Development of the Biochemistry Department

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In 1947, when the Edsel B. Ford Institute for Medical Research was begun, the course to be followed in developing a Department of Biochemistry was self-evident. Nationally the shortage of trained personnel resulting from World War II was acute. Locally research facilities were in that contemplated stage which prospective staff members analyze with a dubious facial expression. On the other hand, the possibility of starting with graduate students, and building up personnel and facilities together, was wide open. Under an arrangement made in 1934, with the Chemistry Department of Wayne University (now Wayne State University), seven candidates for the M. S. degree with major in biochemistry had completed the research requirement for this degree in the writer's laboratory, and a doctorate program had been started in 1946. Establishment of certain lines of interest was, therefore, closely intertwined with the thesis topics and subsequent adventures of a series of graduate students.

The first predoctoral fellow in the Department was Paul D. Bartlett, who joined the staff as an associate on July 1, 1948, shortly after completing his doctorate. His thesis (6) and publications from it (11, 12) formed the background for a series of studies on the mechanism of nitrogen storage during induced growth (18, 21, 22, 34, 35, 57, 58). The second predoctoral fellow, William T. Beher, completed his studies for the doctorate in February 1950. His thesis (26) dealt with certain analytical and metabolic problems in the steroid field. Metabolic aspects of his interest in sterols and steroids have been continued in a series of studies of factors influencing absorption, deposition and mobilization of cholesterol (83, 88, 109, 135, 149), while analytical aspects have been developed in studies, carried out in collaboration with Jonathan Parsons of the Physics Department, in which the value and limitations of two methods — x-ray diffraction and infra-red absorption — are explored (106, 107, 108, 123, 153, 157).

Two other students have completed doctoral programs in the Department and embarked upon careers elsewhere. Stanley Ellis, who was graduated in 1951, has had a fruitful career in the laboratories of Herbert M. Evans and Alfred Wilhelmi. While his thesis was concerned with purine precursors (47), his subsequent interest has been in growth hormone and other pituitary factors. Alexander C. Zuchlewski participated in studies of the relationship between growth hormone and insulin (143), investigated effects of growth hormone on activities of glutamic acid dehydrogenase and transaminases (148), and, after completing his Ph. D. degree (90) in 1954, entered Wayne State University College of Medicine as a medical student.

Another line of investigation — enzyme chemistry as such — was begun by James C. Mathies, who joined the staff July 1, 1948, after completing his M. S. degree here and his doctorate work at the University of Washington, Seattle. During the first two years, he participated in an extensive departmental program in which effects of growth hormone on activity of tissue enzymes and coenzymes (15, 16, 19, 45, 51, 55, 63) were investigated. Meanwhile, he supervised construction of a laboratory suitable for enzyme chemistry, and when this was completed, carried out a series of
studies on purification and characterization of alkaline phosphatase (49, 79). Dr. Mathies is now at the Swedish Hospital, Seattle, Washington, and is participating in the development of research facilities there.

The laboratory which Dr. Mathies developed served as the starting unit for a greatly expanded program in enzyme chemistry, developed by Dr. Thomas P. Singer and Dr. Edna B. Kearney, who joined the staff October 1, 1954. The work on succinic dehydrogenase which this team began at the Enzyme Institute of the University of Wisconsin has been continued here, and expanded in collaboration with a series of postdoctoral fellows and visiting scientists. While certain aspects of the program may be described as "purification and characterization", this feature represents obstacles encountered and overcome, rather than the motivation or goal of the journey. Actually, the program is inspired by a lively interest in the mechanism of certain crucial steps in biological oxidation, the comparative biochemistry of the same process in mammals and bacteria, the role of metals, notably iron, in the action of certain enzymes, and many other fundamental problems.

Two organic chemists, Dr. W. M. Holliday and Dr. Milton Madoff, made important contributions in studies involving use of the stable isotopes carbon-13 and nitrogen-15. Dr. Holliday synthesized 3-acetylpyridine with C-13 in the carbonyl group. After feeding this compound, Dr. Beher isolated heavily labeled N-methyl nicotinamide from the urine, thus demonstrating conversion of 3-acetylpyridine, previously considered an antimetabolite for nicotinic acid, into a biologically active nicotinic acid derivative. It has since been demonstrated elsewhere that blacktongue will not develop in dogs if a suitable amount of 3-acetylpyridine is added to the diet at the time when nicotinic acid is removed. Dr. Madoff extended a program initiated by Dr. Bartlett, by synthesizing urea and various amino acids labeled with N-15. Studies in which these compounds have been, or are being, used are mentioned in another section.

Members of the Department have participated in organization and publication of two of the International Symposia (102, 125) in the series which was initiated by the Executive Director, Dr. Robin C. Buerki, in 1953. Some of our more recent studies on effects of growth hormone on nitrogen metabolism were presented in the "Growth Hormone Symposium" (100, 101). Earlier related studies had been summarized in a symposium elsewhere (85). The beginnings of the expanded program in enzyme chemistry were presented in a contribution (126) to the "Enzyme Symposium". International congresses in which staff members have participated include the Third International Congress of Biochemistry at Brussels, in 1955, and International Physiological Congresses at Montreal, in 1953, and at Brussels, in 1956. Before the ten-year period covered in this report ended, arrangements had been completed to participate in the International Congress on Clinical Chemistry in Stockholm, and in an International Symposium on Enzyme Chemistry, in Japan.

Other extramural activities include presentation of lectures and seminars, and participation in scientific organizations. While the writer was on the staff of the Department of Laboratories of Henry Ford Hospital, he was invited to initiate courses in general biochemistry and biochemical methods of analysis in the Chemistry
Department of Wayne University. This activity was continued after the Institute was begun, and eventually led to formation of a Biochemistry Division, with which Dr. P. D. Bartlett and Dr. W. T. Beher have continued to collaborate. The writer also gave an annual series of 12 lectures on intermediary metabolism, in the Department of Physiological Chemistry, from 1949 until 1955.

In 1954, Dr. W. T. Beher gave an invited lecture at North Central College, Naperville, Illinois. Dr. P. D. Bartlett has given seminars dealing with protein metabolism, at Wayne State University, and in the basic science series of Henry Ford Hospital.

Dr. Edna B. Kearney and Dr. T. P. Singer have given joint lectures dealing with the action of succinic dehydrogenase, and with metabolism of sulfur containing amino acids, at Western Reserve University, University of Wisconsin, Naval Medical Research Institute, and University of Michigan. Dr. Singer also presented a seminar at Michigan State University, and a lecture on “Experimental Foundations of the Concept of Metal-Flavoprotein Catalysis” in the Frontiers in Chemistry series of Wayne State University. Dr. Vincent Massey, on completion of a two-year postdoctoral fellowship in the Enzyme Division, presented lectures dealing with electron transport mechanisms and the role of metals in biological oxidations, at the universities of Minnesota, Utah, and California, and at Oak Ridge National Laboratories. Miss M. G. P. J. Warringa, a Fulbright fellow, also concluded the fellowship with a tour that included seminars on “Succinic Dehydrogenase Action in Obligate Anaerobes”, given at seven major universities and national laboratories.

The writer was a member of the American Board of Clinical Chemistry for 6 years, serving as vice-president and as secretary-treasurer, and is currently vice-president of the American Association of Clinical Chemists.

Analytical work involved in studies of the Department of Pediatrics has been performed by assistants in the Biochemistry Department throughout the ten-year period, and transfer to new quarters has only recently been completed. In its initial stages, the Endocrinology Laboratory program was also housed with Biochemistry. In both these instances the programs were directed by the heads of the corresponding clinical departments; also in both instances, an assistant from the Biochemistry staff was transferred to the clinical department to facilitate continuity of projects in progress at the time of separation.

The goal which has been reached during the ten-year period since the Department was begun is the establishment of three active divisions: Nutrition and Metabolism, Bio-Organic Chemistry, and Enzyme Chemistry. Each division has a chief and a senior associate with complementary but independent programs. The three divisions have a strong common interest in metabolic processes.