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STANLEY ROSSITER BENEDICT

1884—1936

A Biographical Memoir by ELMER VERNER MC COLLUM

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Biographical Memoir

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Stanley R. Benedict.

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It is not possible to give an accurate account of the scientific work of Stanley Benedict without at the same time discussing the parallel history of the researches of Otto Folin. The objectives of their researches were identical, and notwithstanding the difference in their ages, their years of creative work nearly coincided. The lives of both were characterized by sustained endeavor to discover truth. It is the merit of these two men that they succeeded, through many years of intensive investigations, in devising and refining analytical procedures for the determination of minute amounts of the principal nonprotein constituents of blood and urine so that, for the first time, chemical analysis became a highly useful technic for the discovery of the chemical processes in the normal functioning of the body. These new methods also advanced to an astonishing degree the effectiveness of studies of the chemistry of pathological metabolism. In the entire history of biological chemistry no two individuals excelled these men in achievement. In the application of chemistry to the solution of biological problems, their work opened a new era, so that, in respect to knowledge of metabolism, historians will discuss the state of this department of science as it existed before and after Folin and Benedict.

Stanley R. Benedict was born in Cincinnati, Ohio, March 17, 1884, the son of Professor Wayland Richardson Benedict and Anne Kendrick Benedict and his death occurred on December 21, 1936. Stanley's father was professor of philosophy and psychology at the University of Cincinnati. His mother was a teacher and writer. She contributed stories to The Outlook, Independent, Examiner, etc. His maternal grandfather, A. C. Kendrick, was professor of Greek, Hebrew and Sanskrit at the University of Rochester, and a member of the committee for the revision of the King James Version of the Bible.

Stanley grew up in Cincinnati. He was next to the young-

est of six children. A sister, Dr. Mary K. Benedict, was at one time president of Sweet Briar College, but gave up educational work for the practice of medicine in New Haven, Connecticut. In a personal communication she told the writer of this memoir that at home the Benedicts lived in an atmosphere of intellectual inquiry and discussion, and that the family gathered every evening for a short time to listen to reading aloud by the father. They listened to philosophical theory, poetry, Dickens, Uncle Remus, and many more authors.

Stanley was educated in the public schools in Cincinnati, and at the University there. As a boy he planned to practice medicine, and his undergraduate studies at the University included a good many of the medical subjects. However, he became interested in investigative work during his undergraduate years, and abandoned medicine for teaching and research. He was greatly influenced in his undergraduate years at the University by his association with Dr. J. F. Snell, who had earlier worked with Wilbur O. Atwater, famous for his untiring studies in the composition of foods, their digestibility and calorie values, and for his studies on the energy requirements of human subjects at rest and doing various kinds of work. Dr. Snell was, therefore, familiar with all that was known about various aspects of biochemistry, including nutrition. Dr. Snell gave Stanley an insight into the methods and technics of research. It may well have been owing to this association that Stanley went to Yale University for post-graduate study in physiological chemistry. At Yale was the laboratory which had been made famous by Russell H. Chittenden, the first well-trained physiological chemist in the United States. Chittenden had, a few years before Stanley entered Yale, become Director of the Sheffield Scientific School, and his distinguished pupil, Lafayette B. Mendel, had taken over the supervision of graduate students and much of the teaching, but Chittenden still continued to give each year a course in nutrition and one in toxicology. So all the graduate students came intimately into contact with both of these superior men. In 1906, Stanley received his

B.A. degree at the University of Cincinnati and went to Yale, where he received his Ph.D. under Mendel in 1908.

The atmosphere of the laboratory of physiological chemistry in those years was highly stimulating. Mendel was at the height of his powers, intensely enthusiastic, studious and a great teacher. No other physiological chemist had so great an influence upon the medical profession as did he, until after Folin and Benedict had made places for themselves as outstanding contributors to the chemistry of physiological processes. Mendel was a great success as a lecturer, and he kept his graduate students occupied with reading in the fields of physiology and biochemistry, so that most of the more important researches of the past and present were critically examined.

The writer became well acquainted with Stanley during the school year 1906-'07, while working in Mendel's laboratory. We sometimes took long walks together in the environs of New Haven and discussed many topics in biochemistry and the future opportunities for research. Stanley was highly enthusiastic about his laboratory work and his reading in scientific literature. He was fast becoming a highly educated specialist. He was to me a congenial companion with a fine sense of humor. and given to poking a little fun at any one with whom his academic activities brought him in contact, who either kept an untidy desk or who was unskillful in manipulations of chemicals or apparatus. His frequent expressions of skepticism concerning statements of men or books on topics which we discussed showed that he was never superficial in his thinking, and never awed by authority. In all our conversations it was evident that he was a thinker and a critic with uncommon natural endowments.

Under Mendel's direction he studied the paths of excretion of several inorganic elements during his post-graduate years but his originality was apparent even at this time. He independently described a new procedure for separation of barium, strontium and calcium, and a new method for distinguishing between glucose and lactose before completing his work for his degree.

The year 1906 marked a turning point in the history of bio-

chemical studies. Otto Folin published in Volume 13 of the *American Journal of Physiology* three papers which immediately brought him to distinction. The first of these described a new system for the analysis of urine for urea, ammonia, creatine, creatinine, and uric acid. Methods hitherto available for quantitative estimation of these substances were either seriously unspecific, as in the case of urea, or required relatively large samples for analysis, as was the case for uric acid. His new procedures were regarded by biochemists and physiologists as so great a step in advance that Harvard University created a professorship in biochemistry for the humble chemist working in the laboratory of the McLean Hospital for Mental Diseases at Waverley, Massachusetts.

Immediately, in laboratories here and abroad, analyses of urines were made from patients with various kinds of disorders. and the more fertile-minded began to set up experiments on animals for the production of pathological states, and to study the composition of the urine by Folin's methods. Folin, himself. did little further in the way of application of his methods to the study of urines. Instead, he turned his attention to refining and improving analytical methods to a degree which would make possible the determination of the constituents of urine in small samples of blood. He was the first, apparently, to realize that it is much more important to know what the kidneys have failed to excrete, among the products of metabolic activity of the body, and which products, accordingly, accumulate to harmful concentrations in the blood, than it is to know what and how much of these have cleared the kidneys. So he reaped a second great triumph when he first made public the technics by which such analyses could be accomplished. Under his leadership investigators turned at once to the applications of his smallsample, high-accuracy methods to the study of normal and pathological problems in physiology. Folin introduced the colorimeter into biochemistry when he employed this instrument for the quantitative estimation of creatine and creatinine, using the color reaction for creatinine described by Jaffe in 1895. This test depended upon the formation of a red color when a solution of creatinine is treated with picric acid and sodium hydroxide. It reveals the presence of creatinine in a dilution of 1:200,000.

With the publication of Folin's analytical methods for determining quantitatively the principal constituents of urine, clinicians had for the first time methods applicable to the study of patients on a day-to-day analysis of the blood and urine, and the study of disorders of metabolism by the new technics spread rapidly.

For many years the question of the extent of protein digestion in the alimentary tract, the nature of the products absorbed, and the manner in which they were disposed of in the body after being absorbed, had been debated, but no data existed on which a decision between conflicting views on any of these problems could be based. Folin and his students were able to secure data on the concentration of urea, and ammonia in deproteinated samples of blood from branches of the mesenteric veins, the portal vein, the liver, systemic blood and muscle and organ extracts, the samples being taken simultaneously. The non-protein, non-urea, non-ammonia N was correctly judged to consist largely of amino acids. These data afforded an explanation of the course of events in protein digestion and the distribution of amino acids to the tissues during and after the absorption period.

Matters stood thus when Benedict entered upon his vocation of research and teaching. His first appointment was at Syracuse University, where he remained but one year. He then took charge of physiological chemistry at Cornell University College of Medicine, in New York City. Graham Lusk, the distinguished physiologist, was responsible for Benedict's appointment. Benedict often spoke in terms of esteem of Dr. Lusk.

Benedict now entered with enthusiasm upon his career as an improver of analytical methods. Reference to the list of titles of his publications reveals better than can any brief description the nature of the problems which occupied his atten-

tion, and only a few comments on his work will be necessary here.

Benedict found on critical study of the method of Folin for the estimation of urea in urine that along with the decomposition of urea into ammonia and carbon dioxide, some creatinine and uric acid were likewise decomposed to yield the same products. This fact, of course, meant that the values for urea by Folin's method were too high. Benedict proceeded to develop methods for changing urea into its hydrolytic products by gentler means and so arrived at a procedure which gave more nearly accurate values for urea, even when minute samples were analyzed.

Every method which Folin described during the following years was immediately submitted to a critical study and was modified and improved in some important detail by Benedict. Methods for uric acid, creatine and creatinine, total sulfur, sugar, etc., which were devised by Folin, and which at the time of their publication were the best ones known, were, within a few months, tested by Benedict and improved in various ways. It was inevitable that the regular appearance of these follow-up critical studies and replacement of methods devised with great astuteness by Folin, should cause him some irritation. Yet Benedict's great contributions to analytical biochemistry did not in the least detract from the high eminence which was accorded to Folin by chemists, physiologists and clinicians. Folin showed his broadmindedness and tolerance through all the years of Benedict's criticism and replacement of Folin's methods by Benedict's modifications of these methods by always remaining on good terms with him. Indeed, one summer Folin placed his private laboratory at the disposal of Benedict for work which he knew was directed toward improvement on one of his analytical methods.

Especially noteworthy were Benedict's researches on methods for the determination of glucose in blood and urine. Accurate determinations necessitate the finding of chemicals which are reduced by glucose but not by any other substances in blood. Other reducing substances exist in blood and urines, so the older methods for sugar estimation gave results which were too high. Benedict was untiring through the years of his active life in working toward this objective, and he appears to have achieved the limits of accuracy in this important analysis which has such great significance in the study of normal and perverted carbohydrate metabolism.

Neither Folin nor Benedict was devoted to the study of analytical methods as the primary objective. Both had in mind the application of such methods to the study of normal and pathological body chemistry. This fact is emphasized in the case of Benedict whose first appointment at Cornell University Medical College was in clinical pathology. It was two years later (1912) that he was appointed professor of physiological chemistry, a position which he held with distinction until his death. For many years he supervised the research work on cancer at Memorial Hospital, in New York.

The data which were obtained by application of his methods for sugar, creatine, creatinine, purines, ruic acid, sulfur, glutathione and ergothioneine, were the subject of much reflection by Benedict with a view to discerning meaning and interpretations which advanced knowledge. One triumph in this field was his discovery in blood of a sulfur compound hitherto unsuspected as a blood constituent, and which he named *thiasine*. This he later identified as ergothioneine, hitherto known only as a constituent of ergot.

Another discovery of great interest and importance was the existence in beef blood of a compound of uric acid with blood protein. From this compound uric acid is liberated by boiling with hydrochloric acid, but not without some destruction of uric acid. He found that when uric acid was determined in blood with and without the usual precipitation of protein by ammoniasilver-magnesia reagent, the results when the protein precipitation was omitted, were increased by as much as 800 per cent over those obtained in the standard procedure. In chicken blood samples, the increase due to combined uric acid was only about 20 per cent, when the combined uric acid was determined along with the free form. Benedict isolated from ox blood, after

acid hydrolysis of the protein-uric acid complex, as much as 6.7 mg. uric acid, when the colorimetric method showed a total content of 7.0 per cent. This combined uric acid was all in the red cells.

His studies of uric acid metabolism brought to light a biochemical discovery of great interest to geneticists as well as to physiologists and biochemists. Long experience with dogs as experimental animals for the study of metabolic problems had led to the belief that this species dealt with uric acid in a manner different from man and monkey. The latter excrete most of their purine end-products of metabolism derived from degradation of nucleic acids ingested with the food, and those originating from intermediary metabolism, in the form of uric acid. The dog excretes, instead, allantoin. Allantoin is derived from uric acid by the opening of one of its rings, hydrolytically. This process requires the intervention of a hydrolytic enzyme of highly specific nature. In the course of his work with dogs, whose urines were analyzed for uric acid, Benedict observed certain individuals which differed from ordinary dogs in that they excreted uric acid instead of the usual end-product allantoin. Further inquiry showed that the dogs which differed from the usual pattern of purine metabolism and followed the human pattern, were the Dalmatian (Spotted Coach dog) breed. This breed lacks the enzyme which converts uric acid to allantoin, so this substance is excreted without alteration.

Benedict designed and carried through a number of experimental studies on the influence of specific metabolic disturbances on the behavior of malignant tumors. He was one of the earliest investigators to attempt to disturb the metabolic processes of tumors in order to cause regression. He studied the influence of induced diabetes (phlorhizin) on implanted "Buffalo rat sarcoma" on rats. The animals were placed on a carbohydrate-free diet and were at the same time rendered diabetic through the injection of phlorhizin. This treatment was followed by regression of the implants provided they were still small when the treatment was begun. He (with Lewis) found that the changes in the composition of the urines of rats under this treatment, were duplicated in all respects in a human subject made diabetic by injection of this drug.

He tried (with A. H. Rahe) the influence of diets such as would supply but limited amounts of several of the then known micronutrients (vitamins) on the growth and regression of several types of implanted tumors. This field has since been much more thoroughly explored in the light of more extended knowledge of the astonishing number of essential nutrients not known to exist in 1917, when these studies were made.

Among the most interesting results obtained by Benedict and his associates (especially K. Sugiura) in their studies on malignancy, was the observation that when Rous chicken sarcoma was fractionated by means of half-saturated ammonium sulfate, the tumor-producing substance was carried down by the globulin fraction, apparently none being left in the albumin fraction.

Other efforts to reveal important facts concerning the control of tumor growth, involved studies on the effect of certain dyestuffs on the growth and transplantability of tumors; the influence of high-fat diets; deprivation of animals of vitamin A; the effects of anemia-producing diets; the influence of adrenaline administration, etc. on the ability of animals to sustain the growth of tumor implants. At the time his experiments were conducted in this field the ideas involved in planning the studies were new and novel.

Benedict's services as editor:

Notwithstanding the regular teaching of physiological chemistry to medical students, and his constant occupation with post-graduate students and assistants and associates in the planning and supervision of his many researches, Benedict gave a great amount of time to editorial work. Beginning in 1912, he supervised the Biological Chemistry Section of *Chemical Abstracts* throughout the remainder of his life. In 1925 he accepted the editorship of the *Journal of Biological Chemistry*, a labor to which he gave much time and effort, which ended only with his death.

Miss Mary F. Smalley, who was associated with Benedict

throughout the entire period of his service as Editor of the *Journal of Biological Chemistry*, said in a letter to the writer soon after Benedict's death: "The same characteristics that he showed in his scientific work and in handling the manuscripts submitted to the Journal were evident in any phase of the management and publication of the Journal that he undertook; a quick understanding of any question; a direct and concise reply, so carefully worded that there could be little chance of misunderstanding; his great feeling of responsibility for the Journal in its business administration as well as for the papers published in it.

"Any suggestion or plan that affected the Journal he was willing to consider; he was also ready to reconsider, and discard, any of his own directions or suggestions that did not prove feasible. This attitude, of course, added interest and stimulation to the work of this office. Even when he was ill he continued to take care of as much business as he could in addition to the consideration of manuscripts."

Stanley Benedict as others saw him:

Many chemists knew little of Benedict other than through reading year by year his papers in which the shortcomings of a long list of analytical procedures, especially those devised by Folin, were described, and improvements on these procedures were made available. Folin's name was most often recurring in these criticisms only because he was the foremost man of his generation in breaking new ground in devising analytical technics. The general impression gained by many of Benedict's readers was that he was rather unfriendly to Folin. Folin, himself, did not think so, nor did any of us who knew him intimately.

In earlier pages the writer has attempted to give a clear picture of Stanley R. Benedict as a scientist, and of the high standards of his contributions. It is believed that Stanley would value even more than he valued his scientific reputation, the reputation which he had in his personal relations. Soon after Benedict's death the present writer sent letters to a number of persons who had had close contact with him as associates or

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students or in the editorial work which is such a fine monument to his industry and interest in the development of biochemistry. The following excerpts are from replies of a German immigrant who served as analyst in Benedict's laboratory for many years, from foreign students, and from his American students. One learns from these excerpts that he was a kind, patient man, who took pleasure in helping others. He was capable of intimate and lasting friendship, and especially among the humble workers about him he had most devoted friends.

Miss Mary F. Smalley, from whose letter I have already quoted, wrote: "While Dr. Benedict could not approach many people easily, I know of many evidences of his deep interest in the welfare of all connected with him. . . . It is not easy to write about Dr. Benedict, for he did not let many know him well. Yet one cannot have been associated with him as long as I was and constantly have seen his methods in dealing with manuscripts and other matters without a certain knowledge of the man and a great respect for his aims and the courage required to carry them out. He was far from indifferent to the criticism he provoked, but accepted this as inevitable."

Emil Osterberg was a member of the staff and associated with Benedict in a number of his researches during a period of twenty-five years. Mr. Osterberg wrote: "The first time I met Dr. Benedict I said to myself, here is where I will have to watch my step. He looked to be a hard man to please. However, it didn't take long for me to find out he was the finest and most good-hearted man I have ever been associated with in my forty-three years experience in laboratories. It was a pleasure to work with him. Once I saw him very happy: when I found uric acid in the Dalmatian dog's urine. The experiments with that dog pleased him immensely.

"During the war in 1917, we tried different methods for making Dakin's solution. One day there was a leak in the chlorine tank, and Dr. B. became more ill than I did. So on the way to the train he got very sick and went to the hospital. I believe he was never in good health after that accident. One of the colored porters was taken sick. He had a paralytic stroke and was unable to work any more, and was left helpless, with a large family and no income for their support. Dr. Benedict came to the rescue and helped them along. He was always willing to help, and give good advice to everybody. His memory I will cherish as long I as I live."

Olive Hoffman wrote: "Professor Benedict's was an august presence behind which was hidden a shy and sensitive one. This last would not be touched until the first was well worn. As a student of his, the quality which I most appreciated was his patience-one for the lack of which he has often been criticised; not patience of expression, nor with the mechanics of the laboratory, nor with the individual's technique, but in waiting for results. He could wait a long time and not chafe. There would be long silences and no outward encouragement but, if he thought the project worth while, he simply waited. The student might muddle along until he solved the problem, or in desperation sought the Professor. If the latter happened the critical ax usually did not fall. If the former there was a 50:50 chance. At any rate if the point was adequately defended nothing was permitted to interfere with the project, and there was that protection, political and financial, for which a laboratory worker is eternally grateful.

"Once his reserve had been broken, the consistency with which he regarded that individual's ensuing work and opinions sometimes became a fault. To some this made for biased judgment. To others it was the signal for proving him wrong. The latter attitude gave him pleasure, perhaps rather more if he were right. . . Independence of thought and action was not frowned upon by Professor Benedict. . . In the laboratory he was a strict disciplinarian. Less than the usual rest periods were taken (no rule against them). . . . His austerity pervaded the laboratory but I am not sure it was invited. There was no illusion that the function of the laboratory was other than work.

"Much of his graduate teaching was done by analysis of past progress, discussion of which was made in the seminar. At first he would tell us personal anecdotes and characteristics of outstanding biochemists. During the course of the seminars, as this or that paper was discussed, he would take us into the other worker's laboratory by more of these personal anecdotes."

Dr. Isaac Neuwirth, who majored in Benedict's department as a post-graduate student, and who worked with him continuously from 1915 to 1936, said:

"To me, Dr. Benedict was BIG in every sense of the word —big as a man, big as a scholar, big as a scientist. . . Dr. Benedict was a very *human* individual, although to many he may not have appeared as such."

From Dr. William H. Summerson's reply the following is quoted: "His lectures were frequently devoted almost entirely to an exchange of opinion between himself and the members of the class regarding some phase of the subject on which he felt the class should have reasonable opinions and be able to defend them. The picture I am trying to paint is that of a man with a clear and logical mind, wholeheartedly interested in his work and its development by himself and by others, and scrupulously fair in his dealings with his fellow workers. He had a tolerance of other people's weaknesses, but it was a critical tolerance rather than a passive acceptance. He was an inspiration to me, and as far as I could see, to all those students who came into contact with him."

Dr. K. Sugiura, who worked continuously with Benedict from 1917 to 1936, wrote of him: "His charming smile and his gracious manner impressed me greatly. I thought of him as a great teacher, and my future adviser. . . During my twenty years of association with Dr. Benedict, I never saw him with an angry face. . . Dr. Benedict was well liked by his students. . . . He was an unselfish man. He gave full credit to his associates in many joint scientific discoveries, and was intensely pleased to do so."

Dr. Joseph C. Block, who was associated with Benedict for many years in research said of him: "While he was always critical his criticism was constructive and tempered with kindness. . . . I never heard him swear. . . . In one of his rare con-

fidential moods he told me that he would prefer teaching philosophy to biochemistry. . . . He loved to tinker but he was not very skillful with his hands. . . . He was rather generous with money, at one time when he found out that I was rather hard up he felt very much hurt because I had not come to him for a loan. . . . He had a very quick temper but if he hurt anybody by his words his regrets were forthcoming immediately. . . . He was very bashful in the presence of ladies. . . . He was very kind to animals. Whenever he had to inflict pain, for instance, like an injection, he would always talk very kindly to the animal during the whole procedure."

His sister, Dr. Mary K. Benedict wrote that he was always fond of cats. She once saw five saucers on the kitchen floor at one time, containing different morsels for his cat, so that it might make its choice of what it liked best. . . . that once a bird built its nest over his front door, and he would not disturb it, so used the kitchen door until the bird had left its nest . . . that he became fond of photography early in life and did some fine amateur work. Dr. Neuwirth also said that one of Stanley's favorite activities, during his mature years, was taking pictures.

Dr. A. Goudsmit, Jr., wrote: "When Mrs. Goudsmit and I came to this country in September, 1933, as Fellow of the Netherland-American Foundation, Dr. Benedict was the first educated American we met. I remember very vividly how he appeared to us that morning behind his desk: his peculiar head, decidedly too small for the size of his body, looking as if it had been the subject of a smallpox attack and as if it was exposed to the influence of a rough climate at all times; his conspicuously erect posture, walking as well as seated; his continuous smoking; his matter-of-fact and direct way of attacking the problem in hand; all these things impressed us at our first encounter of the typical sea captain. And he has many times since done so. . . . Socially, he no doubt was ex-Because he left the city every night he tremely retiring. made it all the more difficult for his associates to have contact with him outside of 'business.' Only a very few favorites of

his department, and I suspect still less outside of it, were ever invited out to his Westchester house."

Dr. Jeanette A. Behre, who was for years associated with Benedict as a student, and later in research, wrote of him:

"I think of Dr. Benedict as a person of unusual vitality. His personality always completely dominated the department.... There was something magnetic about his personality and something fundamental about his enthusiasm for scientific work which could not help being inspiring. . . . He disliked most social gatherings although he could be delightful company. . . . The country appealed to him partly because he was very sensitive to noise. but he also had a sincere and fundamental love of nature. . . . He had many inner resources and interests. He had studied philosophy intensively at one time and philosophical speculation always had a particular fascination for him. He read literature and poetry. . . . Conrad was one of his favorite books, and he liked Poe's poetry, to mention only a few. He always had definite and original reactions to whatever he read. He was also fond of detective stories. He did a great deal of photography, and in summer especially, he enjoyed his motor boats. I cannot hope to describe his sense of humor, which was an intrinsic part of his personality and which could be both witty and whimsical. None of his friends can ever forget its particular quality nor the expression on his face when something amused him. He had a quick temper. which he often regretted, and which many people found hard to understand. There are plenty of us who have been hurt at times by his frank criticisms. No one who really knew him could fail to appreciate his directness and sincerity or to realize his fundamental kindness. There are many people who could testify to his consideration and generosity, to his genuine sympathy for personal troubles which were brought to him and to the great amount of help and encouragement which he gave not only to professional associates but also to many other people with whom he came in contact. He had a standard of personal integrity from which nothing could make him deviate and he was never afraid to fight for what he considered just

or right. Perhaps relatively few people realized that in spite of his assurance he was very sensitive to criticism and deeply modest about himself and his own accomplishments."

Stanley Benedict's wife, Ruth Fulton Benedict, a distinguished anthropologist, whom he married in 1914, said that in his adult life he never had chemicals nor chemical books at home. All the time outside the office and laboratory was devoted to recuperating his energies and in these relaxation periods he turned to hobbies which would take his mind off his work. Two of these hobbies were special favorites—engines which he set up and took to pieces, whether they were in pumps, boats or automobiles; and photography, where he especially enjoyed playing with different chemical processes in developing and printing.

His summers were devoted to recuperation as far as his duties as editor of the Journal would allow. He loved the isolation and leisure of a New Hampshire summer; for many years he spent the entire summer vacation period on the shores of Lake Winnepesaukee. Still more he enjoyed traveling, and went to the Canadian Rockies or to Mt. Ranier Park or took the boat trip to Alaska or to the North Cape. He struggled always, under the difficulties of an unusually high blood pressure, and solved these difficulties as far as he could by leading a regular life with as few intrusions as possible.

Stanley Benedict's qualities may be summarized by saying that he was a man of superior mental endowment, who delighted in constructive thought; whose interests aroused activity in experimental inquiry. He was strongly motivated by a sense of duty, and served well his fellow scientists and mankind in general by his researches and editorial work.

As a teacher and director of research and as personal counsellor he sustained high standards, and in return he won from those associated with him, respect, admiration, friendship, loyalty and gratitude.

STANLEY ROSSITER BENEDICT-MC COLLUM

Honors and memberships in scientific societies:

Member of the National Academy of Sciences American Association for the Advancement of Science American Society of Biological Chemists (President 1919-1920) American Physiological Society Phi Beta Kappa Corresponding Member of the Societé Biologie de Paris Sigma Xi Alpha Omega Alpha The Harvey Society Associate Fellow of the New York Academy of Medicine

KEY TO ABBREVIATIONS USED IN BIBLIOGRAPHY

Am. J. Cancer = American Journal of Cancer

Am. J. Physiol. = American Journal of Physiology

Arch. Int. Med. = Archives of Internal Medicine

Biochem. Bull. = Biochemical Bulletin

Biochem. J. = Biochemical Journal

J. Am. Chem. Soc. = Journal of the American Chemical Society

J. Biol. Chem. = Journal of Biological Chemistry

J. Cancer Res. = Journal of Cancer Research

J. Lab. Clin. Med. = Journal of Laboratory and Clinical Medicine

N. Y. Med. J. = New York Medical Journal

- Proc. Am. Soc. Biol. Chem. = Proceedings, American Society of Biological Chemists
- Proc. Soc. Exp. Biol. Med. = Proceedings, Society for Experimental Biology and Medicine

Surg. Gynec. Obst. = Surgery, Gynecology and Obstetrics

Zeit. physiol. Chem. = Zeitschrift für physiologische Chemie

BIBLIOGRAPHY

1903

(With J. F. Snell) A method for the estimation of chlorides, bromides and iosides. J. Am. Chem. Soc. 25, 1138-41.

1907

- Detection of barium, strontium and calcium. J. Am. Chem. Soc. 28, 1596-98.
- Detection and elimination of reducing sugars. J. Biol. Chem. 3, 101-17. The detection and estimation of reducing sugars. N. Y. Med. J. 86,

497-9.

A note on the reduction of alkaline copper solutions by sugar. Biochem. J. 2, 408-11.

1909

The estimation of total sulfur in urine. J. Biol. Chem. 6, 363-71.

Preparation of glyoxylic acid as a reagent. J. Biol. Chem. 6, 51-2.

- (With L. B. Mendel) Paths of excretion of inorganic compounds IV. Excretion of magnesium, and V. Excretion of calcium. Am. J. Physiol. 25, 1-22, 23-33.
- (With F. Gephart) Estimation of urea in urine. J. Am. Chem. Soc. 30.

1908-1909

A reagent for the detection of reducing sugars. J. Biol. Chem. 5, 485-7.

1910

The influence of salts and non-electrolytes upon the heart. Am. J. Physiol. 22, 16-31.

1909-1910

(With T. Saiki) A note on the estimation of purine nitrogen in urine. J. Biol. Chem. 7, 27.

A note on the estimation of total sulfur in urine. J. Biol. Chem. 7, 101-2.

1910-1911

The estimation of urea. J. Biol. Chem. 8, 405-21. The determination of total sulfur in urine. J. Biol. Chem. 8, 499-501.

1911

(With J. R. Murlin) Determination of the amino-acid nitrogen in the urine. Proc. Soc. Exp. Biol. Med. 9, 109-11.

1913-1914

(With J. R. Murlin) Note on the determination of amino-acid nitrogen in urine. J. Biol. Chem. 16, 385-8.

1914

A modified Hempel gas pipette. Biochem. Bull. 3, 1.

Studies in creatine and creatinine metabolism I. J. Biol. Chem. 18, 183-90. (With E. Osterberg) Studies in creatine and creatinine metabolism III. J. Biol. Chem. 18, 195-214.

- (With H. B. Lew) The influence of induced diabetes on malignant tumors (including a case of human phlorhizin glycosuria). Proc. Soc. Exp. Biol. Med. 11, 134-6.
- (With E. Osterberg) The influence of feeding upon a cidosis in the phlorhizinized dog. Proc. Soc. Exp. Biol. Med. 12, 14.

1915

(With Ethel Hitchcock) Colorimetric estimation of uric acid in urine. J. Biol. Chem. 20, 619-27.

Colorimetric estimation of uric acid in blood. J. Biol. Chem. 20, 629-40. Studies in uric acid metabolism I. The uric acid in ox and chicken blood. J. Biol. Chem. 20, 633-40.

- (With J. C. Bock) An examination of the Folin-Farmer method (Colorimetric) estimation of nitrogen. J. Biol. Chem. 20, 47-59.
- (With R. C. Lewis) A method for the estimation of sugar in small quantities in blood. J. Biol. Chem. 20, 61-72.

1916

Reply to Wood and McLean. J. Cancer Res. 1, 227-30. Uric acid in its relation to metabolism. J. Lab. Clin. Med. 2, 1-15.

1917

(With A. H. Rahe) Studies in the influence of various factors in nutrition upon the growth of experimental tumors. J. Cancer Res. 2, 159-78.

(With R. C. Theis). Analysis of the blood of cancer patients for the non-protein constituents. J. Cancer Res. 2, 511.

1918

(With E. Osterberg) Studies in carbohydrate metabolism I. J. Biol. Chem. 34, 209-16.

(With E. Osterberg) A method for the determination of sugar in normal urine. J. Biol. Chem. 34, 195-201.

A modification of the Lewis-Benedict method for determination of sugar in blood. J. Biol. Chem. 34, 203-7.

(With J. C. Bock) A new form of colorimeter. J. Biol. Chem. 35, 227-30.
(With K. Sugiura) Nutritive value of the banana. J. Biol. Chem. 36, 171-9.

Preparation of Dakin's solution from liquid chlorine by the gravimetric method. Surg. Gynec. Obst. 27, 386-7.

1919

The determination of sugar by the modified picric acid method. J. Biol. Chem. 37, 503-4.

(With K. Sugiura) The action of radium emanation on the vitamine of yeast. J. Biol. Chem. 39, 421-33.

(With K. Sugiura) The nutritive value of the banana. J. Biol. Chem. 40, 449-68.

1920

The determination of small quantities of sugar in the urine, including observations on the polysaccharide content of human urine. Proc. Soc. Exp. Biol. Med. 17, 183.

1921

- (With E. Osterberg) The effect of certain blood constituents on picrate solutions. Arch. Int. Med. 27, 135-6.
- (With E. Osterberg) A method for the determination of sugar in normal urine. J. Biol. Chem. 48, 51-7.
- Crystalline uric acid compound in beef blood. Proc. Am. Soc. Biol. Chem., J. Biol. Chem. 46, v-vi.
- (With T. P. Nash, Jr.) The ammonia content of the blood and its bearing on the mechanism of acid neutralization in the animal organism. J. Biol. Chem. 48, 462-88.
- (With Ruth Theis) Distribution of uric acid in the blood. J. Lab. Clin. Med. 6, 680-3.

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- (With H. J. Allen) The occurrence of creatine and creatinine in blood. Proc. Am. Soc. Biol. Chem., J. Biol. Chem. 46, xxi.
- (With Elizabeth Franke) A method for the determination of blood volume. J. Lab. Clin. Med. 6, 618-24.

1922

The determination of uric acid in urine. J. Biol. Chem. 51, 187-207.

- (With Elizabeth Franke) A method for the direct determination of uric acid in urine. J. Biol. Chem. 52, 387-91.
- (With J. A. Behre) Creatine and creatinine metabolism. JV. The question of the occurrence of creatinine and creatine in blood. J. Biol. Chem. 52, 11-33.
- A method for the purification of picric acid for creatinine determination. J. Biol. Chem. 54, 239-41.

The determination of uric acid. J. Biol. Chem. 51, 233-38.

(With A. R. Davis and E. B. Newton) The combined uric acid in beef blood. J. Biol. Chem. 54, 595-9.

1923

- (With J. C. Bock) Combined colorimeter and nephalometer. U. S. Patent No. 1,456,964.
- (With E. Osterberg) Sugar determination after subcutaneous injection of glucose in the dog; including a discussion of the paper on observations on carbohydrates by Folin and Berglund. J. Biol. Chem. 55, 769-94.
- (With E. Osterberg) Studies on creatine and creatinine metabolism.V. The metabolism of creatine. J. Biol. Chem. 56, 229-52.
- (With T. P. Nash, Jr.) The mechanism of phlorhizin diabetes. J. Biol. Chem. 55, 757-6.
- (With K. Sugiura) The adequacy of certain synthetic diets for the nutrition of the pigeon. J. Biol. Chem. 56, 33-44.

1924

- (With T. P. Nash, Jr.) The ammonia content of the blood. Zeit. physiol. Chem. 136, 130-3.
- (With Ruth C. Theis) The determination of phenols in blood. J. Biol. Chem. 61, 67-71.
- (With Ruth C. Theis) A modification of the molybdate method for the determination of inorganic phosphorus in serum. J. Biol. Chem. 61, 63-66.
- A reaction given by insulin solutions in vitro. Proc. Soc. Exp. Biol. Med. 21, 529.

1925

- (With T. P. Nash, Jr.) The mechanism of phlorhizin diabetes II. J. Biol. Chem. 61, 423.
- (With R. C. Theis) Inorganic constituents of the serum in cancer. J. Cancer Res. 8, 499-503.
- The determination of uric acid in the blood. J. Biol. Chem. 64, 215-19. The determination of blood in sugar. J. Biol. Chem. 64, 207-13.
- (With K. Sugiura) The influence of certain limited diets upon tumor susceptibility and growth in albino rats. J. Cancer Res. 9, 204-15.

1926

The estimation of sugar in normal urine. J. Biol. Chem. 68, 759-67.

- (With T. P. Nash, Jr.) The site of ammonia formation and the role of vomiting in ammonia elimination. J. Biol. Chem. 69, 389-96.
- (With E. B. Newton and J. A. Behre). A new sulfur-containing compound (Thiasine) in the blood. J. Biol. Chem. 67, 267-77.
- (With J. A. Behre) A colorimetric method for determining acetone bodies in blood and urine. J. Biol. Chem. 70, 487-94.
- (With K. Sugiura) The influence of insufficient diets upon tumor recurrence and growth in rats and mice. J. Cancer Res. 10, 309-18.

1927

- (With E. B. Newton and H. D. Dakin) Thiasine, its structure and identification with ergothioneine. J. Biol. Chem. 72, 367-73.
- (With K. Sugiura) Fractionation of the Rous chicken Sarcoma. J. Cancer Res. 11, 164-86.

1928

The determination of blood sugar, II. J. Biol. Chem. 76, 457-70.

1929

- A note on the purification of picric acid for creatinine determination. J. Biol. Chem. 82, 1-3.
- (With E. B. Newton) The use of molybdic acid as a precipitant for blood protein. J. Biol. Chem. 82, 5-10.
- (With J. A. Behre) Occurrence and determination of thioneine (ergothioneine) in human blood. J. Biol. Chem. 82, 11.

The question of the origin of urinary ammonia. J. Biol. Chem. 82, 673-8. Determination of sugar in blood. J. Biol. Chem. 83, 165-8.

- (With E. B. Newton) The use of tungstomolybdic acid as a precipitant for blood protein. J. Biol. Chem. 83, 357-60.
- (With E. B. Newton) Studies on the non-sugar reducing substances in blood and urine. I. Glutathione and thioneine in blood. J. Biol. Chem. 83, 361-5.

(With K. Sugiura) The action of certain dyestuffs on the growth of transplantable tumors. J. Cancer Res. 13, 340-58.

1930

- (With K. Sugiura) A critical study of vitamin A and carcinogenesis. J. Cancer Res. 14, 306-10.
- (With K. Sugiura) The influence of adrenaline on the growth of carcinoma, sarcoma and melanoma in animals. J. Cancer Res. 14, 487-501.
- (With K. Sugiura) Influence of high-fat diets on the growth of carcinoma and sarcoma in rats. J. Cancer Res. 14, 311-318.

1931

The analysis of whole blood. I. The precipitation of proteins. J. Biol. Chem. 92, 135-9.

II. The determination of sugar and of saccharoids (non-fermentable reducing substances). Ibid. 141-59.

(With J. A. Behre) III. Determination and distribution of uric acid. Ibid. 161-9.

1933

(With Gertrude Gotteschall) The analysis of whole blood. IV. The determination of glutathione. J. Biol. Chem. 99, 729-40.

1935

(With J. A. Behre) The presence of creatinine in the blood. J. Biol. Chem. 110, 245-8.

1936

- (With J. A. Behre) Some applications of a new color reaction for creatinine. J. Biol. Chem. 114, 515-32.
- The effect of an anemia-producing diet on the growth of carcinoma, sarcoma and melanoma in animals. Am. J. Cancer 26, 115-23.

1937

(With J. A. Behre) The precipitation of creatinine rubidium picrate from blood plasma filtrate. J. Biol. Chem. 117, 415-22.