



Adolphe Vorderman's 1897 study on beriberi: an example of scrupulous efforts to avoid bias

Jan P Vandenbroucke

Department of Clinical Epidemiology, Leiden University Hospital, Leiden University Medical Center, CO-P, PO Box 9600, 2300 RC Leiden, The Netherlands
Email: j.p.vandenbroucke@lumc.nl

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When excerpts from

Vorderman's work were seen by Iain

Chalmers he originally thought that it might have been a controlled trial because the observations seemed so well-controlled.

Close reading of the

complete original Dutch text by Jan Vandenbroucke showed that it was an observational study, but with unusually tight

This paper highlights Adolphe Vorderman's investigations of the causes of beriberi using epidemiological observations among prison inmates in the Dutch East Indies (today Indonesia) in the 1890s.¹ His investigations are featured in the James Lind Library because of Vorderman's scrupulous efforts to avoid bias. He built a number of methodological safeguards into his investigations, both to avoid being deluded by others, and to reduce the likelihood that he would, when collecting and analysing the data, delude himself by potential prejudices about the hypothesis that he was investigating.

The story of the discovery of the nutritional cause of beriberi (a lack of vitamin B₁) is often recounted as that of a few heroic studies. On the side of 'basic science', the highlights are the experiments done by Christian Eijkman in the 1890s in Batavia, Dutch East Indies (now Jakarta, Indonesia), who found that chickens that had developed a beriberi-like illness when fed polished rice, did not do so when they were fed unpolished rice. Later, Frederick Gowland Hopkins, Eijkman's co-Nobel prize winner, did biochemical experiments in Cambridge, UK, and coined the idea that particular food substances, later called 'vitamins', were necessary for human growth and development.

As far as human experimentation is concerned, two reports in particular have received attention. In 1906, Baron Takaki published an account in *The Lancet* of an investigation done two decades earlier, which had been prompted by a severe epidemic of beriberi among Japanese sailors during a long sea voyage. Takaki arranged for a similar ship to follow the same long-distance route but with a much more varied diet for the

sailors: and many fewer cases of beriberi were observed among sailors during the second voyage.^{2,3} The other experiment was organized by William Fletcher in 1905 and was reported in *The Lancet* in 1907. It involved assigning inmates of a mental asylum in Kuala Lumpur, Malaya, alternately to either polished or unpolished rice, and showed that unpolished rice offered protection against beriberi.^{4,5}

As is often the case, the development of insights into the causes and prevention of beriberi was a much more tortuous process. Among others, Eijkman was initially not convinced that a nutritional deficiency was the cause of the disease – he was more inclined to think that there was a poison in polished rice. Eijkman's successor in Batavia, Gerrit Grijns, carried out several more experiments and proposed that the disease was caused by 'partial hunger', that is, a lack of particular food substances, and this corresponded to the theories of Frederick Gowland Hopkins. Several more people contributed shrewd observations that gradually reinforced the case for believing that a nutritional deficiency caused the disease. Vitamin B₁ was only isolated and purified much later. The ups and downs of different competing theories, infectious, poisons and, nutritional deficiencies were described in Kenneth Carpenter's monograph in 2000.

Adolphe Vorderman (1844–1902), a Dutch government doctor who worked in the Dutch East Indies, was one of the people who made careful observations on groups of humans receiving differing diets. His contribution was exceptional because of the elaborate precautions that he took against potential biases in his investigations, which went a long way beyond what one

precautions against bias, including bias due to self-delusion by scientists. We thank Harm Beukers for providing the original Dutch text. First version published as Vandembroucke JP (2003). Adolphe Vorderman's 1897 study of beriberi among prison inmates in the Dutch East Indies: an exemplar of scrupulous efforts to avoid bias. JLL Bulletin: Commentaries on the history of treatment evaluation (www.jameslindlibrary.org). Excerpts translated from Dutch to English by Jan P Vandembroucke; original texts, translations and additional material are available on www.jameslindlibrary.org where this article was originally published.

ordinarily sees in observational research, even today.¹

Vorderman described how in 1895 he had spoken with Christian Eijkman, not long before the latter's departure for Europe due to ill health. Eijkman had told him about his observations that chickens fed polished rice developed a neurological disease that might resemble beriberi, which disappeared when they were fed unpolished rice. This reminded Vorderman of a fleeting idea that he had once had: that beriberi was never seen in some prisons but frequently in others. He thought that this might be associated with the type of rice that the inmates received: 'whole' or unpolished 'red rice'; or 'peeled' or polished 'white rice'.

To avoid relying only on his own observations and memory for this initial impression, Vorderman started his observations by writing to all the prison medical officers in two parts of the Dutch East Indies, including prisons that he had never visited himself. He asked the medical officers (i) whether they had seen beriberi in the prisons for which they were responsible; and (ii) what type of rice was being given to the inmates. In his own words:

My remark, that in accordance with the results of his (Eijkman's) experiments with poultry, I recalled never to have seen Beri-beri in prisons where red rice was used as the main nutrition but that I had always seen white rice given as the main nutrition in prisons where Beri-beri occurred, prompted Dr Eijkman to ask me whether he might use this at some point in time. For my part, there was no objection. Only, I wished first to have data from all prisons of Java and Madoera, not only for the sake of completeness, but also to verify whether this peculiarity was also present in the prisons that I had not so far visited.

Therefore, I wrote a letter to all Heads of the Local Governments, with questions about the main type of nutrition of the prisoners, and about the occurrence of Beri-beri among these people, without, however, mentioning any possible relation between these two factors. (page 2).

As the results of Vorderman's initial survey confirmed his impression, he requested and was granted permission to proceed to a more extensive

investigation. He planned to visit all prisons on several islands in the Dutch East Indies, to collect specimens of the food given to the inmates, and to personally check records on the occurrence of beriberi. The latter was often documented quite well, since beriberi in its end stages was grounds for release from prison (hence, some cases of simulated disease also occurred!).

Vorderman was much preoccupied with the possibility of bias – even if he did not use the word or referred to any theoretical textbook describing the notion. His mission had the official aim of 'looking into the health status of prison inmates'. However, the fact that he wanted to do the food sampling was kept an official secret, to prevent the possibility that rumours about the investigation might lead the local suppliers of the food to the prisons to change the kind of rice that they provided (see p. 3). In his own words:

Mention of this special part of the aim of the visit was kept secret, however, to prevent it becoming known, so that the Chinese suppliers who delivered the food would show types of rice other than the one they usually provided. (p. 3).

In each prison he visited, he went to the food supply, sampled it and mailed the sample under seal to the capital, Batavia, for further analysis. To keep the mission secret he refrained from making any comment about whatever he had found locally, even if the condition of the food was appalling. In his own words:

Even if the rice was of inferior quality, or if there were other remarks to be made about the food, these were temporarily withheld, to prevent the Chinese suppliers guessing the special aim of the mission, and warning each other about my visit. (p. 5).

In each prison, he obtained the statistics of beriberi relating to the year before his visit. Back in Batavia, he asked several experts to analyse and classify the rice samples by origin and composition. Laboratory assistants removed impurities, checked chemical composition, and used the services of a local Chinese rice vendor with a good knowledge of the types of rice to analyse the samples. However, all of these people were kept unaware

of the origins of the samples, as the bottles were marked only with alphabetical letters or numbers. In his own words:

The expert [who assessed the rice, transl.] did not know anything about the places where the samples were taken, because they were presented to him by the dozen, in small bottles marked only by a letter or number. His brief was: determine whether the rice came from Saigon, Rangoon or Siam. (page 5).

After initial verification, each batch of 20 samples was shown to a European rice vendor who sat on a committee with the acting medical director of the laboratory, Dr Roll, and a local officer of health of Batavia, Gerrit Grijns (who had taken on Eijkman's work when Eijkman retired). It soon dawned on Vorderman that many mixtures of rice were present, not just a contrast between 'white polished' and 'red unpolished', so he developed a finer classification. He also went one step further in his attempts to be as 'unpartisan' as possible (as he called it himself): only after the finer classification of the rice samples had been established, and each prison assigned to one of the categories of rice, did he communicate his findings about the statistics on beriberi among the inmates in each prison to his medical colleagues. In his words:

Only after the categorisation of the different prisons according to the types of rice had been established were the statistics that I had collected about Beri-beri sufferers and prisoners given to the above named medical doctors, to be ordered in the columns of appendix 10. (page 58).

The results of his analysis were eventually presented in his report, showing the strong association between type of rice and frequency of beriberi.¹

Although Vorderman's 1897 report mentions that beriberi had disappeared in prisons and the army when the type of rice had been changed, it attracted severe criticisms. His critics suggested that he had not ruled out an infectious cause of the disease, superimposed upon malnutrition; that other nutrition factors might be playing a role; and so on. These criticisms led to more experimental studies in chickens (by

Grijns, among others) and more investigations in humans.

For example, a controlled trial of mung beans among mental patients in the Dutch East Indies was published by Hulshoff Poll in 1902. This showed that there was no beriberi in the pavilions where patients were given mung beans, in contrast to the inmates in pavilions where the rice had been disinfected (as a precaution against infection!), where 42% had beriberi. Strangely, the author of these observations nevertheless concluded that the cause of the disease was infectious, reasoning that the addition of mung beans had led to better nutrition and therefore less infection.⁶ This incorrect inference might be why this interesting experiment has not survived in medical memory.

One forceful believer in the nutritional origin of beriberi was Baron Takaki, who blamed the beriberi in the Japanese navy in 1882 on a diet with too high a proportion of carbohydrates. In 1906, he reported that a subsequent change of nutrition in the navy had virtually wiped out the disease.² Still, the experimental work by Eijkman's successors clearly pointed to a specific deficiency factor in unpolished rice. Large-scale experimental evidence in humans came with the results of the controlled trial of different types of rice in asylum inmates in Malaysia, done by William Fletcher, who was careful, however, not to commit himself to a specific mechanism.⁴

All this work ultimately led to the award of a Nobel prize to Eijkman and Gowland Hopkins, as well as to the discovery of vitamin B1, the deficiency of which causes beriberi.^{7,8,9}

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