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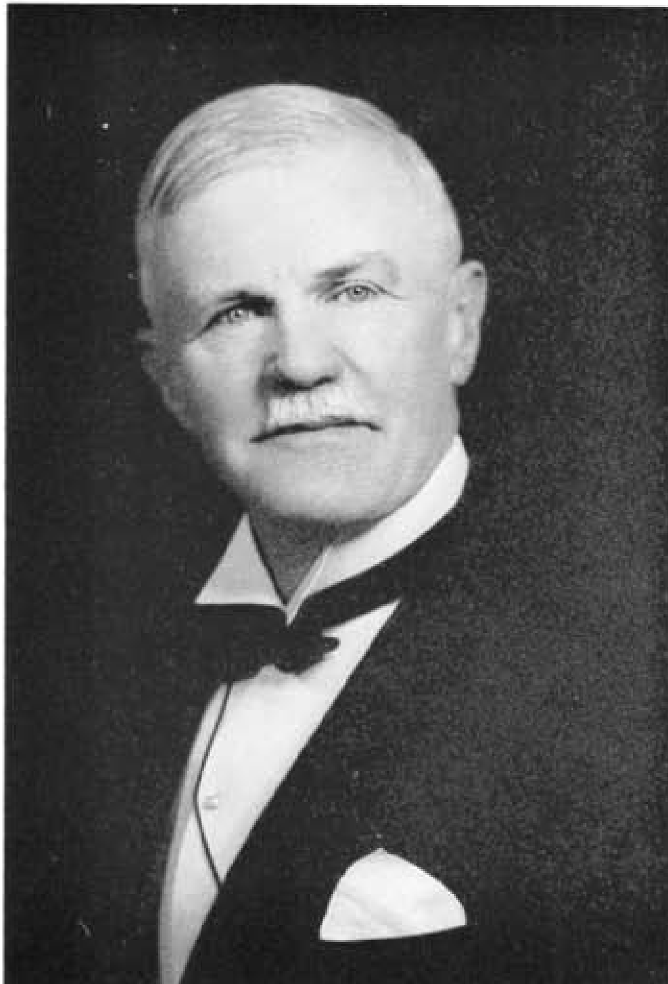
FRANCIS GANO BENEDICT

1870—1957

A Biographical Memoir by

EUGENE F. DUBOIS AND OSCAR RIDDLE

Biographical Memoir



Francis G. Benedict

Photo courtesy of W.C. Tracy

FRANCIS GANO BENEDICT

October 3, 1870—May 14, 1957

BY EUGENE F. DuBOIS AND OSCAR RIDDLE

FRANCIS GANO BENEDICT was trained as a chemist at Harvard and Heidelberg. At Wesleyan University he shared in important biochemical studies, and while there developed a capital mechanical device. As director (1907–1937) of Carnegie Institution of Washington's Nutrition Laboratory, in Boston, he became one of America's leading physiologists and perhaps the foremost investigator of gaseous metabolism of his time.

He was born October 3, 1870, in Milwaukee, Wisconsin, the son of Washington Gano and Harriet Emily (Barrett) Benedict. A paternal ancestor was Thomas Benedict, who came from England about 1645 and settled near Providence and Pawtucket, Rhode Island. Frank was named for another paternal ancestor, François Gano, who, during a religious war, escaped from his native France in a whiskey barrel. When Frank was seven years old, the family moved to Orange Park, Florida, and in his eleventh year they moved to Boston. He belonged to a musically inclined family that added piano lessons to his public school education in these various cities.

When about thirteen years old he attended a lecture in Boston by Professor James F. Babcock on "A Basket of Coal," which opened his eyes to the wonders of chemistry. Thereafter he set up a laboratory in the cellar of his home where, without supervision, he performed experiments and fortunately avoided blowing himself to pieces. One suspects that the outfitting and prolonged maintenance of this self-made laboratory must have developed some of the mechanical skills, and familiarity with numerous gadgets which were later of much use to the builder of ingenious devices for measuring the heat production of man, mouse, and elephant.

For one year following his graduation from public high school in Boston, Frank studied chemistry exclusively, at the Massachusetts College of Pharmacy and later, while an advanced student at Harvard (1892–1894), he also served as instructor in chemistry at that college. He entered Harvard at the age of nineteen. There, he had the most important experience of his life in his association (as pupil and assistant) with Josiah Parsons Cooke, the professor of chemistry. He was granted the A.B. degree in 1893, remained for a year of graduate study, and obtained the A.M. in 1894. These five years at Harvard were years of exceptionally hard work which excluded all extracurricular activities. Indeed, the usual games and sports remained always foreign to the boy and man. His father, a business man, disapproved of collegiate training for the son, wished for him a career in business and music, and frowned upon sports because they might disable the hands for piano playing. At the end of an additional year of graduate study, chiefly under Victor Meyer, Heidelburg University granted him a Ph.D., *magna cum laude,* in 1895.

As research assistant to Professor W. O. Atwater, he began an association with the chemistry department of Wesleyan University, Middletown, Connecticut, in the autumn of 1895. Here Dr. Benedict advanced from instructor to professor (1905–1907). From 1895 to 1907 he also held an appointment as physiological chemist in the U. S. Department of Agriculture, and from 1896 to 1900 as chemist at Storrs Experiment Station. In these several posts at Middletown his research was closely associated with that of the distinguished physiological chemist, Dr. Atwater, and the transformation of chemist to physiologist got well under way. In these early years Dr. Benedict made what he regarded in 1924 as his first important contribution to science. In his own words:

"The development of the closed circuit respiration apparatus and calorimeter at Wesleyan University is, in my judgment, the most important mechanical contribution I have been privileged to make. This was developed from the ground up, based upon the idea that if the actual amount of oxygen absorbed by the human body in life processes could be directly measured such a measure would have great significance in the comparison with the simultaneous heat production."

Similarly one could note that, also in 1924, he regarded his study of the chemical composition of the atmosphere, particularly its oxygen content (1912), as the most important *chemical* study he had ever made.

Early in the Wesleyan period, in 1897, Frank was married to Cornelia Golay, of Brewer, Maine. Their maternal grandfathers were brothers, and both were physicians. Mrs. Benedict was a Vassar graduate trained in zoology and biology. Somewhat later, at the Nutrition Laboratory where physiological studies predominated, she shared fully in the conduct and publication of several valuable studies. That the Middletown researches with the calorimeter were of much significance in medicine was early recognized by at least three medical leaders of the day—Doctors Welch, Billings, and Keen. Largely through their initiative the Trustees of Carnegie Institution of Washington were led to establish the Nutrition Laboratory in Boston, and Dr. Benedict was appointed as its director (1907–1937). Built alongside Harvard's Medical School, this soon became famous as one of the leading research laboratories of America.

While the new laboratory was under construction, early in 1907, the Benedict family made the first of its many trips to Europe. Establishing his wife and his daughter, Elizabeth, in Geneva, Frank began an acquaintance with most of the leading physiologists of Europe, and brought back to his unfinished laboratory a fresh view of results, methods, equipment, and persons currently connected with the evolving problems and purposes of that new laboratory. All this he regarded so highly that he planned thereafter to repeat these visits at approximately three-year intervals. With the exception of the years of the First World War, this was done. On these trips abroad he lectured most liberally, often in German or French. Though he was relatively inactive in the strictly professional societies of his own country, the work of few American physiologists was so quickly and widely known in Europe as that of Benedict.

At the Nutrition Laboratory his research activities were divided, necessarily, between the devising and adequate testing of new or simplified appliances and the actual use of these instruments in studies on those vital activities which were his main objective and interest. Though little more than a casual reference to these numerous appliances and instruments can be made in these pages it should be observed that they constitute a major contribution to physiology. He built two "small" calorimeters of the Atwood-Rosa type and devised several much smaller and relatively inexpensive instruments for measuring the oxygen consumption as a means of estimating the energy production. One such device is the small "Benedict apparatus" since used widely in hospitals and doctors' offices for measuring the metabolism of patients (1916–1918). Other devices were adapted to measuring the heat production of man and of animals varying greatly in size—from the 8-gram dwarf mouse, the rat, and the pigeon to the python, the steer and the 4,000-kilogram elephant.

One of the writers of this memoir was a follower of Benedict in the field of calorimetry and metabolism.

In the Russell Sage Institute of Pathology, Bellevue Hospital, New York, we built a human calorimeter for the study of disease—following closely the design and experimental method used by Benedict in his 'small' calorimeter. We there found that the Benedict apparatus and methods of calculation were extraordinarily accurate. When I later used his smaller, simpler universal or unit apparatus and the Benedict-Collins small spirometer these also were found to be accurate and very useful. In the course of this work I had to study all of Benedict's publications in great detail, and I do not remember finding a single miscalculation, or a statement that was not supported by evidence. (E. F. D. B.)

Dr. Benedict repeatedly said that the unifying aim and objective of most of his studies was to uncover the laws governing those vital activities most closely related to heat production and heat loss in the human and animal organism. Pursuit of this aim committed him to several types of precise measurement: direct measurements of the heat given off by the body; quantity of carbon-dioxide produced; more especially, the quantity of oxygen consumed; loss in weight of the body from hour to hour; losses from each of the several paths of heat loss; the temperature of the skin and body trunk; and several of the metabolic accompaniments of muscular work, such as walking, riding a bicycle, and stair climbing. One particular and quite comprehensive program of study emerged during his first decade at the Nutrition Laboratory and this was destined to become his foremost interest during the last half of his studies there. This involved a wide survey of the comparative metabolism of animals. His initial concentration on the human being was, in a sense, a preparation and part of this broader study. He came to regard both small and large warm-blooded species as the more essential part of this program. Of the cold-blooded animals, only representatives of large species—large snakes and giant tortoises—were included, since Krogh and others had undertaken adequate studies of the smaller species.

With these aims, and through use of his several types of calorimeters during a span of forty years, Benedict and his many collaborators added much to our understanding of heat production and heat regulation in humans and animals, in infancy and old age, in races, sexes, hybrids, and several other related subjects. More especially, he examined with much skill and success the conditions requisite for a measurement and calculation of the so-called "basal" metabolism in man and a score of species of other mammals, birds and reptiles, and he greatly extended our knowledge of the comparative metabolism of vertebrate animals.

Harris and Benedict (1919) provided standards based on age, sex, height, and weight which are still most useful for comparing the metabolism of a patient with that of the normal person. With Osborne he determined the heat of combustion of several vegetable proteins. An intensive study of the respiratory metabolism in diabetes by Benedict and Joslin is one of the most important ever made of that disease. With Carpenter he provided sound information on a variety of topics that included the respiratory exchange, metabolism during rest and during fever, and the stimulating effect of nutrients. With one or another collaborator he made several studies on the physiological effects of alcohol. With R. C. Lee he studied lipogenesis in the goose, and hibernation in the woodchuck. Other collaborators were numerous, some of them working elsewhere than in Boston (Ritzman, MacLeod, DuBois, Fox, Riddle, Sherman, Steggerda, Wilson). Results from this large group of studies—even a list of the problems more or less successfully attacked—must remain unnoted here. The variety and scope of those numerous studies is indicated in the appended Bibliography. Many of those results were brought together, and subjected to scholarly analysis, in the last (1938) of Dr. Benedict's monographic publications, *Vital Energetics: A Study of Comparative Basal Metabolism*. This book is the outstanding classic in his field of study; it is one of the classics of physiology.

Of course, it cannot be assumed that all of Benedict's published views on basic questions of respiratory metabolism remained unchanged during his long career, nor that some of those views remained unchallenged by colleagues in this field of study. In earlier years Benedict considered "basal" values as more firmly fixed than was consonant with his later findings in several species of animals. In contrast to the constancy observed in humans (except in emotional disturbances, 1935) he concluded (with Ritzman, 1935) that, "In view of the lability of the basal metabolism of dairy cows, the concept of constancy in basal metabolism of animals must be revised." Less marked lability he had earlier observed (with Riddle, 1930–34) in doves and pigeons, and he was later to find (with Lee, 1937–38) surprising fluctuations in the goose and in the non-hibernating phase of the woodchuck.

As a part of comment on this topic perhaps a reference to a personal experience of each of the two writers of this memoir is not inappropriate. One of us collaborated with Benedict during a period of almost ten years.

At the beginning of this work, done with doves and pigeons in my laboratory, I found him quite reluctant to grant the possibility that the hormones (other than that of the thyroid) may be a significant factor or factors in the heat production of animals—more especially, the possibility that they are responsible for temporary and cyclical increases in heat production. Later results—obtained both in our collaboration and in the work of others—apparently made that view acceptable to him, but he developed no program for a personal study of that area. Actually his later interests centered more and more in the comparative basal metabolism of adults of various species (1938)—not that of the individual, the sex, or even the race. Interestingly enough, this restriction of main interest seems in the end to have resulted in an extension of his concept of lability and of multiple causation within both areas—that of heat production in different species, and at different periods in the adult individual. In his final monograph (1938), dealing with species difference in adult animals, he lucidly documented his confidence in a fairly wide divergence and inequality of the basal heat production of the various warm-blooded species, in the lability (occasional) of basal heat production, and in the views that heat production is far more meaningful than heat loss, and that heat production varies in response to a wide and still inadequately explored range of conditions and tissue stimuli. (O.R.)

The other author of this memoir was brought up in a school of nutrition that considered the surface area an important factor in basal metabolism, though the school never stated very clearly whether or not it considered surface area a causal factor.

Benedict, on the other hand, maintained that if the surface area were useful in estimating the normal metabolism that this was in more or less accurate relationship—but not causal. As a result of this difference in theory he and I had a long controversy in the literature.

Fortunately, it was always a friendly controversy. Indeed the hotter the arguments the stronger our friendship became, and we both enjoyed the dispute which stimulated some of our best work. Eventually Benedict and I came to almost the same viewpoint in a position almost halfway between the two extremes. The question is still the subject of dispute, and may long remain unsettled. (E.F.D.B.)

Early critical comment maintained that Benedict's lack of initial biological training led the Nutrition Laboratory to a too restricted program of studies and to occasional errors of procedure. In regard to the latter he was indeed frustrated in his study of the periodic (monthly) variation of the metabolism of women through failure to recognize that ovulation, not menstruation, was the critical time and point in such a study. His avoidance of the field of vitamin research—a large area of nutrition whose emergence practically coincided with the founding of his laboratory—disappointed many during one or two decades. In retrospect it can be seen that the unfolding of both the vitamin story and that of the gaseous metabolism warranted the establishment of separate laboratories or institutes. Perhaps the same observation applies to the circumstance that the Nutrition Laboratory remained aloof from the quite coincident and highly significant development of knowledge of cellular respiration and the enzymes involved in that process.

Benedict's disagreements with Rubner, as recorded in the literature, relate especially to the use and significance of surface area in calculations of heat production and to the role of temperature in metabolism measurements made for comparative purposes. In his private notes for the year 1913 he wrote: "It is always a matter of great regret to me that Prof. Rubner is so disinclined to discuss scientific matters. I have never been able to draw him out to any length in scientific discussion either in his visit to America or later in my visit to Berlin." Mentionable too is Benedict's unreported attempt, some twenty years later, to lessen this area of controversy through friendly and prolonged personal correspondence. This effort, however, was a deep disappointment to Benedict. When he later wrote (1938) his summarizing monograph, *Vital Energetics,* these disagreements were candidly but most courteously reexamined.

Though only the studies of a later day can properly assess some of Benedict's theoretical views, it is perhaps significant that those most familiar with his total contribution are commonly the ones most impressed by the magnitude and coherence of that contribution. Added to indispensable and often expensive instrumentation, made quickly available to colleagues, was a steady flow of the results of keen observation and accurate measurement. During forty years he was a careful planner of experiment and a meticulous guardian of method. Continuously, he was a source of science-building fact. Ultimately, a foremost designer of the outlines of whatever respiratory metabolism now seems likely to contribute to the comparative physiology of man and other air-breathing vertebrate animals.

The list of Dr. Benedict's publications includes nearly 300 titles. Thirty-three of these exceed 100 pages, and eight of them contain from 301 to 712 pages. This list does not include his 30 Annual Reports as director of the Nutrition Laboratory to the Trustees of Carnegie Institution on the accomplishments of the year in his laboratory. Though his collaborators did much of this writing, he was a prodigious writer, commonly using the rather unusual method of dictating to a secretary or dictaphone. This sometimes resulted in books or papers that were too long, but it was his way of making the results of his studies available to others. Thirty-five contributions were published in foreign journals in French or German.

Here one may reflect momentarily on one circumstance that was peculiarly—probably vitally—favorable to Benedict's highly productive career. This sustaining circumstance was his early and influential association with the Carnegie Institution of Washington. During the decades in which his work was planned and done, most of his colleagues in physiology could find only meager financial support for either their research or their more expensive publications. Though the apparatus he developed was exceptionally expensive, though the use of this equipment in actual research often required uncommonly costly assistance and materials, and though the cost of publication of a stream of monographs was beyond the resources of nearly all American universities, these restraining barriers were avoided or minimized for him. The resources and foresight of Mr. Andrew Carnegie, sustained by the vigilant interest of officers of the institution he founded, continuously smoothed the way for the personal bent and talents of this investigator.

Frank Benedict was elected a member of the National Academy of Sciences in 1914, of the American Philosophical Society (1910), of the American Academy of Arts and Sciences, and of the Society of American Magicians (1930); of the Boston Branch of this society, in the twenties. He received the medal of the National Institute of Social Sciences in 1917, "in recognition of his valuable contributions to human energetics and the alcohol problem"; and the gold honor medal of the University of Hamburg in 1929, "in recognition of his successful work in metabolism and physiology." He was an honorary member of scientific or medical societies centering in Paris, Brussels, Halle, Budapest, and Vienna. Honorary Sc.D. degrees were conferred by Wesleyan University (1910) and the University of Maine (1924). He was given an honorary M.D. by the University of Würzburg in 1932.

Benedict held quite inflexible views on some social questions. He was an enemy of alcohol, but an honest enemy. His published researches on this substance are unbiased accounts of its physiological effects. In the days when Maine was a prohibition state, he once assumed chief responsibility for stopping the illegal sale of liquor in Machiasport by apprehending the seller. The family of the latter were friends of the Benedicts, but Frank considered this neighbor a menace to the town. He was highly suspicious of the power of labor unions and strongly resented it when, on one occasion, the union tried to get him to discharge some of the nonunion workers in his laboratory. Again, during the construction of his laboratory he was bothered by some plumbing inspectors. To settle this matter, he himself took the examinations and became a licensed plumber. Thereafter he proudly showed this license not only to inspectors, but to visitors as well.

Frank Benedict was a large man, always dignified and impressive. He was full of energy, always interesting in his conversation, considerate of others, good natured, kindly, self-confident. He was also impatient with excuses, and could be sharply critical of an inadequate performance or of an individual not accommodated by his standards. He was scrupulously careful in financial matters. He had a lively sense of humor, and was unusually good as a lecturer—well understanding the art of showmanship; his talks were always well planned and clear, appropriately illustrated with lantern slides and a few anecdotes. He had a strong aversion to profanity and shady stories. Inwardly, he was religious. Magic and the piano, "played for my own amazement," were his chief hobbies. His color-blindness failed to destroy his pleasure in circuses and museums. Beyond these hobbies was his lifelong interest in international amity. This he pursued through a voluminous correspondence with his many friends in Europe and Japan— in addition to the visits, lectures, and use of European publication facilities already noted. A hard worker in the laboratory, his happiest hours seem to have been those spent in his summer home at Machiasport with its beautiful view of the coast of Maine.

On his retirement as director of the Nutrition Laboratory, November, 1937, he widely advised his colleagues that this also marked the termination of his scientific efforts and interests. During the earlier years that followed he sometimes left his Machiasport home for lecture tours—using "Magic and Science" and "The Physiology of the Elephant" as subjects. He suffered an almost fatal accident in April, 1940, when struck by a taxicab in downtown Boston. After a long convalescence, he again lectured occasionally, but usually found it better to spend the winter months in California, New York City, or Florida. Though unable to travel to California (or elsewhere) during his last years his former visits there had permitted him to be close to most of those who survived him—his widow, Cornelia Golay Benedict; his daughter, Elizabeth Harriet (now Mrs. Henri Hänggi); and his grandchildren, Dr. Cecil E. Leith and Cornelia Sarah Garbesa. He died in Machiasport on May 14, 1957.

Frank Benedict had the good fortune to use a talent and a durably strong hand in creating both basic and applied physiology in America, and to pass along that creation and related American learning quickly and persuasively to Europe. He was a citizen and untiring worker much honored at home and abroad.

KEY TO ABBREVIATIONS

Am. Chem. Journ. = American Chemical Journal
Am. Journ. Diseases Children = American Journal of Diseases of Children
Am. Journ. Obst. Gynecol. = American Journal of Obstetrics and Gynecology
Am. Journ. Phys. Anthrop. = American Journal of Physical Anthropology
Am. Journ. Physiol. = American Journal of Physiology
Ann. Physiol. = Annales de Physiologie
Arch. f. d. ges. Physiol. = Archiv für die gesamte Physiologie
Arch. Intern. Med. = Archives of Internal Medicine
Biochem. Ztschr. = Biochemische Zeitschrift
Boston Med. Surg. Journ. = Boston Medical and Surgical Journal
Bull. Soc. Scient. d'Hygiène Alimen. = Bulletin de la Société Scientifique d'Hygiène Alimentaire
Chinese Journ. Physiol. = Chinese Journal of Physiology
Deutsch. Arch. f. klin. Med. = Deutsches Archiv für klinische Medizin
Indus. Eng. Chem. = Industrial and Engineering Chemistry
Inst. Expt. Med., Leningrad = Institute of Experimental Medicine, Leningrad
Journ. Am. Chem. Soc. = Journal of the American Chemical Society
Journ. Am. Med. Assoc. = Journal of the American Medical Association
Journ. Biol. Chem. = Journal of Biological Chemistry
Journ. Mammal. = Journal of Mammalogy
Journ. Med. Research = Journal of Medical Research
Journ. Nutrition = Journal of Nutrition
Journ. de Physiol. et de Path. gén. = Journal de Physiologie et de Pathologie générale
New Eng. Journ. Med. = New England Journal of Medicine
New York Med. Journ. = New York Medical Journal
Proc. Am. Acad. Arts Sci. = Proceedings of the American Academy of Arts and Sciences
Proc. Am. Philos. Soc. = Proceedings of the American Philosophical Society
Proc. Am. Soc. Animal Nutrition = Proceedings of the American Society for Animal Nutrition
Proc. Nat. Acad. Sci. = Proceedings of the National Academy of Sciences
Schweiz. Med. Wochenschr. = Schweizer Medizinische Wochenschrift
Sci. Am. Supp. = Scientific American Supplement
Sci. Monthly = Scientific Monthly
Skand. Arch. f. Physiol. = Skandinavische Archiv für Physiologie
Storrs Agric. Expt. Sta. = Storrs Agricultural Experiment Station
U. S. Dept. Agric., Office Expt. Stations = United States Department of Agriculture, Office of Experiment Stations
Univ. New Hampshire, Agric. Expt. Sta. Tech. Bull. = University of New Hampshire, Agricultural Experiment Station Technical Bulletin

Verhandl. d. phys.-med. Gesellsch. zu Würzburg = Verhandlungen des physikalische-medizinische Gesellschaft zu Würzburg
Yale Journ. Biol. Med. = Yale Journal of Biology and Medicine

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