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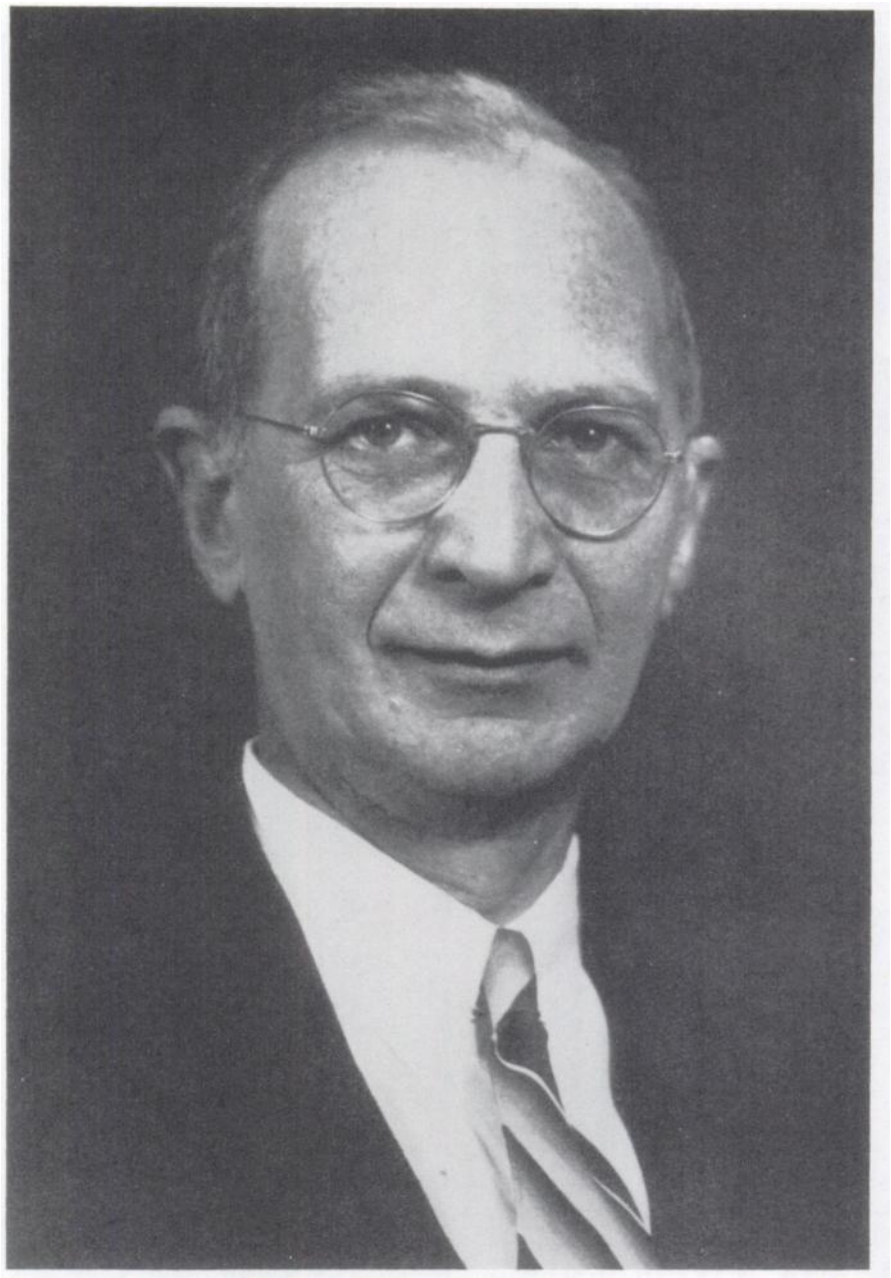

ALFRED THEODORE SHOHL

Alfred Theodore Shohl (1889–1946)[1]

A Biographical Sketch

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Alfred Theodore Shohl was trained as a physician, but he devoted his adult life to laboratory studies of the inorganic elements in nutrition. His special interests were concerned with calcium and phosphorus interrelationships in experimental rickets, and acid-base balance in physiology. He was a charter member of the American Institute of Nutrition and served a term on the Board of Editors of the Journal of Nutrition. Most of his scientific papers dealt with some aspect of mineral metabolism which he defined as "the study of the role of the minerals in the structure and function of the human body." His views were summarized in his book, Mineral Metabolism, published in 1939 as one of the American Chemical Society's series of scientific monographs. He was an enthusiastic experimenter, perfected a number of excellent methods of analysis of biological materials and devised several ingenious pieces of apparatus for laboratory use.

Shohl was born 29 December 1889 in Cincinnati, OH, of parents who had migrated from Germany late in the 1800's. His father, a successful businessman, was characterized by an old-world kind of courtliness and a sense of obligation to do things for his fellow man and for the community in which he lived. This sense of duty was inculcated into his three sons, one of whom unfortunately died young while still a student of engineering. Another became a well-known attorney who was also active in civic affairs in Cincinnati. The son who is the subject of this biographical sketch attended the Walnut Hills High School in Cincinnati, which had earned a reputation for its solid preparation of boys and girls for college and for life as adults. From there he went to Harvard College, from which he was graduated in 1910.

While an undergraduate, Shohl became interested in theoretical chemistry and in general physiology and began some experimental studies with Prof. G. H. Parker in the department of zoology. These studies led to the publication of "The reaction of earthworms to hydroxyl ions." It is characteristic of his later work to note that in the course of this study the young investigator devised a simpler and better method of testing the reactions of his unusual experimental animals. While a medical student, he and W. S. Wright worked with Prof. Walter B. Cannon. This work led to a paper in 1911 by Cannon, Shohl and Wright entitled "Emotional glycosuria." The authors showed that a cat kept in a cage excreted considerable quantities of sugar in its urine when it was frightened by bringing a barking dog nearby. The effect, the authors believed, was caused by the release of epinephrine into the blood stream.

As a student, Shohl was greatly influenced by the teachings of Prof. L. J. Henderson, whose book, The Fitness of the Environment, appeared in 1913, while Shohl was an upperclass student in the medical school. Years later as a member of Prof. L. B. Mendel's department at Yale, Shohl graciously gave on request a series of lectures and discussions on the physical chemistry of the body fluids, with the view of helping graduate students in Mendel's

[1] See National Auxiliary Publications Service document no. 03615 for 8 pages of supplementary material, a bibliography of Shohl's publications. Order from NAPS c/o Microfiche Publications, P.O. Box 3513, Grand Central Station, New York, NY 10017. Remit in advance, in U.S. funds only $5 for photocopies or $3 for microfiche. Outside the U.S. and Canada add postage of $3 for photocopy and $1 for microfiche.

department to better appreciate the Silliman lectures soon to be delivered by L. J. Henderson. Some student notes of Shohl's lectures taken at the time reveal the practical nature of Shohl's thinking; he presented the subjects of acidity, weak and strong acids, buffer values, etc., from the laboratory point of view. Each lecture ended with the presentation of a number of problems for students to solve, the arithmetic being purposely made simple, to focus attention on principles.

When Prof. Henderson came to New Haven, he paid a social visit to Shohl in the laboratory before the first of his series of lectures which when published were called simply "Blood, a study in general physiology." Shohl's thinking and experimenting in the field of mineral metabolism were guided by the conviction that the maintenance of the constancy of the composition of body fluids, as taught by Henderson and also included in what Cannon came to call "homeostasis," determined much of what could be observed in the behavior of the mineral elements in health and in disease. In turn it could be said that many of Shohl's observations on the actions of the minerals in the body constituted data in support of Henderson's and Cannon's picture of what Claude Bernard originally called the "milieu intérieur."

After graduation from Harvard Medical School, Shohl spent a year as an intern in Boston and Montreal. His family urged him to enter private practice as a physician, but he wanted to do laboratory work on problems of clinical interest. In those days there were not many openings in clinical departments for persons who wanted to devote their full time to research rather than the treatment of patients. He found a position, however, as assistant in pediatrics at Johns Hopkins University under John Howland and W. McKim Marriott. He remained there for 2 years and then from 1917 to 1920 served as an assistant in the department of urology at the same university.

Part of this time, however, was spent in the army during World War One in the section of the Sanitary Corps headed by John R. Murlin, and he saw service in France. Asked what he did during the war, he was apt to brush off the question or humorously tell about his spending considerable time, on his own initiative, to develop a new method of slicing bread. Shohl had observed that the American soldiers had a habit of throwing away what they called the "heels" or two end-slices of the loaf, and his new method of slicing would prevent that. He demonstrated his new technique for conserving bread to his superior officer who happened to be a Frenchman. The latter looked on with an obvious air of boredom and, when the exuberant Lieutenant Shohl had completed his demonstration, shrugged his shoulders, threw up his hands and said, "But why? I like ze crust."

After the war, Shohl returned to Hopkins and transferred to E. V. McCollum's department of chemical hygiene in the School of Public Health. There he served as an associate professor during the academic year, 1920–1921, before accepting an appointment at the same rank in the department of pediatrics at the Yale Medical School. In 1927, he transferred to the department of physiology and physiological chemistry, because the newly appointed head of the department of pediatrics wanted to appoint his own staff.

Shohl had the highest regard for McCollum, a feeling which was reciprocated. "He was kind and fair to me," Shohl said. "When I reported to him, he first showed me around the laboratory. When we came to one room, he said that I could work there on anything I wished to do unless I chose to work with rats, and then he would like me to discuss the matter with him first. Nothing could have been fairer than that."

During his association with three different departments at Johns Hopkins University, Shohl made a number of studies which illustrated the importance of acidity in determining the course of certain chemical reactions and the efficacy of some drugs. Hexamethylene tetramine, for example, was widely used at the time for the treatment of urinary infections, commonly caused by *E. coli*. Shohl demonstrated that the efficacy of the drug, which depends upon its conversion to formaldehyde, re-

quires that the urine have an acidity equal to pH 5.4 or less. With John H. King, Shohl published three noteworthy papers on the determination of the acidity of gastric contents by the use of a convenient indicator method which he devised, and he described the interpretation of the results of such tests, still in use today, clearly and understandingly. He also worked out the effect of different acidities on the determination of calcium in biological materials by precipitation of calcium oxalate, and generously made his information available before publication to F. F. Tisdall who used it in developing the Kramer-Tisdall method for the determination of calcium in blood serum.

While at Johns Hopkins, Shohl performed some of his initial studies of mineral metabolism beginning with the work that led to two papers with A. Sato on the determination of base balance in infancy. He also began an intensive study of the scientific literature on the inorganic elements in nutrition and their interrelationships. He used some of this material in the preparation of his review, entitled "Mineral metabolism in relation to acid-base equilibrium," which appeared in Physiological Reviews in 1923, after he had gone to New Haven.

It was in New Haven that he began his studies of the relationships of calcium, phosphorus and vitamin D in the diet, using puppies and young rats as experimental animals. There were 15 papers published between 1927 and 1936 under the general heading "Rickets in rats." Using this animal, he was able to show that the amounts as well as the ratios of calcium to phosphorus in the diet determined whether rickets or normal bones were produced, in the absence of vitamin D. He also clarified the nature of rachitic tetany and studied other problems of clinical and scientific interest.

In the early 1920's there was introduced the practice of requiring senior medical students at Yale to perform some piece of original research and write a thesis as a prerequisite for graduation. Some of these theses were of excellent quality and were published in scientific journals. Shohl could suggest numerous problems and was eminently qualified to guide interested students in their efforts to meet this requirement. One study concerned the refractive index of breast milk serum, principally for the purpose of distinguishing between human milk and cow's milk. The milk from wet nurses at the time was becoming an article in demand, and its dilution with cow's milk was possible and, regrettably, sometimes occurred. The method developed enabled the ready detection of 10 percent or more cow's milk in human milk.

Shohl built up his section on pediatric research by employing two young women as technical assistants. One of these was Helen Bennett (Brown) who with Shohl's assistance enrolled for graduate work in Mendel's department and obtained her Ph.D. in 1930. Between 1926 and 1934, Shohl and Mrs. Brown collaborated in work described in 16 research papers and Mrs. Brown published several on her own. Shohl was a critical reader and careful worker, and sometimes, because of his outspokenness, he antagonized others, but he was a joy to work with in the laboratory. He was a tall man, well-built and stood out in any group. Those who worked for him or with him were intensely loyal to him. One afternoon in 1928 after Shohl had transferred his activities to Mendel's laboratory, a tall young man crossed the street from the hospital and strode into the room where Shohl was busily engaged in some task which he instantly stopped. The visitor was Dr. A. M. Wakeman, one of the twin sons of Dr. Alfred J. Wakeman of the Connecticut Agricultural Experiment Station, both of whom became physicians. The young man was bubbling with enthusiasm as he bade farewell to Shohl, with whom he had worked and published two papers. Promising to write, he left. There were tears in Shohl's eyes after the door closed. "What's wrong?" he was asked. He replied in a low voice, "I hate to see that boy go. He is leaving for Africa to work with Noguchi on yellow fever. I have a feeling that he isn't coming back"

That year Helen Bennett married a young lawyer named Brown, who planned to begin his career in Cleveland, OH. She asked Shohl if he could help her find a lab-

oratory position there, and he wrote a letter to Dr. H. J. Gerstenberger, who was professor of pediatrics at Western Reserve University. The latter did have an opening and, when Mrs. Brown reported for work, asked her what Shohl was doing. This conversation led to Shohl's going to Cleveland as associate professor of pediatrics in charge of pediatric research. There he remained for 5 years and then went to Boston where he served as an associate in the department of pediatrics at Harvard from 1934 until his death in 1946. The position he had left in pediatrics at Yale was filled by the appointment of Daniel C. Darrow and, at Western Reserve, by Paul György. Shohl was one of the pioneers who helped establish full-time research in clinical departments on a firm basis.

His years in Boston were particularly pleasant and rewarding. Among the persons whose names appeared with his as coauthors of scientific papers were Kenneth D. Blackfan, Louis K. Diamond, Sidney Farber, S. B. Wolbach and Elsie MacLaughlin. They studied the pathology of experimental rickets, the action of dihydrotachysterol on various types of experimental rickets, the effect of intravenous administration of casein hydrolysates or of mixtures of crystalline amino acids in solution to infants, especially those with acute gastrointestinal disturbances, and various simplified methods of measuring red cell volume for hematological studies. During the course of his continued studies of experimental rickets at Harvard, Shohl made the interesting observation that citrates served a useful purpose by promoting the calcification of the bones. Later, with Allan Butler, it was shown that the administration of citrates to rachitic children could cure rickets without the giving of vitamin D.

Shohl's last paper was on nitrogen and fat metabolism of infants and children with pancreatic fibrosis, with Charles D. May and H. Schwachman published in 1943. The last years of Shohl's life were marked by recurring illnesses until, finally, on 25 March 1946 he succumbed to a heart attack. He was buried in a little cemetery on a hilltop in Wolfeboro, NH, not far from his longtime summer residence on the shores of Lake Winnipesaukee, whose clear waters offered inspiration as well as respite from his thinking and writing about the problems of nutrition of infants in health and in disease.

Shohl liked few things better than working in the laboratory. He was a competent glass blower and enjoyed making apparatus to fit a special need. He described new and simpler methods for calibrating small pipets and burets. He also described a tube for the convenient determination of both pH and carbon dioxide on a single small sample (such as 0.1 ml) of blood plasma or serum. His brief note describing this device is illustrated by a drawing which Shohl proudly stated had been made by his son, Theodore. The boy, who was then about 10 years old, had indeed worked hard at his task and produced a commendable drawing.

Some of Shohl's apparatus and suggestions are revealing of the times when he worked. For example, his directions for making solutions of glucose and of sodium bicarbonate for intravenous administration, which were useful directions, remind us today that there was a time when all solutions for parenteral administration to patients had to be made up in the laboratory or hospital that wanted them. In 1931, Shohl described a frame for holding small rats for photographic or operating purposes. The principal reason for developing this apparatus was to avoid exposure of one's fingers to Roentgen rays while holding rats for x-ray photographs. At the time, the dangers of Roentgen rays to the operators of x-ray equipment were recognized and were being publicized. Many x-ray photographs previously included pictures of the tips of two thumbs and index fingers of the experimenter who was holding the little animals spread-eagled for the pictures.

Shohl's versatility and creativeness made him a valuable member of the White House Conference on Child Health and Protection, which was active from about 1929–1932. This conference was initiated by President Hoover and financed by private funds. Shohl was made a member of the committee on nutrition, which published a

book-length report in 1932. He contributed most of the material on minerals in nutrition, the pages dealing with food analysis and other material. The report summarized what was known at the time concerning infant and child nutrition, recommended areas for further study and exerted considerable influence for many years.

Prof. Mendel suggested to Shohl that he put together the information he had shared with the White House Conference, plus other material, as a volume for the American Chemical Society's series of scientific monographs, of which Mendel was an editor. That is how Shohl's book, Mineral Metabolism, came to be written. As has been mentioned, it was not published until December 1939. The book is in its way a small classic. Shohl compiled in brief, almost laconic form a vast amount of information, critically evaluated, concerning the physiology of the body as viewed through the behavior of its inorganic constituents. In his evaluation of data in the literature, Shohl was always looking for a complete understanding according to basic principles. He was elated, for example when, while studying published data concerning the concentration of chlorine in the body at different ages, he found a rational explanation of why its concentration (and that of sodium) decreased with age, while the concentration of all other major mineral elements increased. Older workers had frankly stated that they were puzzled. Shohl listed all available data and then tried relating the concentrations to the water content of the body. To his delight, the relation proved to be roughly constant as, he said later, should be expected if osmotic pressure is to remain constant in the body fluids. Shohl's book remained on the recommended reading list for students at Harvard Medical School for more than 25 years after its publication.

In his book and in some of his scientific papers, but more often in personal conversation with friends, Shohl mentioned three unsolved problems concerning balance studies in nutrition and their use and interpretation. One was the fact that with each increment of increased intake of calcium, experimentally with young adults, correspondingly greater retentions of this element are found. The question then arises: What is the calcium requirement? A relatively recent paper by Hegsted (J. Nutr. *106*, 307-311, 1976) indicates that this question has not yet been answered satisfactorily. Another problem was the fact that in infants the feeding of cow's milk formulas, unless the milk is greatly diluted, produces greater retentions of nitrogen, calcium and phosphorus and greater gains in body weight. Are faster growing babies better off in the long run than babies reared on human milk? The consensus of leading pediatricians has favored better growth-producing feedings, but there always was, and still remains, the specter such as McCay's observations, that restriction of food early in life produced slower growth but prolonged the life span of his rats.

The third problem Shohl did try to solve but without success. He fed rats diets which differed considerably in the ratio and level of calcium and phosphorus and found, even when the animals had nearly reached mature body weights, that the balances of calcium and phosphorus continued to reflect the ratio in the diet consumed. Thinking that this phenomenon might involve, if long continued, a change in body composition, Shohl killed his animals and determined their composition in terms of calcium and phosphorus. He found no differences in composition. The interpretation of his data from balance experiments and the data from body composition simply failed to supplement each other. Shohl often expressed a wish to continue experiments to try to resolve the puzzle, but facilities and time, especially time, during an all too short lifetime did not permit.

Shohl was married twice. His first wife was Alice Eichberg of Cincinnati who had attended the same high school as Shohl and then graduated from Bryn Mawr College. She died after a brief illness in 1929, leaving two young children. In time, these children, Jane and Theodore, became physicians, Jane also earning a Ph.D. in psychology. She and her husband, Dr. Charles G. Colburn, and family now live in Westford, MA. Theodore is now a practicing

surgeon in Anchorage, AK. Shohl's second wife, Florence, was a daughter of Dr. and Mrs. Cozad of Cuyahoga Falls, OH. After working with the Grenfell Mission in Labrador, she was employed as a technician at the Babies and Childrens Hospital in Cleveland and worked for a while with Shohl. She became a devoted mother to the two small Shohl children, helped Shohl with the manuscript of his book and nursed him during the distressing illnesses the last years of his life. They had one daughter, now Kathryn Shohl Scott, who lives in Washington, DC with her husband and children. Florence Shohl continued to live in their home in Cambridge, taught in public and Quaker schools in Massachusetts for about 25 years and then died of cancer. Shohl is now survived by three children and 12 grandchildren, two of whom bear Alfred as their middle names in his honor. Shohl was only 56 years old when he died but he left a heritage which seems to grow, as memories of him who got so much fun from working in the laboratory seem to intensify and not fade with the years.