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Special Note

Kazimierz (Casimir) Funk – Pioneer in Vitaminology – 101 Anniversary of His Discovery – Special Note

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Short life story and scientific activity of Kazimierz (Casimir) Funk is presented. His achievements and pioneer work in vitaminology is summated on the occasion of 101 anniversary of the introduction of this topic into food and nutrition sciences.

His long biochemical scientific itinerary is presented starting from Switzerland, France (twice), UK, USA (twice) and Poland. Most of his discoveries or studies were linked with vitamins, but also with other nutrients (carbohydrates, amino acids, trace elements) or bioactive substances *e.g.* hormones and their synthesis. It is worth mentioning that Dr. Funk looked always at food constituents as factors affecting health and/ or preventing diseases.

We in Poland are very proud of his scientific achievements considering that Dr. Funk is the significant milestone in developing food and nutrition science worldwide.

INTRODUCTION

In 1912 Kazimierz Funk (Photo 1), based on his research invented the term "VITAMIN" [Funk 1912, 1913] and therefore this word for the first time blazed across the printed pages [Harrow, 1955; Berger, 2010].

The first part of this word implicated in Latin "*vita*" – life and the second "*amine*" – since the discovered by him substance(s) was (were) belonging to a group of organic compounds known as "amines".

Although at present several vitamins do not contain the amine group (*e.g.* fat-soluble vitamins or ascorbic acid) this name was accepted worldwide, especially in food and nutrition sciences, for 13 or 14 substances representing bioactive organic micronutrients [Harrow, 1955].

They are not significant dietary sources of energy (but act in rather small amounts) and are not synthesized in the body of man (and most animals). Most of them are participating in many enzymatic processes, therefore are often recognized as co-enzymes. These organic micronutrients are essential for human health and development during all stages of man's or animals' life cycle.

When in deficiency called often hypo– or a–vitaminose – such syndromes are appearing as: blindness, rickets, neuritis, scurvy, beri-beri, glissitis, pellagra, anemia, neural tube defects or fatigue. Therefore most vitamins are included in the Dietary Reference Intakes (DRI) or Dietary Reference Values (DRV). Recently, Tolerable Upper Intake Levels (UL) or Safe Upper Levels (SUL) are also suggested.

PHOTO 1. Casimir Funk photo (source: www.wikipedia.org).

In turn, Guideline Daily Amounts (GDA) are becoming more and more popular in practice for consumers and food industry or pharmacy. As in this area of food and nutrition sciences a Polish citizen Kazimierz Funk played a crucial role it is worthwhile to remind his life story rich in many events particularly on the occasion of the 101st anniversary of introducing vitaminology into the world of scientific literature.

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TABLE 1. Main places and dates of Kazimierz Funk's life and work.

Country	Period	Places
Poland	1884-1900	Warsaw (one year - 1886 - Funk was in hospital near Augsburg, Germany for orthopedic treatment)
Switzerland	1900-1904	Geneva and Bern Universities (PhD – 1904)
France	1904-1906	Paris – Pasteur Institute
Germany	1906-1916	University of Berlin and Municipal Hospital in Wiesbaden
England	1910-1915	Lister Institute of Preventative Medicine in London (discovery of vitamins), London Cancer Hospital Research Institute, University of London (D.Sc.)
USA	1915-1923	New York City – The Harriman Research Laboratory, New Jersey – Calco Company in Bound Brook, New York City – Columbia University's College of Physicians and Surgeons
Poland	1923-1927	Warsaw – State Hygiene's School, Department of Biochemistry
France	1928-1939	Paris – Grémy's Factory and Rousell Company
USA	1939-1967	New York City – US Vitamin Corporation, Funk Foundation for Medical Research

Source: own compilation

PROFESSIONAL LIFE OF K. FUNK

Funk could be called as a "travelling scientist" as he lived and worked in many places and countries. The most of them are shown in Table 1. In travelling so much was easer, as he knew Polish, Russian, German, French and English languages.

He was born in Warsaw on 23 February 1884. His father, a well-known dermatologist and his mother Gustawa Zysan enrolled Kazimierz in the public gymnasium in Warsaw, but as the education was difficult there (Poland was under Russia's control) he was also tutored at home. Later he went to study biology in Geneva and Bern Universities in Switzerland, where he studied chemistry, physics, zoology and biology and obtained PhD under the leadership of professor Stanisław Kostanecki in 1904. After that period he moved to the Pasteur Institute in Paris cooperating among others with Gabriel Bertrand in the field of biochemistry of sugars and proteins, soon afterwards (in 1906) he moved to the University of Berlin and worked in the laboratories of professors Emil Abderhalden and Emil Fisher.

In London (1910-1915) Dr. Funk was a scholar at the Lister Institute of Preventive Medicine and started his work on dihydroxyphenylalanine (known as "dopa"), but soon became interested in beri-beri disease.

This disease was common among oriental people consuming polished rice and was manifested by peripheral nerves that caused pain and paralysis, usually followed by death. Funk was feeding among others pigeons or chickens using polished rice and discovered that they were recovering from polyneuritis gallinarum and were regaining growth when fed rice-bran.

He soon published an article: "Chemical Nature of the Substance Which Cures Polyneuritis in Birds Induced by a Diet of Polished Rice". This paper was followed by many other articles on beri-beri, but the crucial one was published in the Journal of State Medicine: "The Etiology of Deficiency Diseases" in 1912, where for the first time the term "vitamine" was introduced to the world-wide literature [Funk, 1912]. Dr. Funk proposed also that at least four vitamins were preventing (anti-) beri-beri, scurvy, pellagra and rickets. Later it was established that vitamins are part of the chemical make-up of several enzymes (biological catalysts) necessary for many functions of living human or animal body [Kraemer *et al*., 2012].

These publications earned him great public recognition and in 1913, when Dr. Funk began working at the London Cancer Hospital Research Institute, he published his first book: "Die Vitamine" translated in 1922 into English and then again in German "Die Vitamine" in 1924 [Funk, 1913, 1922, 1924].

Before leaving London for the USA Dr. Funk worked also as a biochemist at the Cancer Hospital Research Institute, where several investigations including thiamine association with carbohydrate metabolism were studied (Figure 1). They were linked with cancer problem showing that some substances in food are enhancing and some just opposing cancer growth. Therefore, it could be said that some connection between diet and cancer may occur.

Due to several reasons, including war time, Dr. Funk left Europe on 18 February 1915 for the USA, having an opportunity to continue scientific work at the Harriman Research Laboratories in New York City. Some experiments were devoted to the development of chemical industry in the USA (*e.g.* benzonaphtol, atophan, salvarsan or adrenaline). However Dr. Funk left these Laboratories and was appointed in the pharmaceutical department of the Calco Co. in Bound Brook N.J., where he was helping in manufacturing benzoic acid or atophan.

His suggestions to industry for some topics in the field of vitamins were not accepted with great enthusiasm. However, some progress has been done and with the collaboration with Dr. H.E. Dubin, such a product like "Oscodal" (concentrated fraction of vitamin A and D) appeared on the market and was accepted as the first vitamin product by the American Medical Association (A.M.A.). Also some nutritional studies were initiated at the Biochemical Department of the Columbia University (*e.g.* material which promoted bacterial growth was strongly associated with its vitamins content or amino

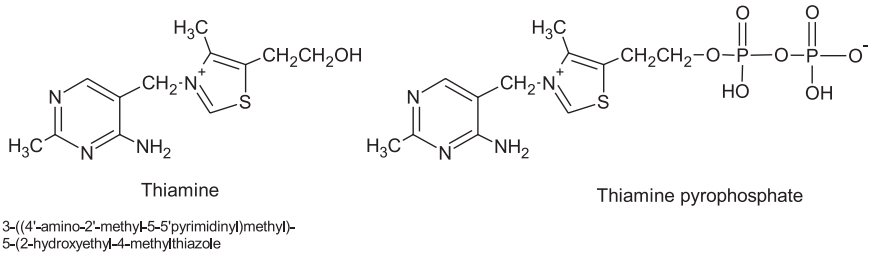

FIGURE 1. Structure of thiamine and thiamine pyrophosphate. Free thiamine is depicted as the free base form (adapted from Gregory [1997]).

acids). This kind of research was seldom referred to Dr. Funk, who was also pioneer in this area of research [Harrow, 1955].

Dr. Funk worked also in the pharmaceutical firm Metz and Company in New York City as well as between 1918-1923 he held an academic position at the Columbia University's College of Physicians and Surgeons where his interest was concentrated on the synthesis of adrenaline.

During Spring in 1923 Dr. L. Rajchman (from the League of Nations and National Health Institute in Warsaw) visiting New York invited Dr. Funk to fill the post as a biochemist in this Institute in Poland. Therefore, the next place for Dr. Funk research and stay during 1923-27 became Warsaw.

Although Dr. Funk became also a citizen of the USA (in 1920) he returned to Poland as recommended by Dr. L. Rajchman and was assigned two small laboratories at the State School of Hygiene in Warsaw (later State Institute of Hygiene – PZH) obtaining Rockefeller Fellowship and some financial support to purchase needed equipment. His activities were concentrated mainly on production and distribution of insulin, but also on several vitamins (mainly B complex).

Dr. Funk and his coworkers were also interested in how to measure dietary provision of some vitamins by determining their excretion with urine (as no more needed). Several other works were also performed in the field of biochemistry and nutrition related to protein (casein), nicotinic acid (as part of so called "yellow" enzyme), some hormones (pirocin, pitrescin) or pepsin and trypsin.

Dr. Funk as the chief of Biochemistry Department at PZH, has played an important role in initiating the nutrition science in Poland.

It is worth mentioning that the third edition of his classical book of vitamins [Funk, 1924] was prepared during his work in Warsaw. Also during his stay in Poland Dr. Funk was able to visit several scientific places or attend many congresses in Europe *e.g.* in Copenhagen, Malmo, Lund, Bucharest, stopping in Lwów (meeting with a famous Polish biochemist – Prof. Parnas), then Stockholm (here in 1926 Danish scientists were recommending him to the Nobel Prize for his works on vitamin), Leningrad (lecture on his work related to hormones and meeting with I. P. Pavlov - Nobel Prize winner discussing the physiology of digestion), Moscow (visiting Prof. Bach in the Biochemical Institute) *etc*.

Stay and works of Dr. Funk inspired many of his followers in Poland and as a matter of fact the author of this Note was working in this laboratory later on to continue and develop many research programmes related particularly to vitamin determinations, especially vitamin A, carotenoids, metabolism, evaluations of human needs or recommended daily allowances *etc*.

Unfortunately Dr. Funk left Poland for France in 1927, but his name is included on a special marble table among all leaders in the building of the Institute of Hygiene (PZH).

During 1928-1939 Dr. Funk was in Paris, where he first accepted position at the pharmaceutical House of Grémy (producer of sera and vaccines). He was interested in study of sex hormones, but soon left Grémy and established the "Casa Biochemica", where he worked among others on chemical differentiation between male and female hormones related to age especially in urine.

Also some studies were undertaken on insulin and antianemic factor (from liver or yeast).

During 1929-1939 Dr. Funk worked also as a biochemist for the Rousell Company and in 1936 with Dr. H.E. Dubin he published: "Vitamin and Mineral Therapy". Among many statements there is one very important that "Lack of particular vitamin leads eventually to a particular nutritional disease …. making body susceptible to attack of certain infection".

Funk's daughter Doriane was helping him in laboratory, by especially taking care of animal (cats, chicken) colony. Also several scientific papers were published with his son Ian Funk on hormones or pyridine derivatives in nutrition.

During his stay in France Dr. Funk collaborated also with various American firms in different fields of nutrition, *e.g.* in the production of nicotinic acid, and maintained connection with the US Vitamin Corporation.

Before WW II Funk's family left France for the USA arriving in New York on October 5, 1939. After living France Dr. Funk began working for the US Vitamin Corporation and with its support he became a head of the Funk Foundation for Medical Research.

In addition serving as a consultant for the US Vitamin Corporation he developed the production of nicotinic acid and nicotinamide, so Funk with his children as helpers was still close to nutrition science.

In the USA Funk with his wife, daughter Doriane and son Ian, who after medical studies in psychiatry were helping him in a contract as consulting chemists to the US Vitamin Corporation and with his friend Prof. Benjamin Harrow at the City College of New York published several papers with him, particularly on male hormones.

Dr. Funk developed also theory on interrelationships between vitamins and minerals.

As a matter of fact this led to the preparation of the product known as "Vi-Syneral" as Funk always considered that vi-

TABLE 2. Present status of existing vitamins.

Water soluble		Fat soluble	
Vitamin B_1	Thiamine	Vitamin A	Retinol
Vitamin B_2	Riboflavin	Provitamin A	β-Carotene
Vitamin B_3	Niacin	Vitamin D	Calciferol
Vitamin B_5	Pantothenic acid	Vitamin E	Tocopherol
Vitamin B_6	Pyridoxine	Vitamin K	Phylloquinone
Vitamin B_7	Biotin		
Vitamin B_9	Folic acid		
Vitamin B_{12}	Cobalamin		
Vitamin C	Ascorbic acid		

Between following years the above vitamins were discovered (1831-1941), isolated (1831-1948), had established structure (1930-1956) and synthesized (1933-1972).

Source: compiled from: Micronutrients…, [2011].

tamins act in the body not independently but with other food components particularly with trace elements.

Funk was also occupied with the cancer and its possible treatments and investigations of such subject as diabetes. In 1912 he was pioneer as vitamin-conscious, but became also cancer-conscious. So in conclusion K. Funk strived always to work for better life of man.

As a matter of fact The Funk Foundation for Medical Research was incorporated in 1947 under the laws of the State New-York, as a nonprofit organization to investigate cancer and other significant and related medical research problems [Harrow, 1955]. The subject of cancer goes back to 1915 (in Switzerland) and 1926 (in Warsaw) showing cancer-stimulating and cancer-reducing substances. But this field of actions is far beyond this Special Note and deserves another publication.

CONCLUSIONS

Kazimierz (or Casimir as an anglicized form of his given name) **Funk** died in New York at the age 83 in November 19, 1967.

He could be called TRAVELLING SCIENTIST: Poland (twice), Switzerland, France (twice), Germany, Great Britain, USA (twice), survived two World Wars, and was always faithful to his scientific career in organic- and bio-chemistry. However his very hard work was always linked with nutrition science, medicine and health.

Sometimes his life was more that of a poet than of a scientist [Harrow, 1955; Griminger, 1972] serving a man in his endeavour to combat under- or mal- nutrition world-wide.

Even after his retirement he was in touch with fields of his interest serving humanity, publishing over 140 scientific papers, many reviews or articles incl. unique books on vitamins (in English, German, Russian or Polish). It should perhaps be proper to mention here that Dr. Funk was often in touch or co-working scientifically with several compatriots *e.g.* B. Fejgin, Z. Kołodziejska, S. Kostanecki (his PhD adviser), S.K. Kon, A. Lejwa, L. Rajchman and several others.

Present status of existing vitamins is summarized in Table 2. Some of the authors are also considering, that choline [Kraemer *et al*., 2012] or carnitine and B_{17} (Laetrile, amygdaline) might be or are belonging to the vitamin group or pseudovitamins group (some authors in Machlin [1984]).

Dr. Funk is recognized world-wide as one (Polish) milestone in developing nutrition science [Berger, 1988] frequently contributing to several other fields (*e.g.* medicine, pharmacy) or discovering interrelationships of vitamins with other nutrients or food substances.

It is a pity however that despite his nomination to the Nobel Prize among many vitaminologists [Souganidis, 2012] he was not successful winner, however Sir Frederic Gowland Hopkins in his Nobel Lecture (Dec. 11, 1929) mentioned that he (Funk) has not received too much, but to little credit for his vitamin work as a whole [Hopkins, 1949; Harrow, 1955].

Also it is strange that in the Handbook of Vitamins [Machlin, 1984] only few sentences were devoted to K. Funk in the chapter on thiamine, referring to his publication in the Journal of Physiology (London) in 1911 and that Carpenter [2012] when writing on this vitamin discovery did not mention Funk at all.

But we in Poland and particularly nutritionists are very proud of Kazimierz Funk – the visionary and pioneer in vitaminology linked with many aspects of human health [Berger, 1988, 2010].

In our Faculty building (Human Nutrition and Consumer Sciences at WULS) there is permanent exhibition on Kazimierz Funk and his achievements in vitaminology. His hard work will constitute everlasting contribution to better life of man and good example for his followers in further development of human nutrition sciences.

NOTE

The author of this Special Note was working for several years (before leaving as a Rockefeller Fellow to Cornell University USA in 1957) in the State Institute of Hygiene (PZH) – Nutrition Division, where Dr. Funk had his Biochemistry Laboratory (1923-1927).

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