

## Medicine in Stamps

# Christiaan Eijkman (1858–1930): The vicar of vitamins

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The nascent science of medical microbiology flourished during the 19th century. During this time, Louis Pasteur, Robert Koch and others isolated pathogenic bacteria, developed the germ theory of disease and refined methods of heat sterilisation, sanitation and vaccination. In this flurry of discovery, a team of Dutch physicians and microbiologists, including Christiaan Eijkman, sailed to the East Indies on a state-sponsored mission to find the bacterial cause of beriberi. A chance encounter with sick chickens tested Eijkman's scientific skill and his creative ability to consider alternative theories, which ultimately led to the discovery of vitamins.

### SON OF AN EDUCATOR

Christiaan Eijkman was born on August 11, 1858 in the small town of Nijkerk, Holland. His father served as a school headmaster and prized education highly. Shortly after Eijkman's birth, the family moved with their seven children to Zaandam, a small town near Amsterdam. Christiaan became a student in his father's school, and began to develop his intellectual curiosity under close guidance and supervision. Although well-respected and well-educated, the senior Eijkman was not well-compensated, and the approximately 6,000 guilder price tag for his son's medical education was out of reach. Fortunately, a government-sponsored programme subsidised Eijkman's medical education in exchange for service in the Dutch East Indies (present-day Indonesia).

**DUTCH EAST INDIES** The Dutch military stationed Eijkman as the medical officer of the villages of Semarang and Tjiltjap. The young doctor was amazed

at the large number of previously healthy soldiers who were debilitated by a disease called beriberi, which caused peripheral neuropathy, muscle pain and atrophy, cognitive dysfunction, heart failure and death. The medical community called it *polyneuritis endemica pernicioso*, but preferred the term "beriberi", which is derived from the Sinhala phrase "I cannot, I cannot", uttered by victims of the disease. During this time, the field of microbiology was flourishing, and the medical world witnessed the remarkable discoveries of agents of devastating diseases such as anthrax, cholera, diphtheria and tuberculosis. The germ-theory of

disease was in vogue, and Eijkman obsessively sought the microbial agent that causes beriberi. In 1885, he travelled to Berlin to study with Koch, who only three years earlier, had discovered the bacteria that was responsible for cholera and tuberculosis.

**BERIBERI BACTERIUM** The epidemic of beriberi in the East Indies had generated significant concern in the Dutch government, which commissioned a research team to find its cause. Pathologist

Cornelis Adrianus Pekelharing and neurologist Cornelis Winkler led the mission, and they enlisted Eijkman as the team's third member before setting off for Java on their mission.

Before long, Pekelharing isolated a *Micrococcus* from the blood of some beriberi patients and from the filtered air of patient wards. The organism seemed to cause polyneuritis, but Eijkman was skeptical about this putative beriberi agent, as it did not quite fulfill Koch's postulates. He had injected cultured *Micrococcus* as well as blood and urine from beriberi patients into chickens, rabbits, dogs and monkeys, but could not consistently transmit the disease. Even



when the animals did develop polyneuritis, it was only after weeks or months of injections, and Eijkman then could not successfully reculture *Micrococcus* from his experimental specimens.

**CIVILIAN CHICKENS** After Pekelharing and Winkler returned to the Netherlands in 1887, Eijkman remained behind to direct a permanent laboratory and medical school in Batavia (now Djakarta). Until this time and despite devoted effort, no animal equivalent of beriberi existed. When “[a] disease, in many respects strikingly similar to beriberi in man, suddenly broke out in the chicken-house at the laboratory in Batavia”, Eijkman immediately recognised the research opportunity and closely examined the birds through autopsy, histological examination and careful documentation of their symptoms and disease progression. He named the chickens’ malady *polyneuritis gallinarum*, since it was essentially identical to *polyneuritis endemica perniciosa* or human beriberi. Initially, Eijkman maintained a microbiological hypothesis of causation until he made the following observations: when he separated the chickens into control and experimental groups and attempted to infect the latter with blood from beriberi chickens, he found, to his surprise, that all of the birds, including the controls, contracted the disease. More tellingly, a new group kept in a thoroughly sanitised chicken-house without any contact with the sick birds also came down with the disease.

As suddenly as it had developed, the disease cleared up, the affected chickens recovered and no new cases emerged. Eijkman learned that during the outbreak, the chef of the military hospital had fed the chickens with leftover military-grade polished white rice. When a new chef refused to allow military rice to be used as feed for “civilian chickens” and returned them to their usual unpolished brown rice, the sick birds improved and other birds stopped developing beriberi. These observations led Eijkman to quickly suspect the role of diet, and he soon confirmed that the chickens that were fed polished rice “were attacked with the disease after 3–4 weeks... whereas controls which were fed unpolished rice remained healthy... [and] birds suffering from the disease could be cured by a suitable alteration in diet.” Eijkman next enlisted the help of Adolph Vorderman, Inspector of Public Health of Java, who surveyed the 101 prisons and over 300,000 inmates in the East Indies for cases of beriberi. They found that beriberi deaths were about 300-fold higher in prisons that served polished rice.

**VITAMINS** Although confident of his observational data, Eijkman remained unsure of the mechanism by which rough rice prevented beriberi. Rice consists of a carbohydrate grain surrounded by a protein sheath. Unpolished (rough or brown) rice includes both the core and envelop, but it rots quickly and could not be stored for long periods. In contrast, polished or white rice is mechanically processed to remove the sheath, leaving just the carbohydrate grain, which greatly lengthens its shelf life. Eijkman hypothesised that a toxin was present in polished rice that was normally neutralised by something in the protective sheath. He extracted this “antineuritic principle” with water, and this cured beriberi when administered to afflicted chickens. His colleague and successor Gerrit Grijns eventually demonstrated that the cause of beriberi was neither an infection nor a toxin in polished rice, but the deficiency of a “protective nutrient” in the outer sheath lost during polishing.

Casimir Funk was the first to claim to have isolated Eijkman’s antineuritic principle in 1911, and thinking that it was an amine, named it a “vital amine” or “vitamin”. He had in fact isolated niacin, the cure for pellagra, and not thiamine, the protective nutrient for beriberi. It was Donath and Jansen, Grijns’ successors at the Batavia laboratory, who finally isolated thiamine or vitamin B<sub>1</sub> in 1926 from the sheath of unpolished rice.

The concept that a micronutrient deficiency can cause illness revolutionised medicine, and spawned the subsequent discovery of myriad life-saving vitamins and minerals. Although decades would pass before the validity and repercussions of Eijkman’s research were fully appreciated, his role in the discovery of vitamins earned him the Nobel Prize in 1929.

## BIBLIOGRAPHY

- Bruyn GW, Poser CM. The History of Tropical Neurology: Nutritional Disorders. Sagamore Beach: Science History Publications, 2003.
- Carpenter KJ. The Nobel Prize and the Discover of Vitamins [online]. Available at: [nobelprize.org/nobel\\_prizes/medicine/articles/carpenter/index.html](http://nobelprize.org/nobel_prizes/medicine/articles/carpenter/index.html). Accessed August 2011.
- Carpenter KJ, Sutherland B. Eijkman’s contribution to the discovery of vitamins. J Nutr 1995; 125:155-63.
- Christiaan Eijkman: The Nobel Prize in Physiology or Medicine 1929, Biography [online]. Available at: [nobelprize.org/nobel\\_prizes/medicine/laureates/1929/eijkman-bio.html](http://nobelprize.org/nobel_prizes/medicine/laureates/1929/eijkman-bio.html). Accessed August 2011.
- Verhoef, J. Christiaan Eijkman: Early Nobel Winner for Beriberi Research. American Society for Microbiology News [online] 1998; 64(12). Available at: [newsarchive.asm.org/dec98/feature2.asp](http://newsarchive.asm.org/dec98/feature2.asp). Accessed August 2011.