

This problem might not be deemed so important if employment by the Federal Government were a minor factor in the whole scientific employment pattern. It is already a major factor in certain fields, and its importance may extend to other fields as time goes on. Furthermore, the problem of meaningful B.S. degrees extends far beyond the Civil Service. The weakness of this degree as a criterion has frequently been embarrassing throughout the war period. It was a big factor in the Selective Service situation. Had professional B.S. curricula existed, it is possible that the Selective Service System would have been able to use them as criteria of minimum preparation for use in screening out those who should be given special consideration as scientists, thus obviating some of the cases of flagrant misassignments of scientific personnel. In assigning Federal fellowships or Federal monies for students in the early part of the war, the lack of such a recognized curriculum, or at least of some recognized standard of minimum preparation in the fields of interest, was felt.

Discussions on the proper type of organization for the mobilization of scientific personnel in wartime have been numerous during the war and since V-J Day, many of these have taken place among military personnel. Perhaps some type of organization similar to the Medical Corps will arise in time. If so, scientists will need to be commissioned from civil life

on the basis of accomplishment. Again, a meaningful B.S. degree is necessary.

The present National Research Foundation Bill, sponsored by Senators Magnuson, Kilgore, *et al.*, (S. 1850), calls for the establishment of fellowships for advanced study. The same problem of threshold preparation for applicants will arise, and the existence of a meaningful B.S. degree would again be useful. The dominant role of American scientific education in the world today will mean that foreign students will come here more and more and that our students will go abroad. The American degree will then become to a greater and greater extent world currency in this field. It would be better in this connection, too, if a more uniform measure of accomplishment were represented by our B.S. degree.

These are indications that the Federal Government is being called on more and more frequently to deal with persons on the basis of their academic accomplishments. The law and regulations based on the law require the existence of definable terms. The B.S. degree at the present time is frankly not a sharply definable term. The ACSP is not presuming to suggest any particular action, but does feel a responsibility to present to the scientific population a situation which seems worth describing and which does seem to merit most thoughtful consideration.

Canadian Researches on BAL (British Anti-Lewisite)

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ONE OF THE OUTSTANDING ACHIEVEMENTS in the field of chemical warfare research in World War II was the discovery by Peters, Stocken, and Thompson of the antidotal action of 2,3-dimercapto-propanol (BAL, British anti-lewisite) to lewisite and other arsenical compounds. Two reviews of work on BAL have been published recently. The first of these was by Peters, Stocken, and Thompson (3), and the second, which dealt particularly with researches on BAL in the United States, was by Waters and Stock (11). The purpose of the present article is to review briefly some researches on BAL conducted on behalf of the Directorate of Chemical Warfare, Department of National Defence, Ottawa.

Work on BAL was started in Canada late in 1941. The first investigation undertaken was a comparison of the antidotal activity and toxicity of BAL with those of a series of related compounds. In the course of this work the following thiols were synthesized

(4, 12): 1,2-dimercapto-ethane, 1,2-dimercapto-propane, 1,3-dimercapto-propane, 1,2,3-trimercapto-propane, 1,2-dimercapto-n-butane, 1,3-dimercapto-2-propanol, 2,2'-dimercapto-diethyl ether, 3,3'-dimercapto-dipropyl ether, and 2,2'-dimercapto-diisopropyl ether. These compounds, together with 1- and 2-mercapto-propane and 2-mercapto-ethanol, were tested for antidotal activity to lewisite and toxicity when applied to the skin of the rat (6, 12). None of the compounds tested was found to be superior to BAL as an antidote to lewisite. Although none of the monothiols tested showed antidotal activity under the above conditions, all the dithiols and the trithiol studied gave evidence of some antidotal activity. Only in the case of 1,3-dimercapto-2-propanol did this activity approach that of BAL, however, and this compound proved to be much more toxic than BAL.

Rats usually die within 24 hours after the application of lethal amounts of lewisite ($2 \times LD_{50}$) to the skin. Almost invariably, however, the lives of the

animals are saved if BAL is applied to the dosed area of skin not later than two hours after dosing with lewisite. Even when treatment with BAL is delayed for a longer period, the animals sometimes survive (6). Protection against the systemic effects of lewisite in rats also occurs when BAL is applied to a skin site other than that contaminated with lewisite (15), or when BAL in propylene glycol solution is administered by intramuscular injection (13). Protective action is also obtained when BAL is applied to the skin two hours, or sometimes even longer, before application of lewisite to another area of skin (15)—a finding which can be explained by the low rate of percutaneous absorption of BAL in the rat (10, 15).

When applied to the skin of the rat, BAL exerts an antidotal action to sodium arsenite ($2 \times LD_{50}$) administered by intraperitoneal injection (2). When rats are dosed intraperitoneally with lethal amounts of cadmium chloride, they sometimes survive if treated percutaneously with BAL. There is evidence, however, that under some conditions deleterious effects follow the administration of BAL to rats poisoned with cadmium (1).

The finding of the Oxford workers (3) that there is an increased urinary excretion of arsenic following the administration of BAL to rats dosed with lewisite was confirmed and extended. Whether BAL is applied to the skin site contaminated with lewisite, or to a separate site (14), or given by intramuscular injection (13), the arsenic content of the urine excreted during the 24 hours after dosing with lewisite ($0.5 \times LD_{50}$) is markedly increased when the BAL is given immediately, one or six hours after the lewisite. When the administration of the BAL is delayed for 24 or 48 hours the effect on the urinary excretion of arsenic in the succeeding 24 hours is much less marked. The fecal excretion of arsenic is not influenced to a significant extent by BAL treatment.

Although BAL exerts an antidotal action in sodium arsenite poisoning, its influence on arsenic excretion under these conditions is slight (2). On the other hand, whereas rats given intraperitoneal injections of cadmium chloride ($0.5 \times LD_{50}$) show almost no urinary excretion of cadmium, they excrete considerable amounts of cadmium in the urine when also treated with BAL. This tends to prevent the accumulation of cadmium in the liver which occurs when BAL is not administered (1).

Radioactive BAL, i.e. 2,3-dimercapto-propanol with radioactive sulfur (S^{35}) incorporated in the molecule, was synthesized (7) and used in studies of the absorption and metabolism of BAL (5, 8, 9). The radioactive compound was obtained by allowing 2,3-dibromo-propanol to react in methanol with sodium

hydrosulfide which had been prepared from hydrogen sulfide containing H_2S^{35} .

BAL penetrates skin rather slowly. In experiments with radioactive BAL the average rate of percutaneous absorption of BAL in the rat over a period of six hours was found to be 0.38 mg./cm.² skin/hour (8). This value is of the same order as that obtained in preliminary experiments on the rate of absorption of BAL from human skin (5). When radioactive BAL dissolved in propylene glycol is injected intramuscularly into rats, it passes rapidly from the site of dosing, for almost no S^{35} is present in the dosed muscle six hours after injection (9).

In experiments in which radioactive BAL is administered to rats percutaneously (8) or intramuscularly (9), S^{35} is distributed throughout the organism and, apart from somewhat higher concentrations in the intestine and its contents and in the kidney, it does not appear to accumulate preferentially in any of the main organs. The most striking feature of such experiments is the rapidity with which S^{35} is excreted in the urine. For example, after an intramuscular injection of a solution of 20 mg. of radioactive BAL in propylene glycol, the amounts of S^{35} present in the urine at 6, 12, and 24 hours after injection corresponded to 45.5, 71.0, and 81.3 per cent, respectively, of the radioactive BAL administered (9). A similar rate of excretion of S^{35} is observed when radioactive BAL is administered to the rat by application to the skin (8). Studies of the thiol content of the urine and other observations suggest that little of the S^{35} in the urine of rats dosed with radioactive BAL is in the form of unchanged BAL (5).

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References¹

1. BERENBOM, M. Unreported observations.
2. MANSON, L. A., ZBARSKY, S. H., and YOUNG, L. Report C.P. 85, 1945.
3. PETERS, R. A., STOCKEN, L. A., and THOMPSON, R. H. S. *Nature, Lond.*, 1945, 156, 616.
4. SIMPSON, S. D. Report C.P. 48, 1944.
5. SIMPSON, S. D. Unreported observations.
6. SIMPSON, S. D., and YOUNG, L. Report C.P. 49, 1944.
7. SIMPSON, S. D., and YOUNG, L. Report C.P. 79, 1945.
8. SIMPSON, S. D., and YOUNG, L. Report C.P. 80, 1945.
9. SIMPSON, S. D., and YOUNG, L. Report C.P. 84, 1945.
10. SIMPSON, S. D., ZBARSKY, S. H., and YOUNG, L. Report C.P. 63, 1944.
11. WATERS, L. L., and STOCK, C. *Science*, 1945, 102, 601.
12. YOUNG, L. Progress Report No. 21, 1942.
13. ZBARSKY, S. H. Unreported observations.
14. ZBARSKY, S. H., MANSON, L. A., and YOUNG, L. Report C.P. 72, 1944.
15. ZBARSKY, S. H., SIMPSON, S. D., and YOUNG, L. Report C.P. 64, 1944.

¹ The reports to which reference is made were submitted to the Director of Chemical Warfare, Department of National Defence, Ottawa, Canada.