On this cold wintry day in December, 1921, George Conrad was browsing the shelves of his favorite book store. There, nestled on the shelf between textbooks of surgery, he found a treasure bound in rich burgundy with 1-centimeter-tall gold lettering, written by Edward B. Vedder, M.D., Captain in the U.S. Army Medical Corps, and published in 1913. This accounting of an illness was already acclaimed a masterpiece. Vedder had been awarded the Cartwright Prize of the Alumni of the College of Physicians and Surgeons, Medical Department of Columbia University (New York). Clutching the book to his chest with his left hand as if afraid he would lose it, George reached for his wallet to make the purchase.

"Vedder could have titled it Kakke," George noted as he related his good fortune to son, Charles, years later. "This book, like so many other classics in medicine, provided informative reading that linked basic, clinical and population-based sciences. An abstracted summary that appeared in the Appendix on page 412, and which was translated into English from turn-of-the-century German literature, led me to the original paper published in 1899. This clinical report provided useful teaching material for my students."

This paper also provided much entertainment for the Conrad family as they exchanged yet another public health conundrum. George dubbed his fictionalized version of the report "Dark Voyage of the Fearless Eagle." A gentle summer breeze blew across the North Sea as the Fearless Eagle (der Adler), prepared to depart Hamburg in July, 1898. This steamer would make its first voyage to East Asia, a nonstop journey to Hong Kong that would take several months. Standing at the helm was Captain Tritthart, his ordinarily stern face creased by the slightest of smiles on this important occasion. A plume of smoke wafted skyward from his trusty pipe as Tritthart gripped the tiller and scanned the navigator’s map that would guide them into the North Atlantic. A knock at the door interrupted his concentration and engaged his startle response. “Enter!” he exclaimed.

As if walking on eggs, 28-year-old Dr. Bernhard Nocht made his way into the cabin. Nocht, a naval physician, would care for the ship’s crew while satisfying his wanderlust to visit distant shores. He reported that rations on board, including citrus fruit from Spain, baked bread, fresh vegetables, and fresh as well as canned meats, had passed his personal inspection. Further, all hired men were fit for the long journey.

The arduous 60-day voyage on the high seas proved uneventful, and import goods were delivered on time in early September.

There followed a six-week stay in Hong Kong, during which time Bernhard enjoyed its many treasures. The Captain kept the crew mindful of the ship’s timetable. Asian exports had to be promptly loaded for the return voyage. As added incentive, he noted that by maintaining schedule, the return voyage would reach Germany in time for the Christmas holiday.

Tritthart also searched for men who could serve as stokers, fueling the ship’s hungry furnace. Twenty-three men would ultimately be hired, but only after Bernhard’s physical examination had pronounced them fit. All were of fine physique, and Bernhard had found no evidence of communicable illnesses such as measles, scarlatina, tuberculosis or smallpox. None were jaundiced nor had body lice or dermal eruptions, and none had cardiac murmurs, ascites, peripheral edema or neurologic deficits. To accommodate their dietary preferences, Bernhard ordered crates of dried fish and white rice for the journey to Hamburg. The Chinese crew would not begin work until the steamer was back in Hamburg. They therefore would be passengers on this return voyage. By October 16, the Fearless Eagle was back at sea on its way to Hamburg. No illnesses appeared among European or Chinese crews during the uneventful 8-week voyage.
By mid-December, the Hong Kong-based crew were actively involved in their physically demanding chores aboard the steamer. It was on December 26 that Bernhard found Li Ming and Song Yang had taken ill. Each complained of poor appetite, malaise, nausea and generalized weakness. There was a loss of power in lower extremities, and with a slow, deliberate gait each hobbled about using ropes, hatches or dockhouses to steady themselves. They further reported numbness and a prickling sensation to the soles of their feet. In recent days, Li Ming had also developed swollen facies and legs, a bounding, rapid pulse and neck vein distention. Bernhard arranged for both men to be admitted to a hospital. Li Ming died soon after admission.

Captain Tritthart summoned Bernhard to his cabin to ascertain why these men had taken ill. Bernhard reported sadness and surprise at this unexpected turn of events. The Chinese crew were presumptively healthy, and each had been carefully examined for illness prior to their hire. Food had not spoiled and water tanks were well maintained. The steamer was in good sanitary condition and did not harbor pestilence. If these men had been ill with infection when they came on board in Hong Kong, he could not discern what disease had a latency period of some 70 days, and why others had not taken ill. Tritthart and Nocht could only guess at the possibilities, but infection seemed improbable.

The Fearless Eagle departed for Boston on December 27. Out to sea but a few days, the steamer was engulfed by the first of several hurricane-like storms. The Chinese crew, barefoot and without proper clothing, were not prepared for these adverse conditions. Their exposure to the elements was constant as they traversed the flooded front deck several times daily to reach their living quarters. They frequently suffered upper respiratory infections.

It was January 8, 1899, two weeks after their departure from Hamburg and 13 weeks since leaving Hong Kong, that Wong Shown reported ill. His legs and face were swollen and he noted pains in both calves and chest. Bernhard found Wong to have a rapid but regular, bounding pulse. By percussion there was no evidence of cardiac enlargement. Over ensuing days, compressive dressings proved useful in reducing ankle and leg edema; however, Wong developed a progressive paralysis of his lower extremities and remained confined to his quarters for the remainder of the journey.

Perplexed and frightened, Bernhard struggled to contain his sense of helplessness. Crew members asked him to see Wong San on the evening of January 19. Wong San was the fourth member of the Chinese crew to fall ill and the third with swollen facies and leg edema. Pitting edema also involved the abdominal wall and thorax, and there was percussion dullness in keeping with bilateral pleural effusions. Over ensuing days Nocht applied compressive leg dressings, warm poultices of aromatic scammony to the chest, while feet were inuncted with oils of cloves and mace mixed with oil of rose. Little seemed to help. His desperation growing, Bernhard turned to a decoction of Sarsaparilla roots in the hopes of dispelling the evil humor through sweat and urine. An extract of aloes was used as a cathartic. Despite these efforts, Wong San suddenly collapsed and died the evening of February 1.

On January 29, yet another crew member, Wong Sui, was stricken in the same way as his coworker. His symptoms were less advanced, but his fear overwhelming. Violent storms again appeared to further prolong the journey. On February 8, Wong Sui, his feeble voice barely audible, attempted to speak with fellow crew members as they left guard duty. He was found dead in his berth an hour later. Bernhard noted that he had developed marked edema of face, trunk and legs.

The seriousness of the emerging epidemic escalated the fears of other crew members. Together with relentless storms and exhausting labor, the spirit of all crew members was slipping away. The men wondered as to the “Jonah” that caused such bad luck. They began to whisper amongst themselves: it had to be the Captain’s fault, or perhaps tragedy was his fate. Who else was there to blame? They questioned whether it was advisable to ever sail with him again.

Between February 16 and mid-March, 1899, five additional members of the Chinese crew would be stricken with the ailment that featured facial and peripheral edema. Most had rapid heart rate. All told since the departure of the Fearless Eagle from Hong Kong on 16 October, ten cases had appeared, of which 5 failed to survive. By early April, out of desperation, Captain Tritthart arranged for the remainder of the Chinese crew to be placed aboard a steamer bound for East Asia, and so ended the epidemic aboard this steamer.

The 54-day voyage to Boston had taken longer than expected. Exhausted and perplexed, Bernhard Nocht and Captain Tritthart sat down to survey the epidemic and the circumstances that had befallen their hard-working Chinese crew. There had been several intrinsic difficulties. First, the crew was reluctant to bring their ailments to attention for fear of retribution. As a result, they only presented when their illness and symptoms were far advanced. Second, they did not trust the European physician. Third, detailed clinical evaluation had been hampered by the weather, the crew’s obligatory responsibilities and inadequate quarters for health care. Finally, Bernhard admitted that his understanding of the illness was hindered by limited onboard medical literature.

Captain Tritthart insisted that if such a tragedy was to be avoided in the future, it was mandatory that contributing factors be examined. Nocht provided his perspective, addressing the crew’s living conditions, the climate encountered during the voyage, and the crew’s nutritional status.

The men had been provided larger than recommended quarters that were well ventilated, and this was true for
journeys between Hong Kong and Hamburg and Hamburg to Boston. No prior Asian inhabitants had occupied these quarters. Tritthart added it was policy after each 6-week voyage that living quarters be disinfected; indeed, prior to leaving Hamburg they had also been painted. They concluded that living conditions could not have been contributory. This could not be a "place infection," an illness endemic to a disease-laden ship.

The journey between Hamburg and Boston had been prolonged by adverse weather, and members of the Chinese crew were not properly clothed and regularly had taken ill with common colds. Could this have made them more susceptible to the illness?

Drinking water was considered noncontributory. It was available to all sailors and was replenished during each voyage at ports frequented regularly by many vessels. Despite recommendations for a diverse diet, the Chinese crew preferred their own rations that included fish, white rice and various spices. A separate kitchen had provided them privacy and the opportunity to prepare their dietary intake according to custom and preference. Rice purchased for the crew was considered to be of the highest quality. The same could not be said for the fish. The crew had preferred half-cooked fish and dried fish. As adverse weather prolonged the voyage, rations became low. Discovery of spoiled fish, which the crew might have consumed, led to prompt disposal. The crew rebuffed recommended European fare, even though none of the Europeans aboard had taken ill. The importance of fish to the epidemic could therefore not be discounted.

**What is your diagnosis and what is its causality?**

*Answer:*

The illness, known as *Kakke* (disease of legs), was endemic to China at the turn of this century, particularly at such ports as KiangChow, Foo Chow and Hong Kong. In 1897, 10,000 cases would appear among Hong Kong's 250,000 inhabitants. It was prevalent throughout East Asia, including the Philippines, Malaysia and Indonesia. In Indonesia it was called beriberi (BB). Beri refers to weakness and the duplication was used to accentuate meaning (very weak).

Its origins were debated for many years. The Chinese felt BB was caused by a gaseous poison that originated from the earth. Feet in contact with earth were therefore first affected. Pasteur's germ theory and the emergence of microbiology as a discipline in the latter part of the 19th century led many to believe a disease could only be caused by a positive agent (e.g., infecting organism or toxin). While theories varied, a variety of organisms were held responsible for BB. Studies did not support one another. Each touted a new organism. Diet was considered of lesser importance. Its relevance slowly gained credence from several parts of the world.

**Atjeh, Dutch East Indies, 1874.** To combat BB prevalent amongst the Dutch East Indian fleet, native sailors had their predominant rice diet modified to include European foodstuffs. A marked decline in incidence followed. In 1875 several of the fleet's ships travelled to New Guinea. During the voyage the crew reverted back to native rations. Many of those who remained behind maintained the European diet. Only those who resumed their rice diet during the voyage, or those who refused to switch over to the varied diet in Atjeh, developed BB. Thereafter, a European diet became compulsory ration for the fleet, and as Van Leent reported in 1880, BB had disappeared from warships.

**Tokyo, Japan, 1882.** Kanehiro Takaki, a medical officer in the Japanese Navy, emphasized the importance of diet in preventing BB. His hypothesis: too little nitrogenous substances, too much carbohydrate. He convinced a sceptical Japanese admiralty to initiate dietary reforms. Voyages would provide more fresh meat and vegetables; barley occasionally would be substituted for rice. In 5 years BB was eliminated from the Japanese Navy. Takaki would later become an Admiral.

**Java, Dutch East Indies, 1883.** Christiaan Eijkman, a microbiologist, went to Java to find the organism responsible for BB. He made an accidental discovery. Domestic fowl fed surplus cooked rice from the wards of the military hospital developed a BB-like neuritis. He termed it *polyneuritis gallinarum.* When these chickens were returned to their usual low-grade, uncooked rice diet, they recovered. He was unable to demonstrate chicken-to-chicken transmission and could not induce the illness in chickens given blood or body fluids taken from affected humans. The rice used in the hospital kitchen was milled, and referred to as polished or white rice. During milling the outer bran coating was removed.

Chickens became an animal model vital to the study of BB, including the isolation and identification of BB-preventing substance. A.G. Voderman, a colleague of Eijkman, surveyed several hundred thousand prisoners in 101 Java and Madeira prisons in 1885, testing the bran coat hypothesis. An astounding difference in the incidence of BB was observed, depending on whether prisoners were served polished or unpolished rice. Both Eijkman and Voderman, victims of their microbiology training, searched for responsible microorganisms.

In 1912, Casimir Funk would present results of his epidemiologic and experimental studies that identified the importance of minute quantities of substances found in foodstuffs in preserving normal metabolism and human nutrition. He termed these substances vitamins. Absence of a vitamin from the diet led to a new concept: consumption of a ration lacking a definitive chemical substance could lead to a disease of deficiency.

The clinical presentation of BB was related to the degree
and duration of the dietary deficit. Milder cases were associated with polyneuritis (dry BB). More severe cases included cardiac involvement and serous effusions (wet BB). Cardiovascular manifestations included vasodilatation, reduced renal blood flow with sodium and water retention, and biventricular failure. An acute fulminant form included dyspnea, palpitation, and chest pain. Heavy muscular work together with a chronic deficiency of moderate severity and high carbohydrate intake was likely the case in the Hong Kong crew, and favored the appearance of wet BB. A chronic deficiency with caloric restriction and inactivity favored dry BB.

Manila, Philippines, 1909. Edward Vedder’s studies had shown that rice polishings contained a specific BB-preventing substance which was lacking in white rice. He had partially characterized the substance: it was soluble in alcohol and insoluble in ether, and was diffusible through parchment membrane, indicating it was of low molecular weight, and strongly absorbed by bone char. Robert Williams, a chemist, came to work with Vedder and was given the task of further characterizing and isolating the substance. Williams returned to the States in 1915 and pursued his quest for many years.

In 1927 the vitamin was isolated in pure form by Jansen and Donath, and by Williams and coworker in crystalline form in 1933. Soon after World War II, Juan Salcedo would demonstrate that BB could be prevented in the Peninsula of Bataan, the Philippines, by artificial enrichment of rice with this vitamin, termed B1 or thiamine.

Postscript

Today, thiamine deficiency is associated with specific dietary habits such as food faddism, weight reduction, or anorexia nervosa. It may yet occur in those lands where polished rice is the staple dietary cereal. A partial deficiency may be seen with increased requirements attendant with pregnancy, lactation, hyperthyroidism, and likely is associated with other deficiencies that include riboflavin and niacin. Chronic alcoholism most commonly accounts for thiamine deprivation in the U.S. The degree and duration of the deficiency generally determine clinical manifestations: polyneuritis (dry beriberi) is seen in milder forms; cardiac involvement (wet beriberi), with a moderate deficiency; and encephalopathy in severe cases.