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EARLY DAYS OF NUTRITION RESEARCH IN THE UNITED STATES OF AMERICA

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SIGNIFICANT developments in nutrition in the United States began early in the last quarter of the 19th century. This review covers the subsequent period of approximately 50 years. The developments followed much earlier ones in Europe, which provided background and guidance. The story is an account of the accomplishments of scientists, most of whom were initially trained as agricultural chemists, physiological chemists or physiologists. Many of them pursued advanced study in Germany, and much credit for the early nutrition research in the United States is due to German scientists who provided training and stimulation for the leaders directly responsible.

Among these leaders, first mention should be made of Samuel Johnson (1830–1909). As a student of chemistry in the Sheffield Scientific School at Yale University he was influenced by his professor to make agricultural chemistry his life work. To obtain the necessary training, he went in 1853 to Germany, where he worked under Erdmann at Leipzig and in Liebig's laboratory in Munich. Returning to Yale in 1855, he was appointed Professor of Agricultural Chemistry in 1857. He was the author of seven books and 172 articles on agriculture and agricultural chemistry, most of them dealing with soils, fertilisers and food crops, reflecting his primary research interest. As is mentioned again later, he was also a leader in the establishment of the first agricultural experiment station in the United States and served as its Director for many years. His principal contribution to the beginnings of nutritional investigation was the training and stimulus he gave to students, notably Atwater, Armsby, Chittenden and Osborne.

Wilbur O. Atwater (1844–1907) has long been referred to as the father of the science of nutrition in the United States, a title which seems eminently appropriate as one reviews his career. He received his bachelor's degree in 1865 from Wesleyan University, Middletown, Conn., a small college of liberal arts. Chance acquaintance with some farmers interested in scientific agriculture led him to enter Yale University for study under Samuel Johnson. Atwater received the Ph.D. degree in 1869 and spent the next two years studying in Berlin and Leipzig. During that period he became acquainted with the organisation and activities of agricultural experiment stations in Europe. It was only one of several periods he spent in Europe to learn about experimental methods and results of special interest for his own programme, and also to gather other information to bring back and publish for the use of investigators and for the stimulation of public interest in nutrition.

In 1873 Atwater became Professor of Chemistry at Wesleyan University and joined his former teacher, Johnson, in persuading the Connecticut legislature to appropriate money for the establishment of an agricultural experiment station. Thus the first station in the United States was set up at Wesleyan in 1875 with Atwater as Director and, two years later, was moved to New Haven with Johnson as Director. Another station was established at Storrs, Conn., in 1887 when federal funds were allotted to each state for that purpose, and Atwater became its Director, a post he held for 14 years without relinquishing his professorship at Wesleyan. To coordinate the work of the state experiment stations a federal bureau, the Office of Experiment Stations, was established in Washington in 1888 with Atwater as part-time Director. His three years of service enabled him to establish policies for the Office and to assist state authorities in the inauguration of their programmes. In 1893 Congress voted a special fund for studies of problems in human nutrition, to be made with the cooperation of the experiment stations. Atwater was placed in direct charge of those studies, with headquarters at Wesleyan.

The foregoing account shows that, from the outset of his career, Atwater had a unique opportunity to influence the development of agricultural and nutritional research in the United States. Nutrition early became his major interest. Recognising the need for information on the composition and nutritive value of American foods, comparable with that available in European tables, Atwater had inaugurated a programme in 1879 at Wesleyan and Storrs. When other state experiment stations were established a cooperative project was organised. As a result, Atwater and Woods published in 1896 a compilation of about 2600 analyses of American foodstuffs. This bulletin was republished in 1899 by Atwater and Bryant, with results based on over 4000 analyses, and reissued with corrections in 1906.

After making initial studies at Storrs, Atwater persuaded other experiment stations to conduct experiments on human digestion. In 1899 he summarised the data from 97 digestion experiments, and computed coefficients of digestibility for nutrients of different food groups, and of the "average mixed diet" as determined by diet surveys. He used these coefficients and gross energy values to arrive at his "fuel values": 4, 8·9 and 4 kilocalories per gram of protein, fat and carbohydrate, respectively, for calculating the available energy of mixed diets. He set forth somewhat different factors for individual foods and food groups. He thus established the system which still continues to be used in the United States and several other countries.

In 1886, at the request of the Massachusetts Bureau of Statistics of Labor, Atwater made a study of data which the Bureau had collected on family food consumption and expressed them as daily intakes per head of specific food groups and also of protein, fat and carbohydrate. The results caused him to inaugurate more reliable diet studies by the inventory method, which in turn led to a cooperative project at several experiment stations. As a result, some 350 diet studies were published during the period of fifteen years when Atwater was actively interested in that field. The diet studies were of special importance in arousing widespread interest, among investigators and the public, in nutrition problems, and in encouraging governments to increase their support for investigations on food and nutrition.

Atwater's most important research contributions were undoubtedly in calorimetry. After a visit to Europe which acquainted him with the activities of Voit and Rubner, he returned with the determination to construct a respiration calorimeter for studies with man. The work was begun at Wesleyan in 1892 and completed in 1897, largely through the skill of E. B. Rosa, Professor of Physics. Atwater and his associates used the apparatus to confirm the findings of European physiologists and to provide additional data of great value for solving problems of human nutrition. They demonstrated for the first time that the principle of the conservation of energy applies to the human body. The studies dealt with nitrogen and carbon as well as with energy metabolism. The effects of both physical and mental effort were studied. College students took examinations in the calorimeter. In all, over 500 experiments were made.

Atwater's chief associate in the studies with the respiration calorimeter was Francis Benedict (1870–1957). He was responsible for an important improvement to the original apparatus, which measured carbon dioxide excretion but not oxygen intake. Benedict developed a closed-circuit respiration apparatus which permitted the measurement of both gases. After Atwater's death he continued his career in calorimetry as Director of the Nutrition Laboratory at Boston, established by the Trustees of the Carnegie Institution of Washington through the urging of medical leaders who had become impressed with the significance of the Wesleyan studies for medicine. Under Dr. Benedict's leadership during twenty years that laboratory became famous for its contributions to nutrition and medicine.

Atwater was a prolific writer of popular and semi-popular articles in his broad field of interest. As Director of the Office of Experiment Stations he established the *Farmers' Bulletin*, a periodical designed to provide farmers with practical information based on current scientific findings. He also established the *Experiment Station Record* to furnish workers with abstracts of current investigations in the United States and abroad. In 1897 he made a trip to Russia and arranged to have the results of pertinent research abstracted in English for publication in the *Record*.

In 1903 Atwater visited certain European universities to discuss the possibility of setting up nutrition experiments on an international scale. His proposal evoked considerable interest and he returned to work out more detailed plans. In 1904, however, he became ill and was largely incapacitated from that time until his death in 1907. In the previous year the headquarters of the federally supported nutrition investigations had been moved to the Department of Agriculture in Washington and placed in charge of Charles F. Langworthy, who had been previously associated with Atwater in directing the programme. Langworthy continued to supervise the programme when it was assigned, in 1915, to the newly created Office of Home Economics. The Office was made a Bureau of the Department in 1923 and thus became the centre of studies on human nutrition; today it bears the name of Institute of Home Economics.

The first scientist in America to challenge the current use of the proximate principles as measures of the nutritive values of rations for animals and to produce evidence to prove his point was Stephen Babcock (1843–1931). After postgraduate studies in Wöhler's laboratory at Göttingen, where he received the Ph.D. degree, he returned to serve as chemist at the New York Experiment Station from 1882 to 1888. Here he was assigned the task of analysing the feed and faeces of a cow on a metabolism experiment. When he computed the results on a dry, ash-free basis he noted that they were much alike for the two products. That caused him to lose faith in the value of conventional methods of measuring the nutritive value of feeds. He wanted to set up an experiment to study the question.

The opportunity to make such a study came to Babcock after he moved to the University of Wisconsin in 1888 and became Professor of Agricultural Chemistry and Chief Chemist of the Experiment Station. He was allowed the use of two heifers for the purpose. One was given a ration made up from the maize plant, the other a ration from the oat plant, both rations being alike by conventional methods of feed analysis. Marked differences in milk production resulted. In this limited experiment he lighted the torch for others to carry on. The results led to the undertaking of a much more comprehensive study by Babcock's successor, E. B. Hart (see p. 352).

Babcock became internationally known as the result of his invention, in 1890, of the butterfat test which bears his name. His record shows many other important accomplishments in agricultural chemistry. He was a modest and companionable person whose active mind up to the time of his death at the age of 88 continued to charm and stimulate all who came in contact with him.

A pioneer in animal nutrition whose career resembled Atwater's in several respects was Henry P. Armsby (1853–1921). Like Atwater, he was influenced to take up agricultural chemistry by his studies with Johnson at Yale, where he received the bachelor's degree in 1874. In 1875 he studied in Germany and thus came in contact with Gustav Kühn, Director of the Möckern Experiment Station. He was so greatly impressed by the digestion and metabolism experiments being conducted on cattle with the aid of a Pettenkofer respiration apparatus that this work later became his main interest. Beginning in 1877 he served for four years at the experiment station at New Haven under the direction of his former teacher, Johnson, and also received his Ph.D. degree at Yale in 1879. During this period he was active in research and also began a translation of Wolff's "Landwirtschaftliche Fütterungslehre". He found that so many changes were needed to make the work apply to American conditions that his efforts resulted in a new book, "Manual of Cattle Feeding", published in 1880, which passed through several editions.

After two years of service as Professor of Agricultural Chemistry at the Storrs Agricultural School (now the University of Connecticut), he received a similar appointment at the University of Wisconsin and also served as Associate Director of the Experiment Station. In 1887 he became Director of the newly established Pennsylvania Experiment Station. After 20 years of distinguished service in administering a broad programme, he resigned to become Director of the Institute of Animal Nutrition, established as a unit of Pennsylvania State College primarily to provide additional facilities for his pioneer investigations of energy metabolism, which he had begun several years earlier.

Armsby had long envisaged a programme which he hoped would measure the intake and output of all gases, liquids and solids by experimental animals and thus take account of the final disposition of the total feed intake. Support from federal funds gave him the opportunity to inaugurate such a programme in 1898. After studying existing apparatus used in Europe for calorimetric research on respiration he decided to build an apparatus for cattle based on the principle of the one in use by Atwater for man. A calorimeter which met exhaustive tests of mechanical performance and accuracy was completed in 1902, with the assistance of J. A. Fries, chemist and I. L. Osmond, physicist. With this apparatus he was able to make both direct and indirect calorimetric measurements of the heat produced by farm animals. The apparatus made possible the quantitative measurement of methane production as well as of gaseous exchange. Heat production could be measured both directly and indirectly, with almost perfect agreement between the results obtained by the two procedures.

Armsby made several balance experiments with steers given different feeds and rations. By subtracting from the gross energy of a feed all the metabolic losses, including the heat increment, he arrived at its "net energy" value. Thus he developed his net energy system of evaluating feeds and formulating rations, a system not different in principle from Kellner's feeding standard, based on his "starch values" obtained by the nitrogen-carbon balance method. As a result of his studies Armsby concluded that the computation of rations on the basis of digestible nutrients was erroneous and devised a system which took account of the net energy value of the feeds.

Armsby was the author of a comprehensive book, " Principles of Animal Nutrition ", published in 1903, which was the outstanding publication of that era on the subject. Because of the thorough review of research methods and findings in Europe, it was particularly valuable to research workers and teachers. In 1917, a second book, " The Nutrition of Farm Animals ", was published. This book was as thoroughly documented as the previous one but, written on quite a different plan and broader in scope, reflected the advances in the subject. He recognised that there were " accessory ingredients " which might influence the availability of the protein and energy contained in a feed.

Armsby was one of the founders and the first president of the American Society of Animal Nutrition (later the American Society of Animal Production), established in 1908. He had a large influence in improving the quality of research by its members. He also had an awareness of the problems of human nutrition, as was shown, for example, by his studies on the efficiency of different animal species in producing human food.

Russell H. Chittenden (1856–1943) was another pupil of Johnson at Yale who, in addition to many other outstanding accomplishments, made pioneer contributions to the knowledge of nutrition, especially protein nutrition. After receiving his bachelor's degree from Yale he studied with Kühne at Heidelberg from 1878 to 1879, and thus received the inspiration for much of his later work in physiological chemistry. During this period in Germany he took occasion to visit other laboratories where he became acquainted with many of the leaders in chemistry and physiology and with the work going on under their direction. Returning to Yale, he received the Ph.D. degree in 1880. In 1882 he was appointed Professor of Physiological Chemistry in the Sheffield Scientific School, the first post of its kind in America. He held this post until he retired in 1922. During the last 24 years he served also as Director of the School and was primarily responsible for a considerable expansion of its facilities and for building up an enlarged and strong faculty.

Chittenden was the first scientist in America to challenge the reliability of diet standards based on diet survey data, particularly the recommendations of Voit, Rubner and Atwater, as to protein needs for health. He asked : " What do we really know as to the amount of food the human body requires to meet daily needs under different conditions of life, expecially protein food? " Towards the end of the century he planned an experiment to test that question. A detachment of volunteers from the Hospital Corps of the Army was detailed to New Haven, with a physician in charge, to serve as subjects. Warned by his medical friends about the harm which might result from the food intakes planned, Chittenden decided to experiment first on himself. He studied the effects of reducing the protein and calories in his diet over a period of seventeen months, and estimated the nitrogen content of his urine daily during the last nine. After an initial loss his weight remained stationary. He recovered from a rheumatic trouble in the knee which had failed to respond to medical treatment, and minor troubles such as headaches and bilious attacks disappeared. During the experimental period his protein intake had been about 40 grams daily instead of the 118 grams called for by the Voit standard. He was convinced that this low intake was distinctly beneficial rather than otherwise. He therefore repeated the experiment with soldiers, student athletes and his colleagues over a period of nine months. Personal testimony, athletic performance, photographs and other measures all supported Chittenden's claims for the advantage of abstemious eating. The human experiments were supplemented by extensive studies with dogs.

His results and his interpretation of them were presented at length in two books, " Physiological Economy in Nutrition " (1904) and " The Nutrition of Man " (1907). He stressed the point that appetite is not a reliable guide to nutritional needs and gave physiological reasons for his belief that a high-protein diet was not only unnecessary but positively harmful. He proposed an intake of 60 grams of protein daily for a man weighing 70 kilograms, as one which had a reasonable margin of safety and would ensure good health. He listed the amounts of different foods needed to provide 60 grams of protein. Apart from protein, Chittenden advocated a lower calorie intake than was called for by the Voit standard and stated that such intake should be based on actual need. In this connection he wrote : " But excess food consumption is by no means confined to the protein foodstuffs ; general overeating is a widespread evil, the marks of which are to be detected on all sides, and in no uncertain fashion." This sentiment is widely echoed today. Naturally, his experiments and conclusions did not go unchallenged, in America or elsewhere. They did, however, stimulate further physiological studies to determine actual requirements, instead of relying on the findings of diet surveys, and in turn contributed to the more realistic recommendations in diet standards of today.

Chittenden was an outstanding teacher who trained and inspired many future leaders in physiological chemistry and related fields. As Graham

Lusk said: "He built up the first true school of scientific endeavour concerned with pre-medical education in this country; that is to say, he formed a group consisting of the master himself surrounded by pupils who in turn became masters." His students carried his methods and principles to many medical schools throughout the country. His most distinguished pupil, from the standpoint of later accomplishments in nutrition, was Lafayette B. Mendel, who became his colleague and later his successor.

Chittenden was a man of great personal dignity, somewhat difficult to get to know, but in reality a kindly man who became a lasting and loyal friend of many, both students and colleagues. In retirement, he maintained active interest for many years and continued to be a source of inspiration to staff members and students who sought his counsel. His continuing interest is revealed in his book "The Development of Physiological Chemistry in the United States", published eight years after he retired. He continued to follow those developments until his death at the advanced age of 88.

Thomas B. Osborne (1859–1929) was another of the distinguished pupils of Johnson at Yale. He was first of all a chemist who later became interested in nutrition. A year after receiving the Ph.D. degree in 1885, he joined the staff of the Connecticut Experiment Station at New Haven, where he was active in research until he retired in 1928. At Director Johnson's suggestion he began chemical studies of the vegetable proteins, and continued this work for over 30 years.

For 10 years his chief interest was in the preparation of pure specimens of the proteins of plant seeds. His initial study of the oat kernel, published in 1891, was followed by a series of papers in which the proteins of 32 different seeds were described. Where possible, each protein was investigated by a number of different methods. Next, Osborne's work was particularly directed to the chemical and physical characterisation of those proteins. For about six years, beginning in 1906, he and his collaborators made a series of careful analyses of the amino acid composition of proteins by Fisher's ester-distillation method. Physical properties were studied also. Osborne repeatedly investigated proteins of special economic importance, such as gliadin, zein and casein. As a result of these extensive studies he demonstrated that the number of proteins in plants was much greater than was previously thought and that each of those in a given plant or part of a plant differed in chemical and physical properties from the others. The outstanding characteristic of his work was the thoroughness with which each problem was investigated.

Osborne's amino acid analyses of proteins laid the foundation for the extensive studies of their nutritive value, begun in 1910 in collaboration with Mendel, as discussed later. Osborne was well aware of the earlier ideas that different proteins might differ markedly in nutritive value, but felt that until the proteins in question were well characterised chemically, nutritional studies could not be effectively undertaken.

The first real scientific recognition of Osborne's work came from Germany. Griessmayer published a book in 1897 on vegetable proteins, which includes extracts from Osborne's papers, "to bring to light these treasures buried in their American publications". This encouragement at a time when his work was little understood or appreciated in his own country was of great assistance to him. World-wide recognition came with the publication of his monograph "The Vegetable Proteins", first issued in 1909 and extensively revised in 1924, which summarised much of his work. It became the classic publication on the subject and brought the author many honours from scientific organisations both at home and abroad.

Osborne was of a shy and retiring disposition. He shrank from making a public address or delivering a paper before a large audience. Among a small group of friends, however, he was a gifted conversationalist on scientific topics and public affairs alike. His time was always available for discussion, not only with his colleagues, but also with the many investigators who came from all parts of the world to consult him.

Lafayette B. Mendel (1872–1935), a pupil of Chittenden, received his doctor's degree in physiological chemistry in 1893. After two years' service as Instructor at Yale he went to Breslau to study with Heidenhain and later with others in Germany. Upon his return in 1896 he was appointed Assistant Professor in Chittenden's laboratory and thus began an outstanding career of teaching and research which lasted nearly 40 years.

For some ten years Mendel's research was concerned with problems of gastro-intestinal physiology, the absorption, metabolism and excretion of nutrients, and comparative physiological chemistry. During that period he developed a growing interest in the problems of nutrition and came to the conclusion that only through the use of purified diets could one obtain definite information about the functions and requirements of nutrients, especially of the proteins in which he was particularly interested. He found that Osborne, who had spent many years in isolating and studying pure proteins, was interested in their nutritive value and thus, in 1909, a scientific collaboration was begun which lasted for 20 years. The personalities of the two men were quite different. In contrast to the shy and retiring Osborne, Mendel was a very sociable person with unusually broad interests. Each had a deep regard for the knowledge and professional attainments of the other.

Throughout their joint activities they worked together in the planning and conduct of their experiments and in the interpretation of the results. Their activities represent the most outstanding example of team work in the development of nutritional knowledge in America.

When Osborne and Mendel began their work they were aware of the limited previous studies, notably with gelatin, which showed that all proteins were not of equal nutritive value. They decided to study the importance of the quality of diet protein, and were thus led to consider the amino acids. With the assistance of a grant from the Carnegie Institution of Washington their programme was inaugurated at the Connecticut Experiment Station. Convinced that controlled variations in experimental diets could be accurately made only when the diet consisted of a few purified substances, they decided to employ purified diets with rats. They first gave attention, therefore, to the establishment of a rat colony, and developed appropriate procedures for breeding, feeding and housing.

In initial experiments they found that a purified diet of isolated proteins, starch, lard and a salt mixture was not satisfactory for normal growth, but that a mixture of dried whole milk, lard and starch gave excellent results. They concluded that the milk supplied some essential nutrient other than protein and therefore developed a " protein-free milk " as an ingredient for their basal diet. With this modified diet their experiments revealed wide differences in the growth-promoting powers of different purified proteins. For example, animals failed on zein, could be maintained on gliadin, but grew rapidly on casein. Such studies led to the the supplementation with missing amino acids of proteins found inadequate and thus to the conclusion that some of the amino acids obtained from the hydrolysis of proteins cannot be synthesised in the body and must be considered dietary essentials. Further studies were concerned with the minimum protein requirement for growth and, later, with the requirements of certain amino acids for maintenance and growth. Extensive investigations of the biological or nutritive value of isolated proteins followed. Those studies resulted in the publication of over 100 papers between 1911 and 1927.

Early studies by Osborne and Mendel of the nutritional characteristics of their protein-free milk convinced them that the fat component had some special significance. Following up that conclusion, they found that when butter was added to a diet of dried skimmed milk upon which animals ultimately failed, growth was satisfactory. These results, published in 1913 under the title : " The Influence of Butter Fat on Growth ", provided evidence that butterfat contained an essential growth substance. They noted also that the butterfat cured " inflamed eyes " produced on the basal diet, if the trouble had not progressed too far. Such was their initial contribution to the discovery of vitamin A. Several other studies followed dealing with the distribution of the butterfat substance in foods, its stability, and the harmful effects of its lack.

In addition to collaborating with Osborne, Mendel supervised research on a wide variety of topics in nutritional physiology in his own laboratory. As well as research papers, he published many reviews, semi-popular articles and three books. His last one, " Nutrition, the Chemistry of Life ", published in 1923, is particularly interesting as well as informative. As he took part in the dedevelopment of the science of nutrition he became convinced of its importance in preventive medicine and, through his lectures and writings, was influential in making physicians aware of the fact.

Mendel is affectionately remembered by a large number of students, both undergraduate and graduate, as an excellent teacher. His lectures were based on his broad knowledge of the literature of his subject and were delivered in a careful, yet easy and convincing, manner. A host of graduate students were trained and stimulated by him to pursue and achieve outstanding careers in teaching and research, and to carry on the " Mendel tradition ". Throughout his life he continued to follow their achievements. Mendel's advice was widely sought by executive groups in public health, nutrition and medicine and he performed outstanding public service. He was a delightful man to know personally. Genial in manner, modest regarding his own achievements and conversant with a wide variety of topics, he was always helpful and stimulating to those who sought an opportunity to discuss personal problems, or broader topics.

Graham Lusk (1866–1932) was another pioneer whose major interests and accomplishments were in the study of energy metabolism but whose work was done in medical rather than agricultural schools. Trained as a chemist, he spent four years in postgraduate study under Ludwig at Leipzig and Voit at Munich, receiving his Ph.D. from the University of Munich in 1891. It was from Voit that he received the stimulus and enthusiasm for his life's work. After a period as Instructor and Professor of Physiology at the Yale Medical School, in 1898 he was appointed Professor of Physiology at the Bellevue Hospital Medical College in New York City. In 1909 he accepted a similar appointment in the Cornell University Medical College, where he served for 21 years, retiring only shortly before his death.

When Lusk took the post at Cornell a respiration calorimeter was constructed for studies with dogs and small babies. It was modelled after the

Atwater-Rosa-Benedict type of apparatus in Benedict's laboratory in Boston. Most of the studies dealt with specific dynamic action, although some were concerned with other aspects of energy metabolism, notably basal metabolism. The results of the investigations by Lusk and his associates were published in a series of 42 papers. Several of those associates later became leaders in their own right in calorimetric and other research in nutrition.

Lusk is best remembered by many workers in nutrition for his book " The Science of Nutrition ", of which the first edition was published in 1906 and the fourth in 1928. He stated that the aim of the book was " to review the substratum upon which rests present-day knowledge of nutrition, both in health and disease ". No more recent book has done the job as well in terms of knowledge available at the time. Just before his death he had completed the manuscript of a very brief history of nutrition from the " Ancient World " to " The Modern Phase ". It was published in 1933 under the title " Nutrition ". Lusk was associated with the founding or early development of several scientific societies, such as The American Physiological Society, The American Society of Biological Chemists and The American Institute of Nutrition.

In both his scientific and his private life Lusk was highly admired for his strict code of honesty and his kindness, generosity and unselfishness. He was especially generous in giving financial help to associates and students who were in need of it. He was largely responsible for raising the money for the travel and entertainment of his European colleagues who attended the International Physiological Congress in Boston in 1929.

In 1903 John R. Murlin (1874–1960) joined Lusk's laboratory as Instructor in Physiology and three years later he was appointed to an assistant professorship. At a time when the nutritional value of gelatin was being studied, Murlin made a thorough study with dogs to find out how much of the minimum protein requirement gelatin could replace. He also investigated the nitrogen and energy metabolism of pregnancy in dogs and later participated in studies of human pregnancy and of the metabolism of infants. Murlin was one of the many investigators to become intrigued with the similarity of pancreatic diabetes to diabetes mellitus and the possibility of discovering a therapeutic control of the latter. He devoted several years to an unsuccessful study of the problem, a study that was interrupted by the entry of the United Staes into World War I in 1917.

Murlin volunteered for officer training, which unexpectedly provided the opportunity to make an important contribution to the nutrition of the armed forces. His observations on the army ration at training camp and his suggestions for improvement led to his appointment as Major in the Sanitary Corps and an assignment to organise a Nutrition Division in the Office of the Surgeon General. Under his leadership studies were made of the actual food consumption of trainees and the amount of food wasted. Recommendations were made for improving the nutritional quality of the ration. The result of this pioneer work was to broaden the interest of the Quartermaster Department in feeding the soldier and to make the Medical Department more aware of its responsibility for his nutrition.

While at training camp in 1917 Murlin accepted the directorship of a newly endowed Department of Vital Economics at the University of Rochester, N.Y., and he took up active duty on completion of his army service in 1919. The bequest providing the endowment charged the Department " to conduct instruction and experimentation in physiology, hygiene and nutrition of the human body to the end that human life may be prolonged with increased health and happiness ". Murlin proceeded to develop a programme on this broad basis. The investigations he initiated dealt with different aspects of endocrinology, gastro-intestinal physiology, direct and indirect calorimetry, biological value of proteins, and other subjects. Many of the studies were made on human subjects and significant contributions were made to the technique of nutrition studies in man.

Murlin early saw the need for a journal primarily devoted to the publication of fundamental research in nutrition. He was the prime mover in the establishment of *The Journal of Nutrition* in 1928 and served as its Managing Editor for 11 years. He played a prominent part also in the organisation of the American Institute of Nutrition and served as one of its presidents. In 1919 the National Research Council organised a Committee on Food and Nutrition and Murlin served as its first Chairman.

Murlin was a strong believer in recreation, taking part in several sports and in the care of the grounds and gardens of a lovely home, which was a frequent meeting place for students and colleagues for social activities and also for informal discussion in the broad field of science. Murlin is fondly remembered for his genial hospitality on those numerous occasions.

Edward Brett Hart (1874–1953) was another agricultural chemist who became interested in nutrition. He was a leader in the pioneer studies made early in the present century and in continuing investigations which made the University of Wisconsin famous as a centre of nutrition research. After graduating from the University of Michigan, he worked for seven years at the New York Experiment Station, with the exception of two intermediate years spent in study in Germany. At the New York station he served under Director W. H.

Jordan, whose broad interest in nutrition is shown by his two books " The Feeding of Animals " and " The Principles of Human Nutrition ", published in 1901 and 1912, respectively.

In 1906 Hart joined the University of Wisconsin as Head of the Department of Agricultural Chemistry and Chemist of the Experiment Station where he continued studies, begun in New York, on the chemistry of milk and the metabolism of phosphorus compounds. On his arrival he became acquainted with the results of Babcock's experiments with feeds derived from a single plant (p. 347) and, with Babcock's encouragement, decided to repeat the study on a larger scale. The study was initiated in 1906 in cooperation with Humphrey and later with the assistance of E. V. McCollum and Harry Steenbock. The experiment was begun with heifers which were carried through reproduction and lactation. One group received a ration made up entirely from the wheat plant, another group, from the maize plant and a third, from the oat plant, all three rations being alike according to the conventional method of feed evaluation. There was a control group given a ration made up from all three plants. Striking differences in milk production and reproductive performance resulted. No explanation was possible in terms of the nutritional knowledge available at the time. The findings, published in 1911, stimulated much of the work which resulted in later discoveries on vitamins, amino acids and trace minerals.

As a result of the findings, Hart outlined two general projects for future work : mineral requirements and mineral metabolism, and vitamins and other organic elements. He was instrumental in discovering the necessity of iodine for prevention of goitre in farm animals, and was one of the first to show the toxic effects of fluorine on them. In 1923 he began a study of iron in nutrition, which led to the discovery, made in cooperation with his colleagues, that iron cannot be utilised in building haemoglobin unless it is accompanied by a small amount of copper. His early studies included several on the possible role of protein quality in milk production and on the factors influencing assimilation of calcium by milking cows.

Hart was an outstanding teacher. His lectures were clear and stimulating. He was always helpful to students who came to him for advice. He had great personal charm, a keen sense of humour and an affable manner which made him a very pleasant companion. He always enjoyed getting together with small groups, but did not particularly enjoy scientific meetings and therefore seldom attended them, although he was a member of the Societies concerned. Thus many who knew of his work and would have liked to meet him did not have the opportunity to do so.

Joseph Goldberger (1874–1929) was one of the great men in medicine who made pioneer contributions to nutrition through his studies of pellagra. He showed that it was not an infectious disease but was caused by the lack of a dietary factor which, years later, was recognised as nicotinic acid. Goldberger was born in Hungary, but from the age of seven lived in the crowded tenement area of New York. He received his medical degree in 1892 from Bellevue Hospital Medical College. In 1899 he was commissioned in the U.S. Public Health Service. For some 15 years he was successively engaged in field studies of yellow fever, typhoid fever, dengue fever, typhus and diphtheria, and also devoted considerable time to laboratory investigation of some of those diseases. His field and laboratory studies gave him an unusually fine background of experience for the investigation of pellagra, which he was asked to undertake in 1914, and to which he devoted the remainder of his life.

Endemic pellagra was first reported in the United States in 1907. Two years later it was recognised in 26 states and the large number of cases and deaths reported caused alarm. At the time when the problem was assigned to Goldberger it was believed that the disease was caused by an unknown infectious agent, transmitted in an unknown manner. He immediately went to observe the circumstances under which the disease was occurring. His first series of findings could not be explained by the long held view that pellagra was a communicable disease, and he was led to believe that diet differences were involved. The view was confirmed by his later studies on the diets of those who developed the disease and of those who did not. He next showed that introduction of meat and milk into pellagra-producing diets would cure and prevent the disease. He recognised that, to provide convincing proof that a faulty diet was the cause, he should be able to produce the disease in healthy men. With the approval of the Governor of Mississippi 12 convicts volunteered to submit to the test in return for pardons. A control group was maintained under the same conditions except for diet. Five of the 11 men who completed the study developed pellagra on the diet which Goldberger had previously found associated with occurrence of the disease. In spite of all the evidence, physicians remained unconvinced that pellagra was not an infectious disease. Goldberger recognised that one more experiment needed to be done. All attempts to transmit the disease to animals had failed, but perhaps man alone was susceptible. To settle the point Goldberger tried, by different means, to transmit the disease to volunteers, including himself and his wife. All these attempts failed.

Next, Goldberger began a long series of studies to try to identify the dietary factors responsible for pellagra prevention. In 1925 he was led to the conclusion that a special dietary factor, called the P.P. or pellagra-preventive factor, which appeared to be an unknown vitamin, was responsible for the preventive value. He provided a list of foods for practical use, particularly by poverty-stricken people among whom the disease occurred most frequently. He was actively continuing his studies when he became ill and died of cancer at the early age of 55 years. Goldberger's studies of pellagra were published in 44 papers, which reveal how his logical mind amassed the evidence, step by step, to disprove previous ideas about the disease, to prove that it was caused by a diet deficient in a specific factor and to show how it could be prevented by appropriate diet.

Mary Swartz Rose (1874–1941) was a pioneer in developing the teaching of nutrition and in training women who became teachers of the subject. She also greatly influenced the improvement of nutrition in the home. Her greatest interest was in child health and the contributions nutrition could make to it.

Miss Swartz began her career as a high school teacher and for some years taught home economics. She obtained a Bachelor of Letters degree in 1901 and later entered Teachers College, Columbia University, receiving the Bachelor of Science degree in 1906. Three years of graduate study followed under Mendel at Yale where she received the Ph.D. degree. She then returned to Teachers College, as Instructor in Household Arts, to organise a department of nutrition, and was made an Assistant Professor in 1910. In that same year she married Anton R. Rose, a biochemist whom she had met at Yale. She was appointed Professor of Nutrition in 1921, the first appointment under that title in any American University.

Mrs. Rose's early activities in developing a department of nutrition resulted in the publication in 1914 of the "Handbook of Dietetics", a book which was repeatedly revised and which was used widely in the teaching of the subject. In 1917 came the first edition of her "Feeding the Family", which found wide practical use by homemakers. In 1927 she published the "Foundations of Nutrition", which also became a widely used textbook. She was the author of a small book, "Teaching Nutrition to Boys and Girls", and several pamphlets.

During Mrs. Rose's career of more than 30 years at Teachers College, and in summer schools at other institutions, a host of students received general or specialised training, a development which greatly advanced nutrition education. Many of them became teachers of nutrition in departments of home economics in colleges and high schools, and also in schools of nursing. Others became nutrition workers in departments of public health. Mrs. Rose made a large contribution in extending nutrition education into the home, both through the students she trained and through her books and other writings. She was aware also of the need for and importance of nutrition research and made studies on energy metabolism, nutrition requirements and the availability of nutrients in foods. She conducted an extensive experimental study of problems of teaching nutrition in the New York City Schools.

Despite her very arduous and exacting scientific career Mrs. Rose found a liberal amount of time to devote to her home and family. She was a very gracious hostess and a charming person who endeared herself to students, scientific colleagues and the many others who were privileged to know her.

Henry C. Sherman (1875–1955), who received his Ph.D. in chemistry at Columbia in 1895, became interested in nutrition from his service with Atwater at Wesleyan from 1897 to 1899. Here he was associated with digestion studies and experiments on the effects of muscular work on food consumption, digestion and metabolism. Returning to Columbia, he was rapidly advanced to be Professor of Chemistry and remained in that post, apart from short absences, until he retired.

Sherman made several important contributions to knowledge of mineral nutrition. With human subjects he made pioneer studies of iron, calcium and phosphorus requirements for maintenance. On the basis of his findings he set up diet standards for those nutrients, which found wide use for many years as recommendations for practice. In 1921 he and Pappenheimer produced rickets in rats on a diet high in calcium and low in phosphorus, and prevented the disease by appropriate adjustment of the calcium : phosphorus ratio. Sherman and his students made pioneer contributions in the field of vitamins by developing quantitative biological procedures for estimating vitamins C and A. The methods were used to obtain data for recommendations on diet, and in the subsequent isolation of the vitamins. The work contributed to the discovery that the factor originally called vitamin B consisted of more than one vitamin.

Over his long period of active service Sherman's research dealt with a variety of other topics. He early conducted a survey of the economics of the food habits of low-income groups in New York City which convinced him of the need for nutrition education to improve nutritional status. Later he made extensive studies with successive generations of rats which convinced him that liberal intakes of nutrients were desirable for the promotion of longevity and productive life. He and his associates published many papers on enzymology. He trained many students who later occupied important posts in research and teaching. His belief in the importance of nutrition education, both for the scientist and for the layman, caused him to write several books. The most important one was "Chemistry of Food and Nutrition", first published in 1911 and followed by seven revised editions. From the start it found wide use as a textbook and, in turn, exerted a large influence in improving the food habits of the American people.

Sherman's broad knowledge and interests in nutrition early resulted in calls for public service. In 1917 he served as a member of a Red Cross Team sent to Russia to study the food situation after the revolution. He attended scientific meetings only infrequently and when he did he always seemed anxious to get back to his experimental work and his writing. Nevertheless, he had a wide acquaintanceship among his scientific colleagues who found him a modest, genial and friendly person, as did all who came to know him.

Edward B. Vedder (1878–1952) was a medical officer in the United States Army who, among other outstanding accomplishments, was a pioneer in the identification of beriberi as a deficiency disease. He received the M.D. degree from the University of Pennsylvania in 1902 and was commissioned in the Army in 1903 and assigned to the Army Medical School in Washington. It was during a tour of duty in the Philippines from 1909 to 1912 that Vedder, as a member of the Board of Tropical Diseases, made his studies of beriberi. He demonstrated that it was a deficiency disease by substituting half-polished rice for polished rice in the ration of the Philippine Scouts. He also successfully treated infantile beriberi with an extract of rice polishings. In 1913 he published the classic work, "Beri Beri". It is interesting to note that in 1913 Vedder persuaded Robert R. Williams to begin the chemical studies which led to his synthesis of vitamin B_1 and his establishment of its structure in 1936.

Partly as a result of his own observations, Vedder was one of the early supporters of Goldberger's view that pellagra was a deficiency disease, at a time when that view was rejected by most medical authorities. Later he made important studies of clinical scurvy. He continued to carry out research throughout his Army career, even when assigned to remote posts, and thus made significant contributions to the knowledge of leprosy, sprue, dysentery and syphilis.

Vedder retired from the Army as a Colonel in 1933 and became Professor of Pathology and Experimental Medicine at George Washington University Medical School. Here, along with his teaching duties, he continued research for some 10 years. During the last 15 years of his life he suffered from chronic illness which led to his death in 1952.

Elmer V. McCollum (born 1879), whose name is linked with the discovery of two fat-soluble vitamins and with several other pioneer contributions to nutrition, began his research and teaching career at the University of Wisconsin in 1907. He had previously obtained the Ph.D. degree in organic chemistry at Yale in 1906 and spent an additional year in Mendel's laboratory and Osborne's laboratory, and also had the opportunity to listen to some lectures by Chittenden.

On arrival at Wisconsin McCollum became associated with the feeding experiment with single plants being made under the direction of Hart (p. 352). He was assigned the task of finding out, if possible, why the wheat ration was producing so much poorer results than the others. He decided that a new experimental technique was required. From his reading about the unsuccessful attempts of European investigators to rear animals on purified diets he became convinced that the most important basic problem was to determine why they failed. He decided to undertake studies with rats on purified diets and, late in 1907, set up the first rat colony in America maintained for nutrition studies. His first efforts to rear animals on purified sources of nutrients were entirely unsuccessful. He tried several sources of a given nutrient and in 1912 found that, with the purified diet he had evolved, growth could be obtained when the fat component was supplied by the ether-soluble part of butterfat or egg yolk, but not when the fat was lard or olive oil. Those results were published in 1913 by McCollum and Davis under the title "Necessity of Certain Lipids in the Diet During Growth", a publication which appeared some six months before the similar one by Osborne and Mendel previously mentioned (p.350). McCollum later gave the essential factor the name "fat-soluble A", from which arose the name vitamin A. McCollum and Davis made a series of experiments with foods, notably cereal grains, supplemented with individual or multiple purified supplements, to study the deficiencies of the food in question. They referred to their procedure as the "biological method of analysis".

In 1917 McCollum was appointed Professor of Biochemistry in the newly established School of Hygiene and Public Health at Johns Hopkins University. Here his studies with restricted diets were continued and the chance observation was made that young rats on certain diets developed gross skeletal changes. Dr. John Howland, Pediatrician in Chief of the Johns Hopkins Hospital, examined some of the animals and expressed the opinion that the bone changes were similar to those of severe rickets in infants. A cooperative experiment was planned, under the leadership of McCollum and the paediatricians P. G. Shipley and E. A. Park, to study the cause of the development of rickets in rats, with special reference to the effects of nutritional deficiencies. Studies were made of the effects of deficiencies of vitamin A and calcium, of variations in the calcium: phosphorus ratio and of the contrasting effects of butterfat and cod liver oil as preventives. The investigators were aware of the findings of Mellanby with dogs, that when the vitamin A in butter and cod liver oil was destroyed by heating, the butter no longer protected against rickets but the cod liver oil remained effective. McCollum and his associates sought the explanation by testing both oxidised butterfat and cod liver oil for the prevention of xerophthalmia and for inducing healing in experimental rickets in rats. The oxidised oil was useless for preventing xerophthalmia but still cured rickets. They concluded that the antirachitic substance was a fat-soluble factor distinct from vitamin A; they called it vitamin D. Their results were published in 1922 under the title " An Experimental Demonstration of the Existence of a Vitamin which Favors Calcium Deposition ".

In 1918 McCollum published a small volume entitled " The Newer Knowledge of Nutrition ", which was expanded into a much larger book in 1922. This well documented book interpreted the meaning of the recent discoveries about vitamins, proteins and minerals for the benefit of students, teachers and physicians. The book exerted a profound influence in advancing the cause of nutrition, both by setting forth clearly the " newer knowledge ", and also by indicating problems remaining to be solved and by stimulating research accordingly. Three later editions of the book were published by McCollum and his associates.

McCollum was a great teacher who inspired many students to become leaders in both nutrition and biochemistry. He was an adviser in the broadest sense. His students continued to seek his advice, and many other scientists went to him for counsel on their programmes. All found him ready to take time to talk about their problems and many have given him credit for ideas and stimulation thus received. Both the soundness of his suggestions and his genial manner always made it a great delight to talk with him. His popular lectures have thrilled thousands of listeners, both scientists and laymen. He retired from Johns Hopkins in 1944, but it was only a " formal " retirement. He has continued to have a large influence on the advancement of nutrition and also to charm a host of friends.

In this review the discussion has been limited to pioneers in nutrition whose most active careers fell within the period covered, and to their major accomplishments during that period. Readers familiar with the early developments may properly question the judgement of the author in his selection of the men and events discussed and in regard to his omissions. Here difficult decisions have been required, particularly in view of space limitation. Nevertheless, the preparation of the review has been an enjoyable task because the writer has had the privilege of knowing personally all but three of the men mentioned and in his own career has benefited greatly from the advice and help of several of them.

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