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LAFAYETTE BENEDICT MENDEL

1872–1935

BY

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Lafayette B. Mendel

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To write a biographical sketch of a man in such a way as to make clear what manner of man he was, what the character and extent of his accomplishments, and his degree of usefulness in the scientific world, is a somewhat difficult task especially when the one who essays such a task has been his close associate for forty years or more, and where there is a certain fixed limit to the number of words to be used. Where such a degree of brevity is called for, there must of necessity be careful selection with exercise of good judgment, while the many years of intimate relationship, though affording clear insight into character and activities, may lead to a somewhat biased impression. However this may be, the following sketch will, I trust, give a fair picture of the man and his work.

Lafayette Benedict Mendel was born in Delhi, New York, on February 5, 1872, his parents having come to this country from Württemberg, Germany. The father, Benedict Mendel, was born in Aufhausen, March 4, 1833, and came to the United States in 1851, settling eventually in Delhi where he was a merchant from 1862 to his death in 1907. The mother, Pauline Ullman, was born in Eschenau, February 22, 1844, and came to this country in 1870, being married to Benedict Mendel that same year. Of this marriage there were two children, Lafayette and a younger brother who was frail and who died in 1901.

To Lafayette there must have been transmitted all the mental power and strength of character possessed by the parents, for he was unusually precocious, developing very early a fondness for study and an ability to assimilate knowledge which led to rapid progress, so much so that he presented himself at New Haven for the Yale preliminary examinations in Latin, Greek, and mathematics at the early age of fourteen. His training was at Delhi in the local school, the Delaware Academy, where he completed his preparatory studies and took the final examinations for Yale College in June, 1887. Prior to entering Yale, he went to Albany for a competitive examination through which he hoped to win a state scholarship. In this he was successful, gaining not only a scholarship but confidence in his ability to compete with others older than himself.

Throughout his undergraduate course in Yale College he maintained a fine record for scholarship, graduating with the degree of B.A. in 1891, the youngest man in his class, nineteen years and five months, his senior appointment being a Philosophical Oration, with Phi Beta Kappa standing. During his undergraduate course his studies were largely the classics, economics, and the humanities in general, with only a limited attention to the sciences.

Although the baby of the class, he nevertheless gained wide recognition from his classmates not only for his intellectual keenness, but also because of his winning personality coupled with a measure of good sense and with broad interests tokening a maturity of mind far beyond what would be expected in a youth of his years. In this undergraduate period he showed many of those characteristics which contributed so largely to the success of his scientific career. Not easily swayed by the currents of the moment he was prone to think things through and form his own judgment quite independent of the prevailing sentiment. This habit of thoughtful consideration of all sides of a problem was a striking indication of his mental independence and led many of his classmates to prophesy that young Mendel would go far, a feeling more than justified by later events. As one of his classmates wrote of him in later years, "Destined from the first to be a scholar, as rare then as now, he had his goal, and those who knew him well realized that he would never let anything stand in the way of attainment. Always friendly, he had little time for general conversation. He rigidly adhered to a simple mode of life to avoid distractions. Self-denying, he acquired self-control. Idealistic by nature, he developed spiritual values while devoting his entire life to a search for truth. Tolerant, without prejudice, untrammeled by the ideas of others, he approached his problems with originality and an open mind."

Having completed his undergraduate course and with a graduate fellowship awarded for his successful accomplishments, he returned to Yale in the fall of 1891 and entered the Sheffield Scientific School to take up the study of physiological chemistry with the writer. He had had some physics and chemistry and so was prepared in a way for the work that lay before him, but he was lacking experience in experimental work and found difficulty at first in grasping the full significance of the experiments he was called upon to perform and the proper interpretation of the results obtained. Trained as he was in the study of the printed page with general acceptance of the statements presented, it was not easy to adapt himself to a laboratory procedure where he must collect the facts for himself and then reason out their significance. Difficulties of this character, however, were soon overcome and he made such rapid progress in his studies, with a thesis that had sufficient merit to be given a place in the English *Journal of Physiology,* that he was awarded the Ph.D. degree in 1893. The following year he became my assistant in the Sheffield Laboratory of Physiological Chemistry, followed soon by his appointment as instructor, thus beginning his long term of service as a teacher in the subject to which he had decided to devote his life. During the college year, 1895-96, he was granted leave of absence, the time being spent at the University of Breslau with R. Heidenhain and at the University of Freiburg with E. Bauman in research work with these two eminent physiologists. In 1897 he was given the rank of assistant professor in the Sheffield Scientific School and in 1903 he was advanced to the position of professor of physiological chemistry with membership in the Governing Board of the Sheffield Scientific School.

This somewhat rapid advancement was fully justified by his accomplishments, both as a teacher dealing with undergraduate and post-graduate students, and by his activity in the field of chemico-physiological research. During all this period, indeed up to the writer's retirement from active service in 1922, Mendel took an increasing share in the responsibilities of the steadily growing Department of Physiological Chemistry in the Sheffield Scientific School and after the above date he became the head of the department. In 1921 with the changes incidental to the reorganization of the University, he was appointed Sterling

Professor of Physiological Chemistry in the University, with membership in the faculties of the Graduate School and the School of Medicine, as well as the Sheffield Scientific School, thus binding the Department of Physiological Chemistry more closely to all schools of the University where this branch of science could be of service. His responsibilities were thereby broadened, but he met all the requirements of the new position with increasing success, as testified by the growth in numbers of graduate students coming from other universities throughout the country and indeed from foreign countries, as well as by the greatly increased activity in research.

Dr. Mendel was a born teacher, strengthened by years of hard study and profound thinking. He loved teaching and this phase of his life work he pursued with a wholehearted enthusiasm which he communicated to his students, arousing in them a deep interest in their work. He was gifted with the power of presenting even the more difficult subjects with which he had to deal in a most lucid manner and in language both forceful and readily understandable. But beyond all this he was endowed with qualities that aroused the interest and devotion of his students. As one of his former pupils, now professor of physiological chemistry in a mid-western university, wrote shortly after Mendel's death, "To his students Professor Mendel was more than a distinguished scientist and a great teacher. Somehow, he directed the aspirations and broadened the perspective of those who came under the charm of his personality. He was not content merely to impart facts to, or to perfect the scientific technic of those about him. These things he did, but in addition he implanted ideals—ideals of tolerance, unselfishness, intellectual loyalty and service. . . . His students saw him as the personification of the ideals which they admired. They caught his spirit; and determined, perhaps unconsciously, to 'carry on' in his way. Because of these attributes so difficult to describe and yet none the less real, Mendel won and retained the confidence, the respect, and the devotion of his pupils. He became their guide and counselor." The many students trained under his inspiring guidance now holding university positions of importance in the field of physiological chemistry throughout the country constitute a living testimonial of his wise leadership.

With such a personality added to his broad knowledge and sound judgment, Mendel, approachable, gracious, magnetic, was quite naturally called on during his years of active service to give aid in many projects of a scientific nature. Thus, he served on the Board of Directors of the Russell Sage Institute for Pathology; he was long a member of the Council on Pharmacy and Chemistry of the American Medical Association; he was the first president of the American Institute of Nutrition; successively treasurer, vice-president, and president of the American Society of Biological Chemists; member of the Educational Advisory Board of the John Simon Guggenheim Medical Foundation; councillor of the American Home Economics Association; one of the Commission on Medical Education; a member of one of the sub-committees of the White House Conference on Child Welfare and Development; research associate of the Carnegie Institution of Washington and of the Connecticut Agricultural Experiment Station; official advisor on scientific research to the Protein and Nutrition Division, Bureau of Chemistry and Soils, United States Department of Agriculture; and at the close of the late war he was abroad for a time as a member of the *Commission Scientifique Interalliée du Ravitaillement.* For many years he served as a member of the Editorial Board of the *Journal of Biological Chemistry,* as one of the editors of the Scientific Monograph Series of the American Chemical Society and as a member of the Editorial Board of the *Journal of Nutrition.* In these and many other connections Dr. Mendel gave freely of his time and thought for the advancement of sound knowledge along the lines of his chosen field of work.

But Dr. Mendel's position in the world of science rests mainly upon his accomplishments in research, especially in the field of nutrition, where he made for himself and for the laboratory which he represented a broadly recognized reputation. Examination of the attached bibliography reveals a degree of research activity during the forty years from 1894 to 1934 that is highly impressive. Plainly, there was never an idle moment, but all his energies were directed to the study of a variety of problems, solution of which might throw light on many questions of primary importance. The bibliography is also suggestive of the personal magnetism of the man who could draw and hold so many research workers, ready and anxious to cooperate with him.

In the early period of Mendel's research activity his efforts were directed largely to the chemical aspects of digestion, absorption and secretion with some studies of nitrogenous metabolism and the paths of excretion, especially of certain inorganic compounds. His early work on digestion led to critical study of enzyme reactions, particularly in connection with the digestion of animal and vegetable proteins, using both animal and vegetable enzymes. The proteolysis of a crystalline vegetable protein, edestin, was studied for the first time by him in connection with the writer. These studies led in turn to a chemico-physiological study of various derivatives of the proteins, in which the physiological action of the primary products of digestion was given careful attention. This was at a time when knowledge of the digestive processes involved in the utilization of protein foods was very incomplete and unsatisfactory. Peptones and the several proteoses as normal products of digestion were being given undue prominence in view of later knowledge regarding their ultimate breaking down into the various amino acids. Study of the physiological action of the proteoses gave clear indication that they could not be absorbed as such into the blood since they were so obviously inimical to health. Plainly the ultimate products of protein digestion must be given more thoughtful consideration and attention was being focused more and more on the amino acids present in the protein molecules.

In the space at our disposal it is impossible to consider in detail the many more or less related lines of research carried on by Mendel and his coworkers; all bearing in greater or less degree on the broad subject of nutrition. There are, however, two lines of work deserving of special consideration since they extended over many years and brought results of the highest value in helping to create a new science of nutrition. One line of work had to do with the relationship between the chemical constitution of a great variety of food substances, especially the proteins of vegetable and animal origin, and their physiological or food value, while the other line of work had to do with the accessory factors essential for the normal growth of the young and of the normal health of the adult.

In the meantime Mendel had entered on a lengthy series of chemical studies on growth, in cooperation with a number of co-workers in the laboratory, but in 1911 there appeared a suggestive paper, with Thomas B. Osborne, "on the rôle of different proteins in nutrition and growth." This ushered in a period of cooperative work covering nearly twenty years up to the death of Dr. Osborne in 1929. Dr. Osborne, long connected with the nearby Connecticut Agricultural Experiment Station, had been occupied for many years with a study of proteins, especially those of vegetable origin, devoting much time to the isolation of the pure proteins and to a study of their chemical constitution. He found many striking differences in their content of the various amino acids of which they are composed, differences both qualitative and quantitative. Plainly such differences in chemical make-up might reasonably be expected to have some influence on nutritive values. Some of the amino acids might prove to be essential, others non-essential, to the growth and maintenance of the body. Osborne was primarily a chemist; Mendel versed more fully in the physiological aspects of nutrition and growth; the two making a combination of forces that might accomplish much. In the words of another "the ways of two explorers who started at different points met in a common interest and thus Osborne and Mendel joined hands in the common objective of the study of the problems of nutrition based on the appraisal of the food values of pure chemical substances of various degrees of complexity."

Aided by grants from the Carnegie Institution of Washington, Osborne and Mendel began their classical studies on nutrition with albino rats as subjects. This necessitated first a long series of observations on such animals in captivity, how best to maintain them in good physiological condition with the kinds of food adapted to normal nutrition, using relatively simple diets. They were then ready to begin their experiments proper with purified food products, having in mind especially the relative values of various isolated proteins for the maintenance in normal condition of adult animals and for the proper growth of young animals. In this connection it is to be remembered that, as Osborne found, purified proteins from various sources may differ greatly in their content of the individual amino acids. Thus, for example, of three proteins in the wheat kernel, leucosin contains 6.73 per cent of glutamic acid, while gliadin and glutenin contain respectively 37.33 and 23.42 per cent of this amino acid. Further, leucosin contains 2.83 per cent of histidine, while gliadin contains only 0.58 per cent of this amino acid. Again, leucosin yields 2.75 per cent of lysine, while none of this amino acid is present in gliadin. With such wide differences in chemical structure it would be strange indeed if these three proteins did not have different physiological values.

Recent years had brought new ideas regarding the relation of the food proteins to tissue proteins. With increasing evidence of marked structural differences between the albuminous compounds of different origin, it had become clear that it is impossible to develop noticeable changes in the character of the tissues of animals correlated with the character of the food consumed. In other words, tissue cells and fluids remain characteristic and specific for a species, whatever the chemical make-up of the food ingested. As Osborne and Mendel pointed out, the structural peculiarities which determine the individuality of the proteins are lost by the digestive processes and it is with the amino acids, the final products of the breaking down of proteins that we have to deal in considering the construction or renewal of the specific body proteins. This chemical fixity of the tissues under widely differing nutrient conditions pointed clearly to the supposition that the animal must construct its tissue proteins, by a process of synthesis, from the amino acid fragments furnished by protein hydrolysis. Again, it was a question whether all the amino acids formed by protein hydrolysis are equally indispensable. There was some evidence that the cyclic compounds, such as tyrosine, tryptophane, histidine, and phenylalanine were absolutely necessary for the welfare of the organism while other evidence pointed to the possibility of the synthesis of some amino acids *de novo* in the animal organism.

With such and other related ideas, Osborne and Mendel, keeping clearly in mind that the "processes of replacing nitrogen degraded in cellular metabolism are not of the same character as the processes of growth," or, in other words, that maintenance, repair and growth in the animal organism may be quite different processes, began their experimental work covering this long period of time.

Taking gliadin as one illustration, they found that *grown* rats having gliadin as the sole nitrogenous intake, though this protein lacked glycocoll and lysine, thrived without any evidence of alteration in well being, thus pointing to the conclusion that so far as maintenance is concerned, the protein of the food can differ widely in its amino acid make-up from the tissue proteins of the animal without affecting the well being of the latter. With *growing* rats, however, the story was quite different. Thus, young rats fed on the gliadin of wheat failed to grow, though in other respects they were quite normal. The same results were obtained with gliadin from rye, with the hordein of barley, and with zein of maize. Plainly growth required the presence in the food of certain amino acids not supplied by these incomplete proteins. This view was strengthened by the fact that the introduction of a little tryptophane and lysine with the gliadin or zein caused growth to show itself at once.

Thus, as early as 1912 Osborne and Mendel demonstrated by their many and varied maintenance experiments that "it is possible to maintain rats for periods equal to practically their entire adult lives on foods containing a single purified protein, and also that the successful food proteins may differ very widely in their chemical make-up without affecting the physical well being of the animal to any noticeable extent." In this connection it is to be observed that one rat was maintained in good condition, though without growth, for more than 530 days of adult life on a mixture of isolated food substances containing a single protein and this lacking both lysine and glycocoll; without doubt the longest experiment on record of artificial nutrition, bearing in mind that two years or thereabouts represent the rat's span of life. By experiments of such long duration the possibility of approaching certain of the problems of nutrition, many of them very illusive in character, by "new and hitherto discredited methods of study" was clearly established. Thus, they found among other important facts that "a protein as unlike the tissue proteins as is gliadin can serve for the construction of new tissues through the intervention of the metabolic processes of the mature animal" as was illustrated with a pair of rats maintained for 178 days on gliadin as the sole protein in the diet, four healthy young being produced and reared by them. This naturally involved "not only the construction of the tissues of the young animals, but also the production of the milk by which they were successfully nourished."

The value of the painstaking experimental work of these two coworkers on the nutritive value of isolated purified proteins from many sources, especially various cereal grains, can hardly be overestimated, throwing as it does so much light on the relationship between chemical constitution and biological value; work which has had a marked influence in revolutionizing many of the earlier theories of nutrition. Further, their experiments on the relative value of different purified proteins made it quite clear that *growth* depends on nutritive conditions quite distinct from those required for maintenance. Something more than the proper proportion of essential amino acids seemed necessary if grown rats were to be kept in health and in apparent nutritive equilibrium over long periods of time.

In all their previous experiments with isolated proteins the diet contained a small amount of "protein-free milk." Many lengthy experiments finally led them to the belief that some constituent present in natural milk, distinct from "protein-free milk" is essential for prolonged maintenance. Young rats fed solely upon a natural milk food not only grew from infancy to full maturity, but also gave birth to litters of normal young which in turn thrived on diets like that furnished to their parents. Further, if rats were allowed to grow on the "protein-free milk" food until a decline in growth set in, the addition of a little milk food caused growth to again manifest itself. A second decline in growth was easily averted by further exhibition of milk food. The conclusion was obvious that the milk food contains something that is essential for *both* growth and maintenance.

In seeking for this essential accessory factor in milk, Osborne and Mendel soon found that if the lard of their simple diets was replaced by butter fat, growth and well being were maintained. In the preparation of their "protein-free milk" food, the cream component of the milk was nearly or completely removed, with ultimate decline of growth on such a diet. Repeated experiments showed them that rats which had ceased to grow and were declining on their "protein-free milk" diet at once recovered and resumed a normal rate of growth when a portion of the lard in their food was replaced by a quantity of unsalted butter. Interesting is the conclusion published in 1913: "It would seem therefore as if a substance exerting a marked influence upon growth were present in butter." They at once raised the question "what light does the experience thus far accumulated throw upon the nature of the essential substance, if there be such? Is it organic or inorganic or both?" It is thus seen that they were on the threshold of the discovery of vitamins, or more particularly of the fat-soluble vitamin A, so essential for growth and well being.

Further experiments soon demonstrated that the growth-promoting substance of milk or of butter is associated with the butter *fat* and that the power of the latter must be attributed to something which distinguishes butter from the ordinary fats, for both lard and olive oil were found to lack this growth-promoting power. In addition it seemed improbable that glycerides of any of the fatty acids ordinarily present in foods could be responsible for the promotion of growth, while lecithin and other phosphorus—or nitrogen—containing substances were excluded, since the butter fat contained neither phosphorus nor nitrogen. Cholesterol was also ruled out by the fact that lard contains even more of this substance than does butter fat. What then was the substance possessed of this extraordinary power? In studying this question, Osborne and Mendel began to consider the possibility of an unique class of substances essential for normal nutrition. Thus, they stated in one of their papers, 1913, that "The researches which have been devoted in recent years to certain diseases, notably beri-beri, have made it more than probable that there are conditions of nutrition during which certain essential, but, as yet, unknown substances must be supplied in the diet if nutritive disaster is to be avoided. These substances apparently do not belong to the category of the ordinary nutrients, and do not fulfill their physiological mission because of the energy which they supply." As expressed by another "and as it often happens that a fundamental investigation opens new avenues not anticipated and not envisaged by the explorer, so it came about that the investigations of the food value of pure chemical substances led up to the discovery of the accessory factors essential for maintenance of the normal growth of the young and of the normal health of the adult. Such was the beginning, in this country, of the work on vitamins, work that revolutionized the existing theories of nutrition."

As their studies progressed, the horizon broadened and they soon found that adequate dietaries for growth and normal health required at least two groups of "formerly unappreciated components," i.e. fat-soluble vitamins and water-soluble vitamins. Further, growth-promoting properties were found to be associated with many and widely divergent tissues and fluids, thus implying a fairly broad distribution of these accessory substances. Thus, egg-yolk fat, wheat embryo, yeast, corn germs and glandular tissues showed "a surprising richness in growth-promoting properties aside from their protein and mineral content." Much time was devoted to investigation of the water-soluble vitamins of milk and of yeast, while thought was also given to the distribution of these particular food accessories in the various vegetable and animal tissues in general. Lack of space prevents a full discussion of the great variety of problems studied by Osborne and Mendel in their pursuit of knowledge in this particular field of nutrition. A glance at the attached bibliography, however, will give some idea of the wide scope of their investigations, while examination of the papers themselves will reveal the breadth of vision and the clarity of judgment, of these two gifted coworkers. As expressed by another in referring to their vitamin work, "contemporaneously, investigations on similar lines were initiated in other countries, but in America to Osborne and Mendel belongs the credit of the pioneer work. Indeed, to have been among the first to embark on a road which today is traversed by explorers in many fields of biology is a testimony of great foresight and wide imagination."

Such, very briefly, is a faint outline of two chapters of Mendel's work in the field of nutrition. His mind, however, reached out in many directions, but always with a thought of the bearing of his experimental work on some aspect of nutrition. In the latter part of his life he was much interested in the relation of the chemical character of the fats used as food to the fats present in the tissues of the body.

Having a facile pen and with a broad command of the literature, he was called on to write many reviews dealing especially with nutrition and growth. Thus, in 1916, in the *Ergebnisse der Physiologie,* under the title *"Das Wachstum"* he wrote a comprehensive review of the broad subject of growth with inclusion of all the chemical data then available. The same year he published a book entitled *Changes in the Food Supply and Their Relation to Nutrition,* and in 1923 there appeared another volume, *Nutrition, the Chemistry of Life,* being the Hitchcock Lectures at the University of California for that year. In 1930 he gave the Cutler Lecture at the Harvard Medical School and at Cornell University he lectured on the Schiff Foundation. He likewise gave several of the Harvey Lectures and one of the Herter Lectures in New York dealing mainly with subjects related to nutrition.

Recognition of his broad knowledge and varied accomplishments in his chosen field of work came from many sources. In 1913 he was elected a member of the National Academy of Sciences and the same year the University of Michigan conferred on him the honorary degree of Doctor of Science. In 1927 he was awarded the gold medal of the American Institute of Chemists for his outstanding contributions to chemistry, and in 1930 Rutgers University honored him with the degree of Doctor of Science, while in 1932 Western Reserve University gave him the degree of Doctor of Laws. In 1935 the Chemists Club of New York awarded him the Conne Medal "for his outstanding chemical contributions to medicine." On his sixtieth birthday in 1932 his portrait was presented to him by professional associates and friends and today it hangs on the wall of the seminar room in the Sterling Hall of Medicine and may serve in the years to come as a reminder to future workers in the laboratory of the man who gave of the best that was in him for the development of knowledge in the field of physiological chemistry, a teacher who represented a highly developed form of culture, which was both intellectual and personal.

During the last two years of his life Dr. Mendel suffered a painful illness which confined him to the New Haven Hospital, death coming as a relief from suffering on December 9, 1935. He was married to Alice R. Friend, a graduate of the University of Wisconsin, on July 19, 1917. A very intelligent and cultured woman, her sympathetic and helpful attitude toward his work did much to encourage him, and their life together was a very happy one. Worn out by the physical and mental strain attendant on Dr. Mendel's long illness, she died a few weeks prior to his decease. They had no children.

On April 16, 1936, memorial exercises for Dr. Mendel were held at Yale, in Strathcona Hall, when friends and associates gathered to do honor to his memory. President Angell presided and three addresses were given, by the Honorable Frederic C. Walcott, a classmate of Dr. Mendel, by Dr. Phoebus A. Levene, of the Rockefeller Institute for Medical Research, and by the writer.

In closing this brief review, I add a paragraph made use of previously: Plainly, the accomplishments of such a man as Dr. Mendel, with his broad vision, clear thinking and great industry, coupled with the important scientific data he was continually bringing to light have had, and will continue to have, a marked influence upon the growth of a more definite understanding of the science of nutrition. His love for his work, his enthusiasm over newly discovered facts, his pleasure in a successful experiment made of his labors a perpetual joy, by which his life was kept sweet and peaceful. He realized that no man can accomplish much in science except by lifting his hand and mind honestly to the tasks that lie directly in front of him, and this he did all through life with profit to the science for which he strove and with satisfaction to his own soul. His accomplishments stand clearly revealed in the records of science and in the hearts of his fellow workers.

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