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The Rise of Western "Scientific Medicine" in Japan: Bacteriology and Beriberi

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Introduction

The adoption of Western medicine was an integral part of Japan's modernization from its very beginning,[1] leading ultimately to the introduction of "scientific medicine," a defining characteristic of the modern world. Scientific medicine started as a development in Western Europe, and after considerable conflict, came to be recognized as producing "true medical knowledge." This, in turn, was made universal through exportation.[2] Scientific medicine is based on two distinctive institutions, the hospital and the laboratory, which still prevail today. In hospital medicine, clinical investigation searches for correlations between symptoms and signs of disease, and internal changes of the body. Research focuses on anatomical pathology, and postmortems are routinely performed. In laboratory medicine, causes of diseases are identified by experiments in order to create cures for them. Laboratory research concentrates on living processes like bacteriology, uses living animals for experiments, and depends strongly on scientific instruments like microscopes.[3]

Historical research on Western medicine in Japan so far has paid little attention to the process of adopting scientific medicine. However, the investigations that the Japanese authorities and individual physicians carried out during the early Meiji period to identify the cause of beriberi (in Japanese, *kakke*), temporarily culminating in Ōgata Masanori's[4] (1855–1919) discovery of a "beriberi bacillus" in 1885, present an important case through which we can glean insights from the Japanese experience into the rise of scientific medicine in a non-European society. Because beriberi was not prevalent in Europe when it became a public health challenge in Japan, there were no ready-made containment policies available and the Japanese government had to try controlling this menace single-handed. As Japan had managed to

escape the threat of colonization and could develop quite autonomously, early beriberi research allows us to examine the introduction of scientific medicine in Japan under "laboratory conditions."

Japanese authors who discuss the history of beriberi in Japan dismiss bacteriological research on this disease, and Ōgata's work in particular, as only a diversion from the "true" path of medical progress that eventually led to the discovery of the cause, deficiency of vitamin B_1.[5] The historian of Japanese bacteriology Fujino Tsunezaburō explains Ōgata's work in detail, but does not place it in the context of Japanese beriberi research.[6] In European languages, Ōgata's discovery has been treated almost exclusively with regard to his later dispute with Japan's internationally more famous bacteriologist, Kitasato Shibasaburō (1852–1931). The alleged consequences that Kitasato's critique of Ōgata's findings had for Kitasato's career have been at the center of attention, rather than Ōgata's discovery itself.[7] K. Cordell Carter, too, in his study of the history of beriberi research, does not consider Ōgata's work in detail.[8] This chapter seeks to do so by asking in particular how scientific medicine was adopted in the course of early beriberi research during Japan's early modernization, and what role the germ theory played in this process.

Beriberi as a Threat to Modernization

After the Meiji Restoration (1867–1868), the role of medicine in Japanese society changed dramatically. Medicine was now expected to contribute to the government's policy of modernization, symbolized by the slogan of a "rich country with a strong army" (*fukoku kyōhei*). This shift had already begun under Tokugawa rule at the end of the Edo period, but after the Meiji Restoration, the new government strongly promoted this process. In 1872, an "Office for Medical Affairs" (*Imu-ka*) was created within the Ministry of Education. This was later succeeded by the "Bureau of Hygiene" (*Eisei-kyoku*) under the leadership of Nagayo Sensai (1838–1902) of the powerful Ministry of the Interior. The Bureau was responsible for regulating health care and coordinating the numerous measures that were now taken to defend the public's health. In 1874, the "Medical Act" (*Isei*) established the first national licensing examination for physicians based on Western medicine, effectively abolishing traditional Kanpō medicine.[9]

During this early stage of the creation of a medical administration, beriberi was of little concern. Epidemic diseases such as cholera that threatened almost the entire country captured the attention of the health authorities. However, beriberi's prevalence had risen already during the late Edo period and it had become a permanently present endemic disease. From the great population centers—Edo (later to become Tokyo), Osaka, and Kyoto—the disease had spread to provincial towns and then to rural areas. The thirteenth and the fourteenth shoguns, Tokugawa Iesada (1824–1858) and Tokugawa Iemochi (1846–1866), are said to have both died of beriberi at the ages of 34 and 20, respectively.[10]

Beriberi suddenly moved to the center of attention when during the Seinan civil war of 1877, a large percentage of the troops fell sick with this disease. According to contemporary statistics, the rate of affliction with beriberi in the Japanese army had been 11 percent in 1876, but climbed to 14 percent in 1877, and jumped to 38 percent in 1878.[11] In the Japanese navy, the prevalence was 33 percent in 1878. If beriberi damaged the fighting capabilities of Japan's troops during a civil war this heavily, how much more crippling would the effects of the disease be during a military confrontation on the Asian continent?[12] The Japanese government decided that, in order to protect the combat readiness of the Japanese armed forces, the beriberi problem had to be solved.

However, there was a second important reason why the medical administration became increasingly concerned with beriberi at this particular time. Since April 1876, the Japanese empress suffered gravely from the disease. One year later, she recovered, but then in June 1877, Kazunomiya, the emperor's sister, fell seriously ill with beriberi, and one month later, even the emperor himself contracted the disease. When in September 1877, Kazunomiya died from heart failure caused by beriberi, this was a severe shock to the Japanese imperial family. The trust in Western medicine that had replaced Chinese-style medicine at the imperial court since the Meiji Restoration was deeply shaken and some physicians of traditional Kanpō medicine were reappointed to court offices. While the emperor recovered by the end of the year, he was now sensitized to the problem of beriberi, and his continuing interest in combating beriberi is reflected in numerous recordings in the imperial chronicle.[13] This was especially so since the damage done by the disease was not limited to the imperial family, but every year, there were thousands of victims among the civilian population. Beriberi thus put the supreme aim of Japanese modernization—to become a "rich country with a strong army" in order to remain an independent nation—in doubt.

As the first official measure of research into the cause of beriberi, in December 1877, the Bureau of Hygiene started a national initiative to collect and evaluate all knowledge about the disease available in Japan. In order to include even the most recent observations, Ministry of the Interior officials instructed all public hospitals throughout the country to gather all extant information concerning the pathology and treatment of the disease and to submit it to the Bureau during January 1878. In the internal explanation for this order, the officials of the Ministry of the Interior stressed that beriberi was confined almost exclusively to Asia. Even the foreign physicians who were practicing in different prefectures of Japan since the Meiji Restoration, despite having conducted numerous investigations of the pathology and therapy of the disease and having formulated different theories regarding its cause, had no confirmed insights in either area of inquiry. Therefore, the Bureau of Hygiene wanted to carry out a comparative study of the different academic theories and practical approaches.[14]

The directive of the Ministry of the Interior of December 1877 caused a wave of concern regarding beriberi among Japan's medical community, and

the number of monographs published on the subject rose steeply in 1878. The physicians of Kanpō medicine reacted especially quickly because they viewed it as an opportunity to win support for Chinese-style medicine that was being abolished. Kanpō physicians submitted petitions to the government outlining their treatment methods and claiming that their medicine was equipped with more effective cures for beriberi than Western medicine because they had more experience treating this disease that was prevalent mainly in Asia. In addition to offering their know-how, Kanpō physicians also founded private beriberi hospitals to demonstrate the special effectiveness of Kanpō medicine to government officials and to gain sympathy for Chinese-style medicine among the common people.[15]

An example of the theories drafted by Kanpō practitioners provides the "New Treatise of Beriberi Disease" (*Kakke shinron*) that was published in May 1878 by the famous Kanpō doctor Imamura Ryōan (1814–1890) who had been a court physician of the Tokugawa family. Imamura's work was based on medical theories stemming from the Chinese Tang period. In China, one of the ways that physicians had explained the origins of the disease was the "theory of outer causes" (*gaiinsetsu*) based on a "wind poison" (*fūdoku*) that supposedly originates in the soil and enters the body through the legs. Imamura enriched this theory with his personal experience and in part even included anatomical concepts from Western medicine. He argued that a "poison" would enter the inner organs via the blood vessels and, as the disease progresses, spreads into the heart and lungs where it would cause the characteristic attacks.[16]

Besides the Kanpō doctors, the Japanese physicians practicing Western medicine now paid more attention to beriberi, and this was reflected in Japan's new medical journals.[17] In April 1878, for example, the *Tokyo Medical Journal* (*Tōkyō iji shinshi*), one of the most influential medical periodicals in Japan during the early Meiji period,[18] published a paper "On Beriberi" (*Kakke-ron*) written by the physician Kashimura Seitoku (1857–1902). Kashimura, who later became one of the research directors of the government's Beriberi Hospital, suspected the cause of the disease to be a "malaria poison" (*mararia doku*).[19] In this, Kashimura possibly followed the lead of the prominent army surgeon Hashimoto Tsunatsune (1845–1909) who in 1876 had submitted to the University of Würzburg a German-language dissertation "About the Beriberi Disease," a Japanese language summary of which was printed in the first edition of the Medical Newspaper (*Iji shinbun*) of May 1878. Concerning the origin of beriberi, Hashimoto had quoted different theories, for example the assumption of an inflammation or softening of the spinal cord, but personally he favored a "miasma formation" in swamps as the most likely cause of the "malaria-like" illness.[20] Another medical officer of the army, Ishiguro Tadanori (1845–1941), authored his own "Theory of Beriberi" in August 1878. According to Ishiguro, a "fungus"[21] caused the disease. This "fungus" supposedly formed as the result of transformation processes in the polluted soil of the great population centers, moved from the ground into the atmosphere and entered the human body through drinking water. As a causal therapy, he recommended fighting the "fungus" with quinine.[22]

In the late 1870s, beriberi was increasingly perceived as a threat to Japan's modernization policy. In addressing this threat, Japan was faced with two-fold difficulties. First, in contrast to other diseases such as cholera against which the counterstrategies of Western countries could serve as a ready reference for Japan, beriberi was a disease that was little known in Europe, and Japan had to develop adequate preventive measures by itself. Second, knowledge regarding the causation and treatment of beriberi still either centered on the ancient theories of Chinese medicine or simply echoed versions of the then popular concept of "miasma" proposed by many European physicians.[23] Therefore, the officials at the Japanese Ministry of the Interior decided to make beriberi research a matter of state responsibility.

State-Sponsored Hospital Medicine at the Beriberi Hospital

The national survey of knowledge about beriberi led the officials at Japan's Ministry of the Interior in February 1878 to the conclusion that neither Kanpō nor European medicine provided a satisfactory theory of causation, not to mention an effective method of treatment of beriberi. In a memorandum to the State Council (*Dajōkan*), they requested funds to found a specialized hospital under the direction of the Bureau of Hygiene that would conduct comparative research on beriberi. The Bureau declared that the strengths and weaknesses of Kanpō and European medicine should be compared on the basis of their clinical performance and the origin of the disease should be elucidated through basic research. In spite of the high costs involved at a time of great fiscal strain, three days later, the State Council responded positively to the Ministry's request. The Imperial court, being afflicted heavily by beriberi, participated not only in generously financing the Beriberi Hospital, but also demanded that Kanpō medicine would be included in the trials.[24]

By July 1878, the state Beriberi Hospital opened its doors. The four clinical wards were placed under the authority of four leading physicians. Two of them, Tōda Chōan (1819–1889) and Imamura Ryōan, were representatives of Kanpō medicine, while the other two, Kobayashi Tan (1847–1894) and Sasaki Tōyō (1838–1918), practiced European style medicine. The effectiveness of their treatment plans was to be compared systematically. Ikeda Kensai (1841–1918) and Miyake Hiizu (1848–1938)—leading authorities on internal medicine and pathology—were responsible for basic research.[25]

The clinical side of the state Beriberi Hospital exemplified the multitude of causative theories and therapeutic approaches that were common in Japan at the end of the 1870s. On the part of the Kanpō physicians, Imamura treated his patients according to the established recipes of Chinese-style medicine. Tōda, a former court physician of the Tokugawa as well as the emperor, on the contrary abided by the secret method handed down within his family that was based on the conviction that the cause of beriberi was found in rice. He prohibited his patients from consuming rice and prescribed instead a diet based on Azuki beans.[26] Among the two physicians of European

medicine, Kobayashi believed the precise cause of beriberi to be unknown but suspected a disease process similar to the ideas of Agathon Wernich (1843–1896)—a German lecturer for Internal Medicine at the university in Tokyo—who had pointed out various pathological signs of nutrition deficiencies that were supposedly caused by an inflammation of the digestive tract of beriberi patients. Kobayashi thus implemented a strict regimen of improved nutrition that required his patients to drink large quantities of milk. Sasaki who had studied European medicine with the Dutch military surgeon Johannes L.C. Pompe van Meerdevort (1829–1908), who was probably the first European to describe the Japanese "variation" of beriberi,[27] finally acted like a representative of Ishiguro whose theories and therapy suggestions he followed. Sasaki assumed a "fungus" to be at the root of beriberi and therefore treated his patients "causally" by administering quinine, otherwise addressing only the symptoms of the disease. Despite the variety of therapeutic approaches, there were, in the end, no significant differences between the curative successes of Kanpō and European medicine. Only Kobayashi achieved slightly better results than his colleagues with his nutrition-oriented milk therapy, while Sasaki stayed somewhat behind the field, perhaps because of his focus on fighting the suspected "fungus."[28]

How did basic research fare at the state Beriberi Hospital? While both of the two highly acclaimed research directors installed in 1878, Ikeda and Miyake, left the Beriberi Hospital after only a short period of time, the basic proceedings that they established were followed by their successors. From the outset, the scientific work was based on the assumption that beriberi was an infectious disease caused by a certain "poison" (*doku*) that entered the human body from the outside. The first and most pressing aim of the investigation was to observe the climatic and other circumstances under which the disease occurred in order to identify its "cause" (*gen'yū*) and pathology. If the factors leading to the formation of the "poison" and the mechanism of its entry into the human body were known, then a prevention of the disease would be possible, even if the exact "nature of the disease poison" (*byōdoku no honsei*) could not be fully understood. This pragmatic approach based not on a search for *the* cause, but the factors contributing to causation seemed justified to Ikeda and Miyake as they noted that even in Europe, the nature of many epidemic infectious diseases was not yet fully grasped. They wanted to investigate all circumstances that could possibly produce the disease. If they would remove that "factor which was closest" (*mottomo kin'in*) to the disease, then this should serve as a means of prevention.[29] As a second step, the afflicted organs and the most important symptoms of the disease were to be recorded according to precise clinical observation. The achievements of Kanpō medicine in this area were not considered sufficient as their focus was thought to be different from that of European medicine. Finally, an understanding of the pathology of the disease was Ikeda's and Miyake's third stated aim. Pathological dissections were to be conducted to observe the relationship between organic changes and the clinical course of the disease.[30] This research program at the Beriberi Hospital was thus characteristic of hospital

medicine seeking to identify "factors" causing beriberi that could be linked to the clinical and pathological disease process and that could ultimately serve as a starting point for preventive measures.

The decision to base the scientific work of the Beriberi Hospital on the assumption of a disease poison followed the general trend at the time. In August 1880, the Medical Newspaper published a review of the beriberi research undertaken in Japan until then that included even the views of Pompe van Meerdevort and Antonius Bauduin (1822–1885) who had taught Dutch medicine in Japan during the Edo period (ca. 1600–1868). From this synopsis, it was clear that the majority of the leading Japanese representatives of Western medicine as well as their foreign colleagues believed a miasma to be the cause of the disease.[31]

The Japanese physicians perhaps accepted the notion of a miasma readily because the concept appeared similar to that of the "wind poison" of Chinese-style medicine of the Edo period. How did Japanese physicians of the early Meiji period imagine the miasma and its origin? In an essay on miasmatic disease of September 1880, the physician Satomi Giichirō explained that the exact nature of the miasma was not known, but it was thought that it was a kind of "mold" (*baishū*) that would enter the air with the evaporation of swamp water. In places where the swamps are shallow, the sunlight could reach the bottom and processes of decay would occur in the soil, causing the formation of the poison. Therefore, during hot summers, an especially large quantity of miasma was produced. When there was little air movement in a marshland area, the poison would remain near the swamps and would inflict harm only on the people in its immediate vicinity. Strong winds, however, would carry the miasma even to distant regions particularly threatening the lives of persons of younger age or of those who were weakened by another disease, especially when they were suffering from starvation. To support this theory, Satomi pointed to the example of malaria, which Max von Pettenkofer (1818–1901) claimed was caused by rising groundwater.[32]

During the following years, the researchers at the Beriberi Hospital investigated not only climatic influences but also age, sex, profession, and living conditions as factors of causation, as well as the amount and composition of the patients' urine. They also performed several postmortems.[33] In addition, they searched for explanations for why a change of location had been known since ancient times as the most promising method to treat beriberi and why foreigners were almost entirely spared by the disease. While they recognized the importance of nutrition as a predisposing factor,[34] they interpreted the changes in the spinal cord, nerve, and muscle tissue that were found in the pathological dissections only as symptoms of the disease and speculated that the "poison" was located in the blood. Studies of blood samples were meant to become the focus of research, but they could no longer be carried out as the Beriberi Hospital was closed in July 1882 after only four years of existence, and transformed into a special division within the university.[35]

As the first state-run large-scale medical research project with a modern program of inquiry typical of scientific medicine, the Beriberi Hospital

went far beyond traditional approaches and was a novelty in Japan. It differed profoundly from other specialized beriberi hospitals based on localistic theories of disease. At the Japanese government's Beriberi Hospital, an ambitious program of hospital medicine was aiming for the discovery and confirmation of causative factors of beriberi. Patients served as a resource for medical research, and while postmortems did not readily become a matter of routine because of conflicting Japanese customs, they still formed a central part of the research program and were carried out by (foreign) experts with maximum circumspection.

The integrated research efforts did not, however, lead to the hoped-for breakthrough. The scientific results were meager compared with the huge financial investments and a starting point for preventive measures was not identified. The clinical observations, too, were not particularly startling because they largely replicated earlier work of European physicians practicing in Japan. The pathological research received little in the way of stimulus as only six autopsies could be undertaken in the years 1878 to 1880. In half of the dissected corpses, a disease other than beriberi was the cause of death, so only three postmortems could really contribute to beriberi research. Furthermore, all documented pathological studies were carried out at the university—not at the Beriberi Hospital itself—by a foreign physician, the German lecturer Erwin Baelz (1849–1913) who had been appointed Professor of Internal Medicine in 1876.[36]

While the research program based on hospital medicine did not succeed in identifying the cause of beriberi, the Beriberi Hospital nonetheless deeply influenced the Japanese medical community because it shaped a network of physicians committed to the conceptualization of beriberi as an infectious disease. As many of the doctors that had been affiliated with the Beriberi Hospital would later rise to positions of leadership in Japanese academia and the medical and military administrations, they would exert considerable influence in favor of research and health measures based on their causal perception. However, much to their irritation, it was the epidemiological approach based on nutritional theories that increasingly received attention during the following years.

Epidemiological Work and Experiments with the Barley–Rice–Diet

The naval surgeon Takagi Kanehiro (1849–1920) had been interested in beriberi since his youth. His father, who at the end of the Edo period had served in a military unit that guarded the Imperial palace in Kyoto, had told him about the disease that had cost many samurai their lives. In the troops, the samurai had thought that the disease was caused by the food that they were given and they had called the packages in which their rations were delivered "beriberi boxes."[37] In 1872, when Takagi entered the Japanese navy as a medical officer, he was immediately confronted with beriberi because the disease affected one third of all sick navy sailors, and it was clear that

mainly beriberi patients occupied the two naval hospitals.[38] In 1880, after his return from five years of study at St. Thomas Hospital in England, Takagi devoted much energy, as head of the Tokyo naval hospital, to research on beriberi. He found great differences in the prevalence of the disease between the crews of different warships. In his search for the reason for these discrepancies, he first examined clothing and shelter of the sailors, but they turned out to be mostly uniform and he thus excluded them from the list of possible explanations. Only in the provisions did he detect significant variations among the crewmembers because sailors were given cash allowances for the free purchase of foodstuff. Takagi, therefore, concentrated his efforts on the improvement of the sailors' rations.[39]

Takagi was reportedly motivated by thinking "of the future of our [Japanese] empire, because, if such a [bad] state of health went on without discovering the cause and treatment of beriberi our navy would be of no use in time of need."[40] In 1882, two events made Takagi's work even more pressing. First, during the journeys that the Japanese fleet undertook during the Korea incident of July and August 1882, up to a third of the crew of the great flagships fell sick with beriberi and the combat readiness of the Japanese navy was seriously called into question. Second, the intense threat posed by beriberi was demonstrated by the occurrences during a trip of the training ship *Ryūjō*. The *Ryūjō* set sail in December 1882 with a crew of 376 sailors, headed for New Zealand, South America, and Hawaii. During the ten months until its return to Japan, 169 persons contracted beriberi, 25 of whom lost their lives.[41] After these events, Takagi was granted the opportunity to personally explain his ideas about fighting beriberi to the emperor. Based on successful trials on patients at the naval hospitals in early 1883, Takagi succeeded in reforming navy provisions first from white rice to a Western diet, later to a mixture of barley and rice.

Takagi attempted to demonstrate the effectiveness of the new provisions for the prevention of beriberi quasi-experimentally. He asked that the warship *Tsukuba* follow the same route as the *Ryūjō*, and he successfully requested that this time it be fitted out with new provisions that included meat and condensed milk. When the *Tsukuba* returned to Japan in November 1884, of its crew of 333 men, only 16 had contracted beriberi. The prevalence statistics for the navy as a whole, too, apparently confirmed the effectiveness of Takagi's forceful measures: While from 1878 to 1883, the incidence of beriberi among sailors had been as high as 41 percent, this figure dropped to 13 percent in 1884.[42] In March 1885, Takagi personally reported to the emperor his progress in fighting beriberi in the navy.

Outside of the navy, too, Takagi promoted his belief that the cause of beriberi was found in the diet based on white rice. Already in 1883, he presented his ideas for the first time before the "Great-Japan Private Society for Hygiene" (*Dai-Nihon shiritsu eiseikai*). In 1884, he published a table with instructions for the prevention of beriberi by means of correct nutrition that was distributed to all prefectures.[43] In order to lend scientific support to his empirical findings, Takagi reverted to the older theory that beriberi was

caused by too high a proportion of carbon and too low a proportion of nitrogen in the diet.[44] In January 1885, on the zenith of his success after the completion of the *Tsukuba*-experiment, Takagi advertised his ideas again in a lecture "On the Prevention of the Beriberi Disease" before the Society for Hygiene.[45] Faced with Takagi's successes in the navy, even medical officers in the army began changing provisions. After Horiuchi Toshikuni (1844–1895) had successfully introduced a barley–rice–mixture at his division based in Ōsaka from 1884, most other army units had followed suit by 1890.[46]

In early 1885, the Meiji government began formal proceedings to bestow on Takagi an honor in recognition of his extraordinary achievements in fighting beriberi. On February 5, the Decoration Bureau (*Kunshō-kyoku*) in charge of conferring orders, asked the Ministry of Education for an evaluation of Takagi's scientific work, and the Ministry in turn requested that the university provide expertise. In its answer sent to the Ministry on March 26 for forwarding to the Decoration Bureau, however, the university faculty strongly denied Takagi's ideas. The academics argued that the cause of beriberi could not be reduced to dietary factors alone and that beriberi was a communicable, miasmatic disease. It would be highly unlikely that somebody through one or two experiments of only a few months duration could discover the cause of this disease and develop a method of prophylaxis. Finally, the faculty cast doubt on the specificity of Takagi's preventive measures against beriberi by observing that an improved diet contributes to the prevention of almost *every* disease. The group of experts who took a stance against Takagi's work included Harada Yutaka (?–1894), Ikeda Kensai, Ishiguro Tadanori, Hashimoto Tsunatsune, and Miyake Hiizu—all formerly affiliated with the government's Beriberi Hospital—as well as Ōsawa Kenji (1852–1927), Ōgata Masanori, Ise Jōgorō (1852–?), and the foreign lecturers van der Hayden and Julius Scriba (1848–1905).

In addition to their negative memorandum, individual university faculty opposed Takagi's ideas publicly. Particularly Ōsawa, who had become Japan's first professor of physiology after a period of postgraduate studies in Germany, expressed his concern that the spread of Takagi's views would lead to confusion in Japanese society. Ōsawa possibly considered it a danger that Takagi's beriberi theories might be understood as an endorsement of the dietetic theories of Kanpō medicine, such as those proposed by Tōda Chōan. This appeared even more concerning as the representatives of Western medicine had been fighting hard to discredit Chinese-style medicine.[47] Ōsawa not only doubted Takagi's hypothesis, but also in a second step, using physiological data, tried to prove scientifically that the barley-rice-mixture proposed by Takagi was not superior to a pure rice diet.[48] However, the known epidemiological facts pointed out by the British doctor William Edwin Anderson (1842–1900) already in 1878 would have been sufficient to prove wrong Takagi's assumption of a dietetic imbalance between carbon and nitrogen as the cause of beriberi.[49]

Ishiguro, too, published a new monograph about the beriberi disease, *Kakke-dan* (1885), in which he strongly criticized Takagi's ideas. While he

conceded that diet played an important part in causing beriberi, he refused to accept Takagi's theory that the disease could be explained *solely* by factors of nutrition. He could not imagine that Takagi's therapy of providing patients with a mixture of barley and rice would be of any use in the struggle against the disease. Instead, he recommended as preventive measures an enhanced ventilation of troop barracks, a general improvement of foodstuff, and plenty of exercise.[50] Since Ishiguro was one of the highest-ranking medical officers of the army, his outright denial of the reforms implemented in the navy effectively slowed the learning process in the army.

Takagi's reforms, based on epidemiological studies and quasi-experimental support, received much attention, but his nutritional theories threatened the concept of beriberi as an infectious disease cherished by many influential members of Japan's medical establishment at the university and the army. By successfully opposing Takagi's decoration and scientifically undermining the rationale that he gave for his reforms, the members of this establishment prevented official recognition of Takagi's theories and managed to keep the race for the highly contested cause of beriberi open. Experimental proof of the infection theory, that is, the discovery of an actual beriberi germ, would be the ultimate weapon to restore the balance of power between the two parties.

Beriberi, Germ Theory, and Early Japanese Bacteriology

In their efforts to raise doubts about Takagi's apparent successes, his opponents appeared entirely vindicated when only a few weeks later, in April 1885, Ōgata Masanori published his discovery of a germ causing beriberi. Ōgata's discovery temporarily confirmed the germ hypothesis of beriberi and thus proved the theory of beriberi being an infectious disease championed by Takagi's opponents. How was it possible that only a few years after the unsuccessful application of hospital medicine at the Beriberi Hospital, Ōgata could present a discovery based on the germ theory using the even more advanced techniques of laboratory medicine?

After the closure of the Beriberi Hospital in 1882, great hopes were pinned on bacteriological methods that had been so successfully applied to medical research in Europe, to fulfill the commitment of understanding the infectious cause of beriberi. Baelz who had participated in the pathological research at the Beriberi Hospital and who had profited most from it, first began implementing this agenda in Japan. In August 1882, he published an article in German "On Infectious Diseases Prevalent in Japan" that drew on "almost 6 years of experience at the heavily patronized inner clinic and policlinic of the university hospital in Tokyo that during this period were run under my direction." Baelz stressed that beriberi would be a "miasmatic infectious disease" and pointed to the startling "analogy with malaria." He "most decidedly" opposed Wernich's view that suggested a connection between *Kakke* and pernicious anemia. While bacteria had "not yet been

identified in the blood" of beriberi patients, Baelz thought "it not unlikely that a parasite which until now has just escaped our research, will be found in there [i.e., in the blood] or the tissue."[51] Regarding bacteriological investigations of beriberi, Baelz wrote:

> From our present [scientific] position, the conception of Kakke as a miasmatic infectious disease almost brings about the duty to find the supposedly organized poison; most likely is the expectation that it is a body belonging to the group of fission fungi ["Spaltpilze"]. Based on this assumption, already for many years I have been trying to find such a body, be it in the blood, be it in the mainly affected organs, the nerves. Until now in vain. However, I do not give up the hope with the help of the recently so much perfected methods, especially Koch's staining procedure, still to reach the aim anyway and [I] will therefore continue the microscopic investigations further. Several times I believed to have found a specific Micrococcus, but since the finding was different in different preparations, I do not yet dare to view the same as the cause of Kakke.[52]

While Baelz began applying bacteriological methods to beriberi research, how prepared was Japan's medical community for the advent of bacteriology? Bacteriological topics had been introduced first by Japan's journals of medicine. In the *Tokyo Medical Journal* of 1878, an unidentified author reported on "Methods to exterminate Bacteria" (*Bakuteria o bokumetsu suru no hō*). The writer stated that microorganisms were a product of fermentation processes that could be observed under a microscope at a magnification of 800 times. The author claimed that for a physician it was most important to know how to fight bacteria, and then he discussed how different substances had proven to be of varying usefulness.[53]

Miyake Hiizu's book "General Theory of Pathology" (*byōri sōron*) that was published in 1879 contributed greatly to a more detailed knowledge of bacteriological facts in Japan. In drafting the manuscript for this book that went through several editions and was widely read, Miyake consulted Felix Victor Birch-Hirschfeld's *Textbook of Pathological Anatomy*[54] in addition to four other foreign works. Birch-Hirschfeld's text included the most recent findings of bacteriological research,[55] and based on this, Miyake gave a detailed overview of "schistomycetes" ("fission fungi") under the heading "plant parasites."[56]

Robert Koch's (1843–1910) discovery of the tuberculosis bacillus was transmitted to Japan only with a few months delay when Baelz explained Koch's work to the university students immediately before the summer vacation of 1882.[57] A written account of Koch's work reached the Japanese medical press the following year when Sakaki Junjirō (1859–1939), a physician who studied in Germany at the time, briefly communicated the experimental proceedings of Koch and his theory of the causation of tuberculosis.[58] However, the implications of Koch's discovery were not immediately grasped by the entire Japanese medical community and articles concerning bacteriological topics remained rather an exception in Japanese medical reporting.[59]

Therefore, foreign doctors were the ones who first applied bacteriological techniques to beriberi research. Van der Hayden of Kōbe was among the first physicians in Japan who—based on microscopic inspections of the blood of beriberi patients—claimed that "bacteria" or "micrococci" were the cause of the disease. In 1882, a Japanese medical journal briefly reported that van der Hayden had observed changes in the presence of bacteria in the blood of beriberi patients in correlation with the progress of the disease.[60] American missionary doctor Wallace Taylor (1835–1923) received attention even beyond Japan's shores with his finding of "spores" in the blood of beriberi patients.[61] In autumn 1884, he decided to investigate their link with the disease preparing cultures of the suspected germ and infecting laboratory animals with it. The infected creatures soon exhibited symptoms that according to Taylor were similar to those of human beriberi patients. He observed that the germ that he called "Beriberi Spirilum" was present in rice where cooking would not destroy it. This fit well with the folk wisdom of the Japanese people that the cause of beriberi was found in rice.[62]

Meanwhile, the interest in bacteriology grew considerably in Japan. In the introduction to its series "Overview of the Discovery of 'Bacteria' " (*'Bakuteria' hakkensetsu no shūshū*) of spring 1883, the *Tokyo Medical Journal* noted that during the past few years in the West, bacteriological theories had been increasingly discussed. It was expected that they would radically change the development of medicine. The paper pointed out that the example of tuberculosis had shown how the face of pathology was completely altered by the discovery of bacteria.[63] When one year later, in May 1884, the same journal published a series of articles on "Methods for the Observation of Bacteria" (*Bakuteria kensatsuhō*), the work and proceedings of Koch and Louis Pasteur were introduced in detail.

Only two years after Koch's discovery, the stage was already set for the first bacteriological debate among Japanese physicians. In 1884, the army surgeon Watanabe Kanae (1858–?) announced his discovery of a "Micrococcus Beriberi." Watanabe's investigation was driven by his conviction that the cause of beriberi should not be left to discovery by someone from the Western hemisphere because the disease was mainly prevalent in the Eastern hemisphere. Watanabe claimed to already having recognized in 1881 that the cause of the disease was a bacterium. He reported that in August 1882, when investigating the blood of patients, he had successfully identified the germ and that he had now reached the firm conclusion that this "parasite" (*parashiitsu*) and the beriberi disease were in an "inseparable relationship" (*aihanaru bekarazaru kankei*). The number of germs, it was argued, would correlate with the gravity of the illness. In the blood of patients with severe beriberi symptoms, there were more micrococci than in the blood of those who had only mild complaints. In addition, Watanabe had confirmed that the germ was not found in the blood of healthy persons and of patients suffering from a different disease. Watanabe apparently followed some of the causal criteria postulated by Koch as he reported that he had also tried to transmit the disease to animals, but that this work was still in progress.[64]

Hiroi Komaji and two other physicians thoroughly reviewed Watanabe's claims. The three critics imagined beriberi to take its course from a physical "predisposition" (*soin*), which when the "cause" (*gen'in*) was added, would lead to the outbreak of the disease in which food, clothing etc. would form promoting "circumstances" (*shoin*). They concluded that the question whether beriberi originated in the "conditions of everyday life" (*seikatsuhō*) or was caused by a "specific germ" (*toku'i dokuso*) could not yet be decided. Although they themselves were of the opinion that the cause of beriberi was a specific microorganism, they doubted Watanabe's discovery and regarded the true germ as still unidentified. They argued that already in 1871, Dutch and British physicians had discovered a "fungus" that was later recognized as having already been known and that it was probably similar to Watanabe's discovery. There were many conditions that a proposed beriberi germ had to fulfill. Hiroi and his colleagues called for Watanabe to try the method that Koch valued so highly: to isolate the organism and then to infect laboratory animals with it. They concluded that at the present stage of research, foodstuff and clothing could still not be excluded as causes of the disease.[65]

Ōgata's Discovery of Beriberi Germs and the Power of "Laboratory Medicine"

When Ōgata Masanori returned from postgraduate work in Germany in December 1884, Japanese physicians had already joined Baelz and other foreign colleagues in the hunt for the supposed beriberi germ. Japan's medical community was also sufficiently informed to critically evaluate hasty bacteriological discoveries. When upon his return, the university and the Ministry of the Interior both immediately employed Ōgata to head their respective bacteriological laboratories, he made it his highest priority to identify the cause of beriberi with the bacteriological techniques that he had studied in Germany.

Ōgata was the son of a family of physicians from Kumamoto in Kyushu where he began studying medicine before moving to the university in Tokyo. After graduation in 1880, he assisted Baelz with his work on beriberi. In January 1881, Ōgata received a government scholarship for study in Germany where he first concentrated on physiology and hygiene at the University of Leipzig, Baelz' Alma Mater. Later, Ōgata moved to Munich where he continued research on hygiene with Pettenkofer.[66] In 1884, two years after Koch's discovery of the tuberculosis bacillus, Ōgata spent several months in Berlin to learn bacteriological techniques at the Reichsgesundheitsamt. It is likely that Ōgata acted on orders from Nagayo, the powerful chief of the Bureau of Hygiene, because the Ministry of the Interior offered to bear his expenses during his stay in Berlin.[67] Since Koch was visiting Egypt and India at that time, his assistant, Friedrich Löffler (1852–1915), initially instructed Ōgata.[68]

Ōgata's laboratory in Tokyo had already been partially prepared with government help upon his return: Shibata Tsuguyoshi (1850–1910) of the

Ministry of the Interior who had visited Berlin to attend the hygiene exhibition of 1883, had transported part of the valuable equipment on his return trip to Japan; Ōgata brought the rest with him.[69] He received blood and tissue samples from the beriberi department at the university[70] and examined them at the Tokyo Laboratory for Hygiene of the Ministry of the Interior that was equipped with three Zeiss microscopes with immersion lenses for maximum magnification.[71] At the university, Tsuboi Jirō (1862–1903) was assisting Ōgata while at the Tōkyō Laboratory, he was aided by Kitasato who had concluded his medical studies at the university three years after Ōgata. In addition, Ōgata was expected to train three physicians—Kako Tsurudo (1855–1931) of the army, Kuwahara Sōsuke of the navy, and Suga Yukiyoshi (1854–1914) of the Okayama Medical School—in bacteriological techniques.[72]

Only four months after his return from Germany and only a few weeks after Takagi's report on his nutritional experiments, the great investments in Ōgata's education and research appeared to pay off when on April 6, 1885, Ōgata published in the official government gazette (*kanpō*) a formal "Report about the Discovery of the Beriberi Bacillus" (*Kakke byōkin hakken no gi kaishin*).[73] Ōgata claimed to have isolated a hitherto unknown microorganism from the blood of beriberi patients and the tissue of deceased beriberi victims. Ōgata declared that he could breed this microbe in pure culture and that after inoculation in laboratory animals, it produced symptoms and pathological signs that closely resembled those of beriberi patients.[74] In composing his report, Ōgata emphasized from the beginning that he had followed Koch's example by successfully isolating the bacillus *and* infecting laboratory animals with it and that he had therefore concluded that it was the cause of disease.[75] In a short span of time, Ōgata had thus successfully raised the quest for the cause of beriberi to a new level by bringing the pinnacle of scientific medicine, laboratory medicine, to bear on this task.

During the following weeks, Ōgata held two public lectures about his discovery at the invitation of the president of the university, Katō Hiroyuki (1836–1916), and the director of the Bureau of Hygiene, Nagayo. Among the audience were not only faculty members of the university, but also leading representatives from government, medicine, and the military.[76] In front of a blackboard with explanatory drawings, Ōgata had installed microscopes through which the visitors could observe his "beriberi bacillus." In addition, cultures of the bacilli growing on different media were exhibited. In his speech, Ōgata explained his methods of investigation in detail. To further substantiate his findings, he also presented laboratory animals whose hind extremities were paralyzed, apparently in a way characteristic of the symptoms of beriberi.[77] In quickly presenting his preliminary results to the public, Ōgata thus made intensive use of many of the new forms of visual and "functional" representation of his "discovery" that communicated laboratory medicine's claim to objectivity.[78]

At the end of his presentation, Ōgata turned to his competitors. After criticizing aspects of Taylor's work, he particularly stressed the fundamental

differences between the implications of his discovery and the theories of the also present Takagi.[79] After Ōgata had finished, Takagi had the opportunity to respond. In the face of Ōgata's overwhelming experimental evidence, Takagi attacked from a pragmatic viewpoint: Ōgata's discovery was not very practical, because if it held true, then all physicians would have to be equipped with expensive microscopes to diagnose beriberi with certainty. In addition, Takagi doubted that Ōgata's research would lead to an improvement of beriberi treatment. This argument was indeed powerful. Already in 1881, an essay about the beriberi disease by Baelz had disappointed the Japanese readership because the author did not derive recommendations for therapy from his bacteriological theories.[80] The publishing house resorted to printing advice from an unidentified source in the next edition of the journal.[81] As Takagi did not have the training needed to directly question Ōgata's laboratory evidence, he chose to contest Ōgata's results on the grounds of usefulness instead.

Finally, Ishiguro addressed the audience and lavishly praised Ōgata's discovery. According to Ishiguro, Ōgata had used such precise research methods as had been unknown to "oriental people" (*tōyōjin*) and most of the Western physicians practicing in East Asia. Ishiguro was also deeply impressed by the opposing views of Ōgata and Takagi, both of whom were his personal friends. His speech ended with an appeasing gesture stressing the stimulating effect that differences in opinion would have on true scientists.[82]

Ōgata's discovery left a deep impression on the medical community in Japan, even causing a small bacteria boom. Already a few weeks later, the *Tokyo Medical Journal* reported that Joseph Disse (1852–1912), a German lecturer at the university, had also discovered a beriberi "fungus" that resided at different locations in the spinal chord.[83] In a letter to the journal, Taylor once more called attention to his discovery of the "Beriberi Spirilum."[84] Ōgata himself continued his investigation of the "beriberi bacillus" that he also proudly presented in a German medical weekly in the same year.[85] After having been appointed professor at the university to teach hygiene,[86] one year later, he published a second report about his work on the beriberi germ.[87]

In spite of the generally favorable response to Ōgata's discovery, many Japanese doctors still harbored reservations and judged his findings not yet sufficiently confirmed. In response to a question concerning the beriberi disease, Yamazaki Motomichi of the Society for Hygiene for example, answered that the cause and pathology of beriberi were still unknown. He himself believed that Ōgata's bacillus was indeed the cause of the disease, but that this result still awaited validation. Moreover, Yamazaki combined the germ theory with the older miasmatic disease concept explaining that beriberi was an infectious disease that was contracted from the soil.[88] In a monograph on beriberi published by Harada, the author also stuck to the hypothesis of a miasmatic infectious disease.[89] Ōgata's discovery was thus smoothly integrated into a germ concept that differed from Koch's: Many Japanese physicians believed germs to be miasmatic in origin. Like many of

their European colleagues, most Japanese doctors embraced Koch's concept of specificity—that pathogenic organisms could be produced only from organisms of the same species—only many years later.[90]

While Japan's medical circles were not uncritical, it was hard not to be impressed when confronted with Ōgata's cutting-edge laboratory methods that were modeled on Koch's example, in combination with the authority that Ōgata's study at the Reichsgesundheitsamt in Berlin had conferred on him. Physicians based in Japan did not dare to challenge Ōgata's findings as forcefully as they had done before with Watanabe's claims. This role finally fell to Kitasato who for a short period had been Ōgata's assistant in preparing the discovery of the "beriberi bacillus" before leaving to work with Koch in Berlin. There, Kitasato had the chance to study the methods of the new laboratory science over a much longer period than Ōgata had done. This put Kitasato in a position to criticize Ōgata's work on beriberi as a specialist of bacteriology, and this lead in 1888 to the much-discussed controversy between him and Ōgata. However, being a bacteriologist himself, Kitasato did not explicitly doubt that the cause of beriberi was a germ; he only questioned that *Ōgata*'s "beriberi bacillus" was that germ.

Supported by laboratory medicine, Ōgata's discovery gave the physicians championing the infectious disease theory of beriberi nonetheless more than just a short-lived opportunity to draw attention away from Takagi's practical successes. The doctors at the university and in the army found lasting support for their position through Ōgata's discovery because by introducing laboratory methods, Ōgata had raised the demands placed on a scientifically acceptable causal explanation to a level that Takagi could not match. While the nutritional origin of beriberi postulated by Takagi was too unspecific to satisfy the standards of evidence inspired by "classical bacteriology," Takagi's work did not yet exhibit the combination of work in epidemiology and hygiene with the laboratory search for a specific cause that became characteristic of tropical medicine after 1900.[91] Proposing a cure without being able to establish a suitable cause put Takagi in a position similar to that of the ousted Kanpō physicians with their time-tested therapies based on speculative theories. In the navy, the incidence of beriberi continued to drop rapidly from two-digit levels to 0.6 percent in 1885 and even 0.1 percent in 1886, and Takagi's practical successes received international recognition,[92] but he could win only a few followers because of his unconvincing theoretical explanation. By raising the standards of what is scientific, Ōgata's discovery had effectively shifted the balance in the debate.

Conclusions

The integration of medicine into Japan's modernization policies from the middle of the nineteenth century[93] found its expression in the particular arena of beriberi in the intensive search for the cause of this disease that prompted the government to step in and seek to control it. However, after a government-sponsored research program of hospital medicine failed to

identify a specific cause of beriberi, the "true" origin of the disease remained contested between physicians favoring empirical conceptions based on nutrition and those believing in theories of infection as proposed by many representatives of Western medicine. In the race for the identification of the cause of beriberi that ensued, both sides, using government resources, turned to experimental approaches to prove their ideas. The physicians, preferring the evolving germ theory of beriberi, countered the practical successes of their competitors with findings produced with the modern methods of scientific medicine that they speedily introduced into Japan. In the field of beriberi research, Japan completed the transition from hospital medicine to laboratory medicine, which had taken many decades in the West, in only seven years. Although the discoveries made in the laboratory were met with skepticism, the outcome of this contest was a lasting stalemate in which supporters of nutritional concepts succeeded in implementing prevention measures against beriberi while backers of germ theory managed to block official recognition of nutritional ideas.

The adoption of scientific medicine with its experimental approaches in Japan was strongly driven by the perceived economic and military need to control endemic beriberi, facilitating the supply of massive state resources. Individual physicians from both conceptual camps involved in beriberi research repeatedly stated that they regarded their work as being of national importance. However, perceiving the control of beriberi as a precondition for military preparedness was not peculiar to the Japanese. During the modernization process in many countries, efforts to fight disease created a rising interest in the identification of necessary causes whose removal could serve as preventive measures.[94] The Dutch colonial authorities in Indonesia, for example, saw "conquering beri-beri [. . .] as a necessary condition for winning the Atjeh wars" and this perception formed the background for the mission by Pekelharing and Winkler arriving in Java in 1886 to investigate the disease's cause.[95] In Japan, the physicians at the state's Beriberi Hospital also sought to find a cause whose removal would allow the control of the disease—a necessary cause. Thus in Japan at the end of the 1870s and in the early 1880s, a similar shift from primarily considering disease symptoms to a concern with etiology can be observed, as it has been pointed out for beriberi research published in the Dutch language around the 1880s.[96] This interest in the *cause* of beriberi provided the link between the perceived need to control the disease and the ensuing research agenda that led to the ready adoption first of hospital medicine and then of laboratory medicine in Japan.

While hospital medicine soon reached its limits because the desired findings were not readily forthcoming, it prepared the ground for the next stage of the quest into beriberi's causation by forging an influential group of physicians supporting the model of infection. When the temporary void left by the lack of practical results from the Beriberi Hospital was filled by the nutritional approach advanced through experimental means, the leap from hospital to laboratory medicine was quickly taken. Germ theory arrived on the scene at a moment when Japan's medical elite was acutely absorbed in the

search for the origin of beriberi. However, the transition from hospital to laboratory medicine was possible not just because germ theory had penetrated the Japanese medical community during the preceding years, but also because at this moment the Japanese government's program to send students abroad produced a person—Ōgata Masanori—who seemed fully equipped to successfully implement the most advanced program of research available at the time, laboratory medicine.

The acceptance of a beriberi germ by the Japanese medical community was helped by its apparent close resemblance to indigenous theories of a "wind poison" evaporating from the soil and entering the body via the feet, that appeared compatible with the disease's particular epidemiology, and that was supported by influential foreign physicians believing beriberi to be a miasmatic infection. The rapid adoption of the germ theory in Japan in the context of beriberi research is thus also an instructive example of local appropriation and demonstrates that "there was no 'germ theory of disease' transcendent over time, but rather many different germ theories of specific diseases being debated in specific communities, times, and places [, . . . and] particular understandings of the germ theory were [indebted] to preexisting traditions of explaining disease."[97] It also exemplifies the difficulty of the diffusion of a highly codified scientific discipline, even under the conditions of the seemingly well organized Japanese modernization process. Even in Japan, with its hired foreign teachers and its great number of physicians studying at leading academic institutions abroad, the "laboratory practice that developed [. . .] in the first wave of enthusiasm for the 'miracle-making' science [bacteriology] often failed to conform to the discipline's new, more stringent professional standards."[98] Therefore during the early development of bacteriology in Japan, debates centered on the technical aspects of bacteriological work, and like similar discoveries of beriberi germs for example in South America,[99] early Japanese announcements were rejected because they did not conform to the high standards of bacteriological research. However, these technical "teething" problems were largely overcome after researchers like Kitasato returned to Japan who had the opportunity to undergo much more in-depth training in the new scientific methods than their predecessors.

While the will to remove beriberi as an obstacle to Japan's modernization and the ensuing struggle over the disease's causal explanation accelerated the introduction of scientific medicine to Japan, this did not necessarily bring the "fruits of progress" to the Japanese people. Especially in the army's medical corps, physicians committed to the germ theory of beriberi and supported by bacteriological findings continued to exert a strong influence. Ishiguro in particular repeatedly resisted attempts to reform the army's rice-based diet, ultimately at great cost. Ten years after Ōgata's discovery, during the Sino-Japanese war of 1894–1895, casualties caused by beriberi were nine times higher than those due to combat action. And in 1904–1905, when Japan's victory over a major European power in the Russo-Japanese war was celebrated by many Japanese as proof of the success of Japan's modernization policy, this triumph was tarnished by the fact that more than

200,000 Japanese army soldiers or almost 20 percent of total army personnel in the field in Japan and Asia fell sick with beriberi, many of them dying from the disease.[100] Several decades after the Meiji Restoration and the beginning of Japan's modernization policy, modern medicine provided leading physicians with a scientific rationale to effectively oppose prevention measures against beriberi, the effectiveness of which had been demonstrated "only" empirically.

NOTES

1. Christian Oberländer, *Zwischen Tradition und Moderne: Die Bewegung für den Fortbestand der Kanpō-Medizin in Japan* (Stuttgart: Franz Steiner [Medizin, Gesellschaft und Geschichte, Beiheft 7], 1995), pp. 51–65.
2. Andrew Cunningham and Bridie Andrews, "Introduction: Western Medicine as Contested Knowledge," in *Western Medicine as Contested Knowledge*, ed. Andrew Cunningham and Bridie Andrews (Manchester: Manchester University Press, 1997), pp. 1–23; here pp. 8–9, 12.
3. Andrew Cunningham and Perry Williams, "Introduction," in *The Laboratory Revolution in Medicine*, ed. Andrew Cunningham and Perry Williams (Cambridge: Cambridge University Press, 1992), pp. 1–13; here pp. 2–5.
4. Personal names are given in the customary order in the native language of the person. Where they are known, the years of birth and death of people are given.
5. See, e.g., Yamashita Seizō, *Meijiki ni okeru kakke no rekishi* (History of the Beriberi Disease in the Meiji Period) (Tokyo: Tōkyō Daigaku Shuppankai, 1988), p. 295; Itakura Kiyonobu, *Mohō no jidai* (The Age of Imitation) (Tokyo: Kasetsusha, 1988), p. 299.
6. Fujino Tsunezaburō, *Fujino, Nihon saikingaku-shi* (Fujino's History of Japanese Bacteriology) (Tokyo: Kindai Shuppan, 1984), pp. 105–114.
7. James Bartholomew, *The Formation of Science in Japan* (New Haven: Yale University Press, 1989), p. 81.
8. K. Cordell Carter, "The Germ Theory, Beriberi, and the Deficiency Theory of Disease," *Medical History* 1977, *21*: 119–136.
9. Oberländer, *Zwischen Tradition und Moderne*, pp. 61–64.
10. Yamashita Seizō, *Kakke no rekishi: bitamin hakken izen* (History of Beriberi: Before the Discovery of the Vitamin) (Tokyo: Tōkyō Daigaku Shuppankai, 1983), pp. 183, 191, 220, 356–358.
11. Heinrich Botho Scheube, "Die japanische Kak-ke (Beri-beri)," *Deutsches Archiv für klinische Medizin* 1882, *31*, 1 and 2 (May 30): 141–202; 3 and 4 (July 13): 307–348; *32*, 1 and 2 (November 8): 83–119; here pp. 148–149.
12. Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 89, 335–336.
13. Ibid., pp. 24–27, 43.
14. Kōseishō Imukyoku, *Isei hyakunenshi shiryōhen* (Hundred Year History of the Medical Law: Sources) (Tokyo: Gyōsei, 1976), pp. 52–53.
15. Oberländer, *Zwischen Tradition und Moderne*, pp. 86–92.
16. Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 260–261.
17. William Johnston, *The Modern Epidemic: A History of Tuberculosis in Japan* (Cambridge, Mass.: Council on East Asian Studies, Harvard University, 1995), p. 188.

18. Ibid., p. 188.
19. Kashimura Seitoku, "Kakke-ron" (On Beriberi), *Tōkyō iji shinshi* (Tokyo Medical Journal) April 10, 1878, *16*: 5–13; here pp. 5, 10.
20. Hashimoto Tsunatsune, "Kakke shinsetsu" (New Theory of Beriberi), *Iji shinbun* May 11, 1878, *1*: 1–13; here pp. 2–4.
21. In addition to the term "bacteria," other expressions were frequently used in Japan. For example, the term "fungus" (*pirutsu*) was common. Hashimoto Tsunatsune described the pathogen of diphteria as a "fungus" that enters the mouth from the atmosphere (Hashimoto Tsunatsune, "Kōtō 'Jifuterichisu' no setsu" [On "Diphteria" of the Throat], *Tōkyō iji shinshi* February 22, 1879, *48*: 1–13; here pp. 4–12).
22. Ishiguro Tadanori, *Kakke-ron* (Theory of Beriberi) (Tokyo: Eirandō, 1878), pp. 3, 5, 21.
23. For a more complete overview of the theories of beriberi's causation that Japanese and foreign physicians of the Meiji period proposed, see Christian Oberländer, "The Rise of Scientific Medicine in Japan," *Historia Scientiarum* 2004, *13* (3): 176–199; here pp. 177–180.
24. Oberländer, *Zwischen Tradition und Moderne*, pp. 83–84; Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 95–97, 100.
25 Kakke Byōin, *Kakke byōin daiichi hōkoku* (First Report of the Beriberi Hospital) (Tokyo: Kakke Byōin, 1879).
26. Ibid.
27. Heinrich Botho Scheube, "Die japanische Kak-ke (Beri-beri)," *Deutsches Archiv für klinische Medizin* 1882, *31*, 1 and 2 (May 30): 141–202; 3 and 4 (July 13): 307–348; *32*, 1 and 2 (November 8): 83–119; here p. 147.
28 Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 179–181, 185, 193, 196, 207.
29. Kakke Byōin, *Kakke byōin daiichi hōkoku*, pp. 89–90, 92.
30. Ibid., pp. 90–92.
31. "Naika senmon shokai" (Internistic Meeting), *Iji shinbun* (Medical Newspaper) August 15, 1880, *29*: 1–21.
32. Satomi Giichirō, "Miasma shobyō" (Miasmatic Diseases), *Iji shinbun* September 15, 1880, *30*: 1–3.
33. Kakke Byōin, *Kakke byōin daini hōkoku* (Second Report of the Beriberi Hospital) (Tokyo: Kakke Byōin, 1881), p. 77.
34. Ibid., pp. 117–118.
35. Yamashita, *Meijiki ni okeru kakke no rekishi*, p. 229 note 22.
36. Heinrich Vianden, *Die Einführung der deutschen Medizin im Japan der Meiji-Zeit* (Düsseldorf: Triltsch Verlag [= Düsseldorfer Arbeiten zur Geschichte der Medizin 59], 1985), p. 134.
37. Takaki Kanehiro, "Three Lectures on the Preservation of Health amongst the Personnel of the Japanese Navy and Army. Lecture I," *The Lancet* May 19, 1906: 1369–1374; May 26: 1451–1455; June 2: 1520–1523; here p. 1370.
38. Yamashita, *Meijiki ni okeru kakke no rekishi*, p. 334.
39. Ibid., pp. 339–340.
40. Takaki, "Three Lectures," p. 1370.
41. Yamashita, *Meijiki ni okeru kakke no rekishi*, p. 338.
42. Ibid., pp. 333, 343–352.
43. "Kakke gen'in" (Cause of the Beriberi Disease), *Tōkyō iji shinshi* December 27, 1884, *352*: 1666.

44. Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 339–340.
45. Takagi Kanehiro, "Kakke-byō yobō-setsu" (About the Prevention of the Beriberi Disease), *Dai-Nihon shiritsu eiseikai zasshi* (Journal of the Great-Japan Private Society for Hygiene) 1885, *22*: 1–20.
46. Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 399–401.
47. Oberländer, *Zwischen Tradition und Moderne*, pp. 65–106.
48. Ōsawa Kenji, "Bakuhan no setsu" (About the Barley-Rice-Mix), *Dai-Nihon shiritsu eiseikai zasshi*, July 18, 1885, *26*: 1–13 and August 18, *27*: 1–16.
49. William Anderson, "Kak'ké," *Transactions of the Asiatic Society of Japan* October 27, 1878, *6* (1): 155–178; here pp. 155, 169–170, 175. An overview is given by Carter, "The Germ Theory," pp. 126–127.
50. Ishiguro Tadanori, *Kakke-dan* (About Beriberi) (Tokyo: Eirandō, 1885).
51. Erwin von Baelz, "Ueber die in Japan vorkommenden Infectionskrankheiten," *Mittheilungen der OAG* August 1882, *27*: 295–319; here pp. 304–307, 315.
52. Ibid., p. 304.
53. "Bakuteria o bokumetsu suru no hō" (Methods to exterminate Bacteria), *Tōkyō iji shinshi* January 25, 1878, *12*: 14–17.
54. Felix Victor Birch-Hirschfeld, *Lehrbuch der pathologischen Anatomie* (Leipzig: F.C.W. Vogel, 1877).
55. K. Cordell Carter, "Koch's Postulates in Relation to the Work of Jacob Henle and Edwin Klebs," *Medical History* 1985, *29*: 353–374; here p. 365.
56. Fujino, *Fujino, Nihon saikingaku-shi*, pp. 44–45.
57. Ibid., p. 91.
58. Sakaki Junjirō, "Kekkakusho ha hatashite densenbyō nari" (Is Tuberculosis really an Infectious Disease?), *Tōkyō iji shinshi* May 5, 1883, *266*: 12–16; here p. 13.
59. Johnston, *The Modern Epidemic*, p. 191.
60. "Kakke kanja no ketsueki kensa" (Examination of the Blood of Beriberi Patients), *Tōkyō iji shinshi* July 8, 1882, *223*: 30–31.
61. See, e.g., "Kakké, or Japanese Beri-beri," *Lancet* June 30, 1887: 233–234; here p. 234.
62. Wallace Taylor, "Kakke ichimei beri-beri no gen'in" (The Cause of *Kakke* or Beriberi), *Tōkyō iji shinshi* August 8, 1885, *384*: 998–1001.
63. " 'Bakuteria' hakkensetsu no shūshū" (Overview of the Discovery of "Bacteria"), *Tōkyō iji shinshi* April 28, 1883, *265*: 5–10; May 12, *267*: 8–12; May 19, *268*: 6–9; here p. 5.
64. Watanabe Kanae, "Kakke byōdoku hatsumei-ron" (About the Discovery of the Beriberi Agent), *Tōkyō iji shinshi* September 27, 1884, *339*: 1207–1211 and October 4, *340*: 1241–1247; here pp. 1208–1211; 1242–1246.
65. Hiroi Komaji et al., "Kakke gen'in-ron" (About the Cause of Beriberi), *Chūgai iji shinpō* (International Medical Review) January 10, 1885, *115*: 15–19; January 25, *116*: 23–25; February 10, *117*: 20–22; February 25, *118*: 19–22.
66. Itakura, *Mohō no jidai*, p. 290.
67. Fujino, *Fujino, Nihon saikingaku-shi*, p. 102.
68. Itakura, *Mohō no jidai*, p. 290.
69. Fujino, *Fujino, Nihon saikingaku-shi*, pp. 102–103.
70. Ōgata Masanori, "Kakke byōdoku hakken" (Discovery of the Beriberi Disease Poison), *Tōkyō iji shinshi* April 11, 1885, *367*: 454–457; April 18, *368*: 492–497; April 25, *369*: 517–522; here p. 454.
71. Fujino, *Fujino, Nihon saikingaku-shi*, p. 105.
72. Ibid., p. 104.

73. Yamashita, *Meijiki ni okeru kakke no rekishi*, p. 298.
74. Ōgata, "Kakke byōdoku hakken," pp. 454–455.
75. Carter, "Koch's Postulates," p. 361.
76. "Kakke byōdoku hatsumei dai-enzetsukai kiji" (Report on the Great Lecture Event concerning the Discovery of the Beriberi Disease Poison), *Tōkyō iji shinshi* April 18, 1885, *368*: 507–510.
77. Ibid., pp. 507–508.
78. For the use of different methods of representation in bacteriology, see e.g., Thomas Schlich, "Linking Cause and Disease in the Laboratory: Robert Koch's Method of Superimposing Visual and 'Functional' Representations of Bacteria," *History and Philosophy of the Life Sciences* 2000, *22*: 43–58.
79. "Kakke byōkin hakken enzetsu" (Lecture on the Discovery of the Cause of the Beriberi Disease), *Chūgai iji shinpō* April 25, 1885, *122*: 24–26; here p. 25; "Dainikai kakke baikin enzetsu" (Second Lecture on the Beriberi Germ), *Chūgai iji shinpō* May 10, 1885, *123*: 25–27; here p. 26.
80. Erwin von Baelz, "Kakkebyō-ron" (About the Beriberi Disease), *Chūgai iji shinpō* March 25, 1881, *26*: 1–8 and April 10, *27*: 1–10.
81. "Igaku shinsetsu" (New Medical Theories), *Chūgai iji shinpō* April 25, 1881, *28*: 1–3. Concerning the discovery of the microorganism causing tuberculosis, too, some authors criticized that this would not contribute to the treatment of the disease (Johnston, *The Modern Epidemic*, p. 191).
82. "Kakke byōdoku hatsumei," pp. 509–510.
83. "Isshū no kin" (A Kind of Bacteria), *Tōkyō iji shinshi* May 2, 1885, *370*: 578.
84. Taylor, "Kakke ichimei beri-beri no gen' in," p. 998.
85. "Untersuchungen über die Aetiologie der Kakke," *Aerztliches Intelligenzblatt* November 24, 1885, *32*, *47*: 683–686.
86. Yamashita, *Meijiki ni okeru kakke no rekishi*, p. 298.
87. "Kakke byōgen kensa" (Investigation of the Cause of Beriberi), *Tōkyō iji shinshi*, April 3, 1886, *418*: 428–433; April 10, *419*: 465–470; April 17, *420*: 501–505; April 24, *421*: 537–544; May 1, *422*: 571–576; May 8, *423*: 600–607; May 15, *424*: 634–641.
88. Yamazaki Motomichi, "Kakkebyō ōtō" (Answers concerning the Beriberi Disease), *Dai-Nihon shiritsu eiseikai zasshi* July 25, 1885, *26*: 53–58; here p. 53.
89. Itakura, *Mohō no jidai*, p. 250.
90. For details concerning the debate about specificity during the early development of bacteriology, see Pauline Mazumdar, *Species and Specificity. An Interpretation of the History of Immunology* (Cambridge: Cambridge University Press, 1995).
91. Ilana Löwy, "Yellow Fever in Rio de Janeiro and the Pasteur Institute Mission (1901–1905): The Transfer of Science to the Periphery," *Medical History* 1990, *34*: 144–163; here p. 162.
92. See, e.g., Takaki, "Three Lectures."
93. Oberländer, *Zwischen Tradition und Moderne*, pp. 44–45.
94. K. Cordell Carter, "The Development of Pasteur's Concept of Disease Causation and the Emergence of Specific Causes in Nineteenth-Century Medicine," *Bulletin for the History of Medicine* 1991, *65*: 528–548; here p. 544. See also Thomas Schlich, "Die Konstruktion der notwendigen Krankheitsursache: Wie die Medizin Krankheit beherrschen will," in *Anatomien medizinischen Wissens. Medizin, Macht, Moleküle*, ed. Cornelius Borck (Fischer: Frankfurt a.M., 1996), pp. 201–229.

95. Harmke Kamminga, "Credit and Resistance: Eijkman and the Transformation of Beri-beri into a Vitamin Deficiency Disease," pp. 232–254; here p. 236.
96. Ibid., p. 238.
97. Nancy J. Tomes and John Harley Warner, "Introduction to the Special Issue on Rethinking the Reception of the Germ Theory of Disease: Comparative Perspectives," *Journal of the History of Medicine* 1997, *52*: 7–16.
98. Löwy, "Yellow Fever," p. 144.
99. Ibid., p. 144.
100. Yamashita, *Meijiki ni okeru kakke no rekishi*, pp. 440–465.