

E.V. McCollum: Doyen of Nutrition Science

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The year 1979 marks the centennial of the birth of Elmer Verner McCollum. He was born on a Kansas farm homesteaded by his father in 1863 and received his academic training in chemistry at the University of Kansas and at Yale University. As a member of the faculty of the College of Agriculture at the University of Wisconsin from 1907 to 1917, he gained widespread attention for his pathfinding discoveries in experimental nutrition. From 1917 until his retirement in 1944 he was Professor of Biochemistry in the School of Hygiene and Public Health at Johns Hopkins University where his continuing achievements in research, stimulating leadership in nutrition education, imaginative influence on the food industry and wisdom in the formulation of public policy regarding foods and nutrition gave him unusual distinction and international acclaim.

At Kansas the faculty member most influencing young McCollum was Edward Bartow; at Yale it was Lafayette B. Mendel; and at Wisconsin it was clearly Stephen M. Babcock. At Johns Hopkins, Edwards A. Park was his most stimulating colleague and very close friend.¹

Five Contemporary Pioneers Who Shaped the McCollum Contributions

In order to set the stage, it is important to identify a few of the great nutrition pioneers who interacted with McCollum during his most productive years. Five such nutrition giants

were Graham Lusk (1866-1932), Lafayette B. Mendel (1872-1935), Lord Boyd Orr (1880-1971), Henry C. Sherman (1875-1955) and F. Gowland Hopkins (1861-1947).

Over several decades Lusk was the most influential of the investigators in human and animal calorimetry in this country. Before his death, Lusk gave consideration to the great importance of the newer knowledge of nutrition. In his last book, in 1932, he made reference to the new developments and the new authorities by stating that, "The works of McCollum, of Mendel and of Sherman are available."² As early as 1917 Lusk evaluated McCollum's work by stating that he "brought forth new and surprising facts about foods and their physiological effects."¹

Mendel was involved in the selection of McCollum for the faculty position at Wisconsin. In 1912, following a visit with him at Madison, Mendel wrote to his research associate, T.B. Osborne, "I saw under what conditions McCollum had to work. He has rats in his office ... His working conditions are very bad."³ Such conditions, however, began to improve, particularly after vitamin A was discovered. McCollum and his former teacher occasionally had differences of opinion, but they were always friends and allies in public issues and professional matters concerning nutrition.

Orr and McCollum were close friends with much in common, especially in the development and promotion of sound measures to eliminate malnutrition throughout the world. A measure of their mutual interests was the selection of these two men to be the recipients of the Borden Centennial Awards in 1958 when the 100th anniversary of the founding-

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of The Borden Company was celebrated.⁴ In his autobiography Orr referred to McCollum as "the doyen of American Nutrition workers."⁵ Sherman was a prolific and widely respected writer of general textbooks and comprehensive technical reviews and for more than 50 years he and his associates engaged productively in sound and significant research on various nutrition topics. McCollum's extensive personal notes and papers give appreciative attention to the thoroughness and accuracy of Sherman's famous book, *Chemistry of Food and Nutrition*.

F.G. Hopkins, in England, was the pioneer who in 1906 postulated the existence of "accessory food factors" from experiments similar to McCollum's,^{6,7} His findings and insights greatly influenced McCollum's work.

Development of a Rat Colony

In 1907, McCollum, who wanted to know why animals limited to the known major components of diets promptly failed in health and survived only a few weeks, decided "the most important discovery to be made in nutrition would be the elucidation of the cause or causes of these failures."⁸ It seemed clear that rats would be the most useful experimental animals.

The first experiments began in January 1908. This was to be the first ongoing colony of rats for experimental nutrition studies. Twelve young albino rats were purchased with six dollars of his own money from a pet dealer in Chicago. After about five years a few other albino rats were obtained from regular stock of Henry H. Donaldson. These were interbred with the McCollum stock. About 1915 McCollum obtained some of the yellow and piebald laboratory rats used by William E. Castle in genetic studies at Harvard University. He interbred these rats with his mixed strain of albino rats "and so mixed the colony thoroughly and ever after kept a colony of hybrid rats of these strains."⁹ He confided to W.D. Salmon of Alabama Polytechnic Institute that his development of an experimental rat colony underlay all his successes in nutritional science.⁹

When McCollum moved from Madison to Baltimore in 1917, he also moved a stock of

50 females and ten male rats with him. The rest of the colony was left at the University of Wisconsin.

The second ongoing colony was started in July 1909 by Osborne and Mendel at Yale to study the nutritional value of various proteins. Its development and use during their several years of highly fruitful work together are graphically detailed by Becker.³

In a retrospective review of some of his contributions, which was published less than a year before his death, McCollum observed that¹⁰ "The rat has had a long history of evil deedsBut caged and used intelligently the rat has at last conferred very great benefits on mankind."

Biological Methods for the Analysis of Foods

In his first year at the University of Wisconsin, McCollum assiduously studied the various compilations on foods and nutrition and standard methods on the determination of the nutritive value of foodstuffs. It became clear to him that the accepted methods were grossly inadequate for the evaluation of nutritive value and a biological assay was needed. In 1909, with the help of Marguerite Davis, he began experiments to study the nutritive value of single foods such as wheat, rice, corn and oats.⁹ The plan was to feed groups of weanling rats a basal diet composed largely of the test food plus various supplements such as salts, casein, butterfat and yeast. The rate of growth was the general criterion for judging value of the basic food and the value of the supplements. Occasionally, the effect on reproduction was also studied.

Much useful information was obtained which led to many applications, including attempts to characterize and identify new nutrients. As McCollum recorded more than 40 years later concerning the beginning of this great step forward,⁹"The time was ripe for more systematic experimental inquiry, prosecuted to an extent which would confirm, clarify, extend and unify the isolated observations of importance which were known to practical feeders, or were recorded in scientific journals. Some of these were of importance, but had not been followed up as they should have been by fur-

ther study. I was fortunate to have opportunity and resources for extensive experimental studies in animal nutrition at a most opportune time."

The determination of the nutritional values of foods in terms of specific nutrients, or empirically, the right combinations of foods to achieve maximal complementarity resulted from this concept. The term protective foods also came from this work and the knowledge it provided. The term was first used by McCollum in a lecture at the University of Chicago in 1918.¹ The development of the Basic Seven food groups and later the Basic Four food groups as an aid to nutrition education was derivative from McCollum's early studies.

Discovery of Vitamin A

McCollum and Davis are universally credited with the discovery of vitamin A. Osborne and Mendel at New Haven were close behind. The latter two had been highly successful in studies of the relative nutritional values of isolated proteins determined singly, in combination and with selected amino acid supplements. In some of the studies the basal diets were composed of carbohydrates, fats and inorganic salts, but in many a preparation of protein-free milk was used, to provide a physiologically balanced source of inorganic elements. Using such diets, in 1912 Osborne and Mendel reported that artificial protein-free milk was inferior to natural protein-free-milk. It seemed that the latter provided something important in nutrition other than fat and protein. They speculated that the natural product furnished trace inorganic elements needed by animals.⁷ On the basis of their concepts at that time it appeared that rats could grow without any lipid material in the diet.

In the now classical paper by McCollum and Davis¹¹ the basal rations were "compounded of pure casein, carbohydrates and salt mixtures made up of pure materials, and the same rations in which a part of the carbohydrates was replaced by lard, with a considerable degree of success." On all the rations, however, suspension of growth occurred after 70 to 120 days. They concluded that this was due "to a lack of certain ether-soluble substances in the diet." They added that "these can be supplied by the ether extract of egg or of butter." They

recorded that "In no instance have we obtained such a result from the feeding of lard, or of olive oil." They concluded that this "would lead one to the belief that on these mixtures of purified food substances the animals run out of some organic complex which is indispensable for further growth but without which maintenance in a fairly good nutritive state is possible."

A short time later Osborne and Mendel reported feeding experiments with butterfat added to their protein-free milk diet and confirmed in essence the finding of McCollum and Davis.¹² The newness of the vitamin concept at that time is reflected in their commentary: "Although the data furnished by McCollum and Davis strongly indicated that butter-fat has a marked influence on growth they by no means prove that butter-fat contains something essential for the metabolism of growth, apart from that of maintenance. The added butter-fat may have simply supplied something analogous to the so-called vitamins, which Funk considers to be essential for life . . ." ¹²

Within a year after making their first report in 1913 McCollum and Davis had shown that the essential factor was non-saponifiable and that it could be transferred to other oils. In 1917 McCollum pointed out the analogy between the "xerophthalmia" (his designation) of deficient rats and a disease occurring in humans.¹³

Vitamin Nomenclature

In their application of the biological method for the analysis of polished rice McCollum and Davis in 1915 found that young rats grew and remained free from polyneuritis when they were supplemented with an alcoholic extract of wheat germ as well as with casein, butterfat, and a salt mixture. By that time Eijkman, Funk and others had made progress in determining that the polyneuritis of chickens and pigeons fed polished rice is due to a dietary deficiency.⁷ It was presumed that the curative factor in the wheat germ extracts was identical to the anti-neuritic factor recognized by Eijkman in 1897. On the basis of this work and his own laboratory studies McCollum decided that rats require at least this unidentified nutritional factor as well as the fat-soluble factor he discovered in 1913.

In 1916 McCollum and Kennedy, recognizing the need for appropriate nomenclature, proposed the terms "fat-soluble A and water-soluble B" to designate provisionally the two factors.^{14,15} In 1918 McCollum assumed, as stated in the first edition of his book *The Newer Knowledge of Nutrition*, "that what we designate by each of these terms is in reality but a single physiologically indispensable substance and not a group of substances."¹⁶ This view seemed to be shared by virtually all the investigators at that time.^{7,15}

In the second edition of his textbook, in 1922, McCollum updated his nomenclature. He suggested that since scurvy was a newly recognized deficiency disease, the deficient nutrient could be logically designated water-soluble C. He gave reasons why the terms lipins, accessory food substances and vitamins should not be used. He pointed out that the alphabetical designations used by himself and Kennedy "have found widespread acceptance." He was uneasy about using the term *vitamine* because it "seems to bestow an importance upon these substances paramount to that of other indispensable substances." Owing to the widespread use of that term, however, and Drummond's proposal in 1919 to change the spelling to vitamin, McCollum finally yielded. He said, "This would be in accord with the nomenclature of the hormones and of the alkaloids and indicates nothing of their chemical natures. This seems to be a satisfactory nomenclature to adopt." It was universally accepted.¹⁷

Vitamin D

Rickets, a disabling disease of infancy and childhood, and osteoporosis, not limited to any age category, had ravaged mankind at least 2000 years before vitamin D was discovered. Experimental rickets was first produced in puppies in 1918 in the now classical work of E. Mellanby. It was not until the experimental production of rickets that the dietetic theory of rickets began to be favored over various other hypotheses.

It happened that McCollum and associates in 1918 had for the first time produced rickets in young rats by feeding cereal type diets in

which the calcium:phosphorus ratios were markedly unphysiological. John R. Howland and his associates in pediatrics at the Johns Hopkins Hospital, Edwards A. Park and Paul G. Shipley, became interested. They developed a cooperative program of study in which McCollum and his associate N. Simmonds planned the experiments, produced the animals for study and Park and Shipley performed the bone studies.

One of the most effective rickets-producing diets was number 3143 in the series studied. The calcium phosphorus ratio was about 4:1. The group soon discovered that on this diet and certain others, cod liver oil, instead of butterfat, protected the rats from xerophthalmia as well as from rickets without any adjustment in the level of calcium. For protection from rickets the requirement was much less than for butterfat. This suggested that these two sources of the "fat-soluble A" were dissimilar in their effect on rickets.^{7,15} At that time Mellanby believed that some unidentified fat-soluble factor could prevent or cure rickets. He tentatively suggested that deficiency of "fat-soluble A" might be the cause of rickets. In 1920 F.G. Hopkins showed that the growth-promoting effectiveness of butterfat was lost when it was aerated at 120°C.^{7,10}

Acting on the hypothesis that some factor other than the growth-factor A in cod liver oil accounted for the antirachitic effect, the McCollum group in 1922 aerated butterfat and cod liver oil *athigh temperature* and tested the oils on xerophthalmic rats and rachitic rats. The latter were cured but those with xerophthalmia did not benefit. They concluded that the antirachitic factor was distinct from the fat-soluble A factor and that they had discovered a new vitamin.^{7,15,18}

It may be noted that in the titles of the 30 papers the McCollum group published from 1921 to 1927 describing these studies, it was not until 1925 that they used the terms vitamin D. Until that time the factor was designated only as the antirachitic vitamin.

An important part of the comprehensive program was the development of the so-called "line test" by the McCollum group.¹⁹ Using this sensitive histological procedure rats made extremely rachitic on diet 3143 could be given,

graded amounts of the material being assayed for vitamin D activity. The degree of calcification in the zone of provisional calcification constituted a measure of the vitamin D potency. This soon became the major assay procedure for vitamin D.^{7,15}

One of the two students in the first course McCollum taught at Wisconsin, in 1907, was Harry Steenbock. Eighteen years later Steenbock discovered and patented a process for the production of vitamin D by ultraviolet irradiation which greatly extended the use of vitamin D for man and animals.¹

Other Research Contributions

McCollum and his associates made contributions in many other areas of experimental nutrition.

In 1922 they were the first to describe the gross appearance of dental caries in rats fed faulty diets.²⁰ In 1931 Klein and McCollum showed that diets relatively high in phosphate are probably protective against dental caries.²¹ McCollum, however, always cautioned that the calcium phosphorus ratio must be kept within a fairly limited range for health maintenance.

From 1909 to 1943 McCollum with students and other associates published approximately 40 papers on the indispensability and nutritional roles of magnesium, manganese, calcium, phosphorus, fluorine, aluminum, iron, zinc, sodium, potassium, boron and cobalt.²⁰ This included with E.R. Orent the discovery of the indispensability of magnesium²² and the shared but independent discovery of the indispensability of manganese.²³ A cooperative program with the late R.H. Follis involved the detailed histological examination of many organs and tissues of rats restricted to diets extremely deficient in single indispensable inorganic elements. Necrotic lesions were produced in the heart and kidneys in potassium deficiency.²⁴ This alerted clinicians to the importance of potassium in both enteral and parenteral nutrition. The discovery of unique esophageal and skin changes in zinc deficiency²⁵ was followed by extensive studies of the practical importance of this element in the diet of man.

Other areas of research included vitamin E and nutritional muscular dystrophy,²⁶ metabolic and chemical measures of thiamin deficien-



E.V. McCollum about 1936

cy,^{27,28} nutrition and liver cirrhosis²⁹ and fractionation of amino acid mixtures.³⁰

Promotion of Public and Professional Understanding of Nutrition

From 1916 until the year of his death in 1967 McCollum was an outstanding nutrition educator. In 1916 he wrote a series of articles for *Hoard's Dairyman* on the newer developments—largely his own—of great significance in nutrition. From 1922 to 1946 he wrote 169 articles that were published in *McCall's* magazine. In 1918, acting on behalf of Herbert Hoover and the U.S. Food Administration, he toured the country to inform community leaders and health professionals of the newer knowledge of nutrition. In the same year he published the first edition of *The Newer Knowledge of Nutrition*. Within the next 21 years four other editions were published. In addition, during that same interval he published six editions of *Food, Nutrition and Health*, a book for the lay public.

Other Contributions

Throughout his professional life McCollum had the confidence and attention of many industrial and governmental leaders. He influenced the dairy industry to promote scien-

tific research and a greater production of dairy products. Beginning in 1923 he was the first to emphasize to the baking industry and public the importance to health of substantial use of milk solids in bread baking. He gave support to many organizations whose programs focused on health and the strengthening of family life. This included consulting arrangements with the Merrill-Palmer Institute in Detroit (1919-31), United States Pharmacopeial Revision Board (1932-49), National Advisory Health Council (1933-37), Mixed Committee on Nutrition of the Health Section of the League of Nations (1936-37), and the Scientific Advisory Committee of the Nutrition Foundation, Inc. (1941-53). McCollum was involved in many other services in these general categories.^{1,20}

McCollum was the recipient of honorary degrees from four universities, including Johns Hopkins University, and he had honorary memberships in many significant associations and societies beginning with the American Dietetic Association in 1919 and concluding with foreign member of the Royal Society of London in 1961. He was honorary president of the International Union of Nutritional Sciences in 1955 and of the International Congress on Nutrition in 1960. He received many awards for research and service including the Mead Johnson Award (1940), the Osborne and Mendel Award (1955), The Borden Centennial Award (1957), and the Charles F. Spencer Award (1958).²⁰

Of the many outstanding attributes of McCollum/ a notable one is the broad perspective he held and portrayed, as expressed fittingly in the last chapter of his *History of Nutrition*:¹⁵ "Before the emergence of the science of nutrition many millions of people in every generation, from ignorance, led lives blighted by malnutrition. Inferiority and suffering of domestic animals, with consequent economic loss, was even more widespread throughout the world. The new knowledge brought about improvement of health and its attendant elevation of the status of human life above the sordid, to a degree scarcely equalled by any other agency concerned with the prevention or cure of disease. Implicit in physiological well-being is the prospect for betterment of courage, ideals, purposes, and achievement.

Viewed from this standpoint, the rise of the science of nutrition is one of the greatest events in human history."

A special distinction was the inclusion of McCollum as one of "the twenty-four persons who in North America were judged to have made the most important discoveries in medical sciences in the previous one hundred-fifty years." This recognition is in the Hall of Fame, Museum" of the Rochester (New York) Academy of Medicine (1941). Two additional distinctions are the establishment of the McCollum-Pratt Institute for research at the Johns Hopkins University (1948) and the naming of the principal dormitory McCollum Hall at the University of Kansas (1965).

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