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ROBERT FRANKLIN PITTS

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A Biographical Memoir by

ROBERT W. BERLINER

AND GERHARD H. GIEBISCH

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GERHARD H. GIEBISCH

THE SCIENTIFIC CONTRIBUTIONS of Robert Franklin Pitts have been a major force in molding the shape of renal physiology in the last half-century. There are few aspects of kidney function that he did not explore, and his work illuminated each element that came under his scrutiny. But his contributions to physiology were not limited to the study of the kidney. He produced important work in neurophysiology early in his career, making contributions that for many would be sufficient to lend prestige to the work of a lifetime, but that Bob Pitts was able to accomplish in only a few short years.

Robert F. Pitts was born in Indianapolis on October 24, 1908, the younger of the two children of John Franklin and Estelle Coffin Pitts. His sister Rebecca, three years his senior, has provided much of the information about the family background, childhood, and upbringing of her younger brother. Both parents were members of the Society of Friends and traced their ancestry back to the earliest days of Quakerism. They had known each other since childhood and were married in 1899, moving to Indianapolis the same year. According to Rebecca Pitts: "Because John Franklin Pitts had been a farmer's son, he was ill-equipped for city life, and for several years the young couple was very poor. In fact, throughout

Robert's childhood and youth our circumstances were, though not poverty stricken, certainly marked by severely necessary economies and occasional periods of real hardship. . . . Until Robert was about fourteen his social life was limited to membership in church youth groups. Our parents had strict notions about keeping us at home in the evenings. . . . Such an environment gives lessons in the old Puritan virtues of discipline and industry, economy and careful planning; and my brother learned them very well."

At Butler University, which he entered as an undergraduate a month before his seventeenth birthday, he did very well. According to his sister's account: "He was a member of Phi Delta Theta—a fraternity noted more for football, at least on the Butler campus, than for scholarship. But the Phi Delts were proud of his scholarship . . . and elected him president of the chapter. . . . Although he was never an athlete he was a good tennis player, and in his high school and college years spent many summer afternoons or early mornings on the court."

After receiving the Bachelor of Science degree from Butler at the age of twenty, Bob was awarded a fellowship in biology at Johns Hopkins University. It had been his intention, first expressed at the age of four (!) in admiration of the family doctor, to study medicine. It may be assumed that to obtain a Ph.D. in a basic science was, in view of his financial limitations, a practical step toward his long-term goal. In any case, having had a taste of research in pursuit of his first doctoral degree, it became clear to him that research rather than the practice of medicine was his real passion.

Bob joined the Department of Physiology at the New York University College of Medicine in 1932, fresh from his doctoral work in biology at Johns Hopkins. His dissertation work had dealt with physiological processes in amoebae; having obtained his Ph.D., however, he closed the book on that field and never returned to it. In the 1930s, the NYU Department of Physiology was the center of an intensive exploration of the function of the kidney. Leadership in renal physiology at that time was divided between the group under Homer Smith at NYU and that led by A. N. Richards at the University of Pennsylvania. The approaches of the two groups were quite separate and distinct. Richards and his associates were developing and applying the early and—by latter-day standards—primitive micropuncture techniques. Homer Smith always considered his greatest contribution to experimental physiology to have been the trained, intact, unanesthetized dog. Indeed, except for diversions into work with fish in the summers at the Mount Desert Island Biological Laboratory in Salisbury Cove, Maine, work in the NYU Department of Physiology stuck pretty closely to the intact dog (or occasionally man), and Bob Pitts's work was no exception. In fact, his preference for the intact animal (although not necessarily unanesthetized) was reflected in his experimental work throughout his career, even when most others had shifted, with greatly improved instruments and techniques, to the trail of A. N. Richards and micropuncture.

From 1932 to 1938, Bob Pitts was an active and productive member of the physiology department. His first paper from his new environment at NYU dealt with the relationship between the excretion of inorganic phosphate and the plasma phosphate level in the dog. The subject matter of this work is noteworthy because it was a later and more definitive study of phosphate reabsorption by the renal tubules that led to what most would consider to be Bob Pitts's most important single contribution to renal physiology: his work on acidification of the urine. During this first six-year period at NYU, Bob explored the renal mechanisms involved in the excretion of a number of substances: creatine, urea, xylose, hexamethenamine, ammonia, and phenol red. The work was a significant contribution to the state of the art at the time, although it did not lead to any major new fields of study or new ways of looking at renal function.

During this period, however, Bob found time to enroll as a medical student and, while continuing his work in the laboratory, managed to complete the work for the M.D. degree that he was awarded in 1938. It is clear, moreover, that his completion of medical school was not accomplished in an offhand way: he graduated at the head of his class and received a medal for his work in pathology, as well as the senior prizes in both medicine and surgery! Although he never chose to develop his obvious talent for clinical activities, his thorough grounding in medicine influenced all his subsequent efforts, and he never failed to orient his fundamental physiological work to clinically important problems and to call attention to the relevance of his findings to medicine.

Those whose exposure to biomedical science has been limited to the more recent era of relative affluence and availability of research funds may imagine that Pitts's coworkers and technicians kept things running in the lab with only periodic guidance from him, thus allowing him to continue his research in the laboratory while giving unstinted attention to the medical school curriculum. Nothing could be further from the truth. He did all of his own experiments and all of the analyses himself. It is also probable, although undocumented, that he washed his own glassware. Nevertheless, in that six-year period, he published twelve highly creditable papers, and he was the sole author of eleven of them.

Upon graduation from medical school, he chose to launch into a new field and, as a fellow of the Rockefeller Foundation, he spent a year at Northwestern University in the laboratory of Magoun and Ranson and the subsequent year in the Johnson Foundation laboratories at the University of Pennsylvania with Detlev Bronk. (Both of these were leading laboratories in what would now be called neuroscience.) Although many would hold that one year in a laboratory is hardly enough time to accomplish anything much, particularly in a new field, it is apparent that this rule did not apply in this instance. The immediate output of that brief period was eight papers; for seven of them, Pitts was the senior author. Moreover, he did not merely fall in step with projects already under way. He built his own electronic equipment and launched into a new field: the study of the medullary respiratory centers and related phenomena. The judgment of those familiar with the field appears to have been that these were important contributions to neurophysiology. Some six years later, when he had already established himself as the leading contributor to renal physiology, he was still the author of textbook chapters on the regulation of respiration. In fact, he held what must have been a unique distinction in writing, by invitation, a review entitled "Organization of the Respiratory Center" for *Physiological Reviews* and the chapter on the kidney in *Annual Reviews of Physiology*, both in the same year (1946).

In 1940 he returned as an assistant professor to the Department of Physiology at NYU. For two years he continued his studies on the control of respiration and then moved a short distance up the east side of Manhattan to join the Department of Physiology at Cornell University Medical College. It had been his intention to continue his work in neurophysiology, but the expense of establishing a new laboratory based on electronic equipment, and the difficulty in obtaining financial resources to do so, led him to abandon that plan. All that was needed for his work in renal physiology was a little glassware, some chemicals, and a few trained dogs; so he returned to the study of the kidney. The next four years in New York were a period of productivity that included what Bob himself considered to be some of his best work. It is easy to concur with his judgment without disparagement of the enormous value of his many contributions in subsequent years.

The first few papers that Bob Pitts produced after taking up his position at Cornell dealt with the mechanisms for the reabsorption of amino acids by the renal tubules. He then returned to work on the reabsorption of phosphate, which was described in a paper with Robert Alexander as coauthor: "The Renal Reabsorptive Mechanism for Inorganic Phosphate in Normal and Acidotic Dogs." The essence of this paper was that phosphate was reabsorbed with a saturable transport process and that the capacity of this transport process was not affected by changes in the acid-base status of the animal.

Many years later, in a 1971 paper entitled "Some Aphorisms on Research and Writing," Bob related how this study led to his work on the mechanism of urinary acidification. It seems that Bob presented the results of the study at the Cornell Research Society, where his statement that phosphate reabsorption was not increased by acidosis was challenged by one of his biochemist colleagues. This colleague stated that inasmuch as it was well known that the urine is rendered acid by the reabsorption of disodium phosphate, leaving behind the more acid member of the buffer pair, the reabsorption of phosphate must increase in acidosis when the excretion of acid in the urine is increased. Bob thought for several months about that conflict between theory and data, and he concluded that the phosphate reabsorption data were not wrong but that the mechanism postulated by his biochemical colleague probably was. In fact, Bob's mentor, Homer Smith, the theoretician and philosopher of renal physiology, had suggested a different mechanism some ten years earlier: namely, secretion of hydrogen ion by exchange for fixed cation. Neither hypothesis had ever been tested. Bob decided it was time to do so. The experiment that he designed to examine the alternatives was beautifully conceived to provide a definitive answer. According to Bob's account, and the story is confirmed by Robert Alexander, his collaborator and coauthor of the resulting paper, Bob wrote the entire paper—minus only the data—before they carried out the first experiment! Clearly, the results were all he could have hoped for, showing that hydrogen ion secreted by the renal tubules was indeed responsible for acidifying the urine. The paper, "The Nature of the Renal Tubular Mechanism for Acidifying the Urine" appeared in the *American Journal of Physiology* in 1945. It was considered to be absolutely definitive and a landmark of renal physiology. Bob's older sister tells us that their mother was fond of saying, "Plan your work, then work your plan." Bob had learned the lesson well.

The paper on acidification of the urine established Robert F. Pitts as the leading investigator in renal physiology, but it was only the beginning of a series of studies in which he explored a number of related aspects of renal function: the reabsorption of bicarbonate by the tubules, the factors governing the rate of excretion of titratable acid, and the renal tubular reabsorption of chloride. In addition, a paper with William Lotspeich, "The Role of Amino Acids in the Renal Tubular Secretion of Ammonia," introduced a subject that in later years was to be the focus of Bob Pitts's major line of study.

In 1946 Pitts left Cornell to assume the chairmanship of the Department of Physiology at Syracuse University (the school of medicine that subsequently became the State University of New York Upstate Medical Center). The move was accomplished without any apparent discontinuity in his research. With a new group of younger associates, the work on acidification and bicarbonate reabsorption was extended to the normal human, using the investigators as subjects. The interests of Bob and his series of younger associates were not, however, limited to acid secretion by the tubules and related phenomena; while he was at Syracuse, papers appeared dealing with the effects of adrenal hormones on electrolyte reabsorption and excretion and on the effects of mercurial diuretics. The latter were his first venture into the study of diuretics and their site and mechanisms of action, an area of investigation that was to be an important element of his work over the next decade.

In 1950 Pitts returned to Cornell as the chairman of the Department of Physiology, a position he held until 1973, shortly before his retirement from the university. Bob was a conscientious chairman and a devoted teacher. His lectures were carefully prepared and models of clarity. In addition, he placed great importance on the teaching efforts of the members of his department. He regularly attended *all* the lectures in the course in physiology throughout the period of his chairmanship and participated enthusiastically in the student laboratory exercises.

The stream of published reports of first-rate work was never interrupted during the period of his chairmanship. This was the case despite problems of illness, both of his wife and of himself, that began in the middle fifties and were to plague him through the remainder of his life. His wife was stricken with progressive, incapacitating neurological disease that caused her to be bedridden for many years, during which Bob devoted great personal effort to her care. And Bob himself was the victim of at least three ailments that might have led a less dedicated and determined man to give up. In 1958, when one of us was his companion on a mission to the Middle East for the Unitarian Service Committee, his pockets contained a medicine cabinet's assortment of prescribed medications. Nevertheless, through the years Bob not only continued his extraordinarily productive activities but also adhered to his practice of doing a great deal of the laboratory work himself. In fact, he not only did most of the laboratory work he also built much of his own apparatus, including an early flame photometer for the measurement of sodium and potassium, and later an amino-acid analyzer. Throughout his career he washed his own glassware and insisted that others follow his rigid protocol for achieving adequate chemical cleanliness. He later explained his participation in these activities by noting that "some of my best ideas have come to me when I'm performing some routine analytical chore."

His work explored many areas of renal physiology. He strayed from the kidney only slightly and for a brief period when he, along with Roy Swan and Gerhard Giebisch, defined the extrarenal buffering of acid and base loads. An excellent series of papers dealing with the site and mechanism of action of diuretics, particularly the mercurial diuretics that were then the therapeutic mainstay, appeared seriatim from 1950 to 1962. His studies of the potentiation of the diuretic effect by acidifying salts and of the relationship between structure and activity among the mercurial diuretics led him to conclude that the effect was probably on the transport of chloride and attributable to the intact molecule. This contrasted with the inference of others that dissociation of the mercury was necessary for the effect that was thought to be produced on the transport of the sodium ion. Studies nearly twenty years later with isolated tubules have shown that the Pitts interpretation was correct.

Except for a brief dalliance with the stop-flow method in some of his studies of diuretics, Bob stuck pretty much to the intact kidney, often using the intact dog. Even when his own department became one of the leading centers of micropuncture work, Bob Pitts steered clear of that method. In part, at least, he explained this decision in one of his "aphorisms on research" in the paper referred to earlier. "Pick an area in which there is no, or at least little current research activity," he advised. The reason: The investigator can develop his ideas without pressure to publish to establish priority. He followed his own precepts studiously, followed his own course unpressured by the work of others, and never published a trivial paper or a wrong one.

In the last dozen years of his work, Bob returned to the area that he had opened up in his studies of acidification of the urine and explored that other element in the regulation of acid-base balance, the excretion of ammonia. Almost everything beyond the initial identification of glutamine by Van Slyke and his associates that we know about the sources of ammonia and the renal processes involved in its excretion is based on the work of Bob Pitts.

In 1974 Bob Pitts accepted emeritus status at Cornell and moved to the University of Florida in Gainesville where he held the rank of Research Professor in Renal Medicine and Physiology. Unfortunately, his health, for a long time far from robust, deteriorated further, and he was able to add little to the list of his magnificent accomplishments before his death on June 6, 1977. It might be said that, in the last half-century, if Homer Smith was the high priest of renal physiology, then Bob Pitts was surely the builder of its temple.

AWARDS AND DISTINCTIONS

1948 American Society of Clinical Investigation
1956 National Academy of Sciences
1957 American Academy of Arts and Sciences
1959 President, American Physiological Society
1960 President, Harvey Society
1960 Borden Award in Medical Science
1962 New York University Medical Alumni Award
1963 First Homer W. Smith Award in Renal Physiology
1967 Honorary Master's Degree, Oxford, England
1970 American College of Physicians Award for Distinguished Contributions in Science as Related to Medicine
1972 Association of Chairmen of Departments of Physiology, First Annual Award for Distinguished Contributions to Physiology
1972 Honorary Fellowship Award, Cornell University Medical College Alumni Association

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