

CASIMIR FUNK

(1884–1967)



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— A Biographical Sketch (1884–1967)

“... the deficient substances, which are of the nature of organic bases we will call “vitamines”; and we will speak of a beriberi or scurvy vitamine, which means a substance preventing the special disease.”

The paper containing this sentence was published by Casimir Funk in 1912. In this so-called résumé he tried to show that various diseases listed in the subtitle, such as scurvy and beriberi, were due to nutritional deficiencies, and not to food intoxications or infectious diseases, as was widely believed at that time; they could all be prevented by a complete diet.

The man who wrote this historic paper was born on February 23, 1884, in Warsaw, Poland, the son of Jacques and Gustawa Funk. Jacques Funk was a physician who had specialized in dermatology, and a scientist in his own right: his clinical research resulted in sixty publications, and his reputation had spread beyond the borders of his native Poland, most of which was, at that point in history, under the heel of the Russian Empire.

If Casimir's home environment provided an excellent background for a scientific career, the socio-political conditions did not. After some years of home tutoring, which included extensive reading, Casimir, despite excellent marks, failed to gain entrance into the Russian Government school for ethnic reasons. In fact, there existed a “black market” in secondary school acceptance. Later, entrance was arranged for him, but the timid boy's four years in the dull and anti-Polish Government school were not a complete success. He finished his secondary education as the best student in his class in a better, private, school. A congenital dislocation of the hip had previously brought him for prolonged, though unsuccessful, treatments to Germany and to Austria. The latter was also the family's favorite destination during vacation time. Thus it happened that at age 16 Casimir, whose native tongue was

Polish, was also fluent in Russian and German. Soon he was also to acquire fluency in French: feeling that there was no future for Casimir in Poland, his parents sent him to Geneva, Switzerland, to study biology. He later moved to Berne, where he specialized in organic chemistry; at the age of 20, Casimir passed his oral exams and defended his doctoral thesis on the chemistry of two organic dyes of the stilbene family (1904).

A fair number of Polish and Russian teachers and students could be found in Swiss universities at that time; these included some men of great promise. It is not surprising that this caused resentment, and perhaps jealousy, in some circles of the native-born population. While this did not in any way interfere with Casimir's studies and progress, the sensitive young man was keenly aware of it. Even in later years, in the United States, he never seemed to lose entirely the feeling of being somewhat different, and, therefore, not wholly wanted.

Having finished his graduate work, Casimir went home to discuss his future with his parents, who discouraged him from following in his father's footsteps and studying medicine. He decided to enter the newly blossoming field of biochemistry. At the Pasteur Institute in Paris a chair in biochemistry was already in existence. It was occupied by Gabriel Bertrand, a solitary worker with limited interest in students. There Casimir became involved, among other things, in chemical work with amino acids and organic bases, which was probably the reason for his next move, two years later, to Emil Fischer's laboratory in Berlin. In Paris he also befriended von Euler, who in later years was to receive a Nobel prize in chemistry, and became acquainted with Arrhenius and Metchnikoff. He also seemed to have thoroughly enjoyed the artistic and intellectual life of the French metropolis. While the following

year in Berlin may have been culturally less stimulating, it was of great scientific value to the young scientist. At that time, Berlin was a world center of scientific progress, especially in chemistry and allied sciences. Casimir worked under Emil Abderhalden, who was Fischer's private medical assistant, and their cooperation resulted in several publications. His interests covered various aspects of physiological chemistry, with emphasis on amino acids and protein.

In 1907/08 Funk, who up to this time had been supported by his parents, earned his first money as a biochemist at the municipal hospital in Wiesbaden, Germany. There he adapted Bertrand's assay for sugar to the determination of blood sugar, worked on peptide separation, and familiarized himself with the characteristics of malignant tumors. Still in cooperation with Abderhalden, he undertook research on uric acid metabolism. This finally led him back to Berlin in 1908. Abderhalden's position having changed, relations between the two men became strained, and Funk transferred to the Charité, the University Hospital in Berlin. During his eight months at the hospital, he undertook some respiration studies on babies. Not seeing much hope for a rewarding future at the Charité, he moved to the Lister Institute in London in 1910 on the recommendation of the Englishman Dean, whom he had befriended in Fischer's laboratory.

The Lister Institute, under the leadership of Charles James Martin, was devoted mainly to preventive medicine. In 1911 Funk published his first paper in English — the language of the majority of his later publications — on the synthesis of dihydroxyphenylalanine ("DOPA"). His success in this field was probably instrumental in his subsequent appointment as a Scholar of Lister, with an annual salary of 150 pounds.

The head of the Institute (he became Sir Charles Martin in 1927) was in communication with an English doctor in Malaya, W. L. Braddon, who was interested in beriberi and had published a book about the disease in 1907. Braddon believed that beriberi was caused by a toxin, while Martin thought that an essential amino acid was discarded with the rice

polishings, thus causing a protein deficiency. Funk, given the job of finding the missing substance, discarded the "protein deficiency" theory on the basis of his preliminary experiments, and started to look for some undefined material present in rice polishings, but absent in the polished rice. In 1912 he succeeded in preparing thiamin-containing extracts, first from rice polishings, and later from yeast, milk, and ox-brain. According to Williams (1961) these extracts were relatively low in beriberi-preventing activity. Williams quotes Barger as having suggested in 1914 that the original substance isolated by Funk may have been impure nicotinic acid, the antineuritic properties being due to the impurities. On the other hand, Funk was able, in the same year, to state that "the curative substance is a pyrimidine base, analogous to uracil and thymine . . .", indicating that he must have had a product on hand that contained appreciable amounts of the vitamin. In the following year, he actually isolated and identified nicotinic acid from one of the fractions of his extract, without, however, recognizing its vitamin nature.

To Funk must go not only the honor of preparing the first useful concentrate, however impure, of the antineuritic factor. More important, in this writer's opinion, was his scientific intuition, exemplified in the well-known résumé mentioned earlier, in which he listed a number of deficiency diseases, coined the term "vitamine" deficiencies for these diseases, and even predicted, from the apparent minuteness of the requirements for the proposed micronutrients, that they may be used as, or transformed into, ferments (enzymes). F. G. Hopkins as well as other scientists of that time also believed in the existence of substances, other than the known major nutrients, that were required in small amounts. The boldness of Funk's predictions, however, in this paper as well as in his later book on vitamins (1914) had a profound influence on subsequent work. Scientists began to take an active interest in the new field, which resulted, within 35 years, in the discovery of all vitamins known today, and, incidentally, in the creation of a billion-dollar industry.

At the Lister Institute, Funk worked under rather primitive conditions, either alone or with the aid of a servant not trained in the sciences. While his vitamin theory did not create many converts in the medical profession, he made an excellent impression on Hopkins at Cambridge: Casimir received a Beit Fellowship and the degree of Doctor of Science of the University of London for his efforts. In the spring of 1913 he had also been joined by his parents; Funk senior helped with the collection and evaluation of data and abstracted the literature for his son. The younger Funk, however, was not entirely satisfied, and eventually accepted a position at the Cancer Hospital. There he had at his disposal a micro-analytical laboratory equipped according to the suggestions of the Austrian analytical chemist, Fritz Pregl, and was able to concentrate on vitamin problems and the study of tumors. He was also given an assistant, who later became professor of biochemistry at the University of London, and, for his valuable work as chief of nutrition of the British Government during World War II, was knighted Sir Jack Drummond.

While vacationing with his parents in Ostend, Belgium, Funk met Alice Denise Schneidesch, and was married to her in the following year. During their honeymoon, World War I broke out.

England at war offered a less favorable climate for research, and had less sympathy for foreigners, than the England that had greeted Funk in 1910. He accepted a position at the Harriman Research Laboratory in New York, and arrived there early in 1915. Later in the same year, a son, Ian, was born to the Funks.

At first, Funk was intrigued by the New World. He was especially impressed by the lack of need for registration and identification cards, something that had been developed to a science in the Old World. The first shock came when he saw his new laboratory — a dark room without equipment. While the laboratory problem was eventually solved, the need for research funds forced him to look for industrial connections. After a health breakdown, possibly from overwork, he accepted a full-time industrial position. With deliveries from Germany halted, and the need

for chemicals of all types greater than ever, this was a time of opportunity for the growth of the American chemical industry. Funk, with imagination and skill, became one of the pioneers in the development of this industry.

His first position was not a success; the second position was a great improvement, but required an amount of travel that would make even a hardy commuter shudder. Funk had to get up at five in the morning, take an elevated train to the ferry to New Jersey, then take another train, followed by a trolley, and finally walk in order to reach the Calco Company in Bound Brook, New Jersey. There he prepared cinchophen, benzoic acid, and benzonaphthol, which were all in great demand. While he was apparently happy with the job, a better and geographically more convenient opportunity soon offered itself: a responsible position in the research department of H. A. Metz and Company, with a promise for time to work on vitamins. This position ended his financial worries.

At first, there was little time to continue in his primary field of interest, the vitamins. He had to solve, among other things, Metz's problems in the preparation of salvarsan and neo-salvarsan, which heretofore had been imported from Germany, and organize the industrial synthesis of adrenaline. He worked very hard and, in the words of one of his co-workers, he was a genius at thinking out future research. The success of Funk's activity for the company finally led to greater freedom for himself. Transferred to the Hudson Street Branch in the city, he had the valuable cooperation of H. E. Dubin and Louis Freedman. An early product of the new effort was "Oscodal," a vitamin A and D concentrate, which was the first vitamin preparation accepted by the American Medical Association as an ethical product. The group was less successful, for unexplained reasons, with a B-vitamin product from yeast. From 1920 to 1923 Funk also held the position of Associate in Biochemistry at Columbia University. There he met Benjamin Harrow, who was to become Funk's biographer (1955). This period saw a number of publications with Dubin and Freedman on factors influencing the

vitamin requirements of rats, and on the vitamins in yeast. Freedman, whose doctoral research at Columbia was supervised by Funk, investigated nutritional requirements of yeast and bacteria, methods for measuring bacterial growth, and the use of yeast growth for the assay of B-factors.

Despite progress, Funk was not entirely happy, and a change in scenery seemed in order. The medical director of the League of Nations was then, with the help of the Rockefeller Institute, trying to provide better health services for various countries, and engaged Funk to work for 2 years for the Health Institute in Warsaw, Poland. In 1923, at the age of 39, Funk left New York, making several professional visits on the way, including one to Pregl in Graz, Austria, where he tried to perfect his analytical techniques.

In Warsaw, the family settled in a modest apartment, and Funk faced the problem of setting up a laboratory without sufficient funds for either equipment or chemicals. In order to create an income for his institute, he initiated a small-scale manufacture of insulin, using his own funds as seed money. A severe case of pneumonia, perhaps contracted on one of his cross-country trips in an open Ford to obtain materials, interrupted his efforts. Recovery was slow. His serious illness probably caused concern to the Polish authorities: the family was moved to a small house in the suburbs, and he obtained newer and better laboratories. Money, however, was still in short supply. In 1924, a second child, a daughter, was born to the Funks in Danzig: they felt that in Danzig better medical care would be available than in Warsaw, and had gone there to await the birth of the child.

The Rockefeller Institute was satisfied with Funk's insulin work, extended his stay for another two years, and assigned him \$3,000 for equipment, which he purchased in Berlin. Funk and his cooperators — including S. K. Kon, whom he recommended for a Rockefeller Fellowship, and who later became well known for his nutrition work at Reading, England — published widely on insulin, on vitamin problems, and on methods in nutritional biochemistry, and developed an interest in hormones. The years in Warsaw were fruit-

ful, and certainly stimulating to the local scientific effort. Funk also visited many European laboratories and attended various meetings. Sweden, Rumania and Russia were among his destinations. In Sweden he heard that he was under consideration for the Nobel Prize for his vitamin work. Eventually the Prize went to two other participants in the search for the first accessory food factors: Eijkman and Hopkins. In Russia he lectured on hormones — he still had a fair command of Russian — to a most attentive audience. He visited with Pavlov, and was offered the directorship of a nutrition and hormone institute in Moscow, an offer which he declined.

Their life in Warsaw was not unpleasant, and Mrs. Funk had made many friends. The political situation in Poland, however, was still unsettled. Inflation and starvation were bywords of the scene. The uprising in 1926 under Pilsudski once again brought home the basic instability of the situation. During the uprising, Funk's Institute was hit with shrapnel, and the hall of his apartment riddled with bullets. It was only natural that he decided to look westward again. In the fall of 1927, at the end of his Rockefeller appointment, he left for Brussels, the home of his in-laws. There were frequent contacts with the medical school faculty during his five months' stay, but the relationship did not bloom into a position at the University. In 1928 he moved to Paris to accept a part-time position with the pharmaceutical house of Grémy, which left him time for the effort needed to locate a laboratory suitable for the advancement of his own research interests.

Grémy manufactured sera and vaccines, and needed a research and development center for new products not heretofore produced in France. Funk had been interested for some time in sex hormones, and now submerged himself into a study of the identification of the male hormone in urine. Conditions at Grémy deteriorated, however, and Funk decided to branch out for himself. With the help of grants from various sources he built the "Casa Biochemica," which contained laboratories as well as his home. Various circumstances, including the financial disaster of 1929, brought about a much more modest build-

ing than originally planned, but Funk, with the help of his children and a handy man, was already hard at work in the animal laboratory while workmen were still hammering away in other parts of the building. Harrow, who worked with Funk, vividly described the cluttered laboratory in his biography, but noted that Funk always knew how and where everything was, a lack of identification marks notwithstanding. The years in Paris resulted in work on the chemical differentiation between male and female hormones, a series of papers on the male hormone and the preparation of active hormone extracts from urine, and similar preparations of pituitary gonadotrophic hormone. Another urine fraction yielded an active material that caused hyperglycemia and an increase in acetone bodies in rats. At the same time, the "Casa" turned out an insulin product that was as good as anything imported into France at that time. In the area of nutrition, Funk, in cooperation with Lejwa, found that not only liver, but also yeast contained an antianemic factor for newborn rats, and concentrated the active fraction in both materials. In this connection he helped the Roussel concern, then the second largest pharmaceutical house in France, to prepare an iron-free liver extract that was effective in pernicious anemia.

In 1934 Funk junior first appeared as a coauthor on one of his father's papers, and he continued to cooperate in his father's hormone work until joining the army during World War II.

During this time, Funk also served as a consultant for the U. S. Vitamin Corporation, and in collaboration with American firms developed the production of nicotinic acid and nicotinamide. Even though the investigation of the chemistry of hormones seemed to have been his major interest at that time, he was never far away from nutrition, and, especially, from the area of vitamins.

On September 1, 1939, World War II started with the invasion of Poland by Nazi-Germany. By the time Poland's fate had been sealed with the fall of Warsaw, Funk and his family had already arrived at the port of Bordeaux, leaving their material possessions behind in Paris. According to his biographer, Harrow, these pos-

sessions included all his chemicals, his library, apparatus and valuables, a garden that the family had planted, a Great Dane, three black cats, and hundreds of pigeons, rats, mice, guinea pigs, rabbits, and turkeys. After waiting for a week in Bordeaux, the family was finally able to board a small ocean liner and proceed to New York.

When the Funks arrived in New York, daughter Doriane was 15, and son Ian 24. Ian had studied medicine in Paris, while working at the same time in his father's laboratory, and received the M.D. degree from the Albany Medical College in 1942. Volunteering for service with the United States Army, he was severely wounded in 1944 when his jeep was blown up by a land mine in France. Recovery was very slow. Later, Dr. Ian Funk became head of the Psychiatric Division of the Veterans Administration Hospital in Albany, New York. Doriane, now Mrs. Henry Coenen, followed a college career in pure and applied art, and later also made her home in Albany.

Funk senior worked with the U. S. Vitamin Corporation, for which he had previously consulted, but had time left for independent research. He worked with B. Harrow at the City College of New York, and with I. M. Chamelin at the Welfare Hospital. His interests ranged from trace elements to ulcers, diabetes and cancer, with the latter emerging as his main concern. In 1944, he joined forces with Dr. Edward Jacobs, and once again the scarcity of funds made it necessary for the junior members of the family to help in the laboratory.

In 1945, a patron appeared on the scene in the person of Mr. Spanel, President of the International Latex Corporation. The Funk-Jacobs-Spanel Foundation was set up in 1945 with headquarters and laboratories in Manhattan. In 1946, however, Funk withdrew and returned to full-time employment with the U. S. Vitamin Corporation, which incorporated the Funk Foundation for Medical Research in 1947. Funk was now 63, and this was his last move; he remained with the Foundation until his retirement in 1963 at the age of 79. Much of his work at the Foundation centered around the chemistry of carcinomas, and

on factors influencing the production of ulcers. Funk's interest in oncology had developed early in his career. In 1915, while attempting to diagnose sarcoma by chemical means, he had noted a disturbance of carbohydrate metabolism in the affected birds. In the same year he also published a novel method of an interspecies transfer of a tumor, and again showed some interest in oncology while in Warsaw. After 1951, however, the nature of the development of malignant tumors and their chemistry became his overriding interest. He succeeded in demonstrating hormonal influences on cancer growth, and worked on the concentration of cancer-stimulating and cancer-reducing substances from beef spleen.

Of interest to Funk and co-workers in the early forties was also the action of liver extracts in counteracting the toxic effects of diethylstilbestrol and of sulfanilamide. In the fifties he published several studies on the ulcer problem. He attempted unsuccessfully to isolate enterogastrone, a substance claimed by Ivy to inhibit gastric secretion, and was experimenting with materials showing antiulcer as well as anti-acid secretion activity. Even in retirement, he continued to keep himself informed on developments in his field of endeavor. He died from cancer in the home of his son on November 19, 1967, at the age of 83 and, in accordance with his wishes, was cremated.

The life of some scientists can be partitioned by a biographer into neat little packages marked "private" and "professional." Not so the life of Casimir Funk. Having left his home as a youth, and buffeted by the upheavals of two World Wars, his private life was always closely intertwined with his professional activities. It is also difficult to use a simple label for his scientific career. His strength was in organic and biochemistry, but his work spanned nutrition and medicine, analytical biochemistry and chemical synthesis, oncology and endocrinology. Nutrition must have had a special fascination for Funk, since he frequently searched for implications of nutritional factors within the areas of his respective research interests. He was a hard worker, with a keen mind. According to his co-worker, friend,

and biographer, Harrow, his imagination was sometimes more that of a poet than of a scientist, and often his ideas were ahead of what was warranted by established scientific work. While some may only remember him as the coiner of the term "vitamines," and the creator of a new era in this field of endeavor, he contributed to many facets of biochemical-medical research and to methodology in the pharmaceutical industry. His legacy to the scientific world includes over 140 technical papers, about 30 reviews and non-technical articles, and numerous abstracts of oral presentations, the last one dated 1963.

Funk was of small stature, with a gentle face and blue eyes. A connoisseur of the arts, especially music, he was shy with strangers, but charming with friends. He was a man of strong opinions and definite convictions. His restlessness, in combination with the vagaries of the political destinies of the countries in which he resided, forced him to start many times from scratch. One may speculate how much more he might have accomplished had he been able to concentrate on his interests without pressures of economics and geography. Notwithstanding these obstacles, he has left an indelible mark on many areas of biological research, and enriched science by his work and his vision.

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REFERENCES

1. Funk, C. 1904 Zur Kenntnis des Brasilins und Hämatoxylyns. Dissertation, University of Berne, Switzerland.

2. Funk, C. 1912 The etiology of the deficiency diseases. Beri-beri, polyneuritis in birds, epidemic dropsy, scurvy, experimental scurvy in animals, infantile scurvy, ship beri-beri, pellagra. J. State Med. 20: 341.
3. Funk, C. 1914 *Die Vitamine*. J. P. Bergmann, Wiesbaden.
4. Harrow, B. 1955 *Casimir Funk — Pioneer in Vitamins and Hormones*. Dodd, Mead & Company, New York.
5. Williams, R. R. 1961 *Toward the Conquest of Beriberi*. Harvard University Press, Cambridge.