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BAL (BRITISH ANTI-LEWISITE)*

Compiled by Dr. L. L. WATERS and Dr. CHESTER STOCK

IN a recent issue of *Nature,* Professor R. A. Peters of Oxford has announced the discovery and development during the war years of an effective antiarsenical, 2,3,-dimercaptopropanol.[1] This substance has been called BAL (British anti-lewisite). As its name suggests, BAL is of interest in war medicine as an effective therapeutic agent against both the local and systemic action of certain arsenical war gases. Clinical trials of BAL, conducted as a part of the program of war research, have shown further that the compound is of value in the treatment of types of arsenical poisoning encountered in civilian medicine. Beyond this direct clinical application, the study of the action of BAL has resulted, as stressed by Professor Peters, in an important advance in the understanding of fundamental biochemical mechanisms.

Full details concerning BAL, its chemistry, method of preparation and basic biochemical actions were promptly and graciously transmitted to the United States by Professor Peters and his associates through official channels. BAL itself was received in this country late in 1941. Thereafter an intense program of study, including preparation and manufacture, biochemistry, toxicology, pharmacology, experimental therapeutics and clinical application, was undertaken jointly by the Government agencies concerned. Cooperating in this program were the U. S. Army, the U. S. Navy, the Office of Scientific Research and Development, the National Research Council, the Federal Security Agency.

It is the purpose of this review to give a brief summary of the information on BAL, particularly as it was developed in the United States. As in England, more detailed papers based on the original confidential reports are being prepared for early publication.

* Many of the investigations included in the footnotes have not been published in open literature and the date given is the year in which the work was carried out.

[1] R. A. Peters, *Nature,* November 24, 1945.

PREPARATION AND CHEMISTRY

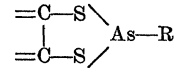
Subsequent to the discovery of BAL by the British, methods of preparation of BAL were studied in the United States so that a process would be available for large-scale manufacture.[2] A modification of the British process was developed involving the bromination of allyl alcohol to glycerol dibromohydrin (83 per cent. yield) followed by reaction in an autoclave with sodium hydrosulfide under 100 pounds per square inch hydrogen sulfide pressure, at 60–70° C. to yield BAL (64 per cent. yield). BAL is unstable to heat and to acids and decomposes during distillation. The British and American investigators independently made the important discovery that 1 per cent. of ammonium hydroxide is an efficient stabilizer during vacuum distillation.

Other methods, as well as many modifications of the above method and a variety of reaction conditions, were studied before developing a process which was operable and which yielded a product of satisfactory quality. On the basis of biological tests BAL produced by the recommended procedure was equal to that produced by the British. This process was expanded to pilot plant scale operation.[3] The pilot plant yields were about the same as indicated above. This pilot plant produced the BAL used by the Services in the form of therapeutic solutions and ointments. An engineering study[4] was also made of a plant capable of producing 200,000 pounds of BAL per year; at that time it seemed possible that there would be a large demand for this material.

Other work on the chemistry of BAL confirmed the demonstration by the British that this and other dithiols form with lewisite and lewisite oxide isolable cyclic dithioarsenites.[5] Further work was conducted on the resolution of BAL into its optically active forms.[6] Investigations[7, 8] were also carried out on the preparation of a considerable number of water-soluble derivatives of BAL and on a large number of analogs.

BIOCHEMICAL ACTION

Peters and his associates[1] found that sodium arsenite and lewisite exerted a powerful inhibitory influence on the pyruvate oxidase system in brain brei, a system dependent upon –SH groups for its activity. They next analyzed compounds of arsenic with an –SH protein product, kerateine. The arsenic content of the arsenic-kerateine compound was found to correspond closely with the thiol content of the parent protein. Further, most of the arsenic present in the treated protein was in combination with two thiol groups. This and other chemical evidence indicated that dithiols added to protein previously treated with arsenic probably compete successfully for the arsenic by the formation of compounds of the type:



These findings focused attention on the theory for which there was already considerable independent evidence[9, 10, 11, 12, 13, 14, 15, 16] that the toxicity of trivalent arsenicals is largely due to their binding of essential thiol groups in enzyme proteins. This concept was supported by the significant observation that dithiols of the BAL type not only prevented the inhibition of enzyme systems by arsenicals but also reactivated these systems when added after inhibition had occurred.[1]

American work has confirmed and extended these observations. The effect of trivalent arsenicals, chiefly of lewisite, on the various classes of enzyme reactions concerned with cellular metabolism have been intensively investigated.[17] From these experiments it is concluded that trivalent arsenicals exert their toxic action by combination with –SH groups of the activating protein of enzyme systems. Tissue respiration is interfered with by the action of the arsenicals on the large group of –SH enzymes essential for carbohydrate transformations and fat metabolism. Lewisite has little effect on co-enzymes or on enzyme systems concerned with protein utilization and synthesis. The enzyme inhibitions produced by lewisite and arsenic can generally be prevented by BAL or other closely related dithiols. Furthermore, even when established, these inhibitions can be reversed by BAL and to a lesser extent by glutathione. Certain of the inhibitions produced by arsine are enhanced by BAL.[18] This is apparently

[2] P. L. Salzberg, W. A. Lazier, M. W. Farlow, W. J. Peppel, G. W. Rigby, F. K. Signaigo, C. G. Wortz, 1942.
[3] H. W. Elley, W. S. Calcott, H. R. Lee, C. F. Belcher, A. J. Wuertz, 1942.
[4] H. W. Elley, C. B. Biswell, J. F. Froning, W. V. Wirth, T. W. Stricklin, Jr., 1943.
[5] P. D. Bartlett, S. G. Cohen, H. J. Dauben, Jr., L. J. Rosen, M. J. Ryan, 1942.
[6] H. R. Snyder, R. L. Kenyon, 1943.
[7] P. L. Salzberg, W. A. Lazier, F. K. Signaigo, A. A. Pavlic, 1945.
[8] M. S. Kharasch, S. Weinhouse, 1943.
[9] M. Onaka, *z. physiol. chem.*, 70: 433–440, 1911.
[10] A. Szent-Györgyi, *Biochem. Jour.*, 24: 1723–1727, 1930.
[11] C. Voegtlin, S. M. Rosenthal, J. M. Johnson, *U. S. Pub. Health Report*, 46: 339–354, 1931.
[12] C. Voegtlin, H. Dyer, C. S. Leonard, *U. S. Pub. Health Report*, 38: 1882–1912, 1923.
[13] R. Labes, *Arch. Exp. Path. Pharmakol.*, 141: 148–160, 1928.
[14] M. S. Kharasch, U. S. Patent 1927, 1, 677, 392.
[15] H. J. Barber, *Chemistry and Ind.*, 49: 802, 1930.
[16] A. Cohen, H. King, W. I. Strangeways, *Jour. Chem. Soc.*, 3043, 1931.
[17] E. S. G. Barron, Z. B. Miller, G. Bartlett, J. Meyer, 1942.
[18] C. J. Kensler, C. P. Rhoads, H. Levy, H. B. Sherlock, C. Brooks, 1943.

related to an inherent toxicity of BAL itself for the enzyme system in question. In reversing enzyme inhibitions produced by arsenic, BAL and other related dithiols exhibit greater affinity for arsenic than do the attacked tissue thiols. This is strikingly brought out in experiments on unicellular organisms.[19, 20] If trypanosomes or spermatozoa are subjected to lethal concentrations of arsenic and observed microscopically they lose all motility and show early degenerative changes. If a dithiol of the BAL type is now added they regain their motility and normal cytologic appearance.[19, 20] Apparently the arsenic is actually removed from the damaged cells as the arsenic content of the supernatant fluid increases after the addition of BAL.[19] Experiments have also shown that the administration of BAL to animals previously poisoned with arsenicals is followed by a marked increase of arsenic excretion in the urine.[1, 19] Except in arsine poisoning no dithiol has been found which is more effective than BAL in preventing and reversing the toxic effects of the arsenicals tested.[18]

BAL is a strong reducing agent and is rapidly oxidized in the presence of catalytic amounts of copper and hemin. In the presence of oxygen, it destroys hemin or oxyhemoglobin by opening the porphyrin ring. BAL reacts instantaneously with methemoglobin and reduces it to hemoglobin. Cytochrome C is kept in a reduced state by BAL and thus interference with cytochrome oxidase activity is produced. BAL exerts an inhibitory effect on brain glycolysis presumably by combining with the metal-protein components which take part in the enzymatic processes concerned. Oxidized BAL itself is an inhibitor of enzyme systems containing essential –SH groups. It also destroys the physiological activity of insulin, possibly by reduction of the –S–S– groups of the insulin molecule. These reactions of BAL[21] may be related to the toxicity of the compound when injected in large amounts.

Working with the –SH containing enzyme, succinoxidase, it has been shown that heavy metals such as Pb, Sb, V, Bi, Cd, Hg and Zn produce complete inhibition and that the enzyme is reactivated on the addition of certain BAL derivatives. This demonstrates that the toxicity of these metals is, like that of As, due to inhibition of –SH enzymes. It furthermore is an indication for experiments designed to test the therapeutic value of BAL in these heavy metal intoxications.[22]

Toxicology and Pharmacology

BAL is not an innocuous substance. With its initial use, Peters and his associates[1] observed profound toxic effects following its administration to rats. When death occurred in these animals, it was usually preceded by violent convulsive seizures. Following the administration of toxic amounts of BAL to laboratory animals, there is usually an initial period of apathy, accompanied by lacrimation, blepharospasm and edema of the conjunctivae. There is copious salivation, and dogs frequently vomit. If the dose is increased, the course is further characterized by an increase in depth and rate of respiration, by muscle tremors of gradually increasing intensity, a rapid, thready pulse, nystagmus, and finally by repeated tonic and clonic convulsions, coma and death.[23, 24, 25]

Lethal amounts of BAL given intramuscularly or percutaneously cause an early transient rise in blood pressure which results from intense vasoconstriction in skin and skeletal muscle.[24] Rapid intravenous injection of large doses of BAL is followed by circulatory collapse. Changes in the electrocardiogram and the cardiac arrest occurring in hearts perfused with BAL solutions give additional evidence of the toxicity of BAL for the heart.

Following the injection of toxic amounts of BAL, the pH of the blood is reduced, as are also the serum CO_2 content and combining power[23, 24] Accumulation of lactic acid and a fall in serum sodium contribute to the metabolic acidosis.[23] Terminally there is a rise in serum amino acids, hyperglycemia, a depletion of liver glycogen and a virtual depletion of intracellular hepatic potassium.[23] The glycogen content of skeletal or cardiac muscle is not materially affected.[24]

The striking physiologic and metabolic changes of BAL poisoning in animals are not accompanied by comparable morphologic alterations. Little is to be seen either grossly or microscopically other than congestion of the viscera, and occasionally accumulation of fluid in the serous cavities or lungs.[23, 24] Lesions of the central nervous system have been described following the injection of certain BAL derivatives.[24]

On the skin of man or animals, BAL causes localized erythema and edema but no necrosis or blister formation. BAL is extremely irritating when applied to mucous surfaces, producing edema and severe ulcerations of the respiratory passages[47] and gastric mucosa of animals.[24] Fortunately, dilutions still therapeutically active, on the order of 5–10 per cent., may be applied to the eye or injected intramuscularly with no lasting ill effects. In man, solutions

[19] H. Eagle, 1942–1943.
[20] J. McLeod, 1942.
[21] E. S. G. Barron, Z. B. Miller, T. P. Singer, J. Meyer, 1943.
[22] E. S. G. Barron, S. Kalnitsky, 1944.
[23] H. Bunting, W. Ordway, H. Harrison, S. Durlacher, W. S. Albrink, 1942, 1943.
[24] McK. Cattell, H. Gold, W. Modell, M. B. Chenoweth, S. Krop, P. Hitchcock, F. Foster, W. F. Riker, 1942–1943.
[25] R. W. Gerard, J. Tobias, A. Potts, C. Lushbaugh, F. Simon, H. Patt, M. Swift, S. Postel, L. Postelnek, 1944.

or ointments containing 5–10 per cent. BAL produce only temporary tearing, lacrimation, blepharospasm and eye pain when instilled into the conjunctival sac.[26, 27, 28, 35, 36] Injected intramuscularly in sterile peanut oil-benzyl benzoate solution, concentrations of BAL of 10 per cent. or less are well tolerated.[29, 30, 31, 34] Inunction of a total of 1 cc of undiluted BAL or of 2 gm in a jelly base does not produce systemic effects in man.[31, 32]

It has been shown that BAL-in-oil injected intramuscularly at a dosage level of 3 mgm per kg produces only the mildest reactions in a small percentage of the individuals tested.[29] If, however, the level is increased to 5 mgm per kg, more than half the subjects experience some or all of the following reactions: nausea, vomiting, headaches, generalized aches and pains, burning sensations in the mouth, nose and eyes, sweating, restlessness, weakness, pain in the limbs, jaws and trunk muscles. The heart rate is often increased and there may be a rise in both systolic and diastolic blood pressure.[29, 30, 31] These signs and symptoms are transient and subside within four hours.

The early samples of BAL produced in the United States by the hydrogenation of the appropriate polysulfides were much more toxic than the BAL received from England.[23] Subsequent syntheses by the modified British procedure yielded a BAL which in toxicity and therapeutic efficacy was comparable to the British samples.[2, 23, 34] This product was eventually established as American Reference Standard BAL,[33, 34] and its physical, chemical and pharmacological properties have served as standards for the control testing of all BAL produced in the United States.[34] The LD_{50} of American Reference Standard BAL for rats is 105 mgm per kg when injected intramuscularly.

Experimental Therapeutics

Beginning in the spring of 1942 a large number of animal experiments were carried out in order to test the therapeutic value of BAL against the arsenicals used in chemical warfare. Most of the experiments were concerned with combatting the local effects of these chemical agents on the eyes and skin. While chiefly of interest to war medicine, the therapeutic results achieved were so striking that they deserve brief mention. It was found, in agreement with British reports,[1] that following the contamination of rabbits' eyes with an amount of lewisite sufficient to destroy the eyes, the local instillation of 5 or 10 per cent. solution of BAL up to 5 minutes after contamination resulted in almost complete recovery.[35, 36] At time intervals longer than five minutes, treatment resulted in progressively less good results, but some improvement was observed even after a treatment delay of thirty minutes.[35, 36]

The effect of BAL on the lesions produced by lewisite and other vesicant arsenicals on the skin of animals was equally striking.[1, 37, 38] Prompt application of solutions or ointment containing the medication prevented these lesions completely.[37, 38] Even after initial erythema had appeared, applications of BAL prevented the further development of the process and were followed by the rapid disappearance of the initial redness.[37, 38]

Accidental contamination of human eyes with lewisite occurred only rarely during the war, so that direct observations on the efficacy of BAL were few. The instances reported would seem to support the results obtained in animals.[39] The use of volunteers made possible extensive therapeutic trials of BAL against the lesions produced by arsenicals on human skin. In such volunteers the material proved just as effective in preventing the development of vesicant lesions after the application of lewisite as it had in animals.[32, 40, 41]

Once the therapeutic value of BAL had been established for arsenical lesions of eye and skin, and its toxicity in these locations had been determined, there remained the problems of the best possible vehicles for BAL, and proper packaging. Cooperative efforts involving much chemical and biological testing by Service and civilian government agencies and by manufacturers culminated in satisfactory issues for the Armed Forces of BAL eye solution,[34, 35, 36, 44, 45] BAL eye ointment[3, 34, 42, 43, 44, 45] and BAL ointment for skin application.[3, 43, 44, 45]

Lewisite and other arsenicals when applied to the skin of animals in sufficient quantity are absorbed

[26] C. P. Rhoads, A. S. Reese, 1942.
[27] M. B. Sulzberger, M. Cuthbert, D. P. Barr, J. McLean, 1943–1944.
[28] R. C. Laughlin, 1944.
[29] H. Eagle, H. J. Magnuson, R. Fleishman, 1943–1944.
[30] H. Gold, W. Modell, McK. Cattell, 1944.
[31] M. B. Sulzberger, R. L. Baer, A. Kanof, 1944.
[32] D. W. Wilson, T. R. Talbot, 1943–1944.
[33] P. L. Salzberg, W. A. Lazier, G. W. Rigby, C. G. Wortz, 1943–1944.
[34] H. O. Calvery, H. A. Braun, D. W. Fassett, O. G. Fitzhugh, C. D. Johnston, W. S. Lawrence, L. M. Lusky, A. A. Nelson, R. B. Smith, Jr., B. J. Vos, Jr., G. Woodard, 1943–1944.
[35] F. H. Adler, I. H. Leopold, A. S. Crandall, W. H. Steele, 1942.
[36] W. F. Hughes, Jr., 1942.
[37] C. B. Marquand, O. E. McElroy, T. W. Kethley, 1941.
[38] M. B. Sulzberger, D. P. Barr, 1942.
[39] Medical Division, Chemical Warfare Service.
[40] D. P. Barr, M. B. Sulzberger, 1942.
[41] W. Bloom, T. Friedman, J. Last, R. Murray, J. Savit, 1942.
[42] J. S. Friedenwald, 1942.
[43] M. B. Sulzberger, D. P. Barr, J. McLean, R. L. Baer, M. Cuthbert, C. Lowenberg, 1943.
[44] P. L. Salzberg, W. A. Lazier, M. W. Farlow, G. W. Rigby, C. G. Wortz, 1943.
[45] P. L. Salzberg, W. A. Lazier, G. W. Rigby, C. G. Wortz, 1945.

and cause systemic arsenic poisoning. The effectiveness of BAL in protecting such contaminated animals from the systemic action of lewisite was early observed by the British investigators.[1] Treatment not only saved the animals but also resulted in increased urinary excretion of arsenic.[1] Work in the United States has abundantly confirmed these observations[19, 23, 29, 46] and has indicated that to obtain this protective action against systemic effects BAL need not be applied directly to the site of lewisite contamination.[23]

As mentioned earlier, BAL was capable of resuscitating microorganisms poisoned by various trivalent arsenicals, including the widely used antisyphilitic agent mapharsen.[19, 20] BAL given intravenously, intramuscularly or subcutaneously also resuscitated rabbits[19] or cats[24] given lethal injections of mapharsen. The longer the delay in treatment after injection of the arsenical, the less effective BAL became in preventing systemic effects. Urinary excretion of arsenic was greatly increased following treatment with BAL. Furthermore, subcutaneous, intramuscular or intravenous administration of BAL prevented the development of systemic arsenical poisoning due to lewisite or phenyldichlorarsine.[19, 29, 47] Application of BAL to lewisite-burned areas combined with parenteral injections was ultimately found to be the most effective method of therapy.[47]

These experiments led directly to further studies in animals of the toxicity and therapeutic effectiveness of BAL in various vehicles, by various routes of administration and on various dosage schedules.[19] The data so obtained made possible the development of a stable sterile preparation of BAL in benzyl benzoate-peanut oil solution, suitable for intramuscular injection.[19] The most effective method of treatment was found to consist of four injections of BAL at two to four hourly intervals, followed by single daily injections for six days.[19] On this schedule, BAL in doses of 1 to 10 mg per kg per injection saved 55 per cent. of the animals from repeated massive doses of mapharsen and delayed death in an additional 22 per cent. Similar results were obtained in the treatment of animals poisoned with lewisite, applied either to the skin,[23] or subcutaneously,[29] and treated with the BAL peanut oil-benzyl benzoate preparation.

The toxicity of this preparation on intramuscular injection in man was then carefully investigated.[29, 30, 31] When it was found that BAL could be injected safely into man in amounts that were therapeutically effective against arsenical poisoning in animals, it remained only to give BAL a therapeutic trial in instances of clinical arsenical poisoning.

There is now evidence from animal experiments that BAL is of value in preventing the development of pulmonary lesions after the inhalation of lewisite,[23, 47] cadmium[25, 47] or zinc fumes.[48] It is also therapeutically active against systemic toxic actions of mercury[49] and possibly zinc. With cadmium, BAL forms toxic complexes in the body that cause serious renal damage although the animal is protected from the systemic action of cadmium itself.[50]

Medical Applications

Toxic reactions in man due to the systemic action of arsenic are observed occasionally during the arsenotherapy of syphilis. Because of the recent widespread use of highly intensive schedules of anti-syphilitic treatment the incidence of such reactions had increased markedly prior to the introduction of penicillin.[51] It thus became feasible to initiate a carefully supervised therapeutic trial of BAL in clinics where patients were being given these intensified forms of treatment.[29] Patients were also available from industrial plants where exposure to arsenicals had accidentally occurred.[52] Up to the present time more than 200 such patients have been studied in the United States and England.[1, 29] The majority of toxic reactions treated have been either arsenical dermatitis or hemorrhagic encephalitis, following administration of mapharsen. Included, however, are some cases of massive overdose of arsenicals and other less common manifestations of arsenic poisoning. Since the majority of the patients observed received conventional supportive therapy and supplementary medication, an exact assessment of the value of BAL was difficult. Also, customary caution with a new and toxic drug limited its use to patients so seriously ill as to endanger life. In spite of the difficulties thus introduced the available data strongly suggest that BAL properly administered is in fact effective in the treatment of patients with arsenical dermatitis, arsenical encephalitis and individuals who have received a massive overdose of mapharsen.[29, 52]

It is probably of value in some cases of blood dyscrasia resulting from arseno-therapy, and it appears to be of no value in most cases of so-called arsenical jaundice.[51]

In addition to its use in systemic arsenical poisoning, BAL has been given preliminary clinical trial in

[46] McK. Cattell, W. F. Riker, G. Rosenfeld, 1944.
[47] H. E. Harrison, S. H. Durlacher, W. S. Albrink, N. K. Ordway, H. Bunting, L. L. Waters, 1943–1944.
[48] A. Gilman, B. P. McNamara, 1943–1944.
[49] A. Gilman, R. Allen, F. S. Philips, 1944–1945.
[50] A. Gilman, R. Allen, F. S. Philips, 1943–1945.
[51] H. Eagle, R. B. Hogan, *Venereal Disease Information*, 24: 33, 1943.
[52] W. T. Longcope, M. M. Wintrobe, J. A. Leutscher, Jr., B. V. Jager, 1943.

mercury poisoning. As was anticipated from preceding animal experiments,[49] the results in these patients are most encouraging.[53]

In conclusion, it should be restated that BAL, discovered in England early in the war, has been developed through the joint effort of many agencies and individuals in Britain and in the United States as a therapeutic agent in local and systemic arsenical poisoning. Further, study of its mode of action has led to definite advances in biochemical theory. Necessary data for the consideration of BAL under the new provisions of the Federal Food, Drug and Cosmetic Act have been submitted to the Administrator of the Federal Security Agency. Although the substance itself and the large body of detailed reports on which this summary is based are not yet generally available, as soon as possible full information on BAL will be submitted to the Council on Pharmacy and Chemistry of the American Medical Association.

The above summary was compiled by L. L. Waters and C. Chester Stock for the following agencies:

1. Medical Division, Chemical Warfare Service, *and* Medical Department, Office of the Surgeon General, *U. S. Army.*
2. Bureau of Medicine and Surgery, *U. S. Navy.*
3. Division 5, Committee on Medical Research, and Division 9, National Defense Research Committee, *Office of Scientific Research and Development.*
4. The Committee on Treatment of Gas Casualties, Division of Medical Sciences, *National Research Council.*
5. Division of Pharmacology, Food and Drug Administration, *and* Venereal Disease Research Laboratory, U. S. Public Health Service, *Federal Security Agency.*

WASHINGTON, D. C.

OBITUARY

RICHARD STANISLAUS McCAFFERY

RICHARD STANISLAUS MCCAFFERY, respected professor of mining and metallurgy at the University of Wisconsin for twenty-seven years, died at his home in New York City on June 12, 1945, in his seventy-first year.

He was born in New York City on June 2, 1874, the only son of Michael and Mary McCaffery. He completed not only his elementary education in New York but also his professional studies at Columbia University, from which institution, in 1896, he received the degree of engineer of mines. In his senior year at Columbia he served as research assistant to Professor Henry M. Howe, one of the foremost metallurgists of that time, who instilled in him the desire for research.

From the time of his graduation in 1896 until 1909 he worked as a mining and metallurgical engineer in various places in South America and in New Mexico and Utah. Before leaving New York for his first assignment in Chile he was married to Kathleen Kirwan, of New York City, on January 27, 1897. Their honeymoon consisted of the trip to Chile to a rough and inaccessible mining camp. He often related to his students how the experience in Chile taught him to be self-reliant and how best to use the materials at hand. Upon his return to the United States in 1900, he became superintendent for the Santa Fe Gold and Copper Mining Company at San Pedro, New Mexico. From 1905 to 1907 he served as manager of the Salt Lake Copper Company at Salt Lake City, Utah, and from 1908 to 1909 he was superintendent for the Tintic Smelting Company at Silver City, Utah.

His teaching career was begun in 1909 as professor of mining and metallurgy at the University of Idaho. Here he remained for five years. Because of his previous professional experiences, he was asked to serve as consultant for many important lead and zinc mining companies in Idaho and he became an authority on the mineral deposits of that state.

In 1914 he joined the faculty of the College of Engineering of this university as professor of mining and metallurgy, and from 1915, for twenty-six years, he served as chairman of his department.

A few years before his retirement from active service, in 1941, his health began to fail. He then moved to New York City, where he and his wife could be near their children. Here he accepted such consulting activities as his failing health permitted. He is survived by his wife, four sons, Richard, Jr., Arthur L., Philip, John K., two daughters, Marian and Agatha (Mrs. Richard Church), and one sister, Nora McCaffery.

As a member of the faculty of this university, his greatest achievement was the development of the young student; his love and interest in them was boundless; he lived with them in his classes; he made it a practice to have them in his home; and he knew them so intimately he called them by their first names. To the student, on the other hand, he was affectionately known as "Mac." His kindly and sympathetic nature lives in the recollections of his students and associates who profited from his friendly advice. It has been truly said by one of his former pupils that he had the rare ability and the rare gift to make the most complicated and difficult problems appear simple and easily understood.

Professor McCaffery was a devout Catholic. He inaugurated discussion groups and was the leader in expounding the Catholic philosophy; and for many years he was a trustee of St. Paul's Catholic University Chapel.

[53] W. T. Longcope, J. A. Luetscher, Jr., 1945.