# A Child of Many Fathers: The Question of Credit for the Discovery of Thiamine, 1884-1936

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Credit for scientific discoveries can be a contentious affair. Not only do the success and failures of individual careers rest on such, but so can matters of national prestige. One of the less-substantial properties of science has to do with the prestige that adheres to credit for uncovering knowledge that is deemed revolutionary. Such prestige is intangible and unquantifiable, and yet seems to possess a great deal of importance, as demonstrated by the recognition given to those researchers fortunate enough to uncover these wonders, and the awards they are given for such. This acclaim many times also expands to encompass the scientists' country of origin, confirming or heralding its status as a technically and scientifically advanced nation.

For thiamine, or vitamin $B_1$, because the process of uncovering its secrets was so convoluted and lengthy, fraught with laboratory errors and mis-drawn conclusions, many scientists became involved in reaching a more perfect understanding of its properties and structure, each making his own contribution to the totality of its knowledge. Despite this, and depending upon who is asked, only two of them are generally recognized popularly, and when they are, as the sole discoverer of vitamin $B_1$: Casimir Funk and Suzuki Umetarō (鈴木梅太郎). But to acknowledge either of these researchers as the discoverer of thiamine would be a mistake. True credit rests elsewhere.

At the turn of the twentieth century, orthodox nutritional theory only recognized proteins, carbohydrates and fats, in addition to salt and water, as necessary for a healthy diet. However, the proliferation of a variety of diseases, including scurvy, beriberi, and pellagra, led to the realization that other nutritional factors were also involved. Vitamin theory states that certain foodstuffs contain trace compounds that are not protein, carbohydrate, or fat in character, but still are essential for proper health, and indeed, life.

Vitamin $B_1$, also known as thiamine, is essential for the proper metabolic health of most vertebrates and some microorganisms. It is a water-soluble vitamin, and in animals is concentrated in the liver, heart, kidneys, and skeletal muscle. Thiamine is important to the body's oxidation processes, particularly those concerned with the metabolism of carbohydrates and fats. It additionally is vital to the proper health and functioning of the cardiovascular, digestive, and nervous systems, and to appetite and growth.

In humans, its deficiency results in beriberi, the onset of which manifests itself as fatigue and drastic weight loss, followed by nervous disorders and atrophy of the muscles, especially in the legs.[1,2] Paralysis and severe pulmonary edema may occur, and death, usually from heart failure, is the result if the condition progresses. As little as 0.6 milligrams of thiamine per day is enough to deter symptoms of beriberi in an average human. Although the disease had been known in China as long ago as 2600 BCE, beriberi reached crisis

1 Williams, et al., *The Biochemistry of B Vitamins*, New York, Reinhold, 1950, 400-401.
2 The term "beriberi" originated in Sri Lanka, from *beri*, the Singhalese word for weakness.

proportions during the nineteenth century due to the impact of certain changes on the eating habits of humans. Processed and preserved foods, which often had removed from them undesirable parts of vegetable and animal products, also could have essential nutrients removed coincidentally.[3]

Investigations into the nature of beriberi were misled initially by its geographical distribution and the sometimes unpredictable conditions under which it occurred. It seemed to concentrate itself in the then non-industrialized regions of the world and was originally thought to be an infection brought about by unsanitary living conditions. The disease was particularly a problem in Asia, where some estimates of resulting deaths reach into the hundreds of thousands. Perhaps for this reason, it was the Japanese who led inquiries into this disorder, which they refer to as *kakke* (脚気).

In the 1880s, Takaki Kanehiro (高木兼寛), the Director-General of the Imperial Navy's Medical Department, made the connection between beriberi and diet. He discovered that up to forty percent of the Japanese Navy was afflicted with *kakke* and instituted various reforms, including less rice, more bread and milk, and improved hygiene in sailors' living quarters. The incidence of *kakke* plummeted from almost two thousand cases in 1879 to zero in 1887, but Takaki attributed improvement solely to an increase in exercise and dietary protein, and a decrease in carbohydrates and fats.[4]

Further inquiries provided limited insight until 1896, when Christiaan Eijkman, a Dutch physician practicing in Java, published a paper that described a beriberi-like disease that the chickens kept by his hospital contracted when fed polished rice.[5] He found that feeding the chickens rice bran, or the husks of polished rice, was curative for the disorder. However, he mistakenly concluded that the chickens metabolized the white rice's starch into a neurotoxin which subsequently was neutralized by some chemical in the pericarp of the rice.[6] Although Eijkman's suppositions were wrong, the news that a physical disorder similar to beriberi could be duplicated in a non-human species created a great deal of excitement among those who would study the ailment in humans.

In 1908, at the urging of the Imperial army, the Japanese government established a commission to deal with the high incidence of beriberi among soldiers and people who had immigrated to the cities from the countryside. Due to his success in dealing with a mulberry blight in 1899 and to his studies under Emil Fischer, Suzuki was among those appointed to investigate.[7] So began his studies on the nutritional value of rice, leading to his discovery of a substance which was neither protein, fat, carbohydrate, nor mineral, the dietary absence of which leads to beriberi and the death by wasting of the patient. For two years, Suzuki's research group, but primarily the Professor and Shimamura Torai (島村虎猪), worked

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3 Leslie J. Harris, *Vitamins and Vitamin Deficiencies* (London: Churchill, 1938), 4.

4 Ibid., 53.

5 Which is to say, rice that has had its pericarp, also known as its bran or husk, removed. The distinction is that between "white" and "brown" rice. The ailment of the chickens is known as "polyneuritis gallinarum." Eijkmann shared the Nobel Prize for Medicine or Physiology in 1929 with Sir Frederick G. Hopkins of England for their work with vitamins.

6 A 1930 journal article reiterating this was written by Yutaka Teruuchi of Keio University. Suzuki wrote a refutation, showing that the toxin theory was not dying an easy death. Umetaro Suzuki, Toshikazu Sahashi, Tsune Ariyama, Nobuzo Nakamura, Nabetaro Hashimoto, and Toshiichi Kasai, "On the So-called Polished Rice Intoxication," *Scientific Papers of the Institute of Physical and Chemical Research 9(3)* (March 1930), 26-27.

7 Fujioka Nobukatsu, *Kyōkasho ga Oshienai Rekishi 3*, Tokyo: Jiyūshugi Shikan Kenkyūkai, 2005, 198.

"without taking even a day's break."[8] In 1910, Suzuki isolated a substance from rice bran which he said possessed anti-beriberi properties. He named it "aberic acid."

On December 13, 1910, at 6 o'clock in the evening, Suzuki presented his paper on aberic acid before the Chemical Society of Tokyo at Tokyo Imperial University's Main Lecture Hall. It subsequently was published in the January 1911 issue of the *Journal of the Chemical Society, Tokio.*[9] On January 7, 1911, he filed his application with the Japanese patent office concerning his method of extracting aberic acid (patent no. 20785), and on July 21, 1911, did the same for a second method (patent no. 21314).[10]

In Japan, the initial reception to Suzuki's paper was cool. His fellow chemists refused to comment on his findings, while the reaction of medical doctors was less ambiguous, bordering on outright hostility.[11] The Imperial army previously had convened a panel of the most prominent physicians in Japan to investigate the prevention of and cure for beriberi, and these worthies were convinced that beriberi was an infectious disease. So when Suzuki was able to definitively assert that he had discovered a factor that would cure beriberi in one hundred percent of cases, the outcry from this faction was profound.[12] "He plagiarized his data," and "he debased scholarship" were among the criticisms heard.[13] This group included one whose reported response was pungent, "I hear Suzuki says rice bran is effective against beriberi. This is idiocy. He can believe what he likes, but if rice bran cures beriberi, then drinking urine will too."[14]

Although Suzuki scrupulously avoids identifying this person, Imperial Army Medical Chief Mori Ōgai (森鴎外, born Mori Rintarō 森林太郎) was a possible source for this damning statement.[15] He was a staunch proponent of the belief that beriberi was a bacteria-caused infectious disease, and refused to modify the diet of the Imperial Army by the addition of barley during the Russo-Japanese War, unnecessarily leading to a quarter-million cases, including roughly 27,000 fatalities.[16] Mori would remain adamantly opposed to a nutritional basis to the disorder and the curative properties of aberic acid/oryzanine until his death in 1922. In fact, out of all the chemists and medical doctors in Japan, the only word of support, albeit distinctly lukewarm, came from Ikeda Kikunae of Tokyo Imperial University's chemistry department. According to Suzuki, he said, "This accomplishment, if true, is

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8 *Kenkyū no Kaiko*, 6. The beriberi research group also included Suzuki's former academic advisor Kozai Yoshinao and Andō Hirotarō（安藤廣太郎). Suzuki, Umetarō, "Chemical Studies of Vitamin-B in Japan," *Scientific Papers of the Institute for Physical and Chemical Research*, 4(63), 1926, 295.

9 *Journal of the Chemical Society, Tokio 32 (Meiji 44) (1911), 4-17*

10 The first patent, no. 20785, was approved on October 19, 1911, while the second, patent no. 21314, gained the same status on December 21, 1911. Suzuki soon changed the name from "aberic acid" to "oryzanine" (sometimes "oryzanin"), naming it after the source of his discovery, the rice plant *oryza sativa*.

11 *Gekidōki no Rikagakukenkyūjo: Ningenfūkei: Suzuki Umetarō to Yabuta Teijirō*, Tokyo: Kyōritsu Shuppan, 1987, 9.

12 *Suzuki Umetarō Sensei-Den*, 9

13 Dōke Tatsumasa in Tsuneishi Keiichi, ed., *Nihon Kagakusha-de*n. Tokyo: Shogakukan, 1996, 145.

14 Suzuki, *Kenkyū no Kaiko*, 10. Also, Yuasa Mitsutomo, *Kagaku-shi*, Tokyo: Tōyō Keizai Shinpō-sha, 1961, 214. This person, who Suzuki identifies only as "some scholar" would later confront Suzuki and call his oryzanin research "a lie" to his face. Suzuki, *Ibid.*, 11. In point of fact, however, the statement is a correct one since, like all water-soluble vitamins, excess thiamine is excreted via the urine.

15 There is also evidence that the source of the "urine" remark was Aoyama Tanemichi (青山胤通), the dean of Tokyo University's faculty of medicine and Mori's main academic ally in the nutrition/contagion controversy. However, according to Alexander Bay, the target of his wrath was not Suzuki, but Tsuzuki Jinnosuke, an army medical doctor. Alexander Bay, "Beriberi, Military Medicine, and Medical Authority in Prewar Japan," *Japan Review*, 2008, **20**:130.

16 Alexander Bay, *Beriberi in Modern Japan*, University of Rochester Press, 2012, 53.

extremely interesting."[17] In the face of a preponderance of criticism, a chastised Suzuki retreated to his lab to confirm his results.[18]

Suzuki had, unwittingly or not, stepped into a dispute over the cause of beriberi that had raged between the Imperial Navy medical department on one hand, and Imperial Army and Tokyo University physicians on the other, since the 1880s. The Navy, because of Takaki Kanehiro's studies, adhered to a nutritional cause, while the Army and the Tokyo Imperial University faculty of medicine had staked their reputations on a bacterial origin. Supporting the bacterial faction's assertion was Mori's experiments on the nutritional value of white rice which seemingly ruled out a dietary basis to the disease. He concluded that an as-yet undiscovered bacilli must be responsible. This thesis gained most of its weight from the institutional authority of its proponents. Further, Mori was very heavily invested in this hypothesis, if for no other reason than admitting that he made an error would be tantamount to accepting culpability for the deaths of thousands of Japanese soldiers.[19]

Suzuki guessed that the widespread criticism of his findings was because he was "neither a medical doctor nor a pharmacist."[20] This seems disingenuous, however, given both his position at Tokyo University, and the fact that his detractors went so far as to involve the newspapers in lambasting him. Although Suzuki could not have been unaware of the feud between the contagion and nutrition factions in the beriberi debate, he still must have been puzzled at the stubborn resistance to his theory which persisted even after he published a number of studies that seemed to conclusively demonstrate that beriberi was a nutritional deficiency disorder rather than a bacterial one, including one involving 20 orphans, aged five to seven, all afflicted with *kakke*, all conclusively cured with oryzanine.[21]

Suzuki probably would have continued his *kakke* experiments, which could perhaps have eventually won over domestic support for publicizing his case internationally, but the advent of World War I superseded his efforts. Prior to the summer of 1914, most of Japan's technical supplies and scientific knowledge came from Germany, as was the case with most of the industrialized world of the time. However, as Japan was an ally of England and the Entente, this source was no longer available. The coming of the First World War, therefore, while an initial blow to Japan's scientific and industrial communities due to the shortages in raw and finished materials that it caused, also created the opportunity to expand production in cheap consumer goods, chemicals, and pharmaceuticals. So it was in 1915 that Suzuki was ordered to cease his beriberi research and devote his energies to the synthesis of Salvarsan,[22]

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17 *Kenkyū no Kaiko*, 8.

18 *Suzuki Umetarō Sensei-Den*, 9. The account of the *kakke* controversy, Suzuki's side of it at any rate, also has appeared in comic form. Although typically (for the genre) overly dramatic, it is, broadly speaking, true to events, even as it wonders why Suzuki did not receive a Nobel Prize. The *manga* version of Suzuki's nemesis is never identified explicitly, and while he does make the "urine" comment, albeit at the Chemical Society conference, his image resembles neither Mori Ōgai nor Aoyama Tanemichi. Itō Tomoyoshi and Morita Shingo, *Eikō-naki Tensai-tachi v.4*, Tokyo: Shūeisha, 1997.

19 Bay, 126. For a more detailed account of the nutrition/contagion debate, see Alexander R. Bay, "Beriberi, Military Medicine, and Medical Authority in Prewar Japan," *Japan Review*, (2008), v20, 111-156.

20 *Kenkyū no Kaiko*, 11. It also could be that the Mori/Aoyama faction saw his assertions as a betrayal, given that Suzuki was both alumnus and faculty at Tokyo Imperial University. Moreover, there may have been some anger at Suzuki for "interfering" in a medical matter that was none of his affair, despite his appointment to the commission. See Bay, Ibid., for examples of this concerning Japan's domestic beriberi debate, and Bartholomew, Ibid., for those in Japan's general scientific community.

21 Suzuki Umetarō, Araki Bunsuke, and Sasaki Sei, "Shōni no Eiyō ni oyobosu Oryzanin no Kōkō ni tsukete," *Tokyo Kagakukai-shi*, 36 (1915), 1153-1171.

22 Also known as arsephenamine, it was discovered by Paul Ehrlich and Hata Sahachirō (秦 佐八郎) in 1910. It was the first drug capable of effectively treating syphilis.

one of the pharmaceuticals previously supplied by Germany, which he did until he was tapped to head a laboratory upon the founding of Riken two years later.

The controversy between whether *kakke* was a dietary malady or infectious disease would not be laid to rest in Japan until Shimazono Junjirō (島薗順次郎) definitively established the connection between beriberi and a deficiency in thiamine, thereby finally silencing Suzuki's critics. Shimazono also worked out preventive dietary measures and received the Japan Academy Prize in 1926.

On August 1, 1911, Suzuki's aberic acid abstract appeared in *Zentralblatt für Biochemie und Biophysik*, a periodical that served as a clearinghouse for research in medicine and the life sciences. Written by someone identified as "Teruuchi, Tokio," it described Suzuki's methodology in great detail, down to specific concentrations of reagents, and the sequence of the various procedures.[23] This did not look to be a unique occurrence for *Zentralblatt*, but seems unnecessary, given that brevity is supposedly one of the conventions involved in writing journal abstracts.

In the December 22, 1911 issue of the *Journal of Physiology*, Casimir Funk, a researcher at the Lister Institute in London, published a paper entitled "The Preparation from Yeast and Certain Foodstuffs of the Substance the Deficiency of Which in Diet Occasions Polyneuritis in Birds."[24] The following May, the abstract of Funk's article made its appearance in the publication, *Chemical Abstracts*, an English-language equivalent of *Zentralblatt.* The abstract of Suzuki's *Zentralblatt* article, although it preceded Funk's paper by almost a year, for some reason or other did not make its own appearance until October 1912. Biochemist Donald Dexter van Slyke, who wrote the abstract to Suzuki's article with the translated title "Oryzanine, a Component of Rice Bran and its Physiological Significance," seemed to be compelled to conclude it with: "The results of the authors constitute a confirmation and enlargement on the discovery of Casimir Funk *of which they were unaware* (emphasis added)."[25]

This sort of editorializing does not appear to have been very common in a publication that was ostensibly a collection of purely scientific abstracts, and indeed, seems a little unreasonable. One might have thought that van Slyke might have been more forgiving of a scientist's lack of awareness given that *Chemical Abstracts* cited literally tens of thousands of scientific journal articles each year. Most especially since van Slyke himself seems to have been similarly unaware of the original citation on Suzuki's oryzanine research from *the Journal of the Tokyo Chemical Society* that *Chemical Abstracts* had published in an earlier edition.[26]

So, despite the fact that his oryzanine article essentially was cited twice in *Chemical Abstracts*, only in Japan is Suzuki accorded credit for discovery of the anti-beriberi factor. Casimir Funk, with varying degrees of indignation, is, even now, derided in Japan as a plagiarist and opportunist. Sekine Hidesaburō (関根秀三郎), an agricultural chemistry professor at Tokyo University remarked,

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[23] Probably Teruuchi Yutaka (照内豊), a Medical Chemist of the Meiji to early Showa eras.

[24] Casimir Funk, "The Preparation from Yeast and Certain Foodstuffs of the Substance the Deficiency of Which in Diet Occasions Polyneuritis in Birds," *Journal of Physiology 43(5), 75-82.*

[25] D.D. Van Slyke, *Chemical Abstracts* 6(3) October-December 1912, 2774-5.

[26] I.K. Phelps, *Chemical Abstracts* 6(1) January-April 1912, 251.

> "Funk used the same procedure as Suzuki, and produced the same substance (oryzanine) … Suzuki introduced the abstract of his results in German in August of 1911 and Funk presented his report in December of that year – from August to December is four months … Funk should have read Suzuki's research result in *Zentralblatt für Biochemie und Biophysik* – at the time, it was a fairly prominent journal and medical doctors, physiologists, and biochemists had to at least browse it, no matter who they were."[27]

It is indisputable that, as a scientist educated prior to World War I, Funk should at least have been passingly familiar with German, and since he was schooled in Switzerland and Germany, most assuredly was quite fluent in that language, and should have been aware of Suzuki's abstract in *Zentralblatt*.[28] After all, Funk's own abstracts were published therein. Notably, in an article carried in the November 1911 edition of the British medical journal *The Lancet*, three months after Suzuki in *Zentralblatt* and one month before Funk's "groundbreaking" article in the *Journal of Physiology*, the authors Funk and Evelyn Cooper announced that the "precise nature of [an anti-beriberi substance] is being at present investigated by one of us (C.F.)."[29] Although this paper does not disclose the precise form that the investigation was taking, and whether it involved laboratory experimentation or a rigorous search of published materials, it also reveals that it was Dr. Charles James Martin, FRS, and Director of the Lister Institute from 1903 to 1930, who apparently suggested that Funk direct his attention to beriberi in the first place.[30] At any rate, if the procedure for extracting the anti-beriberi substance did not originate with Funk, at the very least, academic integrity obliged him to cite his source or face charges of plagiarism.

Nonetheless, the popularity of Funk's invented term, "vitamine," presumably what elision had made of "vital amine," took off.[31] But his motive for inventing the term may not have been of a strictly scientific nature. He said,

> "… I must admit that when I chose the name, "vitamine," I was well aware that these substances might later prove not to be of an amine nature. However, it was *necessary* for me to choose a name that would sound well and serve as a catchword, since I had already at that time no doubt about the importance and the *future popularity of the new field*" (emphases added).[32]

Perhaps this statement may be construed to indicate his intention to link his name to a revolutionary new area of study, and that he may have been searching for a project with which he could elevate himself to prominence, at least within the scientific community. Whether this

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[27] Sekine Hidesaburō, in *Suzuki Umetarō Sensei-den*, p.146. Sekine also was a professor of agricultural chemistry at Tokyo University. He felt that Suzuki should have been awarded a Nobel for his work on vitamins, and felt the same about Takamine Jōkichi and his adrenaline research. *Ibid*., 142.

[28] Fred Jueneman, "Scientists Who Were Shafted," *R & D 39(3),* S1 (2).

[29] Cooper and Funk, 1367.

[30] Ibid., 1267.

[31] Incidentally, the term "thiamine," also known as vitamin $B_1$ comes from the joining of "sulfur-bearing" or "thio-" and "amine."

[32] Funk, *Vitamines*, 36.

is so or not, it must have been quite a disappointment to Funk when he was not awarded the Nobel Prize for their work on vitamin theory. Suzuki must similarly have been disappointed not to have been so honored, if also a touch vindicated to share that non-status with his "rival," Funk.

My criteria for "discovery" of thiamine is admittedly narrow, but I think proper. I define it as being the first to identify the correct molecular formula, as agreed upon by current convention. If another compound were under consideration, it might be necessary to amend the definition to include "identify the correct molecular structure." However, the first scientist to do so was also the first with the correct molecular formula, so for vitamin $B_1$, molecular formula alone is sufficient.

So as to the proposition, who should receive credit for the discovery of vitamin $B_1$, should it be Takaki Kanehiro? His work positing that beriberi was due to a dietary deficiency and his subsequent clinical studies was an indispensable step toward illumination of this matter, but his hypothesis that it was a lack of dietary protein that caused beriberi was erroneous. His contribution to resolving the question of dietary deficiency disease in general, and beriberi in particular, is akin to that of James Lind and scurvy, although a number of successful treatments for that disorder had been discovered, forgotten, then re-discovered over the centuries.

Then should it be Suzuki? The truth is, there is one very large problem with Suzuki's oryzanine research and according him credit for the discovery of vitamin $B_1$. When he broke oryzanine into its constituents, he produced choline, glucose, nicotinic acid, an organic acid he dubbed "alpha," with the formula $C_{10}H_7NO_4$, and a "beta" acid with $C_{18}H_{16}N_2O_2$.[33] The accepted chemical formula for thiamine is $C_{12}H_{17}N_4OS$. While it is possible that Suzuki's method of extraction fractured the vitamin $B_1$ molecule, if this indeed were the case, one would expect the chemical formula "sum" of the two acids to equal that of thiamine. Not only does it not do this, but the sulfur atom is conspicuously missing from Suzuki's results.[34]

But there also are problems with Funk's results. Despite what Sekine Hidesaburō said, Funk's compound was not the same as Suzuki's. Referencing the chemical formula he published for his "vitamine," $C_{17}H_{20}N_2O_4$, the identity of the molecule is not clear. The closest candidate is nicotine salicylate, $C_{17}H_{20}N_2O_3$, which is not a chemical that occurs naturally, and as with Suzuki's results, the essential sulfur atom also is missing.[35,36] So, despite entries in numerous Japanese popular writings, biographical dictionaries and encyclopedias, Suzuki did not correctly identify the pertinent molecule. However, neither did Funk, who to this day, also despite entries in numerous popular writings, biographical dictionaries, encyclopedias and online databases, is accorded the credit for first discovering vitamin $B_1$ (and sometimes A, C, and E) when in fact he is only the second one to *incorrectly* identify it.

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[33] One chemical that shares the same formula with Suzuki's alpha acid is xanthurenic acid, a chemical that is excreted by pyridoxine-deficient animals after being fed tryptophan. If albino rats are fed nothing but fibrin, this chemical will be in their urine. The beta acid most resembles 1-xylyl-azo-2-naphthol, a coloring agent banned by the US Food and Drug Administration. Of course with such large molecules, there are a number of isomers possible which have structure and properties in wide variance to each other. But the ones proposed by myself are the only possibilities listed by the Merck index, or those that come closest.

[34] Suzuki, "Chemical Studies of Vitamin-B in Japan," 296.

[35] It is used to treat nicotine withdrawal, and as an insecticide.

[36] Barend Coenraad Petrus Jansen and Willem Frederik Donath, "On the Isolation of Antiberiberi Vitamin". *Koninklijke Nederlandse Akademie van Wetenschappen* 29 (1926), 1390.

Then what of the two researchers who received a Nobel for their work with vitamins? According to the Nobel Committee that awarded them the 1929 Prize in Physiology or Medicine Christiaan Eijkman was being honored "for his discovery of the antineuritic vitamin" and Sir Frederick Gowland Hopkins "for his discovery of the growth-stimulating vitamins." However, neither did any such thing. Eijkman believed beriberi was caused by a toxin in white rice that was neutralized by some compound found in its pericarp. He never delved deeper into the subject than stating that it was brown rice or its husks that, when fed to chickens, prevented them from developing beriberi-like symptoms.

Likewise, Frederick Gowland Hopkins was at Cambridge University in 1906 when he declared that there were "minimal qualitative [dietetic] factors," which he also referred to as "accessory food factors," that are essential if an animal is to thrive.[37] But if theorizing the existence of unspecified dietetic factors constitutes "discovery of vitamins," then Cornelis Adrianus Pekelharing has a stronger claim to Hopkins' half of the prize. In 1905 he proposed that:

> There is still an unknown substance in milk, which, even in very small quantities, is of paramount importance to nutrition. If this substance is absent, the organism loses the power properly to assimilate the well-known principal parts of food, the appetite is lost and with apparent abundance the animals die of want. Undoubtedly this substance not only occurs in milk but in all sorts of foodstuffs, both of vegetable and animal origin.[38]

Of course, Pekelharing passed away in 1922, thereby making him ineligible for a 1929 Nobel Prize. Although it seems strange to award someone an internationally prestigious medal because he was the second person to make the supposition, the person who proposed it first being dead, Hopkins was nevertheless so honored, even if his "accessory food factors" did not prove as popular a "catchphrase" with the scientific and general public as did "vitamins."

In spite of scientific squabbling and the handing out of medals, research on the anti-neuretic vitamin continued, fortunately, as it turned out. In 1926, Barend Coenraad Petrus Jansen (1884-1962) and Willem Frederik Donath (1889-1957) reported that they had crystallized a thiamine molecule, which they dubbed "aneurine." The ability to crystallize a substance is an indicator that researchers have isolated a pure sample. Unfortunately, the chemical formula they had so elucidated ($C_6H_{10}NO_2$) still lacked a sulfur atom.[39] The next step was to develop a procedure to synthesize vitamin $B_1$, but their omission stymied attempts in this endeavor, and furthermore, cast doubt on their findings.

Finally, in 1934, Robert Runnels Williams (1886-1965) managed to determine the correct molecular formula from a crystallized sample, and two years later, while working for the Merck chemical company, developed a procedure to produce thiamine in the laboratory. Now a pure version of the cure for beriberi was available, rather than the extracts that had heretofore been the only pharmaceutical alternative to a healthy diet. [40] The synthesized version being curative for beriberi conclusively demonstrated that the correct formula had at

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37 *Ibid*., 10.

38 Leslie J. Harris, *Vitamins and Vitamin Deficiencies*, London: Churchill, 1938, 14.

39 C. Eijkman, "Experiments with Jansen and Donath's Antiberberi-vitamin," *Proceedings of the Royal Academy of Amsterdam v.30* (1927), 375-382.

40 R.R. Williams and J.K. Cline, "Synthesis of Vitamin B1," *Journal of the American Chemical Society 58(8)* (August 1936), 1504-1505.

last been determined. Therefore, it is Robert Runnels Williams who should receive final acclaim for discovery of thiamine, since it was he who, not only isolated it in pure form, but also elucidated its structure accurately. Additionally, he was the first to synthesize it, definitively putting a cap on any further dispute as to its molecular formula.

Although Suzuki felt that he had been robbed of rightful acknowledgment for his discovery, unlike many of his supporters even up until the present day, he knew he did not deserve credit for having discovered thiamine. However, in 1926 he wrote, "So I believe, that, my experiments . . . apart from their significance in the genesis of the (sic) beriberi, established the first firm foundation of the Vitamin theory of to-day (sic)."[41] For while he did not correctly chemically identify any one particular vitamin, what he did was even more significant. He took the study of these essential macromolecules from the realm of nutrition, to that of chemistry; to the molecular level.

[41] Umetarō Suzuki, "Chemical Studies of Vitamin-B in Japan," *Scientific Papers of the Institute of Physical and Chemical Research*, 4 (63) (1926), 297.