

# John P. Peters

## 1887-1955

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John Punnett Peters died on Dec. 29, 1955, at the age of sixty-eight, bringing to a close an illustrious career in scientific and academic medicine. Dr. Peters was one of those leaders in American medicine who exemplified in his own life and work the ideal qualities of the scientist, teacher, physician, and citizen.

Were Thomas Carlyle alive today to add to his lecture series "On Heroes, Hero-Worship, and the Heroic in History" he could well use him as "The Hero as Scientist." Beginning in 1916 and continuing for thirty-nine years, a steady stream of articles, monographs, and books, 199 in all, emanated from his pen, each one a significant contribution to the science of medicine. No other single man has done more to make physiology and biochemistry an integral part of medicine today. For thirty-four years at Yale, first as Associate Professor and then as John Slade Ely Professor of Internal Medicine, he maintained a center dedicated to the application of physiological and biochemical knowledge to the diagnosis and treatment of disease in man. In his later years he often quoted Pope's line: "The proper study of mankind is man" to emphasize the importance of directing medical research toward man himself, rather than toward other species. Not one of his own investigations was made on animals. His method of experimental approach remained essentially unchanged throughout his career and could well serve as a model to all clinical investigators. Of prime importance to him was an intimate and firsthand knowledge of the patient and his disease. In the laboratory he insisted on accurate technics, making Yale a model of what a good laboratory of quantitative clinical chemistry should be. He had an intense scorn for those hospitals, no matter how famous, where double standards for "routine" and "research" chemical technics existed, for in his own laboratory the same procedures were applied to both, and duplicate determinations were done without exception in all analyses. This enabled him at any time to use data obtained from patients at New Haven Hospital for the study and interpretation of disease processes. Accurate and detailed records were kept on every determination, often in his own hand, so that he could describe quantitatively the various biochemical changes that take place

in each group of diseases. Description of data was only the beginning of his scientific contributions. His keen critical evaluation of results of others as well as of his own, and his ability to synthesize and clarify his own points of view resulted in major advances in concept and therapy of metabolic disorders. Finally, in attempting to describe his scientific approach, it is worthy of note that he seldom resorted to planned experiments in humans which would involve any hazard, great or insignificant. He was content with studying the changes that nature herself performed in the guise of disease. His research covered a wide spectrum of subjects, including acid-base equilibrium, respiratory physiology, water and electrolyte metabolism, renal disease, thyroid function, pregnancy, cardiac failure, gastrointestinal metabolic disorders, diabetes mellitus, and other endocrine disturbances, and the metabolism of protein, fats and carbohydrates. Dr. Peters' scientific contributions played an integral part in the development and growth of quantitative clinical chemistry, in the broadest sense of the term, from its smallest beginnings to the stature and maturity it fulfills in medicine today. No other single work epitomizes this so well as the monumental "Quantitative Clinical Chemistry" written in 1931 and 1932 with Donald Van Slyke and published in two volumes, "Interpretations" and "Methods." Although he had time to revise only part of this by 1946, it still remains the classic in its field.

John Peters' contributions to diabetes encompassed almost every facet of the problem, twenty-six papers relating to the subject testifying to his interest. An experienced clinician, alert to the nuances of the disease from patient to patient, he strengthened his knowledge by continuous observations in the office and at the bedside over a twenty-four-year period. He had a firsthand experience with the natural history of diabetes and as such was fully aware of the problems of clinical management and the development of the dreaded vascular complications. He coupled this with his laboratory investigations in various spheres. In 1917 he wrote about the relation of adrenalin hyperglycemia to decreased alkali reserve of the blood. In 1923 the effect of infection in diabetes was reviewed. He was interested in the

plasma proteins, particularly in diabetic acidosis, finding that the actual levels were often obscured by the hemoconcentration present. These studies clarified the role of hypoproteinemia and excessive alkali administration in the causation of "diabetic edema." The nutritional disturbances seen in severe uncontrolled diabetes focused his attention on the effects of starvation, culminating in his stimulating paper in 1945 on "Starvation Diabetes, the Reason for the Use of Glucose in the Treatment of Diabetic Acidosis" (*Yale J. Biol. & Med.* 17:705, 1945). This masterful summary of a controversial aspect of treatment is concluded with the following statement: "The ultimate solution of this question must rest upon the sound assemblage of physiological evidence, supported by controlled clinical observations, not by *ad hoc* arguments from particular cases. An attempt has been made to array in some semblance of order the most significant items in the great mass of evidence that carbohydrate should be used in the treatment of diabetic acidosis because it promotes the oxidation of glycogen, supplements the action of insulin, reduces the destruction of protein, and diminishes the production of ketone bodies." The work of Seldin and Tarail in his laboratory caused him to consider the undesirable features of glucose administration—polyuria, loss of salt, and dehydration. He avoided this dilemma in 1954 (*Yale J. Biol. & Med.* 27:152, 1954) by advocating the substitution of fructose for glucose, based on physiological and clinical evidence that "fructose is removed from the blood of the patient with diabetic acidosis as rapidly as it is from the blood of a normal person. . . . Moreover, perhaps because of the advanced point at which it enters the chain of oxidative reactions, a certain proportion of it can be utilized. Although it may contribute to blood glucose, if given rapidly, moderate amounts produce little or no hyperglycemia. Fructose solution is, therefore, an ideal vehicle for the parenteral administration of water in diabetic acidosis and at the same time provides some utilizable sugar."

Other aspects of diabetic acidosis were investigated. As early as 1925, in a study of fifty-three cases of diabetic acidosis, he proved that "in profound diabetic toxemia the salt content of the blood and probably that of the tissues is seriously depleted" thus laying the foundation for the routine use of saline in treatment. The importance of these observations was overlooked by some of the leading diabetic clinics for many years. In 1946 a careful analysis of the 188 cases of diabetic acidosis observed over a period of more than twenty years revealed a striking correlation between the degree of salt depletion, the occurrence of peripheral vascular

collapse, and the mortality rate. Here again careful clinical and laboratory observations resulted in important contributions to rational therapy, the use of saline and plasma expanders (*Yale J. Biol. & Med.* 18:405, 1946).

He next became interested in some of the electrolyte changes in red blood cells in diabetic acidosis, finding that there was extreme depletion of phosphates and base (*Am. J. Phys.* 149:667, 1947). The impairment of the glycolytic process in the blood in some cases of severe diabetic acidosis was found to be correlated with depletion of organic acid-soluble phosphate (*J. Applied Physiol.* 5:647, 1953).

Beginning in 1934 the lipid fractions of the serum in diabetic acidosis and in controlled diabetes were investigated (*J. Clin. Invest.* 13:237, 1934; 14:579, 1935; *Metabolism* 2:120, 1953). The elevation of lipids found in diabetic acidosis was largely due to hemoconcentration. Detailed analysis of seventy-nine diabetic patients not in acidosis showed that the level of cholesterol was not related to severity of diabetes, the amount of fat in diet or the degree of arteriosclerosis. Here again the laboratory helped the clinician clarify his problems, this time in the area of fat metabolism.

Significant contributions were made in other areas related to diabetes. Arteriovenous blood sugar differences in normal and diabetic subjects and the effect of insulin were determined (*J. Biol. Chem.* 80:269, 1928; *Arch. Int. Med.* 43:633, 1929). Four cases of intercapillary glomerulosclerosis with autopsy findings were reported in 1939 (*Arch. Int. Med.* 64:1252, 1939). The rapid intravenous tolerance test, employing 50 cc. of 50 per cent glucose, was described in 1941 (*J. Clin. Invest.* 20:507, 1941). This test is now a standard diagnostic procedure in many clinics, because of the avoidance of variations in intestinal absorption of glucose, and its reproducibility under standard conditions. The problem of diabetes and pregnancy was not overlooked, the clinical experience being reviewed and systematically analyzed (*Yale J. Biol. & Med.* 16:151, 1943).

Last, but by no means least, must be cited the articles summarizing his ideas on the management of diabetes (*Rhode Island Med.* 21:1, 1938; *New Internat. Clinics* 2:171, 1941; *Yale J. Biol. & Med.* 27:53, 1954). The 1954 article can justifiably be called a "classic," written with elegance and felicitous phrase and emphasizing rational therapy based on sound physiological and biochemical facts. This is combined with the realization that the doctor must retain the humanistic and personal point of view. A few quotations will illustrate his approach: regarding objectives, "The objective in the treatment of any chronic disease should be

to enable the patient to enjoy as full and untrammelled a life as possible. Medicine should not be entirely negative and restrictive. It should especially avoid emptying life of the features that give enjoyment and a sense of accomplishment. The therapeutic regime should not make the patient conspicuous; his ailments are his own business. With insulin preparations that are now available the diabetic should be enabled to pursue a normal course of life with no lets or hindrances other than adherence to a diet, injection of insulin, and analysis of urine, except as these may be necessary to meet complicating or associated disorders. The patient with advanced arterial disease cannot profitably return to digging ditches. Since all the activities and vicissitudes of life influence the course of diabetes, no satisfactory therapeutic regime can be established or adjusted in a hospital. Hospitalization is necessary or desirable only for the management of complicating conditions or emergencies." On diet: "To place the full onus for infractions of dietary and other regulations upon the patient is an evasion of responsibility by the physician, whose prior assumption should be that the regime has been improperly devised. To upbraid the patient as if weaknesses were sins may destroy the frank relations that should prevail between physician and patient. To invoke fear is cruel. Lapses should be met with sympathy and understanding, their consequences explained with kindly reason. Self-righteousness on the part of the physician does not benefit the patient. An honest compromise, even though not altogether desirable, may be necessary. A little liberty is better than license." On complications: "A careful investigation of the natural history of diabetes promises greater returns. The sad realization has been reached that a large proportion of children afflicted with the disorder follow the pattern of adults with respect to vascular disease. This majority in both groups is, however, no more important than the minority that mysteriously escapes these evils, or, since the life history of the young diabetic is still to be written, has managed to survive without them far beyond the general expectation. It is too early to congratulate ourselves and somewhat ridiculous to blame patients for the incidence of these associated complicating conditions. Some of the most medically virtuous have succumbed early, while rascals have escaped. I will not say that only the good die young; but experience has convinced me that in this, as in many another panel of life, virtue too often has to be its own and only reward."

No assessment of Dr. Peters' contribution to diabetes can close without citing his critical and encyclopedic

review of carbohydrate metabolism in *Quantitative Clinical Chemistry*. In the first edition published in 1931 this covered 147 pages with 481 references. The rapid growth of knowledge in the field is shown by the increase by 1946 to 273 pages with 1,316 references. Every sentence in the review bears witness to his ability to analyze and synthesize this vast area of metabolism.

Jack Peters' place in American medicine is further strengthened by his influence on students, both undergraduate and postgraduate. In teaching he always aimed at the highest level because he firmly believed that medical students should be treated as adults who were not to be spoon-fed but rather stimulated and provoked to think. Many a student still recalls vividly his quick and caustic remarks when opinions, unsupported by logic or data, were voiced. This uncompromising attitude toward ignorance or faulty reasoning was directed not only at students, but at all levels, so that even his colleagues and peers chose their words with care in his presence. His famous "Metabolism Rounds" at Yale, held thrice weekly, were memorable for many reasons. He spoke softly and with little facial expression, so that from a distance his rounds could be identified by the huddle of his disciples straining to catch his every word (lip-reading became an invaluable aid!). His nimble and facile mind, fortified by his tremendous knowledge of experimental clinical medicine, would frequently leap-frog many steps in the reasoning that culminated in the often brilliant interpretations or diagnoses at the bedside, to the despair of those less well-versed in the field. But as one's own knowledge increased, the appreciation of his abilities increased geometrically, and it is perhaps the young men who were trained in his metabolic service and laboratory who owe him the greatest debt for the stimulation and insight he provided into clinical medicine and investigation. The later years of his life were blessed by the knowledge that so many of his "boys" had gone out to other medical centers to establish islands of teaching and investigation in the metabolic field.

Those who did not see him function in his own hospital environment did not always appreciate his abilities as a physician. In a famous radio debate on the social aspects of medicine late in the thirties, the defender of the status quo of the practice of medicine, confronted by the overwhelming logic and carefully considered facts presented by Dr. Peters, retorted by saying that Dr. Peters might be an authority in chemistry but was not qualified to give any opinion on the subject under debate because he was a "professor" who knew little about patients and disease. In reality Dr.

Peters was an able and expert physician, skilled in every aspect of the care of the patient not only on the organic side but also in the psychological sphere. He was always quick to point out the importance of the emotional aspects, especially the impact on metabolic functions, as in diabetes and thyroid disease. His house officers soon learned not to relegate every emotional problem to the psychiatrist, for Dr. Peters believed strongly that the physician responsible for the organic aspects of disease was best qualified to evaluate these factors. As a full-time teacher on salary, he never collected any fees for himself, yet every patient on his service or whom he saw in his office received from him the best possible type of medical care. This individual approach to the patient, epitomizing the highest level of physician relationship, nevertheless was coupled in his mind with the recognition that the inevitable increase in laboratory medicine would force a great expansion in institutional equipment and in group cooperation of professional and other ancillary medical personnel. He felt strongly that the day had passed when the problems of medicine could be handled by the individual private physician practicing entirely out of the little black bag. Aware also of the economic consequences of the enormous growth in medical knowledge he entered actively into the controversies surrounding methods of medical care and from 1927 until 1954 served as secretary of the Committee of Physicians for the Improvement of Medical Care. As such he frequently became the target for vilification and slander by the more conservative members of organized medicine. He was convinced that comprehensive health coverage was not only necessary but inevitable and that it was the responsibility of physicians to experiment in that direction, just as much as in the problem of disease itself. His great fear was that the medical profession, by blind opposition to change, would lose its opportunity to control and improve the practice of medicine, thus allowing those lay people concerned only with the economics of medicine rather than quality of medical care to develop the pattern and rules.

It was as a citizen that Dr. Peters, the "Hero as Scientist," was best known to the public in the last few years. During World War II he conducted investigations for the Air Force on survival rations and for the National Research Council on nutrition in injury and disease. The Quartermaster Corps used him as a Consultant and after the War he was appointed a Consultant to the Army Medical School. From 1947 to 1954 he served on the Study Section on Endocrinology and Metabolism of the National Institutes of Health in the

Public Health Service. His advice was sought on all sides by many interested in metabolic research and he never failed to give unstintingly of his time and knowledge.

Socially and politically he was a liberal and progressive, a natural consequence of his distinguished American heritage which dated back more than three hundred years to prerevolutionary days. There is a letter on record of one Abigail Peters written to the presiding judge of the Salem assize, protesting the witchcraft trials. His father was an eminent member of the clergy and an archeologist of note who was very active in civic affairs and who had a reputation for being a militant advocate of causes he considered just, often upsetting the complacency of his wealthy New York parish. His scholarship, broad interests, and deep moral sense of social responsibility had a significant influence on his son. With the upsurge of McCarthyism after World War II, Dr. Peters' liberalism became suspect and on the basis of anonymous information he was discharged in 1953 from his position as consultant to the U. S. Public Health Service on its study section for metabolism. This was despite the fact that he had received loyalty clearance in 1949 and in 1952. His case, supported by professors from the Yale Law School and a former U.S. Attorney General, was carried through to the Supreme Court, and resulted in complete personal vindication. To his great sorrow, however, the court failed to rule decisively on the fundamental constitutional question of the right of an accused person to face and crossexamine his accusers. Nevertheless, he had succeeded in calling attention forcibly to important questions of possible encroachment on the basic civil liberties of his fellow citizens.

To describe Dr. Peters as a person is difficult. Dr. J. Russell Elkinton's remarks to the Interurban Club must be quoted: "John Peters was not a simple man in his mental or emotional life, nor was he always an easy man with whom to be associated. Almost every activity that he undertook he undertook with intensity. He was intense, nay even passionate, whether he was playing tennis, growing roses, playing the piano, or indulging in controversy with one of his cherished scientific or economic adversaries. His capacity for criticism was tremendous and often devastating. Perhaps one of the sad ironies of his life was that his criticism was often so penetrating that it was feared, and hence his advice was less sought after and his wisdom was less influential in the world of American medicine than it might otherwise have been. But underneath his critical exterior he had a kind heart; sooner or later

each of his associates came to appreciate this fact as "The Boss" helped him to meet some of the vicissitudes of life.

The genius of John P. Peters consisted to a great extent in the coupling of a razor-sharp critical mind with a profound knowledge of the experimental literature; it can be said that rarely did a problem probed by him remain entirely unclarified, and seldom did the probing thereof fail to open new vistas of inquiry. And yet he was a more complex individual than that. The essence of the man lay in his integrity. Above all else he abhorred hypocrisy, he abominated sham, he deplored complacency. And if he appeared to be hypercritical and to be in constant revolt against the established order, the cause usually lay in his wholehearted

pursuit of the truth as he saw it. Thus to the profession of medicine and to society he brought a mind and a fierce purpose, and his contributions were commensurate."

And finally, the remarks of his attorney, Fowler Harper, Professor of Law at Yale, at the Memorial Service in New Haven serve further to illuminate the portrait of the man: "I think I saw with some clarity the many contradictions of his character—the kindness and the steel, the simplicity and the urbanity, the intricate and the complicated personality, the precision-like mechanism of his mind, the softness and the warmth, the flint-like quality of his courage. In man's long struggle to civilize himself, it would be hard to find better evidence of success."

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## CORRESPONDENCE

To the Editor:

As I have stated elsewhere, observations of symptomatic differences made it evident from the outset that the hypoglycemia of the sulfonylurea drugs is in no sense an insulin hypoglycemia. The mere fact that they are not powerful enough to prevail against the profound collapse of carbohydrate metabolism resulting from total absence of insulin does not imply that this action is insulin-mediated. Insulin accelerates tissue uptake of sugar at the cost of depletion of liver glycogen, while plausible evidence seems to point to an opposite effect of these drugs, namely an action on the liver causing hypoglycemia by increased glycogen storage and diminished discharge of glucose, with less evident augmentation of peripheral uptake. This or any other artificial mechanism may be ground for suspicion of a toxic interference with metabolism and the likelihood of overt injury in the course of time. While it may be granted that the hypoglycemic action is as unphysiologic as the antibacterial action of sulfonamides, the fear of

toxicity except in a few sensitive individuals may be countered by the following considerations. First, the usual effect of hepatotoxins is increase of fat and reduction of glycogen in the liver, and no agent initially increasing glycogen is known to lead to necrosis or cirrhosis. Second, laboratory studies may overlook the fact that utilization of sugar is actually brought about; that is, sugar previously lost in the urine is metabolized, presumably in the peripheral tissues. Third, with recollections of the early debate of overproduction versus underconsumption of sugar, and the modern view that both processes are involved in diabetes, it is conceivable that a slower and more orderly flow of sugar to the blood may precisely suit the need of some patients possessing a moderate supply of autogenous insulin. These theoretical considerations reinforce a clinical experience that small doses of these drugs in suitable patients are truly beneficial.

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## BOOK REVIEWS

COWDRY'S PROBLEMS OF AGEING-BIOLOGICAL AND MEDICAL ASPECTS. Edited by A. I. Lansing, Ph.D., Associate Professor of Anatomy, Washington University School of Medicine, St. Louis, Mo. \$15.00, pp. 1061, 3rd Edition, The Williams and Wilkins Co., Baltimore, 1952.

This book, first published in 1939, has been brought up to date. It is timely, well conceived, and splendidly executed. Every conceivable aspect of the problems of ageing has been ably presented. The forty-eight contributors have been well selected. The magnitude of