was given to this project by a grant from the Josiah Macy, Jr. Foundation to cover the more medical aspects of the investigation. The work of the Cold Spring Harbor group progressed favorably. On 10 March 1943, a conference was called by the Technical Division at Edgewood Arsenal, Maryland, on "Aerosol Therapy of Gas Casualties of the Respiratory Tract." At this meeting the feasibility of aerosol therapy of the lungs by antibiotics was discussed again, and tentative plans were drawn up to proceed with the experimental phase of penicillin aerosol therapy of the lungs. As soon as technical problems, such as choice of nebulizers and particle-size distribution during nebulization therapy, appeared to be solved, Lt. Col. Abramson directed the Cold Spring Harbor investigators to begin the study of penicillin aerosols in animal and man, with a view to utilizing this technique in the treatment of lung infections of all types.

Thus, Bryson (*5*) gives credit to Abramson for the initiation of the penicillin aerosol therapy program. He states, in his report of the work done under contract with the Technical Division:

> Perhaps the most interesting aspect of the work has been the development of penicillin mists for inhalation. We know that many serious lung infections are caused by bacteria susceptible to the action of penicillin. It appeared to our colleague, Major H. A. Abramson (M.C.), that the introduction of penicillin directly to the site of infection might give certain advantages over conventional methods of administering the drug. Clinical studies at the College of Physicians & Surgeons in New York City and St. John's Hospital in Brooklyn have confirmed the value of penicillin aerosols in the treatment of some kinds of chronic and acute pulmonary disease.

Intermediate Phase

Bryson, Sansome, and Laskin, of the Cold Spring Harbor Laboratory, reported their results on penicillin aerosol to the Technical Division early in 1944. It appeared that their results were of the greatest importance. Their findings were as follows:

(1) Simple commercial nebulizers of the DeVilbiss No. 40 type could be used to nebulize penicillin solutions, even in concentrations as high as 200,000 units/cc.

(2) Penicillin was not reduced in potency by the air flow through the nebulizer. Oxygen, similarly, had no deleterious effect.

(3) Penicillin aerosols penetrated into the lungs.

(4) Penicillin from the aerosols diffused into the blood stream and could be recovered in the urine.

(5) Appreciable amounts of penicillin were absorbed through the lungs.

[1] The writer was chief of the Research Branch, Technical Division, OCCWS, at the time this project was initiated.

(6) Concentrations of penicillin much higher than those required for therapeutic efficacy could be safely inhaled by man.

These investigators were instructed by the Chief, Technical Division, to publish their findings at once because of the general importance of their data (*6*). The Chief of the Technical Division, Brig. Gen. Kabrich, thereupon instructed Lt. Col. Abramson to organize and preside at a meeting of interested agencies and to have the Cold Spring Harbor group report their findings to these agencies so that proper coordination of interested research organizations could be made. This meeting, on "Generation of Aerosols for Therapy of the Respiratory Tract," was held on 22 May 1944 at Edgewood Arsenal, with representatives from the following organizations attending: Professional Service, Surgeon General's Office; Preventive Medicine, Surgeon General's Office; Bureau of Medicine and Surgery, U. S. Navy; Camp Detrick, Maryland; Office of the Air Surgeon; Chemical Warfare Laboratory, Ottawa, Canada; Medical Director, Macy Foundation; Biological Laboratory, Cold Spring Harbor; Aerosol Laboratory, Columbia University (Division 10, NDRC); Medical Research Laboratory, Edgewood Arsenal; and Medical Division, Office of the Chief, Chemical Warfare Service. At this meeting the chairman, Lt. Col. Abramson, pointed out that the Technical Division had, through its own researches and through the Biological Laboratory, found that two types of aerosol therapy of the respiratory tract were possible: (1) where low-quantity effects were desirable, and (2) where high-quantity effects were more important. For the first part, it was pointed out that suitable commercial nebulizers had been studied and that further studies of nebulizers were in progress. For the second type, the ordinary atomizer, with a proper tip, could be used directly to the trachea and bronchi. After discussing the various items connected with aerosol therapy of the lungs, the following action was taken: "Study of penicillin aerosols will be undertaken at Columbia University in the Department of Medicine by Dr. Barach, with the support of the Macy Foundation, in cooperation with the Technical Division and the Cold Spring Harbor group."

Clinical Phase

Dr. Barach and his co-workers at Presbyterian Hospital, New York City, collaborated with the Technical Division and with the Biological Laboratory. Their paper (*3*), which was closely followed by that of Olsen (*7*) and others, showed (1) that experimental peritonitis in animals with penicillin-susceptible organisms could be prevented or cured by penicillin aerosol, and (2) that penicillin aerosol could be applied to many clinical entities without damage to the patients.

In addition, evidence was presented which indicated that penicillin-susceptible organisms would disappear from the sputum of certain types of nontuberculous lung infections.

Other papers which appeared in 1945 have shown that penicillin aerosol therapy, as initiated and organized by the Technical Division, its coordinating agencies, and collaborating groups, has become a standard and useful feature in medicine. While there is some controversy as far as technique and dosage are concerned, the outstanding fact is that it is now widely applied, especially in hospital practice to control suppurative diseases of the lungs of all types. It is also being applied in addition to other antibiotics, such as streptomycin (*8*) and hydrogen peroxide (*2*), in an attempt to improve the pathological processes due to the primary and secondary infections of tuberculosis.

References

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2. Abramson, H. A. *Ann. Allergy,* 1946, **4**, 199.
3. Barach, A. L., Silberstein, F. H., Oppenheimer, E. T., Hunter, T., and Soroka, M. *Ann. int. Med.,* 1945, **22**, 482.
4. Bodansky, O. *Science,* 1945, **102**, 517.
5. Bryson, V. *Ann. Rep., Biol. Lab., Cold Spr. Harb.,* 1944.
6. Bryson, V., Sansome, E., and Laskin, S. *Science,* 1944, **100**, 33.
7. Olsen, A. M. *Proc. staff Meet., Mayo Clin.,* 1945, **20**, 184.
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Scanning Science—

Invitations have been sent for the opening of the new halls of ethnology and vertebrate paleontology of the American Museum of Natural History, New York. The reception will be held from two to three o'clock on November 30.

At midnight on November 15th the electric power generated at Niagara Falls was transmitted to Buffalo where it will be used to operate the trolley cars of the street railway.

—27 November 1896