

Christiaan Eijkman: *Simplex non veri sigillum*

Episode 1: More than coffee at Café Bauer

It was a lazy summer afternoon in 1886 in Berlin, Germany at the popular Café Bauer. In one corner, a figure sporting a bushy moustache was hunched over his afternoon coffee, reading a newspaper. It was the 28-year-old Dutch doctor, Christiaan Eijkman. Eijkman motioned to the waiter, who came hurrying over, “I will have another coffee, please.”

“Of course, sir,” replied the waiter, eyeing the Dutch newspaper in front of Eijkman. “What brings you to Berlin?” he asked, unable to suppress his curiosity.

“I have come to study bacteriology with Professor Koch at the University to investigate the cause of beriberi.”

“Beriberi?” inquired the waiter quizzically, “I have not heard of it.”

Eijkman straightened up. “It is a disease prevalent in the Indies that has become an issue of national security in the Netherlands.”

“How so?” asked the overly curious waiter.

Eijkman continued, “Last year, my government sent a naval flotilla to Sumatra to curb pirate operations against merchant shipping. They had to call off the operation on account of the alarming, increasing incidence of beriberi among both the sailors and soldiers.”

The waiter leaned against the table, interest written all over his face. “Fascinating, indeed. It must be a very serious disease.”

Eijkman nodded, “Yes, it is completely debilitating. It involves weight loss, muscle weakness, extreme fatigue, confusion, a loss of the sense of feeling in the limbs, and paralysis. Often, due to fluid collection, it manifests in the swelling of the legs, enlargement of the heart, and heart failure.”

The waiter, realizing that he had not yet attended to the doctor’s request, concluded, “Very impressive work! I wish you every success. I’ll get your coffee immediately.” Eijkman nodded and turned back to the newspaper.

Thereupon, another figure entered the café, striding over to the bar, “One coffee, please. Have you a Dutch newspaper?”

The waiter motioned towards the corner of the room, “The Dutchman over there has our only copy.” The newcomer made his way to the table in the corner, “Let me introduce myself: my name is Cornelis Winkler from Utrecht.”

Eijkman put down his paper and stretched out his hand, “I am Christiaan Eijkman, lately of Amsterdam, but before that from Jakarta, Java.”

Winkler laughed, “What a coincidence! I am about to travel to Jakarta on a government commission to investigate the cause of beriberi. I am a neurologist and have come to consult with Robert Koch about bacteriology.”

Eijkman was astounded, “You don’t say! Why have we not met before? I am a physiologist working with Koch to prepare to investigate beriberi. As you are aware, Dr. Koch has advanced his new germ theory of disease, and I am convinced that our answer lies with that cause.”

Winkler nodded, “Yes, I, too, believe that most disease results from microorganisms that infect the body or from toxins that poison the body.”

The two launched into an animated conversation, forgetting all about their coffees. By the end of their impromptu meeting, they agreed to seek the approval of the commission director, Dr. Pekelharing, for Eijkman to join the commission in Jakarta.

So it was that the medical team, including Winkler’s research leader, Dr. Cornelis Pekelharing, and Eijkman’s research partner, Dr. M. B. Romeny, set out by steamship from Amsterdam on October 22nd of that year. They passed through the recently built Suez Canal and arrived in Jakarta, nearly half-way around the globe, on November 23rd. Their mission? To isolate the cause of beriberi in order to find a cure.

Discussion 1

- *What are the possible causes of disease?*
- *What other diseases have symptoms similar to those of beriberi?*

- *Can you think of any likely causes for the beriberi epidemic?*
- *How would you begin to look for the cause?*

Episode 2: Looking for infection

The first order of business for the team was to set up a laboratory. They obtained two rooms for that purpose in the Central Army Hospital. Fresh with the knowledge and techniques about bacteria that they had learned in Robert Koch's laboratory, the approach was obvious to them. They would search for and isolate the bacterium responsible for beriberi and then show, using various animals, that they could induce the appearance of beriberi just by exposing an animal to it. They tested for the disease scientifically by observing tissue samples containing nerves under a microscope. If beriberi were present, then the nerves appeared disintegrated. During the next eight months, the team was able to isolate a bacterium that they were certain was the right one. There was only one problem: try as they might, they could only observe a few animals which, upon being exposed to the bacteria, would get beriberi-like symptoms.

By the summer, they were no longer so sure about their idea that the disease must be caused by a bacterium. Realizing that the term for the commission was almost over, they met in their laboratory to examine their progress. As usual, Dr. Pekelharing took the initiative, "We must admit that our research up to this point has been inconclusive." Eijkman motioned to speak. "Yes, Christiaan, go ahead," Pekelharing nodded.

Eijkman began, "You realize that we cannot meet Dr. Koch's postulates for establishing the bacterial cause of a disease. We have, for example, not been able to re-infect animals with bacteria developed in cultures taken from other infected animals."

"You are right, of course, Christiaan," said Dr. Pekelharing. The others nodded in agreement.

"In the past," Dr. Winkler interjected, "people have attributed beriberi to insufficient nourishment and to misery. Is that still a possibility?"

Dr. Pekelharing shook his head, "Really, Cornelis, are you saying that the large-scale destruction of the nervous system that we have observed in sick animals is being caused by hunger and grief?" Winkler blushed.

Eijkman laughed at Pekelharing's sarcasm and concluded, "That means that the true cause must be something coming from the outside. Is it a poison or an infection?"

Pekelharing frowned, "Gentlemen, we can't resolve the issue here. I will simply have to write up my report in a cautious way. We are due to leave next week, you know."

Eijkman, again, motioned to reply, "I would like to volunteer to stay behind and continue the investigation."

Pekelharing nodded in approval, "That is certainly noble of you, Christiaan—I will seek approval of the Governor to sponsor you."

The group disbanded, each to begin preparing for the long journey home to Amsterdam. Fortunately, they were successful in obtaining permission for Eijkman to stay in Java to continue the work.

Discussion 2

- *Why was the team uncertain about the cause of beriberi?*
- *List some of the main hindrances to the research team's lack of progress in their search for the cause of the disease.*
- *What advice would you give to the research team?*

Episode 3: The chicken model of beriberi

Christiaan Eijkman was in his laboratory, bending over his microscope, deep in thought. Pounding footsteps came from the distance and entered the room. "Docteur, docteur, the chickens they are sick, the chickens they are sick."

"Slow down, Pierre!" Eijkman laughed. "What is wrong with the chickens?" Pierre was Eijkman's new research assistant from France.

"They are falling over like they are drunk!"

Eijkman straightened up, the tone of his voice rising in sudden excitement, "What? Does it look like beriberi?"

"Yes, yes, I am trying to tell you..." Pierre gestured eagerly as he spoke.

"Then I will have to take tissue and blood samples immediately to see if it is really neuro-degenerative, as beriberi is, and if I can culture a bacterial sample."

The research work now proceeded swiftly. It was soon established that the symptoms were those of beriberi. Eijkman now had an animal model—one

could say a chicken model—for beriberi. He was certain that this was the breakthrough for which he had been looking. To control his experiment carefully, Eijkman brought in chickens from outside the area and divided them into groups in separate cages, then exposed one group to the bacterial culture that he thought carried the beriberi. Something unexpected happened. Chickens from both groups soon exhibited the beriberi symptoms. “That is very strange,” said Eijkman “I had not realized that the disease was so contagious. Likely, the chickens from one group infected the others.” So he started over with disinfected, clean cages and a new group of chickens, this time keeping one cage far away from the other. Again, chickens from both groups developed beriberi symptoms. “That makes no sense whatsoever,” said Eijkman, “There must be another infection pathway of which I am not aware.” Despite the negative outcome, Eijkman let the experiment go on for another few days while he tried to think of something else to do.

What happened next was not only unexpected; it was devastating for Eijkman. Suddenly, both groups of chickens began to recover from the disease. They actually began to run around, again. “Not only are my experiments inconclusive; they are negative. What will I do now?” Eijkman kept to himself for the next few days, reading intensely and often staring blankly into the distance, wondering if he would ever be able to find the cause of beriberi.

Discussion 3

- *Name all the factors that contributed to Eijkman’s confusion during his experimentation with the chickens.*
- *What else, if anything, could Eijkman do to test his bacterial theory?*

Episode 4: Rice is not just rice

Eijkman had let it be known that he was not to be disturbed, yet there was a timid knock on his laboratory door. It was the animal caretaker, Rano.

“Sir, my apologies—I have made a grave error,” he stuttered nervously.

“What is it, Rano?” asked Eijkman.

“Sir, I have been feeding the chickens with leftover cooked white rice from the kitchen.”

Eijkman laughed, “That doesn’t sound too serious—you are certainly not in trouble with me!” “No,

no, you don’t understand—there is a new cook and he says it is against military regulations to feed military rice to civilian chickens.”

Eijkman roared with laughter, “It certainly does not matter to me. You have, however, managed to cheer me up. So what are you going to do about your mistake?”

Rano replied, “Sir, I already made the change weeks ago, but I was ashamed to tell you. I am giving the chickens feed-grade brown rice. Do you think that it will make them sick?”

Eijkman almost jumped, “What? You have fed them differently for weeks?” he exclaimed. Instantly, he thought, “Could that be the cause of their inexplicable recovery?” Eijkman looked Rano straight in the eyes, “Rano, you have done the right thing—you are definitely not in trouble!” at which a very relieved look crossed Rano’s face.

Eijkman’s mind began to spin. Already, he was beginning to contemplate experiments to test the diet of the chickens as he gave the caretaker strict instructions: “Rano, clean and disinfect all the chicken cages, but keep one of the sick chickens here for the next experiment. Also, get me ten new, healthy chickens, at once.”

“Yes, sir, I will do it immediately,” said the all-too-happy Rano as he turned to leave the room.

Eijkman kept the eleven chickens on a diet for five weeks. He fed two of the healthy chickens and the one sick chicken uncooked brown rice. Soon, the sick chicken got well, and the two healthy chickens stayed well. When he fed four of the healthy chickens cooked white rice, they soon all got sick. He then treated two chickens with the bacteria he suspected of causing the disease and fed them uncooked brown rice; yet, they remained healthy. The two remaining chickens—his control group—he kept feeding uncooked brown rice, and they remained healthy.

Eijkman thought about the results and concluded that, without a doubt, feeding white or polished rice resulted in the chickens acquiring beriberi, and feeding them rice containing the bran cured the disease. Yet, he could not explain the actual mechanism at work and continued to puzzle over it, thinking, “There may be some means by which the diet produces poisoning in the digestive system. Perhaps, there is a way to let harmful bacteria grow. On the other hand, perhaps, the bran of the rice contains substances indispensable to life and health that do

not exist in the grain of the rice. I just don't know what it is."

Resolute, he never gave up, ever uncovering new possibilities and undertaking new variations in his investigations in search of the answer. On account of poor health, Eijkman had to leave Jakarta in 1896, never to return, but his move back to Amsterdam did not stop the research efforts, in either Java or the Netherlands, to find the exact cause of beriberi.

Discussion 4

- *What was Eijkman trying to find out with his different versions of diet for chickens?*
- *Why, after determining that a diet of polished rice produced beriberi and unpolished rice cured it, did Eijkman continue to puzzle over the results of his experiment?*

Episode 5: Solving the puzzle

Eijkman's exacting and thorough work opened the way for other researchers to solve the puzzle. Without the foundation that he had laid, finding the solution would have been nearly impossible. Eijkman's successor in Jakarta, Gerrit Grijns, was the first to be able to establish, for certain, that beriberi was caused by a deficiency and not a bacterial infection or some kind of poisoning. He wrote, in 1901, that "There occur in various natural foods substances which cannot be absent without serious injury to the peripheral nervous system. These substances are easily disintegrated, which shows that they are complex substances and cannot be replaced by simple chemical compounds."¹

It remained up to the Polish scientist, Casimir Funk, however, to synthesize the various findings on nutritional deficiency diseases into a theory. He accounted for scurvy, beriberi, and many other diseases as those that break out if "an unvarying diet is partaken of for long periods" because of the "deficiency in a substance which is necessary for the metabolism."² Funk attempted to isolate the beriberi vitamin in 1911 and thought he had done so, but it is likely that his compound consisted mainly of niacin or vitamin B3, which is the factor in the deficiency disease pellagra. Thinking that the substance he had isolated was in the chemical class of amines, he named the newly discovered nutritional substances

"vital amines." Later, when it was discovered that these substances were not amines, their name was shortened to "vitamins."

It was not until 1926 that the substance responsible for preventing beriberi—thiamine or vitamin B1—was isolated by a new research team that had replaced Eijkman in Java.

Soon after Eijkman returned to the Netherlands, he had been appointed as professor of Bacteriology and Hygiene at the University of Utrecht. He became more and more preoccupied with his professorial duties. In 1912, he had taken on the University's rector position. In the following year, when he retired from the position, he gave a public lecture on his research work, which bore the provocative Latin title "Simplex non veri sigillum." Indeed, "simplicity" had not proven to be "a characteristic of truth," as expressed in the epigram. Undeniably, the truth about vitamins uncovered during Eijkman's lifetime had not been a simple matter, but an arduous scientific struggle.

In 1929, Eijkman was awarded the Nobel Prize in Medicine "for his discovery of the antineuritic vitamin," which was somewhat controversial on account of Gerrit Grijns not having been included. The Nobel Committee was not able to award Grijns because he had not been nominated that year. With Eijkman's health rapidly deteriorating, the Committee decided to make the award while they were still able to do so. Christiaan Eijkman died the following year at the age of 72.

Discussion 5

- *Why was it so difficult for the researchers to give up their bacterial theory?*
- *Explain how the epigram, "Simplex non veri sigillum," meaning simplicity is not a seal or mark of truth, applies to the story on Eijkman.*
- *Do you know of any other science story to which this epigram could be applied?*

References

- Allchin, D. (1996). Christiaan Eijkman & the cause of beriberi. In *Doing Biology*, Glenview: Harper Collins, pp. 116–127.
- Allchin, D. (n.d.). Christian Eijkman and the cause of beriberi. In: *Teaching science through history*. Retrieved March 1, 2013 from <http://www1.umn.edu/ships/modules/biol/beriberi.htm>

¹ Quoted in Carpenter (2012) pp. 221–222.

² Funk 1912, p. 341

- Bruyn, G. W., & Poser, C. M. (2003). *The history of tropical neurology: Nutritional disorders*. Canton, MA: Science History Publications.
- Carpenter, K. J. (2000). *Beriberi, white rice and vitamin B: A disease, a cause and a cure*. Berkeley: Univ. of California Press.
- Carpenter, K. J. (2012). The discovery of Thiamin. *Annals of Nutrition and Metabolism*, 61, 219–223.
- Carpenter, K. J., & Sutherland, B. (1995). Eijkman's contribution to the discovery of vitamins. *The Journal of Nutrition*, 125(2), 155–163.
- Carter, K. C. (1977). The germ theory, beriberi, and the deficiency theory of disease. *Medical History*, 21, 119–136.
- Complete Dictionary of Scientific Biography (2008). Eijkman, Christiaan. Retrieved March 18, 2013 from Encyclopedia.com: <http://www.encyclopedia.com/doc/1G2-2830901294.html>
- Erdman, A. M. (1964). Cornelis Adrianus Pekelharing—A biographical sketch. *The Journal of Nutrition*, 83, 3–9.
- Funk, C. (1912). The etiology of deficiency diseases beriberi, polyneuritis in birds, epidemic dropsy, scurvy, experimental scurvy in animals, infantile scurvy, ship beri-beri, pellagra. *Journal of State Medicine*, 20.
- Jansen, B. C. P. (1950). C. Eijkman. *Journal of Nutrition*, 42, 2–8.
- Merritt, C., & Tan, S. Y. (2011). Christiaan Eijkman (1858–1930): The vicar of vitamins. *Singapore Medical Journal*, 52(9), 652–653.
- Rosenfeld, L. (1997). Vitamine—vitamin. The early years of discovery. *Clinical Chemistry*, 43(4), 680–685.
- Verhoef, J. (1998). Christian Eijkman: Early Nobel winner for beriberi research. *American Society for Microbiology News*, 64(2). Retrieved March 1, 2013 from <http://newsarchive.asm.org/dec98/feature2.asp>

Acknowledgment: The author expresses his indebtedness to Douglas Allchin for providing resource materials and the interrupted story approach used in **Christiaan Eijkman: Simplex non veri sigillum** and to Sarah Dietrich for contributing to the basic research.

Christiaan Eijkman: Simplex non veri sigillum was edited by Cathrine Froese Klassen, with the support of the European Commission (project 518094-LLP-1-2011-1-GR-COMENIUS-CMP) and The University of Winnipeg, Canada and is based, in part on **Historical Background: Nutrition**, written by Andreas Junk, and on **Biography: Christiaan Eijkman**, written by Stephen Klassen, Sarah Dietrich, and Cathrine Froese Klassen.

Christiaan Eijkman: Simplex non veri sigillum was written by Stephen Klassen with the support of the European Commission (project 518094-LLP-1-2011-1-GR-COMENIUS-CMP) and The University of Winnipeg, Canada. This publication reflects only the views of the author, and the Commission cannot be held responsible for any use which may be made of the information contained therein.

