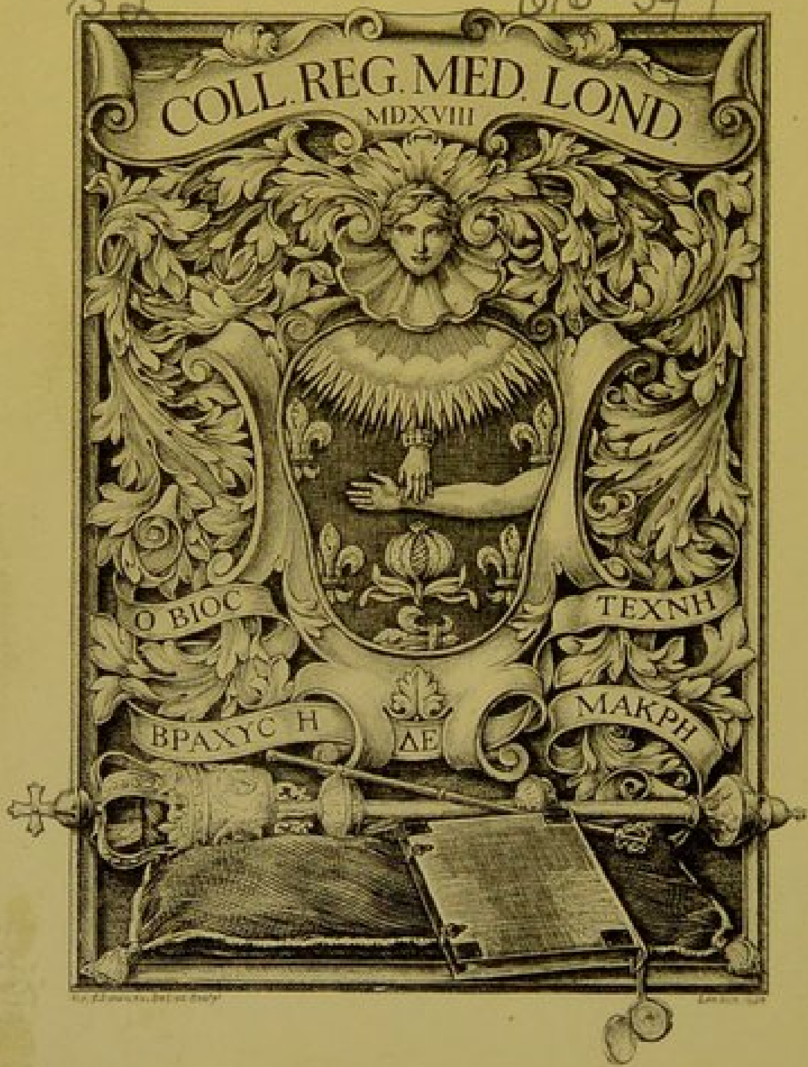
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BERIBERI

BY

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PREFACE.

The entire subject of beriberi has been in hopeless confusion for many years. The ordinary reader who is searching for information on the subject is simply appalled by the mass of literature that has been accumulated, and without special study is quite unable to sift the wheat from the chaff, or the rice from the polishings. And when the reader turns to the recognized standard medical text-books he finds that the authors simply state that the etiology and treatment of beriberi are uncertain, or that when they do furnish answers on these questions, the solutions offered are almost as various as the authorities.

It has been the fortune of the author to be engaged in the experimental study of the etiology of beriberi during the past two years, and in the course of this work he has been obliged to sift the evidence presented in the literature. It is now his hope that a critical review of the entire subject will be of material assistance in clarifying the present confusion.

It is particularly desirable that this should be done at this time for the reason that we may justly claim that within the past few years we have mastered the subject from a practical point of view. We are now in a position to prevent the disease in any community that can and will follow our advice just as surely as we can prevent small-pox and yellow fever.

From a scientific standpoint, the advances made in the study of beriberi in recent years are almost as satisfactory. The main question as to the etiology of beriberi has been settled, and the key to the solution of the minor puzzles that yet remain is in our hands. Moreover, the facts that have been discovered with regard to beriberi have thrown a great light upon other diseases, such as scurvy, and have revolutionized our ideas with regard to the metabolism of the body, although the text-books on physiology have not yet appeared to notice this.

In spite of the great importance of this work, there is, so far as I am aware, no book on beriberi in the English language of a later date than Braddon's (1907), which, moreover, deals with the subject from an entirely different viewpoint. It would appear, therefore, that there is a good opportunity for another book on beriberi.

The literature which I have collected in this work is not absolutely complete, but it is sufficiently exhaustive to enable the reader to verify the statements made.

I am indebted, for permission to use the three colored plates showing magnified sections of rice, to Messrs. Fraser and Stanton, of the Institute for Medical Research, Federated Malay States.

In conclusion I wish to thank the Surgeon General of the Army, who, by appointing me to the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands, has afforded the opportunity to perform this work; the various officers of the army medical corps and practitioners in Manila, who have assisted me in many ways, and the Bureau of Science of Manila, for the use of their library and for many other favors extended during the course of the work.

EDWARD B. VEDDER.

Manila, P. I.
May 1, 1913.

CONTENTS

INTRODUCTION.

Etymology. Many derivations of the word beriberi have been suggested. It may be the Singalese word beri, meaning weak. Reduplication of a word in languages of Malay origin accentuates its meaning or forms a superlative. Thus, according to this principle, beriberi would mean very weak or a great weakness. Meyer-Ahrens derives the term beriberi from words in the Indian dialects, i. e., Bheree or Beri, meaning sheep in Hindostani from the fancied resemblance of the gait of persons so affected to that of a sheep. This same suggestion was made by Bontius in 1642, and was undoubtedly obtained by him from natives. Another Hindu possibility suggested by Herklots is the word Bher-bheri, signifying a sore or swelling. Platteeuw derived it from the Sudanese words biribi or biribit, meaning stiff walking, while Carter claims it comes from Arabic words Buhr (asthma) and bahri (a sailor), since such a form of dyspnoea is frequently encountered among sailors in Arabian waters. It is impossible to definitely trace the origin of the word beriberi, but it is undoubtedly an oriental word and probably from some language allied to or derived from Malay.

Synonyms. There are a large number of synonyms, native names and newly coined anatomical or clinical names for beriberi. The native names are almost as numerous as the countries in which the disease appears. The synonyms and native names include the following:

Brazil: Perneiras (ailing feet).
Ceylon: Formerly called the bad sickness of Ceylon.
China: Kakke (a disease of the legs).
Cuba: Hinchazon (dropsy) de los negros y Chinos.
English: Barbers or barberi is occasionally used.
French: Barbiers.
French Antilles: Maladie des sucreries.
Japan: Kakke or Ashike.
Java: Loempoe.
Malaysia: Kaki lem but (weak legs).
Matto-Grosso: Inchacao.
New Guinea: Pantjakit papoea.
Philippines: Taon, taol and suba (infantile beriberi).

Newly coined descriptive names for beriberi used by certain authors:

Asthma Marinha (Carter).
Hydrops Asthmaticus (Rogers).
Myelopathia tropica scorbutica (van Overbeek de Meijer).
Neuritis multiplex endemica (Scheube).
Paraplegia Mephitica (Swaving).
Panneuritis endemica (Baelz).
Sero-phthisis perniciosa endemica (Wernich).
Synclonus beriberia (Mason Good).

Although such names have a certain value, the word beriberi has been used for hundreds of years to designate this disease and is generally adopted by all authors at present. In the interest of simplicity of nomenclature it is to be desired that no more names be coined for this disease, and therefore the term beriberi will be used in this book, although admitting that we do not know the precise origin or meaning of the word.

Beriberi has often been confused with other conditions. Some observers have failed to distinguish it from anchylostomiasis, pernicious anaemia, sleeping sickness and lathyrism. It is also capable of coexisting with other diseases, such as scurvy (Monteith). Because of these facts, and because it is always desirable to have before the mind a clear picture of the matter under discussion, a definition of beriberi will now be given, although it is fully realized that no brief definition can be wholly satisfactory.

Definition. Beriberi is an acute or chronic disease, characterized by changes in the nervous system and particularly by a multiple peripheral neuritis, with an especial tendency to attack the nerves of the limbs, the pneumogastrics and phrenics. Ordinarily the clinical picture of a peripheral neuritis is combined in varying degrees with cardiac disturbances, oedema, serous effusions and gastro-intestinal derangements. Exceptionally cases occur in which cardiac dilatation and sudden death are the first symptoms observed. It is a disease resulting from faulty metabolism, *usually* only seen in those persons who eat rice as the staple article of diet, and is directly caused by the deficiency of certain vitamines* in the food.

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* A vitamine is a substance which is present in minute quantities in various food stuffs. A certain quantity of vitamines must be supplied if the organism is to maintain a normal metabolism. The deprivation of one of these vitamines results in the production of a certain disease. Thus scurvy is due to the deprivation of one vitamine, while beriberi is due to the deprivation of another or probably of two vitamines.

CHAPTER I

HISTORY OF BERIBERI

Earliest References. The earliest reference to beriberi is to be found, according to Macgowan, in the *Neiching*, which is said to be the oldest medical treatise extant, and is attributed to Hwangti (B. C. 2697). It was possibly common in China at this time and it may have existed even before this period because it is likely that it existed for some time before an account of it was written, and because Chinese customs, food and conditions of life have changed little with the passing centuries, and were probably much the same then as they are now. We should expect that beriberi, a food disease, would be prevalent then exactly as it is now. The Kinki (golden chest), written about 200 A. D. by Chochiyukei, and one of the fundamental books of Chinese medicine, is said to contain a few prescriptions for beriberi.

It seems quite certain also that beriberi was present and known to the Romans in 24 B. C., since Strabo and Dion Cassius describe it or a similar disease which was observed in the Roman army invading Arabia at that time. (Meyer-Ahrens.)

Again Kakko is referred to in A. D. 130 by Chingoho in his "Receipts under the Elbow," so-called because the author was accustomed to carry the book in this manner. The first good description of the disease is found in the Senkinho (thousand golden prescriptions), written by Sonshibaku about 640 A. D. This oldest description of kakke, from which the identity of the disease with beriberi is demonstrated, was translated into German by Scheube, and retranslated is as follows: "Kakke is produced by a gaseous poison. This originates in the earth, from which cold, heat, air and dampness cause it to transpire. The feet rest always on the earth, and therefore the poison attacks the feet first and later the arms, stomach, back, head and neck. At first the patient for the most part does not know he is sick. In some cases the sickness advances gradually, and sometimes it begins suddenly with great unrest, and two or three days later the patient can no longer stand and now becomes aware of his disease for the first time. The symptoms are very insignificant in the beginning, the appetite and general condition remaining good. Sudden weakness of the legs so that walking is impossible is the only symptom. It may affect the head, neck or arms before the legs, and it also can affect the inner organs before there are any other symptoms. When one is infected by the poison, he vomits at the sight of food and even feels revulsion against the smell of it; he suffers from abdominal pain and diarrhoea, or constipation and diminution in the amount of urine, palpitation of the heart and sensitiveness to the light and forgetfulness and delirium. He may suffer also from fever and headache, chills, pain, convulsions, dropsy and impaired sensibility of the abdomen. These are all phenomena and symptoms of kakke. If a slight change in the condition of the patient occurs, it is very dangerous and necessitates quick treatment. If the poison reaches the abdomen the latter may swell up. If the chest becomes full and the breath short, then the patient dies immediately or at least in several days. Experience teaches that cases with great oppression and dyspnoea or violent sweating and alternating heat and cold, quick, short and frequent pulse and obstinate vomiting always end fatally. The dropsy is not an essential symptom, and may or may not be present. Cases with impaired sensation in the abdomen for the most part do not have dropsy of the legs. Three to five days after loss of sensation in the abdomen, the vomiting appears, so that they say that the kakke is penetrating to the heart. In such cases death results in a short time. Damp places and undressing in cold currents of air while overheated are predisposing causes." With a few exceptions, this is a remarkably exact description of beriberi. The allusions to fever, and to alternating heat and cold and violent sweating, make it seem probable that the author may in some particulars have confused malaria or some other febrile disease with beriberi, but we must not expect perfection in 640 A. D. About 750 A. D., Oto wrote a book dealing with kakke, called Gedaihiyoho or the family prescriptions of a provincial official.

Beriberi in Japan. Most of the early Japanese writers appear to have obtained their information from these Chinese sources. The oldest Japanese work in which kakke is referred to under its Japanese name Ashike dates from 808 A. D., and is called Daidoruishinho (a classified collection of prescriptions from the year Daido). This book was written by two physicians, Abe Manao and Idzumo Hirosada, but in this book and in later works kakke is possibly confused with heart and kidney disease, rheumatism, etc. Thirst, diminution of urine, palpitation, dyspnoea, pains in the limbs are emphasized, while paralyses and anaesthesia are barely mentioned.

The most important Japanese work in the history of beriberi is the Koyoigen (prescriptions from a physician's leisure hours). This was written by Kagawa Shuan in 1720, but was edited and many additions made in later years by his son and his pupils. Kagawa the elder says "Kakke or kiakuki (a pain in the legs) as it is now observed is always chronic and death does not occur." He says pain in the legs is the chief symptom. His son adds the following: "According to the authors from the dynasty Kan (Han 202–265) and To (Tang 618–907), the chief symptoms of kakke are weakness of the legs, severe oedema, dyspnoea, palpitation and anaesthesia. This disease was not present among us in earlier times but the pains in the legs and knees were only caused by disturbances in the circulation. True kakke only appeared since the year Horeki (1750) when the original author was already dead, and the symptoms of this disease agree with those of the authors of the dynasties Kan and To referred to. It is commonest in summer and autumn, rare in spring and winter. It usually affects young men, rarely women and children. The disease is very severe and fatal cases are common."

Noro Genjio, a contemporary and court physician to the Shogun, agrees with this statement. Kaempfer, a physician practising in Nagasaki in 1690–1692, and a keen observer, did not describe kakke. Scheube concludes from this evidence that beriberi only appeared in Japan since 1750. This of course is quite possible, but it also seems equally possible that it may have occurred in earlier times and disappeared again before 1720 when Kagawa wrote his book. Beriberi appears in waves or epidemics under certain circumstances and then almost disappears again. This was the case in Manila in 1882, as will be explained later. It is also well known that beriberi attacks certain localities, leaving the rest of a country almost untouched. Scheube himself wrote in 1883 that kakke was almost entirely confined to the larger cities such as Tokio and Kioto, and practically unknown in the country districts. Under such circumstances it seems unsafe to conclude that beriberi was not present in Japan earlier than 1750 simply because one or two observers failed to see it or to differentiate it from other diseases. Bearing in mind the fact that diet in Japan as in China altered little in the course of centuries, it seems quite probable that beriberi has long been present, even though it has only recently been recognized. We have been unable to verify all of these references, but there can be little doubt that beriberi is a disease that occurred and was recognized in very ancient times.

History in Modern Times. Most authors have given to Bontius the credit of being the first European physician to describe beriberi, but they say no more concerning his observations than they do of the reference to the *Neiching*, and Castellani gives the date of his work as 1758–59. The library of the Bureau of Science, Manila, contains a volume published by Jacobus Bontius at Lugdum, Batavia, in 1642, and this is believed to be a first edition. It is entitled "de Medicina Indorum," and is in reality our first book on tropical medicine, containing among other matters descriptions of various eastern drugs, such as santal, betel, cassia, etc., rules for conserving the health in the tropics, and short chapters on beriberi, convulsions, dysentery, cholera, dropsy and other diseases. His article on beriberi is brief and interesting. The original may be found in the appendix, but a free translation is as follows:

Chapter I. Concerning a certain kind of paralysis which the inhabitants call beriberi.

"This is a certain exceedingly troublesome disease affecting the people here which is called beriberi (a word which sounds like the word for sheep) by the inhabitants, I believe because those attacked by this disease walk like sheep, because of their shaking knees and weakened legs. It is a kind of paralysis, or rather a tremor usually affecting the movement and sensation of the hands and feet, but sometimes it attacks the whole body and causes it to shake. The cause of this disease is principally a thick and sluggish phlegmatic humor derived from the nocturnal dampness and from the rains which fall here continuously from the beginning of November to the beginning of May. This humor attacks the nerves, doubtless while men are exhausted by the heat of the day, or at night when they throw off all coverings and blankets, when this humor is generated most easily in the brain and invades the nerves. Now the nights in these regions may be called cold as compared with the heat of the day, and on such occasions, while the limbs are extended, the phlegm insinuates itself between the joints in such a manner that the nerves and ligaments become relaxed.

"Although this disease for the most part begins gradually and invades the body little by little, nevertheless it is sometimes very acute. This is the case when men are fatigued by the heat and drink immediately and copiously a beverage made from the Indian palm. Such an act is no worse than we see done in our own country sometimes in the dog days, when some one who has become overheated by vigorous exercise swallows too greedily a drink of beer or milk, thus not only endangering health, but even at times running a risk of death.

"The symptoms of this disease are readily discernible. Weakness of the whole body is noticed at once by the patient. Movement and sensation, particularly of the hands and feet, are perverted and dulled, and a tingling is often felt in the limbs such as is experienced in cold countries in the fingers and toes during the winter storms, except that in this condition there is not so much pain. Then also the voice is obstructed so that the sick man can hardly speak articulately. I experienced this myself, for while suffering from this disease the sound of my voice was so feeble for a whole month that those sitting next to me could hardly understand me. Besides this, there are often many more signs or symptoms which nevertheless all savor of the cold and sluggish humor, but the chief symptoms have been sufficiently described.

"We have for the cure of this condition remedies which are here set down, by means of which this cold and sluggish humor is dispelled from the sick man. Of itself, for the most part, this disease is not fatal unless it affects the heart or muscles of the chest and in this manner blocks the passage of the spirit and voice. The first thing that is essential in effecting a cure, if it is in any way possible, is to avoid becoming bedridden, and to this end every effort must be made to exert oneself either by walking, riding or by other similar exercises. To run, indeed, is impossible. Hard and even painful rubbing is here of the greatest importance, and is properly performed here by Bengalese slaves and Malaysian women. Our race is not accustomed to exercise or to the baths which are much frequented here. They also prepare warm applications and poultices from scammony which is of an agreeable and aromatic odor. Certainly with us this is not much used; Chamomile and Melilotus take its place. But for dissipating and destroying this humor, in my judgment it is superior. Besides this, the feet and hands are inuncted with the oils of cloves and mace, but mixed with oil of rose, because these are too caustic alone and easily blister the skin. There is also a well-known kind of naphtha, brought from Sumatra and called by the Indians *Minjac Tannah*, which signifies oil of the earth, and which is not inferior to the naphtha known to us as oil of rock, and which gushes from the earth, or is precipitated in the streams under caverns. This oil is held in such esteem by foreigners that King Achinensis, who is the most powerful ruler in these islands, prohibited its export under pain of capital punishment. The inhabitants therefore bring it to us secretly on stormy nights when one of our ships or an English ship is near their shores. This oil, when applied to the affected parts, relieves the patient miraculously. The odor is heavy and carries far, but it is not disagreeable.

"But when this disease is chronic and of long duration nothing is equal to a decoction of the roots of Sarsaparilla (which comes from China) and Guiac, which dispel the cold and sluggish humor through the sweat and urine in a bland and pleasant manner. The action of these drugs should be assisted by evacuating the bowels, for which purpose there is an extract prepared from aloes and gamboge. To let blood is a mistake in this disease, since there is no plethora, but instead a chronic disease, and who does not know that the blood is the source of heat and the fountain of life? The remaining symptoms are dissipated by facilitating sweating and urination and by medicines that strengthen the nerves. Proper exercise and the healing force of nature will cure the remaining manifestations of this disease."

This description of Bontius, while not very extended and mixed with mediaeval conceptions of humors, indicates that he was in all probability describing the disease which we now know as beriberi.

In 1739, Tulpius, a Dutch physician, studied the disease in a person who had returned from the Indies, and his description was followed by several others, including Paxman (1772), Lind (1788), Fontana (1790) and Clark (1792). The description of these authors added some detail to that furnished by Bontius, but it is quite important to note that all described the disease as a form of paralysis. Nothing was said of oedema or serous effusions. Bontius himself devoted another chapter to dropsy, which he said was quite common in the Indies, but in this latter chapter no mention is made of beriberi. It is quite evident that all of these authors were describing dry beriberi.

In 1808 Rogers called attention to the presence of oedema, and proposed the name of hydrops asthmaticus for the disease. In 1812 an attempt was made for the first time by Marshall to describe two different diseases, one in which the paralytic symptoms predominated, and which he called barbiers, and another in which dyspnoea and dropsy predominated, which he called beriberi.

From this time on there was a remarkable difference of opinion as to whether the condition that we now recognize as beriberi should be classified as two diseases or as one disease. Thus, Mason Good, in his study of medicine in 1825, regarded the two different forms as a single disease, beriberi, but the Cyclopaedia of Practical Medicine and the Dictionary of Practical Medicine, published from 1832–1835, discuss in separate articles barbiers and beriberi, although stating that the two diseases are closely allied.

In 1835 Malcolmson made an important contribution to the subject. He found that cases which began as barbiers (dry beriberi) often suddenly assumed the acute and dangerous course of beriberi (wet beriberi), and that beriberi frequently presented the characteristic symptoms of barbiers. Moreover, that cases of both barbiers and beriberi occurred in the same locality, during the same season and under exactly the same circumstances. After this time it became gradually accepted that barbiers and beriberi were one and the same disease, and at the present time the use of the word barbiers is almost forgotten, but all authors speak of dry and wet beriberi. It is most important, however, to remember that this discussion took place with regard to beriberi when we come to consider the relationship existing between beriberi, ship beriberi, infantile beriberi and epidemic dropsy.

In 1865 beriberi was reported from Cuba by Hava, where it had been known under various names, such as Maladie des sucreries and Hinchazon de los negros y Chinos. In 1866 an epidemic of beriberi was reported from Brazil in the province of Bahia by de Moora and da Silva Lima.

In 1877 Wernich described the kakke of Japan, and Van Meedervoort, together with Anderson and Simmons, showed that this was really beriberi. The researches of Baelz and Scheube followed, definitely proving that the disease was a specific form of peripheral neuritis.

Beriberi in the Philippines. An epidemic of beriberi occurred in Manila in 1882–1883. Königer says: "Beriberi had heretofore not been known in Manila. Whether the disease had occurred at all at this place during the last three centuries might perhaps be ascertained from a study of the friars' records. However, it was not known to the inhabitants, including the physicians, some of whom had practised in Manila for more than forty years. I myself, during a practise of three years, had never seen a case of beriberi. This first appearance of the disease in Manila is of particular interest because of the enormous mortality observed during the beginning of the epidemic. This mortality is not surpassed by anything heretofore reported, and is higher than it is stated to be by almost all other observers. The general impression existing among physicians, as well as laymen, during the first part of the epidemic, was that the disease was absolutely fatal. However, during the earlier part of the outbreak I saw several cases which recovered. Still, I think that a mortality of 60 per cent for the first month is by no means too high an estimate. As to the total number of deaths, I have only one reliable observation, according to which, during a period of a little more than two months, over 300 deaths from beriberi occurred in Malabon, a place of about 25,000 inhabitants, situated seven kilometers from Manila. However, it is probable that this place suffered more than any other in the vicinity. The conclusion certainly appears justified that the number of victims in the capital and the surrounding provinces reached several thousand."

While beriberi may have been uncommon in the Philippines in the years immediately prior to 1882, when Königer was practising in Manila, it by no means follows that it had never existed there. The following quotations from "The Philippine Islands," by Blair and Robertson, throw some light on this question. Thus, in volume XV, page 57, in the translation of "Sucessos de las Islas Filipinas," written by Doctor Antonio de Morga of Mexico in 1609, we find the following paragraph: "To assist the chief captain of the fortress of the island of Tidore in Maluco a fleet and soldiers were sent from Manila in 1609. But after reaching Maluco the expedition did not succeed in its object." A footnote by Doctor Rizal says: "This expedition did not succeed because of the development of the disease beriberi among the Spanish forces, from which more than four-fifths of the soldiers died."

Again in volume XVIII, page 222, is a letter to Felipe III. from Alonzo Fajardo de Tenza, Cavite, August 10, 1618, containing the following statement: "All the aid sent last year from this place reached Maluco without suffering any loss on the way either from the sea or from the enemy, as has usually been the case other years. To furnish this aid five ships went laden with supplies and with 15,000 pesos to pay the infantry. Hence our forces there are, for the present, well and even abundantly supplied, although there is some lack of men, because many have died of *bebes*, which is a disease of the legs very common in those islands." A footnote says "this is apparently a reference to beriberi."

Volume XXXV, page 271, in a translation of "affairs in Filipinas" by Fray Joseph Fayol, Manila, 1647, contains the following: "Moreover, there is a disease, known as Verber (i. e., beriberi), which is now prevalent throughout the fleet, by which most of the men have been attacked."

Volume XXXVII, page 28, in a translation of a document by an unknown author, written in 1669, contains this information: "During the interval the said General Rayo was at the point of death; for he was in distress from the dampness of that locality and the disease of beriberi from which he suffered."

While these quotations from old authors cannot be taken as indisputable evidence of the existence of beriberi, yet it is extremely probable that this disease not only existed in the Philippines before 1882, but that it was present and recognized from the very earliest years of the Spanish occupation. It is, of course, impossible to secure any information as to conditions that existed prior to this time.

The above is an extremely brief account of the development of our knowledge of beriberi from 1700–1900. Only a few of the classical works have been mentioned, although the literature of this period, particularly from 1800–1900, teemed with contributions to the subject. To mention each one would be an endless task, and would only result in confusion.

In brief, it may be said that this large amount of literature aided greatly in definitely establishing the symptomatology of beriberi and in fixing it as a clinical entity, but only succeeded in confusing the question of its etiology.

CHAPTER II

THE DISTRIBUTION AND PREVALENCE OF BERIBERI

The practitioner in the United States or Europe who has not investigated the subject can have little idea of the importance of beriberi in many regions, particularly in the Orient. A consideration of the distribution and prevalence of the disease will show that it is about the most important medical problem that the physician who practises in such regions is called upon to face. For while there may be other diseases that are more widely distributed or more fatal, like malaria and plague, yet the etiology and hygiene of these latter diseases have been pretty completely worked out, and the sanitarians of all countries are in pretty general accord as to the method of dealing with them. And although the problem of beriberi is nearing its final solution, and the sanitarian already has sufficient information concerning the disease to enable him to prevent its occurrence, yet it must be conceded that this information is by no means generally accepted or acted upon, and that as a result, with a few exceptions, the areas affected and the prevalence of the disease are increasing rather than descreasing.

Sporadic outbreaks of beriberi have occurred at various times in many countries in which this disease does not ordinarily appear. As illustrations, we may quote the various outbreaks reported from the United States, and the well-known epidemics that occurred at the Richmond Asylum in Dublin, and Suffolk, England, which were reported by Norman. In addition to these well-authenticated cases there are many other instances occurring during famines, wars or in prisons, where symptoms have occurred which may have been in whole or in part of beriberic origin. The cases described by Dechambre as occurring in the siege of Paris in 1870, the so-called Wassersucht der Gefangnisse, and the scorbutic hydraemia which, according to Nocht, often occurs during epidemics of scurvy in Russia, are instances of this questionable occurrence of beriberi. It is probable that beriberi has occurred many times in Occidental countries without being recognized, owing to its comparative rarity, and to the fact that the physicians in these countries are not familiar with the disease. It is clear that if beriberi is caused by a deficiency in the diet, it is quite possible for it to occur in any country whenever circumstances are such that this deficiency exists in the diet of any considerable number of individuals. The instances above quoted are believed to be sufficient to illustrate this point, and no attempt will be made in the following outline of the distribution of the disease to include all of these sporadic outbreaks.

Beriberi is endemic in three principal foci situated in Asia, Africa and South America, of which the Asiatic focus is the most extensive.

Asia. Beriberi is constantly present in Japan, certain parts of China and India, the Philippines, the Dutch Indies and the Malay States. While this statement is simply a bare outline of the endemic territory, it will at once be seen that it includes practically all of the important countries in the far East, which will now be studied in more detail.

Japan. The disease is found in all parts of Japan, from the southernmost islands of Formosa and Kyushu to the Kurile Islands at the extreme north. It was reported in Hokkaido by Grimm, and on the summit of Fuji Yama by Miura. Twenty or thirty years ago it was chiefly found in the large cities, but at the present time it has spread until it may be found practically everywhere, although it is still particularly prevalent in the cities. Concurrently with this increase there has been a very remarkable decrease in the incidence of beriberi in the Japanese navy and army, a fact to which further reference will be made. It is impossible in most of these Oriental lands to give statistics for the whole country, particularly in the earlier years, but some idea of the prevalence and importance of beriberi in Japan may be derived from the following figures.

According to Scheube the reports of beriberi in Kyoto for the years 1875–79 were as follows:

Year.	*Cases.*
1875	225
1876	325
1877	141
1878	1,093
1879	489

Kyoto at this time had a population of 229,000. It is probable that many cases were not reported. At any rate, the figures are much higher in the army during the same period, where the records were more carefully kept.

Thus, according to Anderson, the number of soldiers who had beriberi in 1875 was not less than 26 per cent of the entire army of 17,500 men. In 1876 the Japanese army had 3,868 cases, corresponding to 11 per cent of the total number of 35,300. More detailed figures for the years 1877 and 1878 are given by Scheube, as follows:

1877.				1878.			
Garrison.	Number of troops.	Had beriberi.		Garrison.	Number of troops.	Had beriberi.	
		Total number.	Per cent.			Total number.	Per cent.
Tokio..........	7,700	1,247	16	Tokio..........	13,300	4,880	37
Nagoya........	3,000	102	3	Nagoya........	4,500	1,440	32
Sendai.........	2,800	232	8	Sendai.........	3,100	323	10
Osaka..........	2,200	404	18	Osaka..........	6,400	2,896	46
Hiroshima......	2,100	215	10	Hiroshima......	4,200	932	22
Kumamoto.....	1,800	487	26	Kumamoto....	4,600	3,154	68
Total........	19,600	2,687	14	Total........	36,100	13,629	38

PREVALENCE OF BERIBERI IN JAPANESE NAVY, 1878–83, ACCORDING TO SANEYOSHI.

Year.	Average strength of force.	Cases of beriberi.	Per cent. of cases.
1878..................................	4,528	1,485	32.8
1879..................................	5,081	1,978	38.9
1880..................................	4,956	1,725	34.8
1881..................................	4,641	1,163	25.0
1882..................................	4,769	1,929	40.4
1883..................................	5,346	1,236	23.1

PREVALENCE OF BERIBERI IN JAPANESE ARMY, 1882–84.

Year.	Average strength of force.	Cases of beriberi.	Per cent. of cases.
1882	39,975	7,966	19.9
1883	38,717	7,128	18.4
1884	36,483	9,643	26.7

Later in 1905, during the Russo-Japanese war, bèriberi was prevalent in the army to such an extent that no outside observer during the war had any conception of the facts, and it is doubtful whether they have ever become fully known. Shibayama states: "During the war Japan had 200,000 cases of beriberi in the army, and this was the only ravaging epidemic with which the army had to contend."

China. Beriberi is endemic along practically the entire littoral of China, particularly at the ports of Kiang-Chow, Foo Chow, Hongkong, Swatow, Amoy, Shanghai, Che Foo, Soo Chow, Che Kiang, etc. It is also common in Indo-China along the Mekang and Menam rivers, and at the ports like Saigon and Hue. According to Jeanselme, small foci are spread over the entire extent of French Indo-China, including Vinh, Culao-Gien, Hanoi, Cochin-China, and along the rivers in Tonkin. It is also frequent in the islands near the coast of China, such as Poule-Condore. Statistics from most of these places are very difficult to obtain, and are very unreliable. This is not the case in Hongkong, however, where careful records are kept. Through the courtesy of Doctor Francis Clark, Medical Officer of Health in Hongkong, I have been furnished with the following complete table of the deaths from beriberi in that city from 1891–1910, from which it will be seen that there has been a steady increase in the number of deaths from year to year.

DEATHS FROM BERIBERI IN HONGKONG, 1891–1910.

Month.	1891.	1892.	1893.	1894.	1895.	1896.	1897.	1898.	1899.	1900.	1901.	1902.	1903.	1904.	1905.	1906.	1907.	1908.	1909.	1910.
January	7	15	9	9	3	19	24	11	13	33	26	17	34	30	.....	36	38	47	41	41
February	8	8	7	5	3	15	11	7	10	26	34	24	30	18	.....	23	24	41	24	35
March	19	11	4	9	3	13	10	4	11	27	14	23	29	24	175	26	25	33	35	35
April	5	9	7	10	7	7	11	2	11	30	22	30	24	66	.....	43	47	53	39	44
May	9	12	12	7	8	3	32	6	11	34	26	26	22	105	102	72	46	58	46	44
June	13	6	17	9	9	12	20	7	15	31	16	28	20	56	85	44	44	63	53	39
July	13	17	14	6	10	3	22	10	16	26	23	38	25	84	66	49	57	42	52	38
August	13	16	6	5	20	7	11	12	19	27	40	60	39	101	62	60	63	76	37	67
September	8	9	10	1	19	10	14	5	17	25	47	53	50	88	59	50	42	65	42	54
October	14	5	16	6	13	20	12	14	25	31	44	52	46	62	48	61	60	111	42	60
November	11	10	12	6	28	19	8	17	29	41	51	38	32	105	41	62	48	82	81	58
December	8	19	16	7	21	15	12	22	25	33	38	64	36	.....	40	35	68	65	53	51
Total	128	137	130	80	144	143	177	117	202	364	381	453	387	739	678	561	562	736	545	566

The population of Hongkong during these years is shown by the following table:

POPULATION OF HONGKONG.

Year.	Population.	Year.	Population.	Year.	Population.
1890..........	198,742	1897..........	248,710	1904..........	361.206
1891..........	224,814*	1898..........	254,400	1905..........	377,850
1892..........	231,662	1899..........	259,312	1906..........	329,039*
1893..........	238,734	1900..........	262,678	1907..........	329,357
1894..........	246,006	1901..........	300,660*	1908..........	336,488
1895..........	248,498	1902..........	311,824	1909..........	343,877
1896..........	239,419*	1903..........	325,631	1910..........	350,975

* Indicates census. Other figures are estimates.

When we remember that the average mortality of beriberi is about 5 per cent, it will be seen that the total number of cases in Hongkong must run well into the thousands.

Another estimate of the prevalence of the disease in Hongkong may be obtained from the following table, taken from Hunter and Koch:

ADMISSIONS TO THE TUNG WAH HOSPITAL, HONGKONG, CHINA, DURING THE TEN YEARS 1895–1904, BEING THE YEARS WHEN A REGISTER WAS KEPT UNDER GOVERNMENT INSPECTION, AND AN ACCURATE RECORD MADE OF THE DIAGNOSIS.

Year.	*Admissions.* *Males.*	*Females.*
1895..........................	117..........................	1
1896..........................	136..........................	13
1897..........................	166..........................	15
1898..........................	162..........................	8
1899..........................	265..........................	16
1900..........................	335..........................	25
1901..........................	390..........................	27
1902..........................	409..........................	12
1903..........................	265..........................	17
1904..........................	667..........................	72
Total	2,912	206

We do not know that beriberi is more common in Hongkong than in the other parts of China from which it has been reported, and if Hongkong, with a population of 350,000, has 10,000 cases of beriberi annually, it may well be imagined that millions of cases must occur among the remainder of China's teeming population.

Korea. Beriberi has been reported from the ports of Fooshan, Chemulpo, and is also found in Seoul. The disease is rare among the Koreans themselves, who are said to feed chiefly on peas, and the Japanese and Chinese in Korea furnish almost all the cases.

Siam. Doctor J. Campbell Highet, Health Officer of Bankok, states that beriberi was not reported in Siam previous to 1890, but this does not mean that the disease may not have been present before that time. Even at the present time he says that it is difficult to get any idea of the prevalence of the disease in the general population, but gives the following figures showing the incidence of beriberi in the army, navy and police. He also states that the deaths in these statistics give no conception of the actual death rate, since many serious cases were allowed to return to their homes:

CASES TREATED IN BANKOK, ACCORDING TO HIGHET.

Year.	Cases.	Deaths.
1901–2	1,128	14
1902–3	1,007	81
1903–4	2,615	161
1904–5	2,813	103
1905–6	3,361	92
1906–7	2,712	101
1907–8	2,427	229
1908–9	4,607	282
Total	22,670	1,063

The Malay Peninsula. Beriberi occurs with great frequency throughout all the Malay States. Thus Braddon says: "In the colony of the Straits Settlements and adjacent Native States of the Malay Peninsula, an area about equal to that of England, but with a total population of only a million and a quarter, over 150,000 cases of beriberi have been treated, and 30,000 have died, during the last two decades, in Government hospitals and infirmaries alone. Among the Chinese immigrants into this region, whom it almost exclusively affects, it may be reckoned that of every 1,000 living 120 suffer from it in some degree, 80 are severely attacked, and 16 die of it annually."

Again, according to Braddon, in Perak, one of the largest of the Malay States, there are eleven hospitals. In 1899 in these hospitals there were treated 19,693 patients, of which 2,817 were cases of beriberi.

In Selangor, another large Malay State, there is a pauper hospital at Kuala Lumpur in which from 1891–1893 admissions for all cases were 9,971, of which the admissions for beriberi numbered 2,601.

A good idea of the distribution and prevalence of beriberi in British Malaysia may be derived from the following table, which is abstracted from Braddon's "Cause and Prevention of Beriberi," page 337:

PREVALENCE OF BERIBERI AT 31 DISTRICT HOSPITALS FOR SEVEN YEARS, 1895–1902.

Place.	Admissions, all causes.	Admissions, beriberi.	Deaths, beriberi.
Jelebu	2,924	962	41
Kuala Selangor	1,430	23	7
Kuala Kangsar	11,545	624	45
Tampin	3,397	316	58
Jasin	6,851	903	157
Seremban	12,860	3,385	230
Kuala Langat	1,903	131	51
Malacca	16,687	2,182	394
Kajang	8,227	1,786	144
Sungei Besi	1,714	747	122
Klang	7,554	379	56
Bagan Serai	14,358	214	20
Alor Gajah	6,531	824	54
Parit Buntar	4,285	58	19
Teluk Anson	5,652	315	72
Batu Gajah	26,670	8,938	1,220
Kuala Lumpur	33,735	8,422	1,702
Butterworth	4,824	139	33
Ipoh	24,653	7,643	1,128
Sungei Bakap	3,766	18	4
Bukit Mertajam	3,504	124	29
Gopeng	16,781	4,319	522
Serendah	10,185	2,807	442
Kuala Kubu	15,892	2,019	487
Penang	25,553	2,093	721
Balik Pulau	3,588	183	57
Rawang	7,075	1,897	302
Tapah (5 years only)	12,147	1,704	338
Selama	404	26	6
Kampar	8,082	2,115	173
Larut	27,326	1,729	356
Total	328,936	57,025	8,990

This of course includes only those cases admitted to these hospitals, and takes no account of the mild cases or cases that were treated at home.

Doctor Croucher, Ag. Principal Civil Medical Officer, Straits Settlements, very kindly sent me the following statistics showing the prevalence of beriberi in that colony:

PREVALENCE OF BERIBERI AT STRAITS SETTLEMENTS FOR TEN YEARS, 1901–1910.

Year.	Total deaths from beriberi in the colony.	Total cases of beriberi treated in the various hospitals of the colony.
1901	2,046	1,817
1902	1,607	1,901
1903	1,729	1,919
1904	2,287	2,631
1905	1,888	1,958
1906	1,507	1,971
1907	1,626	1,806
1908	1,900	2,772
1909	1,506	2,118
1910	1,737	2,044

Chinese coolies were imported into Christmas Island, part of the territory of the Straits Settlements, in 1901. Beriberi developed among them as follows:

PREVALENCE OF BERIBERI AMONG CHINESE COOLIES ON CHRISTMAS ISLAND.

Year.	Average Chinese population.	Beriberi.	
		Admissions.	Deaths.
1901	660	670	226
1902	656	673	88
1903	732	587	59
1904	785	971	92
1905	944	489	11

This would indicate that practically the entire population of this island had beriberi.

India. Beriberi is endemic in India in certain restricted regions. It is said to occur in the northern provinces in India, along the east coast and between the coast and the mountains. Jeanselme states that it occurs along the Godavery and Kistna rivers on the eastern coast, and in the centre of India between the Godavery and Nerbudda rivers. Toward the south of India cases become less frequent. This limited distribution of the disease in India is probably due to the fact that the food habits of the different races of India are so rigidly controlled by religion and caste. Thus many only eat cured rice. The Bengalis are said never to have beriberi.

In 1889, Bidie, in writing of the Madras presidency, said: The endemic area of beriberi in this presidency comprises the Kistna, Godavery, Vizagapatam and Gaujan districts, and it also occurs in Nellore and somewhat rarely in Cuddapah and Kurnool. It is more common on the coast than inland, but low-lying places in the valleys of rivers, like Rajahmundry, also suffer. Eyre also reported an epidemic in Madras in 1900. However, Doctor W. R. Macdonald, Health Officer of Madras, states that the deaths from beriberi in Madras are only available for the last six years, as follows:

1905	3
1906	3
1907	0
1908	0
1909	1
1910	4

I have been informed by the Health Officers of Bombay and Cawnpore that there is no beriberi in those cities.

Doctor Frederick Pearse, Health Officer of Calcutta, has also kindly informed me that true beriberi only occurs sporadically in Calcutta, and almost entirely among Chinamen. He says, however: "We have had two or three outbreaks of epidemic dropsy, which is now considered the same disease." Small epidemics have occurred a number of times in the native army.

Dykes reported an epidemic in a jail at Assam in 1904, and in 1908 Daley reported 50 cases in the reformatory school at Alipur (see Appendix, page 3).

Burmah. Beriberi was formerly thought to be very prevalent in Burmah, but Giles said the disease called beriberi there was anchylostomiasis. However, Davis stated in 1887 that beriberi had appeared in three gaols in Upper Burmah at Mimbu and Toung Awinglyi. It has also been reported from Mandalay, and Baker reported an epidemic in a lunatic asylum in Rangoon in 1895, in which 211 out of a total of 233 inmates were affected. Rost also studied the disease in Rangoon.

Ceylon. It was formerly supposed that beriberi was very prevalent in Ceylon, and was called the bad sickness of Ceylon. The result of Kynsey's investigation, however, was to show that anchylostomiasis was exceedingly prevalent in that country and Castellani now states that this so-called beriberi was anchylostomiasis. At any rate, beriberi does not appear to exist there at the present time. Doctor Marshal Philip, Medical Officer of

Health, Colombo, kindly informs me that the first record of a death from beriberi in Ceylon was in 1887. No further deaths appear until 1907, when four were recorded; two in 1908, one in 1909, and four in 1910. All were imported cases.

Sir Allen Perry, Principal Civil Medical Officer of Ceylon, also says: "So far as I know there are no indigenous cases of beriberi in Ceylon. The only cases seen are imported, and the number is small."

The Dutch Indies. Beriberi is endemic in practically all of these islands, and in the past has raged with great severity in some of them. Native soldiers and even Dutch soldiers at Atjeh, Sumatra, have been for many years subject to the disease, although I have been informed that at the present time the Europeans in Sumatra are rarely attacked. The same thing has been true of Java, particularly in Batavia, and of the other islands of this group, including Borneo, the Celebes, Moluccas and New Guinea, and the smaller islands, such as Bintang, Banca and Billiton. Morris reported 35 deaths from beriberi out of a total population of 516 in the Cocos-Keeling Islands from January, 1880, to August, 1885.

It has been said that beriberi has only prevailed in Java during the last four decades, but it probably has been present for centuries, although it has increased greatly in extent and severity during the last few decades. It must be remembered that it was in these islands that Bontius observed the disease called beriberi at that time, and his book, containing the first description of the disease by a European, was printed in 1642, and it is therefore scarcely credible that beriberi was unknown in the Dutch Indies previously to the last fifty years.

According to Van der Burg, the average strength of the Dutch troops maintained in the East Indies from 1873–1874 was 15,200 men. During that period there occurred 17,520 cases of beriberi, and a much higher proportion of the native troops were attacked. The staple diet of these Dutch troops was rice.

The American consul at Batavia, Java, has kindly furnished me with some statistics that indicate the prevalence of the disease in that colony at present. The figures were furnished by the chief of the Civil Medical Service. The figures, however, relate solely to cases observed in civil hospitals, and since the vast majority of a native population never apply for treatment, these cases may be considered as only a small part of the total amount of beriberi in Java:

CASES OF BERIBERI OBSERVED IN CIVIL HOSPITALS IN JAVA.

Years.	Treated.	Deaths.	Percentage.	Population.
1901	4,616	348	7.5	According to census of December 31 1905 in round numbers about 38,000,000.
1902	5,177	336	6.5	
1903	7,719	345	4.4	
1904	4,428	206	4.6	
1905	2,813	139	4.9	
1906	2,704	181	6.7	
1907	1,361	123	9.3	
1908	6,918	508	7.3	
1909	3,870	283	7,3	
1910	2,503	188	7.5	

Doctor Victor G. Heiser, who made a trip through these islands in 1911, informs me that an examination of the hospital records at Rabaul and Kaiser Friedrichshafen in New Guinea and at Samarai in Papua showed that beriberi was very common among dock laborers, those who work on rice plantations, public works, gold mines, saw mills, etc., but that it was seldom encountered among the natives who did not work for Europeans. The disease is also present at Labouan, Sarawak and generally in the English possessions of North Borneo.

The Philippines. Beriberi has been reported from every island of any importance in the group. It occurred in epidemic form in Manila and the surrounding provinces in 1882–1883. Practically no statistics from this time are available, but Königer states that in Malabon, a town of 25,000 inhabitants, there were 300 deaths from beriberi in a little over two months.

American soldiers in the Philippines do not contract beriberi, but the following gives the figures for the Philippine Scouts for the years 1902–1910. The Scouts are native soldiers, but they have American officers. The surgeons are detailed from the regular army, and their records are carefully kept in the same manner as in the regular army. Since 1910 beriberi has been eradicated from the Scouts by a change of dietary:

PREVALENCE OF BERIBERI AMONG THE PHILIPPINE SCOUTS, 1902–1910.

Year.	Mean strength.	Admissions.		Deaths.		Discharges for disability.	
		Number.	Rate per 1000.	Number.	Rate per 1000.	Number.	Rate per 1000.
1902	4,826	598	123.92	29	6.01	2	0.41
1903	4,789	614	128.21	22	4.59	5	1.04
1904	4,610	334	74.62	7	1.52	6	1.30
1905	4,732	170	35.93	6	1.21	1	0.02
1906	4,759	176	36.98	9	1.79	6	1.19
1907	4,679	115	24.58	6	1.28	3	0.54
1908	5,085	618	121.54	7	1.35	13	2.50
1909	5,369	558	103.93	12	2.17	33	5.96
1910	5,422	50	10.00	2	0.36	3	0.55

The following chart, which was kindly furnished by Doctor Victor G. Heiser, Director of Health at Manila, shows the incidence of beriberi in Manila and the provinces so far as the records go:

POPULATION AND NUMBER OF DEATHS FROM BERIBERI OCCURRING IN MANILA AND PROVINCES.

	1901.		1902.		1903.		1904.		1905.	
	Population.	Deaths.	Population.	Deaths.	Population.	Deaths.	Population.	Deaths.	Population.	Deaths.
Manila	244,732	443	244,732	541	232,336	277	219,941	335	219,941	313
Abra	.....	.....	.....	.....	.....	.....	48,280	1	.....	.....
Agusan	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Albay	.....	.....	.....	.....	.....	.....	119,076	30	133,157	19
Ambos Camarines	.....	.....	.....	.....	.....	.....	233,565	84	233,395	109
Antique	.....	.....	.....	.....	.....	.....	111,086	9	131,331	2
Bataan	.....	.....	.....	.....	.....	.....	45,170	25	45,166	20
Batangas	.....	.....	.....	.....	.....	.....	245,001	105	264,695	114
Bohol	.....	.....	.....	.....	.....	.....	268,355	6	271,787	14
Bulacan	.....	.....	.....	.....	.....	.....	226,189	137	226,399	143
Cagayan	.....	.....	.....	.....	.....	.....	133,007	52	142,814	68
Capiz	.....	.....	.....	.....	.....	.....	224,169	181	224,169	80
Cavite	.....	.....	.....	.....	.....	.....	136,836	108	134,779	123
Cebu	.....	.....	.....	.....	.....	.....	668,599	415	701,521	738
Ilocos Norte	.....	.....	.....	.....	.....	.....	.....	.....	176,785	28
Ilocos Sur	.....	.....	.....	.....	.....	.....	177,410	14	223,557	16
Iloilo	.....	.....	.....	.....	.....	.....	.....	.....	394,742	96
Isabela	.....	.....	.....	.....	.....	.....	72,365	20	72,862	16
Laguna	.....	.....	.....	.....	.....	.....	160,513	28	141,589	37
Leyte	.....	.....	.....	.....	.....	.....	.....	.....	441,688	168
Masbate	.....	.....	.....	.....	.....	.....	44,156	5	.....	.....
Misamis	.....	.....	.....	.....	.....	.....	129,239	131	132,601	131
Negros Occidental	.....	.....	.....	.....	.....	.....	302,512	116	312,634	185
Negros Oriental	.....	.....	.....	.....	.....	.....	.....	.....	183,736	27
Nueva Ecija	.....	.....	.....	.....	.....	.....	132,441	75	133,412	99
Nueva Vizcaya	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Pampanga	.....	.....	.....	.....	.....	.....	226,180	25	226,180	43
Pangasinan	.....	.....	.....	.....	.....	.....	444,464	68	436,034	34
Rizal	.....	.....	.....	.....	.....	.....	145,645	84	148,032	95
Romblon	.....	.....	.....	.....	.....	.....	53,048	26	.....	.....
Samar	.....	.....	.....	.....	.....	.....	148,403	76	.....	.....
Sorsogon	.....	.....	.....	.....	.....	.....	123,607	125	124,799	57
Surigao	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Tarlac	.....	.....	.....	.....	.....	.....	134,500	44	134,500	60
Tayabas	.....	.....	.....	.....	.....	.....	.....	.....	201,936	115
Union	.....	.....	.....	.....	.....	.....	131,512	13	135,307	25
Zambales	.....	.....	.....	.....	.....	.....	54,317	6	.....	.....
Total	.....	.....	.....	.....	.....	.....	5,159,566	2,344	6,349,548	2,975

	1906.		1907.		1908.		1909.		1910.	
	Population.	Deaths.	Population.	Deaths.	Population.	Deaths.	Population.	Deaths.	Population.	Deaths.
Manila	219,941	536	223,542	334	223,542	920	223,542	760	234.409	1,478
Abra	.....	.....	.....	.....	54,380	0	61,005	2	.....	.....
Agusan	.....	.....	.....	.....	.....	.....	161,172	2	18,094	8
Albay	.....	.....	174,335	11	233,793	7	241,431	26	245,537	45
Ambos Camarines	228,440	93	164,871	62	228,181	74	236,911	78	242,254	72
Antique	131,330	0	131,330	0	.....	.....	130,891	0	134,400	0
Bataan	.....	.....	45,166	13	45,166	5	.....	.....	46,044	13
Batangas	250,538	32	257,715	31	276,282	50	288,834	52	294,884	79
Bohol	269,223	4	269,223	1	269,223	7	269,223	39	269,223	32
Bulacan	223,327	179	223,327	126	223,935	217	225,766	241	225,756	273
Cagayan	.....	.....	.....	.....	147,930	22	136,896	35	137,155	44
Capiz	224,169	41	224,160	31	226,299	26	220,502	92	225,025	51
Cavite	134,779	80	134,779	23	134,779	38	.....	.....	139,707	62
Cebu	706,147	443	729,981	254	.....	.....	.....	.....	.....	.....
Ilocos Norte	.....	.....	.....	.....	198,195	19	200,735	28	174,644	28
Ilocos Sur	372,631	27	306,546	7	189,279	7	190,079	17	210,831	18
Iloilo	394,742	35	394,742	3	400,037	30	405,868	53	403,260	61
Isabela	68,042	6	68,793	0	68,793	6	.....	.....	.....	.....
Laguna	134,954	25	148,610	14	148,606	34	144,486	66	144,522	55
Leyte	.....	.....	.....	.....	.....	.....	.....	.....	494,602	212
Masbate	.....	.....	43,675	0	.....	.....	.....	.....	.....	.....
Misamis	132,601	68	132,601	55	.....	.....	132,601	86	132,601	87
Negros Occidental	308,544	144	304,642	27	304,668	83	304,668	50	304,668	69
Negros Oriental	.....	.....	190,922	72	194,852	48	.....	.....	.....	.....
Nueva Ecija	133,358	64	132,999	33	.....	.....	132,999	42	132,999	31
Nueva Vizcaya	.....	.....	.....	.....	.....	.....	.....	.....	19,720	14
Pampanga	226,180	47	226,180	35	225,113	43	225,113	56	225,113	109
Pangasinan	.....	.....	436,034	31	436,034	32	439,788	62	439,766	81
Rizal	.....	.....	148,502	110	148,502	245	.....	.....	152,058	251
Romblon	.....	.....	52,848	6	54,532	14	.....	.....	55,559	29
Samar	.....	.....	147,151	43	.....	.....	.....	.....	.....	.....
Sorsogon	122,624	49	120,454	29	120,454	35	.....	.....	.....	.....
Surigao	.....	.....	.....	.....	.....	.....	.....	.....	79,018	6
Tarlac	140,781	25	139,971	11	139,971	37	139,971	22	139,971	42
Tayabas	201,936	73	201,936	41	201,936	31	201,936	31	201,936	68
Union	.....	.....	127,749	14	175,655	27	.....	.....	128,893	16
Zambales	.....	.....	59,198	1	52,974	16	.....	.....	.....	.....
Total	4,624,287	1,971	5,961,982	1,418	5,123,109	2,073	4,569,417	1,840	5,652,739	3,334

DIVISION OF STATISTICS, BUREAU OF HEALTH, Oct. 27, 1911.

Other Groups of Islands. Beriberi has followed Chinese and Japanese laborers with remarkable persistency into almost every place they have gone. This includes Hawaii, Fiji, New Caledonia, New Zealand, the Society Islands and Australia at Sydney and Melbourne. Although beriberi is not very prevalent in Australia except in certain localities, such as among the laborers of the pearling fleets, it is nevertheless fairly widespread. Thus Wetherall, in 1894, reported beriberi in a jail at Wyndham, East Kimberley. In this case 60 native prisoners were fed on a ration consisting of one pound bread, three-fourths pound meat, usually salted, one-half pound rice and three pints of sweetened tea. A number of these natives developed beriberi. Again, Ormerud reported several cases observed in Queensland in 1898. The disease has existed for a long time at Sydney and Melbourne. In 1895 Corlette, discussing the beriberi at Sydney, said that it is difficult to say how long it has existed unrecognized in Australia, but probably for many years, because there is evidence of its presence at least 15 years ago, although so far as known it was confined to Chinese. Molloy, in 1892, asked the question, "Is beriberi endemic in Melbourne?" and cites cases observed in 1888. Graham and Paton described cases among the Chinese in 1893.

Africa. Beriberi is widely distributed in Africa, and this focus is in the process of rapid extension accompanying the march of civilization. It now occurs along most of the east and west coasts of Africa, including the adjacent islands. Saltet and Legrand reported an epidemic at Casablanca, Morocco, among the Senegalese troops at that place. It is especially prevalent along the coast of upper and lower Guinea, particularly at the mouths of the great rivers. It has been reported from Senegal by Lasnet and Firket, from Sierra Leone by Plehn, from Togo and Niger, from German West Africa by Lichtenberg and Plehn, from Gaboon in the French Congo, Congo Free State, Angola (Kopke) and the Soudan.

Sorel reported a very severe epidemic occurring among natives on the Ivory Coast in 1910, in which approximately 900 died, being about 80 per cent of those affected. He states that although not previously reported from this locality, it has nevertheless been endemic for a long time. He makes the interesting point that the use of rice among the natives is entirely unknown. They live on bananas, yams, corn and vegetables.

Bagshawe reported a disease from Uganda called by the natives "Behimbo," but which was probably beriberi. These natives were said to live chiefly on yams.

Proceeding toward the south, it has been reported from Kimberley in Cape Colony, and turning up the east coast from Pietermaritzburg in Natal, and from Zanzibar (Cavalli).

It is common in the islands of Madagascar (Segard), Reunion, Mauritius and Nassibe. It was reported from Ascencion by Randell in 1900.

With regard to Reunion, O'Zoux says beriberi is of recent importation, but it is now endemic. From 1902–1904 it was very violent.

In the Cameroon, Plehn formerly observed only 13 cases in two years, but Lichtenberg, in the year 1896–97, found among 150 auxiliary troops of the garrison 15 cases, of which 11 died. Jeanselme states that the disease first appeared in the Congo State in 1885, but did not spread widely, and that in 1886–87 there was a severe epidemic among the Kaffirs employed in the construction of the railroad.

It is impossible to secure any statistics of value from these countries. I am informed, however, by Doctor Lahn, Director of Health of Cairo, that beriberi does not occur among Egyptians, although imported cases occur at Suez and Port Said. Several cases of beriberi were reported from Omdurman among soldiers in the Egyptian Soudan by Christopherson in 1903. Christopherson states distinctly that rice is a part of the Egyptian soldier's ration, and is consumed in large quantities. The protection enjoyed by the natives of Egypt under natural conditions is undoubtedly due to their dietary habits. Doctor Lahn has kindly furnished me information as to the usual food of the Egyptians, which may be found on page 385 of the Appendix.

South America. Beriberi occurs along the northern and eastern coast of South America, having been reported from Venezuela, the Guianas (Hemeury, Carter), Brazil, Paraguay, Uruguay, and even as far south as Montevideo and Buenos Aires.

It is endemic in Brazil, being common along all the littoral, and in the states of Para, Matto-Grosso and Minas-Geraes, and along the branches of the Amazon. It has been a troublesome disease in the Brazilian navy for at least twenty-five years (Thomson, Silvado).

Proceeding north, beriberi was reported from Cuba in 1865 by Hava.

Panama. Shimer states that, according to the records of physicians practising in Panama, beriberi was unknown among the population of the Isthmus prior to 1887. Moreover, the registers of the French canal company show no deaths from beriberi prior to 1887. In that year a number of Chinese and African laborers were introduced, and the first death from beriberi was reported in July, 1887. The first recorded death from beriberi in the city of Panama occurred in December, 1887, and since that time numerous cases have occurred among the poorer classes and among the colored races. In 1897 the death rate for beriberi among the employees of the French company rose to the alarming figures of 54 per 1,000 per annum, while even in later years, under the American canal commission, the death rate from beriberi has been as high as 2.3 per 1,000 per annum. From the city of Panama 559 deaths were reported from beriberi from 1887 to 1905.

United States. Beriberi is not without interest to the physician in the United States. In 1890 both Putnam and Birge reported a number of cases among New England fishermen, and referred to other cases of what seemed to be the same disease antedating these by ten years.

Bondurant reported a series of 71 cases occurring among the patients in the state insane asylum at Tuscaloosa, Alabama, during the years 1895 and 1896. The first case developed in February, 1895, in a white woman. There were no other cases until the following November, when seven developed. In the next six weeks five more cases appeared, and in September, 1896, 58 cases were recorded. Of the total 71 cases 21 were fatal. Sixty-four of the cases were among white patients and seven cases were among negroes, of which six were fatal.

Beriberi was also reported in 1895 at the Arkansas state insane hospital at Little Rock.

The superintendent of the Texas state lunatic asylum at Austin, in his annual report for 1907, states that in the early part of July an epidemic of beriberi developed in that institution, and that there were over 200 cases, with 20 deaths. The disease was confined to the patients, none of the attendants being affected. It was also stated that since 1891 there had been each year a limited number of cases of the disease, occurring usually in the summer and autumn, but that it had never assumed an epidemic form until 1907.

In the monthly bulletin of the California state board of health for December, 1909, there was published a list of 25 deaths from beriberi reported in California during the years 1907–1909. Of these 22 were Japanese, two Chinese and one German. The list was published with a note saying: "The following list of deaths from beriberi is given to show that this disease is present and widely, though sparsely, distributed. A similar number of deaths in Japan would argue some 500 or 600 existing cases."

An outbreak of undoubted beriberi was reported in South Carolina by Sams in 1910, who reported that similar cases had occurred among convicts near Charleston several times before during the preceding five years. Of the 31 convicts in this epidemic 17 were affected and two died of heart failure. Rice had not been used as food, and it was alleged that the convicts received good and sufficient food. The guards, however, were not affected.

In addition to these cases, beriberi is frequently reported on ships in almost all the larger ports of the United States. Especially interesting in this connection is the beriberi reported by Currie occurring in Chinese fishermen returning to San Francisco from Alaska. It probably occurs unrecognized, especially in institutions, much more frequently than is generally supposed.

Labrador and New Foundland. Little has recently reported the existence of beriberi among the inhabitants of Labrador and New Foundland, who live almost exclusively on fine white flour during certain seasons of the year.

Seasonal prevalence of beriberi. In all countries where the disease is endemic cases of beriberi occur throughout the year, but there are always certain seasons when the disease is more prevalent and may even reach epidemic proportions. The beriberi season, however, falls in different months in different countries, and does not always occur in the same months even in the same country.

Thus Scheube states that in Japan beriberi is at its maximum in June, July and August, and that the most serious and fatal cases fall in the months of July, August and September.

Of 565 cases occurring during the years 1878–1880 the incidence was as follows:

January	14
February	13
March	32
April	50
May	72
June	103
July	133
August	73

September	43
October	20
November	7
December	4
Total	565

Again, the cases occurring in the Japanese army in Tokio during 1879 were distributed by months as follows:

January	60
February	44
March	51
April	84
May	154
June	262
July	644
August	806
September	637
October	160
November	58
December	36
Total	2,996

Doctor Heiser has kindly furnished me with the following data showing the number of deaths from beriberi by months during the years 1911 and 1912:

	1911	1912
January	140	96
February	109	67
March	91	74
April	82	64
May	86	92
June	96	82
July	108	99
August	173	99
September	127	101
October	126	109
November	128	110
December	106	97

It is evident that there is considerable difference as to the monthly incidence of the disease in Manila, but as a general rule it may be stated that there are more cases in September, October and November than during other months of the year.

Many explanations have naturally been offered for the peculiar variations in the incidence of beriberi. It is clear that a disease which ocurs in hot and damp climates, such as the Philippines; in the coldest parts of Japan, such as the Kurile islands; at sea level, or at high altitudes, as on the summit of Fujiyama, cannot depend upon the climate.

Since in some countries the disease appears to be more prevalent during or immediately after the rainy season, some authors have thought that there was a relationship between the amount of rainfall and beriberi. However, Gerrard presented statistics from Selangor, Malay States, for seven years, which indicated that the rainfall, *per se*, did not affect the incidence of beriberi. Braddon has made a careful study of the records of admissions for beriberi, and of the rainfall at 35 different district hospitals between 1880 and 1890, and states positively that there is no definite relation between rainfall and beriberi in Malaya.

In the Philippines the incidence of beriberi appears to bear a relation to the time of harvesting the rice crop. This crop is generally gathered in December. The previous crop is frequently exhausted some time before the new rice is harvested, for the amount of rice produced in the Philippines is far from sufficient, and large amounts must be imported each year. When the old crop is consumed, the imported, or highly milled and beriberi producing rice comes into more general use, and accordingly in the succeeding months there is a marked increase in the number of cases of beriberi. Since the amount of the rice crop varies considerably in different years and in different provinces, the old rice will last longer in some years and places, and the beriberi season is accordingly deferred under such conditions. This is believed to be the true explanation of the seasonal variation in beriberi, at least in the Philippines.

In connection with the distribution of this disease in almost all of these countries it must be borne in mind that our knowledge of their diseases is only partial. For the most part reports are only received from the main towns along the coast or on the river banks, where European or American physicians practise and where hospital facilities exist. In many of these countries the bulk of the people of the interior live and die without ever having seen a physician, and as a result the physicians living in these towns have very little idea of the diseases existing in the interior. For this reason it is quite possible that the distribution of the disease given above is only an outline, and that at least scattered cases may be found practically throughout almost all of the countries that have been named. The above description of the distribution and prevalence of beriberi is believed to be sufficient to indicate the strongholds of the disease and to confirm the statement made earlier that there is no problem in tropical medicine whose solution is more important.

CHAPTER III

THE PATHOLOGY OF BERIBERI

Although beriberi is so ancient, our knowledge of its pathology is quite recent. This is due partly to the fact that pathology is one of the younger of the medical sciences, and partly because Oriental races are so prejudiced against any investigation of the dead body that it is difficult to secure autopsies even at the present day. The real nature of this difficulty may be appreciated from the fact that Scheube only succeeded in obtaining five autopsies on beriberics during a residence of three years in Kioto, and Miura obtained only fourteen autopsies during the years 1878–1888.

In 1844, Wicke decided from a study of the literature that beriberi was caused by a rheumatic affection of the sympathetic nervous system. This, of course, was pure speculation, since he had apparently never seen a case of beriberi or performed an autopsy. The first autopsy of an undoubted case of beriberi was described in 1877 by Wernich. His case was of the acute type, and the post-mortem findings were as follows: Male, 26 years. Musculature of thorax and abdomen oedematous, but not fat. Ascites, Hydrothorax, Hydropericardium (50 cubic centimeters). Cloudy swelling and fatty degeneration of heart muscle. Hypostasis of both lower lobes of the lungs. Spleen small. Cortex of kidneys congested. Mucous membrane of stomach colored slate gray, with punctate ecchymoses. Ileum and coecum very hyperaemic, with haemorrhagic spots. Colon heavily injected. Liver very hyperaemic, with areas of fatty degeneration. Brain, spinal cord and nerves not examined.

A second autopsy of this disease was described in 1879 by Anderson. His case, which was also acute, was as follows: Male, 23 years. *General inspection.* Body muscular and well nourished; face dark; lips blue; lower extremities flecked with purple. *Respiratory system.* Lungs. Bronchi and alveoli filled with foamy fluid. Tissues are doughy and oedematous. The large vessels are filled with dark fluid blood. Pleura normal. *Circulatory system.* Pericardium contains about two ounces clear fluid and a dark blood clot. Vessels much congested. Heart muscle sound and healthy.

Valves normal. All cavities contain clots. Muscle bundles free from any trace of degeneration. *Digestive system.* Stomach contains some foamy fluid and a little milk. Great ecchymoses were found in two places under and into the mucous membrane. Microscopic examination showed that the epithelium was mostly destroyed and the vessels of the muscularis and submucosa were full of blood. *Intestine.* Much congested. Contents fluid and dirty yellow. Submucous ecchymoses in two or three places. Liver, spleen and pancreas hyperaemic. No effusion in abdominal cavity. *Nervous system.* Brain, cord and some nerves were examined, but nothing abnormal found. *Urinary system.* Kidneys hyperaemic. Bladder contained a little urine free from albumen.

Simmons in 1880 reported two autopsies performed on acute cases.

Case 1. Male, 26 years. A few ecchymoses on surface of body. Subcutaneous tissue filled with serum. *Intestinal tract.* Reddish from capillary congestion and rather translucent. The peritoneal cavity contained about 12 ounces of clear fluid. *Lungs.* Oedematous. Left pleural cavity contained 13 ounces clear fluid and the right 5½ ounces. Pericardium contained two ounces of the same clear fluid. *Heart.* Right auricle contained a large clot that filled a two-ounce glass. Half of its inner surface was covered with a white fibrinious substance one-eighth inch thick. The right ventricle contained a large hour-glass shaped clot reaching to the pulmonary valves, and in the smaller branches of the artery were emboli which appeared to have come from this clot. This clot was undoubtedly ante mortem. Valves normal. The ventricles were dilated, their walls thinned, and the whole structure lacked the firmness peculiar to the normal heart. Microscopic examination showed that the muscles had undergone degenerative changes. *Stomach.* Contained eight ounces greenish yellow fluid and the mucous membrane contained a number of dark red or purple flecks. Liver, spleen and kidneys normal.

Case 2. Male, 26 years. Severe general oedema, particularly in the upper portions of the body. The recti had a peculiar yellowish green color and the outer surface of the body was partly sprinkled with greenish gray spots, while other parts showed a bright red dendritic injection. *Peritoneal cavity.* Contained seven and one-half ounces clear serum. Mucous membrane of *stomach* and *intestine* showed signs of congestion throughout entire length. *Liver* dark, but normal. *Right pleura* anterior and upper portion adherent. The remaining part of the cavity contained 14 ounces serous fluid. *Left pleural cavity* free and contained 27 ounces clear serous fluid. *Lungs.*

A high grade of oedema, and a foamy sero-bloody fluid flowed from the cut surfaces. *Pericardium.* Contained one and one-half ounces clear fluid. *Heart* was enlarged, soft, and of a dirty yellow color. The unusual size of the heart appeared to be due to excentric hypertrophy. Endocardium and valves normal. Microscopic investigation showed primary degenerative changes in the muscle. All large venous trunks greatly dilated and filled with blood. The secondary portions of the venous system were also filled with blood. *Brain.* Slight subarachnoid transudation, otherwise normal. *Spinal cord* normal.

Baelz, whose first observations were published in 1882, gives a description of two autopsies as follows:

Case 1. Male, 23 years. Had been sick one-half year and died with acute symptoms. Body rather cyanotic. Anasarca. Badly nourished, muscles flaccid. Muscles soft and clearer than usual. Spinal cord normal, except that the fluid in subarachnoidal space is a little increased and the pia mater is rather hyperaemic. *Brain* apparently normal. *Heart.* Both chambers engorged with coagulated blood, and somewhat dilated. Heart in diastole. Heart wall rather white. Microscopic examination showed cloudy swelling of some fibers and fatty degeneration of others. *Lungs* normal. *Liver* slight nutmeg appearance. Spleen and kidneys normal.

Case 2. Male, 28 years. Sick five months and died with acute symptoms. Badly nourished. Skin dirty color, but no spots. Severe oedema about face, neck and buttocks, and slight oedema in extremities. On cutting into the tissues dark red blood streams out of cut vessels. Muscles soft and flaccid. Subcutaneous tissue full of serum. *Spinal membranes.* From second to ninth thoracic vertebrae were unusually fat and contained punctiform haemorrhages. Posterior half of spinal cord congested, especially in region of filum terminale. In regions of second and third thoracic vertebrae the cord appears rather compressed and on cross section the left side of grey matter was softened. Microscopically there was atrophy of the ganglion cells of the anterior horn. It is possible that these changes were post mortem. Fresh nerve fibers from the sciatic nerve showed nothing.

Heart large and in diastole. Fatty degeneration of left papillary muscle. Fibers of heart wall were normal.

Baelz stated for the first time that beriberi is an endemic form of multiple peripheral neuritis, such as is seen in Europe in sporadic cases. He defines the disease as a miasmatic infection localized in the peripheral nerves, and gave it the name of Panneuritis endemica. He says, "Its nature is that of a true neuritis with degeneration of the fibers quite analogous to that observed in other peripheral paralyses, or to that produced by cutting the nerves."

Ballet (1883) found in a man who had developed beriberi in Brazil, and in whom atrophy of the muscles of the legs was far advanced, atrophy of the ganglion cells of the anterior horn, especially in the lumbar region.

In 1884 Mendes saw changes in the white substance of the cord, particularly in column of Goll, together with atrophy of the grey matter and of the nerve cells without any increase in the neuroglia. He also observed the phenomena of neuritis in the anterior and posterior roots and in the nerves.

Scheube added three more autopsies in 1883. Unfortunately only one of these is of much importance, because his second case was complicated with syphilis of the nervous system and the third case with typhoid fever. Later, however, Scheube obtained further material in Batavia, and thus succeeded in proving from the pathological findings the identity of Japanese kakke and Malaysian beriberi. He was also enabled to make more complete histological examinations, including osmic acid preparations of the nerves. The results of these autopsies are as follows:

Hydropic accumulations in skin and serous cavities.

Anasarca in 11 cases or 55 per cent.

Hydropericardium in 15 cases or 75 per cent.

Hydrothorax in 5 cases or 25 per cent.

Ascites in 10 cases or 50 per cent.

Hydrops of all serous cavities in 4 cases or 20 per cent.

Anasarca and hydrops of all cavities in 3 cases or 15 per cent.

Heart. The heart muscles had undergone fatty degeneration in all cases. In seven cases it was massive. More severe in the right ventricle than in the left. Colloid change was found twice. In two cases there were inflammatory changes consisting partly of a diffuse interstitial infiltration and partly of small disseminated foci.

Dilatation of right heart found in 14 cases or 70 per cent.

Dilatation of both sides found in 4 cases or 20 per cent.

Hypertrophy of left ventricle found in 5 cases or 25 per cent.

Hypertrophy of both ventricles found in 4 cases or 20 per cent.

Lungs. Were usually hyperaemic and oedematous.

Liver and kidneys showed general venous congestion with cloudy swelling and fatty degeneration of the cellular elements.

Spleen usually enlarged.

Intestines. Venous hyperaemia of varying extent and intensity, with frequent small haemorrhages in the mucous membrane.

The Nervous System. Brain. The usual finding in the brain was a venous hyperaemia of the membranes, oedema of the pia, and hyperaemia of the brain. Fluid in the ventricles was increased and there was oedema and anaemia of the brain substance.

Spinal Cord. Macroscopically, hyperaemia of the membranes and serous effusions in the peridural and subarachnoidal spaces. Microscopic examination showed nothing abnormal. In six cases careful investigation was made of sections from all parts of the cord. In one case atrophy and partial loss of ganglion cells of the anterior horn was found, but was thought to be a secondary degeneration, and he considered the softening of the cord described by earlier writers as post-mortem changes.

Nerve Roots. Examined three times and found normal. In one case the connective tissue was infiltrated with nuclei.

The Peripheral Nerves. In all cases the nerves showed more or less severe degeneration and atrophy, corresponding to the paralytic symptoms during life. Osmic acid preparations showed swelling and constriction of the medullary sheath, degeneration into droplets, invasion of fatty granular cells, and finally complete absorption of the medulla and axis cylinder, so that nothing but the empty sheath of Schwann remained. Cross sections stained with carmine also showed loss of fibers, and degenerated fibers which stained uniformly red and in which no distinction could be made between axis cylinder and medulla. The number of nuclei in the endoneurium was increased. The degeneration was most intense in the muscular branches, while the nerve trunks showed only slight changes.

Muscles. Degeneration of muscle fibers went hand in hand with that of the nerves.

Vagus. In nine cases degeneration in this nerve was established.

We have therefore a subacute neuritis and myositis, usually in paraplegic form and affecting first the lower extremities. Scheube asks the question whether the neuritis is primary and followed by secondary degeneration of the muscles, or whether it is possible that they develop pari passu, both being caused by the same agency. He also states that he thinks it likely that the degeneration of the heart muscle is caused by the primary degeneration in the pneumogastric nerve. He concludes that the disease is not of spinal origin, both because he failed to find spinal lesions and from clinical reasons such as the facts that the sphincters are not affected, that there is an early and high grade of muscular atrophy not completely parallel with the paralysis, and because of the reactions of nerves and muscles to electricity. He came to the conclusion that kakke is a multiple subacute neuritis caused by a specific poison.

Baelz, working independently at Tokio, also came to the same conclusion at about the same time.

M. Miura published the results of his 14 autopsies in 1888, and his findings are briefly as follows:

Heart. Dilatation and hypertrophy of the heart without changes in the valves was an almost regular finding in acute cases. The heart muscle was usually normal although in one case there was considerable fatty degeneration.

The Lungs. In three cases severe hyperaemia and massive oedema of both lungs was observed, and the lung capillaries were distended with blood corpuscles.

Kidneys. The gross appearance was normal except for cyanosis in some cases. Microscopically, the stroma was infiltrated with round cells and there was a glomerulo-nephritis.

Spleen. Was usually of normal size, color and consistency, though sometimes atrophic and rarely enlarged.

Stomach. The mucous membrane was swollen and inflamed, and showed a high degree of hyperaemia with numerous ecchymoses and erosions. Microscopically, the gland epithelium was cloudy, but the nuclei were distinct. Between the glands was an extensive round cell infiltration.

Intestines. Findings were not constant, though often a catarrhal condition was found in the small intestine.

Liver. Was of usual size, but hyperaemic, infiltrated with fat and presented an excellent picture of the nutmeg liver. Microscopically the intra- and inter-acinous vessels were dilated with blood cells.

The Skeletal Muscles. Fibers were often encountered showing alterations, consisting of spindle or ball-shaped swellings, and frequent loss of cross striation. Pronounced proliferation of the muscle nuclei was also seen.

The Nervous System. Nothing abnormal was found in the peripheral nerves or central nervous system, either macroscopically or in sections, except that in three cases he found vacuolated ganglion cells in the anterior horn of the cord. The vacuoles were quite numerous in certain cells, but the cell nuclei were unaltered, and Miura did not regard this change as being caused by beriberi.

Pekelharing and Winkler, who worked in Sumatra and Batavia in 1887, published observations based on 64 autopsies which were of the greatest value and may be condensed as follows:

The dead bodies present very different appearances. If muscular atrophy has predominated, the bodies are emaciated, but sometimes muscular atrophy and hypertrophy may be found upon the same body, and the extremities appear swollen. When the cause of death has been a sudden stoppage of the heart, the face reflects the agony suffered. It is blue and swollen, with projecting eyeballs, distended jugular veins, and the mouth filled with froth. Rigor mortis is not peculiar. On making an incision in the skin the presence of serous fluid in the cellular tissue is marked in "wet" cases. The muscles appear brownish in the atrophic form, and in all cases there is generally a profuse oozing of dark red blood from the cut vessels.

Dropsy of the pericardium is a characteristic feature, being present in 62 cases. Pleural and peritoneal effusions were also common, hydrothorax being encountered in 14 cases and ascites in 9 cases out of 64 autopsies.

Ecchymoses were found in 54 cases in the visceral layer of the pericardium and pleurae, but they consider that this was a result of the death agony.

Oedema of the lungs was found 23 times, and also considered as a phenomenon belonging to the last hours of life.

Hypertrophy of the heart was always present, and there was almost always a dilatation of the right side. The left side was also affected, but less frequently. The musculature of the heart was pale, but did not show fatty degeneration.

Liver was often swollen owing to venous hyperaemia and was sometimes a nutmeg liver. There were no pathological changes recorded in the kidney peculiar to beriberi, but venous stagnation was common. No changes in large vessels or other viscera.

Nervous System. Macroscopic examination showed nothing except occasionally local hyperaemia. The peripheral nerves were examined in 85 cases and found to be affected without exception as follows: The nucleated sheath of Schwann remains intact around the medullary substance as it lies agglomerated in masses. In some instances one finds instead of the inter-nodal nucleus two or three nuclei immersed in a mass of swollen protoplasm. The axis cylinder is to be found only near Ranvier's nodes where the medullary substance has often disappeared over a large space. In more advanced stages, by the side of these fibers degenerated into masses, there are some nervous fibers where the medullary sheath has almost entirely disappeared, and only vestiges of it are found as little masses, colored black by the osmic acid. Still more characteristic are certain places where the nerve fibers are filled with a number of little globules colored black, brown or dirty yellow mixed intimately with a frothy mass which becomes a clear rose color when stained by carmine. In this mass or by its side is found one or more nuclei. The number of nuclei has greatly augmented. All phases are found between the massive degeneration and the frothy degeneration. Five peripheral nerves submitted to immediate examination in glycerin with a solution of potash showed an enormous increase of granular nerve corpuscles, and in transverse sections numerous mast cells were found. Sometimes in these sections almost all the nerve fibers have lost their sheath, and some rings colored black have alone been left. Degeneration was found in all the cerebrospinal nerves examined, as well as in the terminal branches of the vagus and phrenic, and they raise the question whether any nerves escape. They were not able to ascertain any changes in anterior roots or at the most only slight ones, but found atrophy of the fibers of the posterior root and also found changes in the ganglion itself in cases of long duration, and in the fibers proceeding therefrom centrally in the columns of Goll. They examined ten spinal cords and found six normal, three with some probable modifications and one with distinct alteration in posterior columns. The change consisted chiefly of absence of medullary sheath around many fibers. In sections at a higher level of lumbar region in the centre of the two posterior columns a degenerated patch in the form of a hammer was found. The tracts of degeneration in which many of the fibers were destroyed approach as they ascend nearer to the central region of the cord. The presence of these degenerated fibers could be traced up through the cervical region through the funiculus gracilis to the nucleus thereof. With regard to the cells in the cord, " in all cords a great number of intact nerve cells were found, with well marked processes, large nuclei and well colored nucleoli, but we also always found some nerve cells which presented slight deviations from the normal. In the first place, the pericellular spaces appeared to us much enlarged. We also found a certain number of nerve cells destitute of processes, no nuclei existed in some and in others the nuclei occupied lateral positions, or actually lay against the linings of the cells. A nucleolus was often wanting and the whole cell assumed a less vesicular form than normal. We also found a few vacuolated cells. The number of these was from one to four in a preparation which contained sixty visible cells. Finally we sometimes saw in these cells a large quantity of pigment." Pekelharing and Winkler thus confirmed and extended the observations of Baelz and Scheube with regard to the characteristic changes in the peripheral nervous system, though they rightly recognized that these changes are not specific for beriberi. They considered the changes in the ganglion cells as secondary.

Bentley in 1893 reported nineteen autopsies of undoubted beriberi cases, giving the clinical history of each case and a detailed account of the conditions found at autopsy. He summarizes the results of these autopsies as follows: "The appearances presented were very uniform, and consisted chiefly in serous effusions into the areolar tissues through the body (this, however, was absent in some of the cases, especially such as had a short duration and had been suddenly fatal). Effusions of varying amount into the chest and pericardium * * * the quantity effused into the latter space has averaged from two to eight ounces * * * more or less serous effusions into the abdomen, but rarely amounting to ascites. In all cases effusion was found in the ventricles of the brain, and also on the surface of the cerebrum itself. The quantity of this was variable. There was effusion under the dura mater of the spinal canal. The heart as a rule was large and flabby, surrounded by deposits of fat. The valves were healthy. In the heart cavities were found generally masses of clot and coagulated lymph. The left ventricle was generally found to be contracted. The right flaccid. The weight of the heart varied from eight to thirteen ounces. The lungs were oedematous. Kidneys were pale and enlarged. Spleen was enlarged, in some cases pale and in others congested. Liver was usually large and congested. Brain was found congested, as well as the dura mater. Spinal cord was found in all the cases enormously congested, softened and oedematous in some." "The muscles in all the cases seen in post mortems were pale and flabby, and in those that recovered also the muscles underwent rapid atrophy." "The heart was in almost all cases found to be very considerably enlarged. In the fifteen cases in which the heart was weighed the average weight was found to be ten ounces." "The most marked changes, however, to which I would draw attention were found in the spinal cord, and it is these which have caused me to hesitate in accepting the general view that the disease is a peripheral neuritis, and not one due to a central lesion. The cord in all cases was found to be in a state of marked congestion." "They (the lesions of the cord) were so gross as not to require the use of the microscope to see them, for in some — only a few hours after death — the cord was soft and diffluent with haemorrhages, marked congestion, and extensive oedema quite sufficient in themselves to cause all the symptoms." *"My observations go to prove that it is a cord lesion which involves both motor and sensory functions of central origin — a subacute inflammation of the spinal cord and its membranes."*

Küstermann (1895) performed an autopsy in Hamburg on a Chinese stoker who had died of beriberi. He found, on examining the heart microscopically, fatty degeneration. In the voluntary muscles, localized loss of the striations and knobby swellings of a few fibers. In the vagi, moderately severe degeneration. In peroneus, high grade of degeneration, loss of medullary sheath and appearances similar to those described as Renaut's bodies. Küstermann also found in the anterior horn of the lumbar cord a few vacuolated ganglion cells, and the nucleus of the vagus in the medulla much inflamed, oedematous and containing a greatly reduced number of shrunken ganglion cells.

From clinical observations in 1896 Correa de Bittencourt thought that the optic nerve, chiasm, the optic tracts, corpora quadrigemina and centres of vision in occipital lobe are all affected in beriberi.

Ellis (1898) thought that in the paralytic form degeneration of motor nerves was the main lesion, while in the wet form the sympathetic nerves and the vagus and phrenics were more frequently affected. Thus, Ellis says, Doctor M. Simon published a paper in which he stated his impression that the oedema may be caused by neuritis of the vaso-motor nerves. I have examined a large number of nerves removed from patients dying of beriberi, and have met with many cases in which all the peripheral neres were healthy, but in which some or all of the following nerves were markedly degenerated, viz., the phrenic, branches of the cardiac and pulmonary plexuses, the splanchnics, branches of the solar and renal plexuses, branches to the mesentery, and vaso-motor branches to the aorta, renal, splenic and tibial arteries. In no case of death from beriberi have I failed to find degeneration of either the phrenic, pneumogastric or branches from the cardiac plexuses, showing, it seems to me definitely, that death invariably occurs in the disease from implication of some of these nerves. The phrenic is the nerve most frequently involved.

Ellis also adds the following pathologic findings: In 125 necropsies I found the average weight of the heart to be 13.37 ounces. The right side in nearly every case being much enlarged. Over the same time 204 hearts from patients who had died of other diseases averaged just under nine ounces. In 125 cases of beriberi, the spleen averaged

9.27 ounces in weight, while the spleens of 204 other cases averaged 6.28 ounces. Kidneys and liver sometimes, though rarely, congested. In the same 125 cases of beriberi there was oedema of the lungs (usually slight) 78 times, hydrops pericardii (varying from one ounce to over half a pint) 81 times, hydrothorax 10 times and ascites five times. Lining membrane of stomach congested in 31 out of 57 cases, especially on ridges of corrugations.

Yamagiwa in 1899 reported the results obtained in a large number of autopsies in Japan, which were briefly as follows:

Anasarca found 49 times out of 90 cases, and it affected the entire body 32 times. The remaining 41 cases were dry beriberi.

Effusions in serous cavities in 122 cases are shown in the following table:

Amount of transudate in cubic centimeters.	51 to 100.	101 to 500.	501 to 1000.	1001 to 2000.	2001 and over.	Not present or less than 50.
Left hydrothorax	21	23	9	4	......	65
Right hydrothorax	14	31	5	3	1	68
Hydropericardium	37	28	......	......	......	57

Bleeding in the serous membranes. Especially in the acute cases.

Ecchymoses in the epicardium and pulmonary layer of the pleura are common.

Heart. By a long series of measurements, Yamagiwa showed that the heart was both dilated and hypertrophied, and that this change was particularly apt to effect the right ventricle. Out of 125 cases he found cloudy swelling in the heart muscles 23 times, fatty degeneration 35 times and no change 67 times.

Lungs. Varying degrees of oedema were found in 80 per cent of the cases.

Spleen. Showed usually a perceptible increase in size.

Kidneys in 83 cases showed cyanotic induration. Out of 101 cases he found some cloudy swelling in 54 cases. It was usually present in the wet cases.

Nervous System. Brain and spinal cord are usually anaemic, with severe venous hyperaemia and oedema of the membranes. Yamagiwa did not examine the central nervous system histologically.

Peripheral Nerves. The changes which have already been described by Scheube were found in seven out of nine cases.

Yamagiwa also thought he found changes in the blood vessels, particularly in the media of the arterioles. In preparations of nerves, muscles and kidneys he always found that the walls of the arterioles were thickened, and the lumen narrowed, and he believed that this was the essential change in beriberi. Thus he says, "The essence of kakke consists in the increased resistance which occurs in the systemic and pulmonary circulations as a result of the contraction of the arterioles." The other changes, including the degeneration in the nerves are only secondary to this primary alteration in the blood vessels.

This theory as to the cause of the pathological changes in beriberi never found any general acceptance, and practically all recent observers have recognized the changes in the nervous system as the anatomic basis of beriberi.

Rumpf and Luce (1900) also performed an autopsy on one case. They described a chronic interstitial fatty neuritis in the peripheral nerves, with considerable loss of medulla and parenchymatous degeneration, and also a connective tissue proliferation.

They also found in the case already described, at all levels of the cord, a recent diffuse parenchymatous degeneration of the medullary sheath with isolated parenchymatous foci in the posterior roots, together with a chronic interstitial neuritis and slight degeneration of the ganglion cells of the anterior horn in all the segments.

In 1901 Jeanselme studied five cases in Saigon and investigated the nerves of the cauda equina. He found the axis cylinder fragmented, and in the medullary sheath were glassy clumps which fill this structure. He believed that this substance was amyloid degeneration of the medulla, but obtained no positive microchemical reaction. He believed that it was the result of action of the toxins of beriberi.

H. Wright in 1901 reported results from eight cases studied in Kuala Lumpur. He also found considerable change in the central nervous system. Thus, he says, "In a careful examination of eight cases of beriberi, I have found changes in those posterior spinal ganglion and anterior horn cells which give origin to the degenerated nerves, and in the combined and hypoglossal nuclei of the bulb in those cases where the fibers from these parts were atrophied. The lesion is scarcely distinguishable from that found in cases of alcoholic polyneuritis."

In one typical case of beriberi, and in which all the peripheral nerves were markedly degenerated, Wright found no change in cells in the cerebrum and cerebellum. In the cord he found a few cells in all sections in a state of moderate chromatolysis, nuclear dislocation, and over staining. Changes were not distinguishable from those of chronic alcoholic polyneuritis. Such cells were found distributed throughout all regions of the cord in the anterior horn and posterior root ganglionic cells. Wright says it appears to me that I have said enough to prove that beriberic neuritis is no exception to the rule that governs in other neuritides, namely, that atrophy or loss of function in the axon leads to or is concomitant with disturbances in its trophic cell.

In a second case autopsied 10 minutes after death he found the alteration in the cells much more general and widespread. "I have never before seen ganglia so profoundly altered as are the lumbo-sacral in this case. Scarcely a cell is normal, more than half of the cells have dislocated nuclei, and very dark or light homogeneous hyaloplasm. A few nuclei have burst and the nucleoli have disappeared. A large number of cells are more positively degraded. Vacuolation, shrinkage, increased density of the whole cell body, and actual disintegration are common. It seems, too, that many cells have disappeared. There appears to have been a severe and rapid cellular atrophy in operation."

Wright describes the process of degeneration of the nervous system in beriberi further as follows: The earliest change in the neurones by the Marchi method is a slight black flecking of the myelin about the nodes or scattered along the internodes. The parent cells are seen by Nissl's method to be slightly rarefied and to have swollen, moderately eccentric nuclei. The Nissl bodies of the processes have almost wholly disappeared or they are extremely tenuous, and the small particles which compose them appear to be slightly dissociated. The Nissl bodies of the periphery of the cell are likewise involved. This part of the cell has the appearance of blued, thin ground glass. These changes are seen in the ventral motor cells of the cord, pons, and bulb. The changes in the sensory cells of the posterior spinal ganglia and corresponding ganglia of the cranial nerves are practically the same.

In Later Stages. The nuclei are all more or less swollen and dislocated, the processes are denuded of Nissi bodies and almost wholly of the fine deposit derived from them. The periphery of the cells is more rarefied; the central Nissl bodies are more diaphanous. The cell becomes more rarefied or sometimes takes on a massive blue coloration, the Nissl bodies having disappeared entirely or having broken down into a fine powdery but dense mass which fills the whole cell except the original site of the nucleus. The latter is widely dislocated, even abutting on or being flattened against the cell wall. It colors more deeply than normal and is swollen.

Still Later. Vacuolation of the cell, rupture of its membrane and that of the nucleus occur with extrusion of the nucleolus and loss or fragmentation of the processes.

Wright arrived at a peculiar theory as to the pathogenesis of beriberi as the result of his studies. He thought that beriberi has a short and obscure incubation period of seven to 20 days, during which time the patient suffers from indigestion. He loses his appetite, and suffers from vomiting, catarrhal diarrhoea and mild fever. The nervous symptoms then appear. The patellar reflex is increased or diminished, and in acute cases paralysis of the muscles of the lower extremities, of the shoulder girdle, arms and hands follow. At the autopsy of such a case one finds a fresh haemorrhagic inflammation of the pyloric portion of the stomach and duodenum, with haemorrhagic erosions. At the bottom of the folds are small punctiform haemorrhages. The first chain of mesenteric glands is often swollen. Microscopically, signs of recent haemorrhagic inflammation with a considerable plasma cell infiltration were found. The superficial mucous membrane is necrotic and infiltrated with a bacillus having constant morphologic characteristics. The bacilli penetrate to the bottom of the mucous glands into the tissues. In one case he found this bacillus in all the organs. He therefore concludes that this gastro duodenitis is the primary lesion, and the presence of this bacillus in the mucous membrane is the pathognomonic sign of the disease. In the heart Wright found almost always more or less fatty degeneration of the muscle, principally of the right ventricle. In all acute cases the vagus shows changes which by the Marchi method show as fine black spots in the medullary sheath. In such acute cases, although the degree of paralysis may be slight, round droplets of altered myelin may be seen. True degeneration of the peripheral nerves is only seen in those cases called by Wright residual paralysis of beriberi. He says: "The chief anatomical changes in fatal acute beriberi are, then, the primary gastro duodenitis with an associated bacillus. A bilateral symmetrical toxic change in the peripheral terminations of many or few sensory motor and autonomic neurones with axonal reaction in their parent cells. In all rapidly fatal cases the nervous system of the heart is most deeply and widely implicated."

Usually, however, the disease progresses further, and the toxic material produces the degeneration of the heart nerves and the motor, sensory and vaso-motor nerves, resulting in the picture described by older authors as true beriberi. Of the primary gastro duodenitis there is nothing to be seen in such cases. At this time a third to a half of the medulated fibers of the vagus are degenerated, and degenerated cells are found in the nucleus ambiguous and in the central nucleus. The peripheral nerves also show the chronic degeneration, which also progresses centrally, and numerous degenerated cells are found in the spinal ganglia and in the anterior horn. In older cases degeneration of the fibers of the column of Goll in lumbar and sacral areas may be seen.

Glogner in 1903 observed advanced fragmentation and segmentation of the heart muscle in a number of cases of beriberi, and thought that it was independent of nervous changes.

A further contribution to the pathology of beriberi in later years is the article of Herzog (1906), who gives the details of eleven autopsies. The following embodies in condensed form the summary of the pathology given in this paper: The skin of the corpse is pale, often with cyanotic patches. The superficial veins discharge a large amount of dark fluid blood when cut, and in all cases of "wet" beriberi the subcutaneous tissue is oedematous, particularly in the anterior thoracic region and the anterior surfaces of the lower extremities. Hydropericardium, ascites and hydrothorax are frequent, a total of 256 collected cases having hydropericardium in 66 per cent. Sub-epicardial and sub-pleural petechiae are also frequently found. The heart most constantly shows characteristic changes. The myocardium, particularly of the right ventricle, is hypertrophic, though the left ventricle may also be enlarged. The myocardium is often cloudy or mottled as the result of diffuse fatty degeneration. The right ventricle is also apt to be dilated. Lungs are usually oedematous and congested. Kidneys are markedly congested, and some cloudy swelling and fatty degeneration are often found. Liver is congested, and may be a typical nutmeg liver. Stomach and intestines are often hyperaemic, with ecchymoses in mucous membrane, probably as the result of a purely mechanical passive process, i. e., the general venous congestion. The peripheral nerves show no gross changes.

Microscopic Changes. Myocardium usually shows more or less loss of striation of its fibers, which are also finely vacuolated. Fragmentation and segmentation also occur. (See figures 1–3.)

Lungs show congestion of interalveolar capillaries.

Kidneys. Cloudy swelling and fatty degeneration of tubular epithelium of moderate degree.

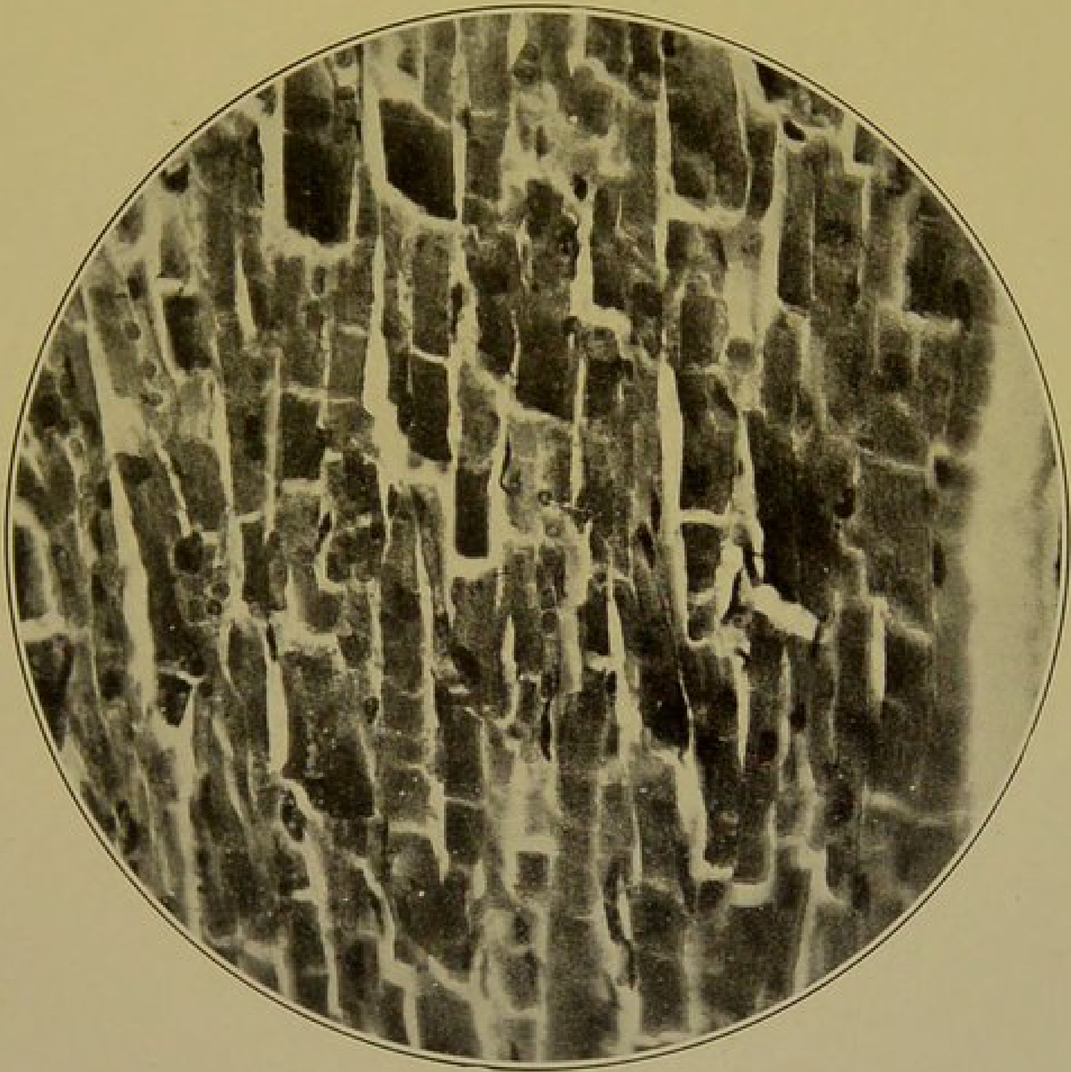

Figure 1. Section of Myocardium from case of beriberi, showing segmentation and fragmentation.

Liver. Great congestion of intralobular capillaries, with cloudy swelling, fatty degeneration of cells and interlobular inflammatory foci caused by infiltration of small round cells.

Figure 2. Section of Myocardium from a case of acute wet beriberi, showing more advanced fragmentation. [From article by Herzog, and plate lent by the courtesy of The Philippine Journal of Science.]

Stomach and duodenum. Dilated and congested vessels are common.

Peripheral nerves. Degeneration of myelin sheath, which is broken up into balls and beads, finally disappearing. Axis cylinders may also

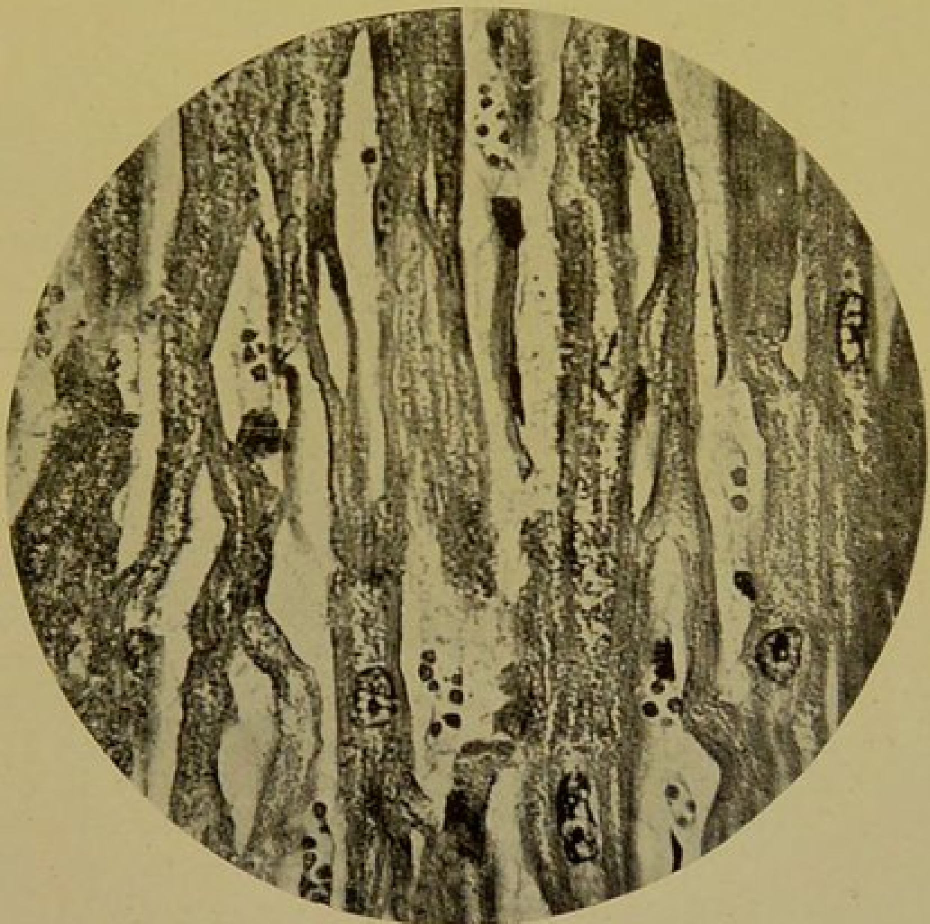

Figure 3. Section of Myocardium from a case of sub-acute wet beriberi, haematoxylin-eosin stain, showing loss of striation, vacuolation and granular degeneration. [From article by Herzog, and plate lent by the courtesy of The Philippine Journal of Science.]

show distortion. The nuclei of the neurilemma are proliferated, but the process is chiefly degenerative. (See figures 4 and 5.)

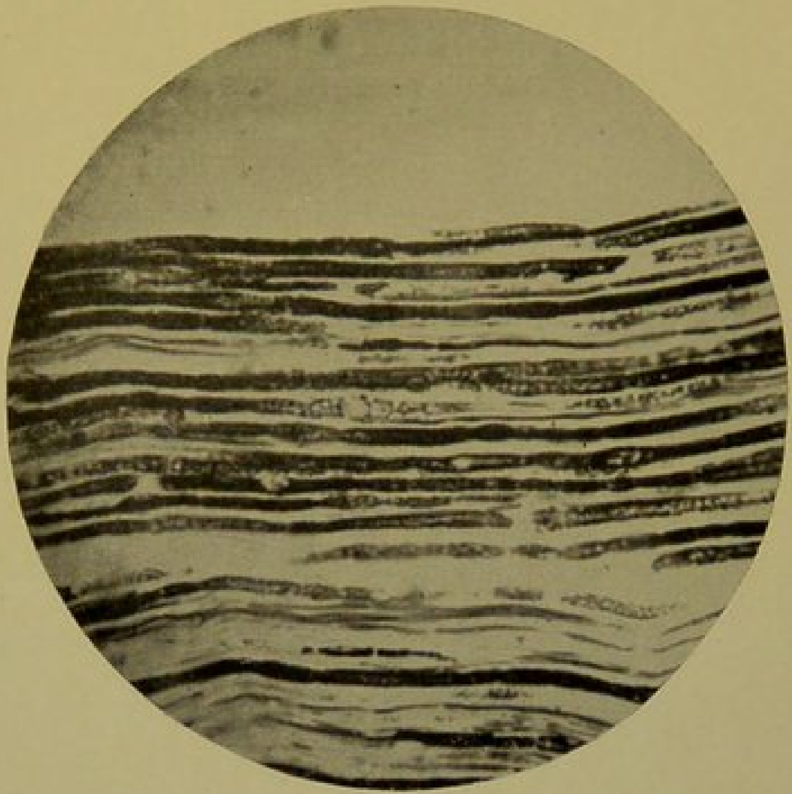

Figure 4. Longitudinal section of popliteal nerve from a case of acute beriberi. Weigert-Pal Stain, showing different degrees of degeneration of the medullary sheath. [From Herzog, plate lent through the courtesy of the Philippine Journal of Science.]

Muscles. Outline of fibers indistinct, and sarcoplasm swollen or shrunken away from the sarcolemma.

More recently, in 1907, Dansauer has investigated cases of beriberi in German Southwest Africa. He made teased preparations of the vagus and peroneus stained with osmic acid, and believes the diagnosis of beriberi can be made from the black colored areas so obtained. This, however, only establishes the presence of degeneration, and there is no means of telling whether this degeneration is caused by beriberi or by some other of the numerous causes of nerve degeneration.

Holcomb, in 1908, found in two fatal cases from a Brazilian naval vessel, hyperaemia of the stomach and duodenum, haemorrhages in the villi, slight necrosis in the lymph follicles of the duodenum and upper jejunum. From the upper portion of the jejunum he cultivated a bacillus similar to the colon bacillus.

Rodenwaldt, in 1908, in two cases studied by Giemsa's modified stain for Nissl bodies, demonstrated changes in a number of cell groups of the anterior horn of the cord and in the column of Clarke similar to those of alcoholic neuritis and following amputation. The cells are swollen, divested of processes, and the Nissl bodies more or less broken down. Occasionally he also found vacuoles. He found that advanced changes could often be found in the peripheral nerves by the Marchi method when these same nerves showed little or no change by ordinary

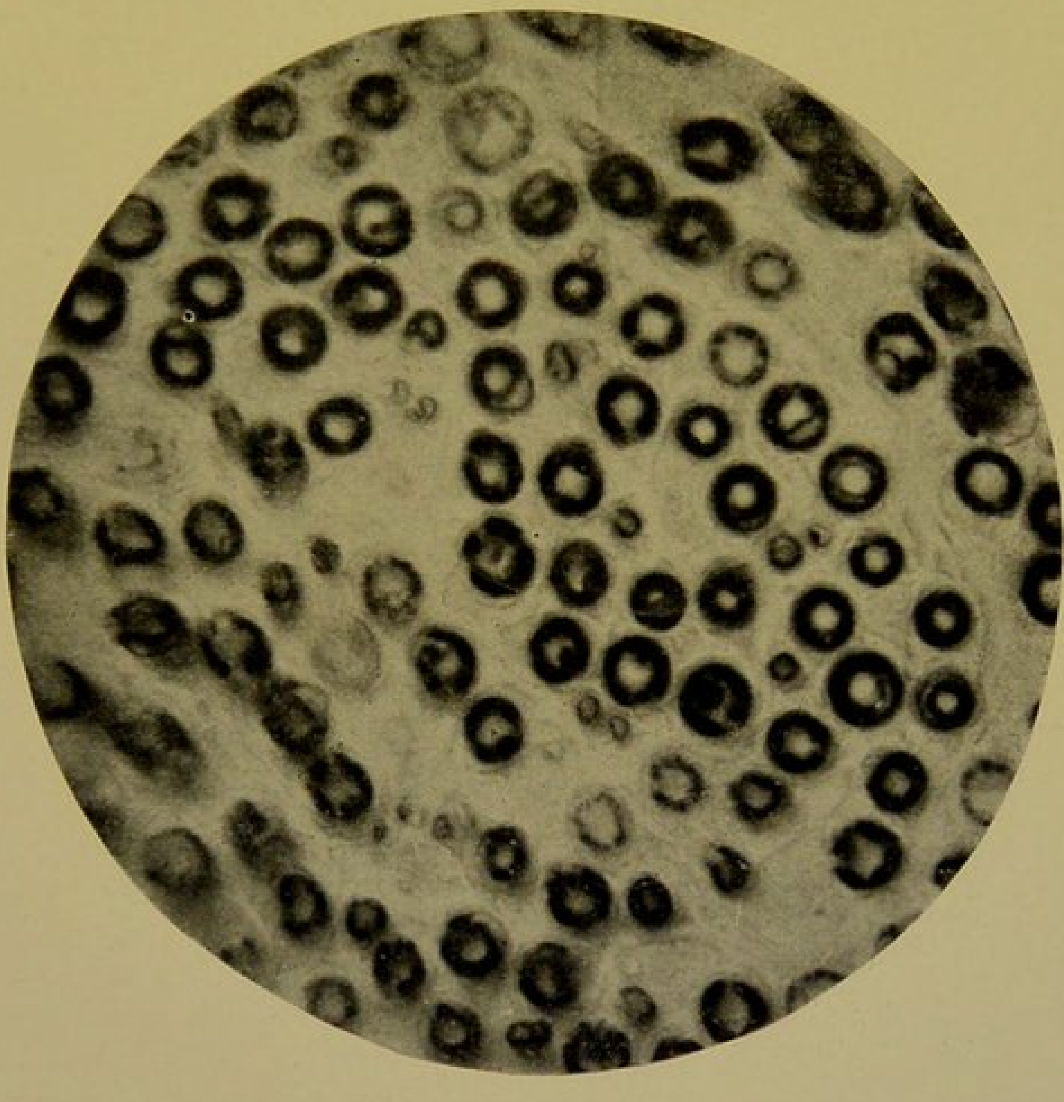

Figure 5. Cross section of popliteal nerve from an acute case of beriberi. Weigert-Pal Stain. Also shows varying degrees of degeneration of the medullary sheath. [From Herzog, plate lent through the courtesy of the Philippine Journal of Science.]

staining methods, and thinks that part of the discrepancies in the observations of different authors are due to this fact, and that if the Marchi method were applied to the cord the majority of cases would show degeneration of the fibers of the cord. The same thing is true for Nissl's method for the nerve cells. He found marked changes in the cells of the cord in both cases by this method which would have been overlooked if other staining methods had been used. He believes that the degeneration of the cells in the anterior horn is secondary to the degeneration in the peripheral nerves.

Dürck (1908) made a careful study of the pathological anatomy of eleven cases of beriberi in which the autopsy was performed immediately after death. Unfortunately several of his cases were complicated with intercurrent diseases, such as sprue, dysentery and typhoid fever.

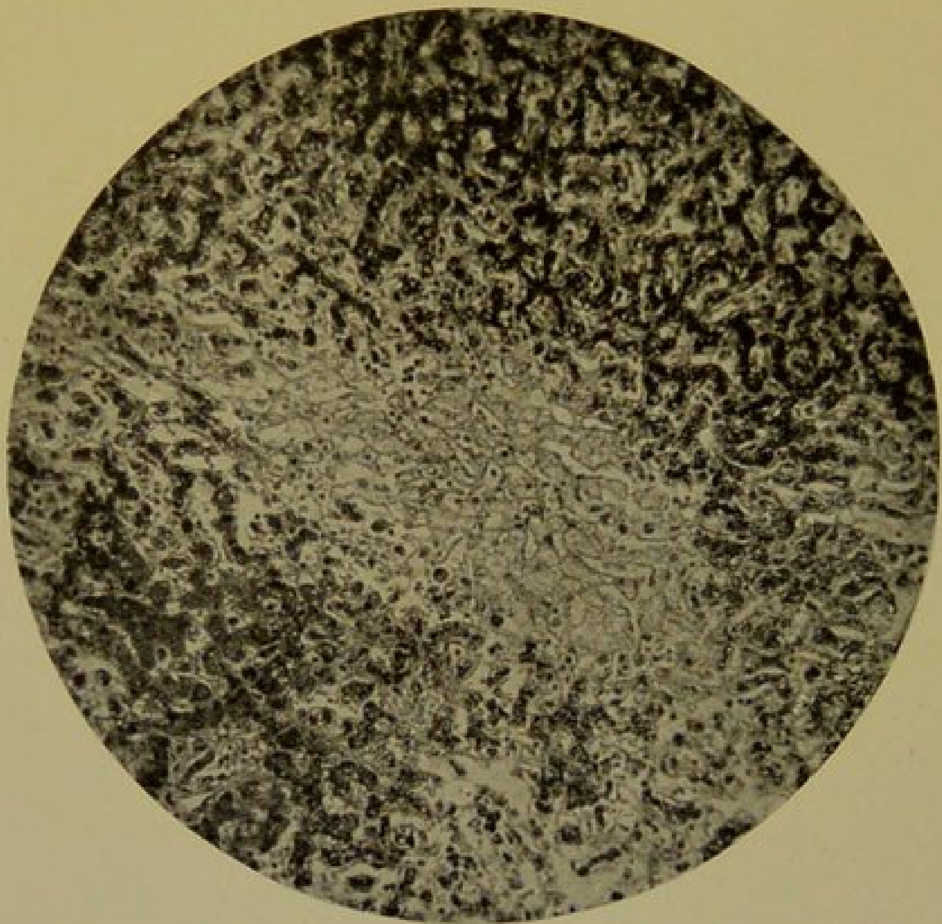

Figure 6. Section of liver from a case of acute beriberi, showing fatty degeneration and necrosis in the central area of the lobule. Haematoxylin and Eosin stain. [From Herzog, and plate lent through the courtesy of the Philippine Journal of Science.]

He gave a brief clinical description of each of these cases, followed by the autopsy findings, including both gross and microscopic anatomy. The gross pathology of these cases is practically the same as that described by the previous observers quoted. Dürck, however, investigated the nervous system quite minutely. He studied particularly the peripheral nerves from both extremities, the pneumogastric, and the cord, using several methods. In some cases they were preserved in Orth's fluid, from which they were transferred without washing to 70 per cent alcohol and subsequently embedded in celloidin. He used Marchi's, Weigert's and other modern methods. He says that the osmic acid methods used by almost all investigators from Baelz and Scheube down to Dansauer are primitive and only demonstrate fat, which can be found in any degeneration of the nerves from any cause; and that they do not demonstrate the essential changes, but on the contrary obscure all of these finer alterations. His book contains many excellent plates illustrating the conditions found in these cases. The changes in the peripheral nerves vary from the slightest periaxial or medullary degeneration in a few fibers up to complete destruction of the entire nerve. In these latter cases the secondary bundles consist of a mass of richly nucleated protoplasm formed entirely of the cells of Schwann. This represents a complete Wallerian degeneration, in which the nerve fiber is transformed into a cylinder containing nucleated neuroplasm. In some of his cases the pneumogastric nerve was hardly affected, while in others it showed much more advanced degeneration than was seen in the peripheral nerves of the extremities.

The spinal cord was studied in nine cases, in all of which certain changes were found. These also ranged from the slightest alterations in the finer structure of the ganglion cells up to complete symmetrical sclerosis of the columns of Goll and Burdach. Tigrolysis of the grey substance in certain ganglion cell groups could almost always be demonstrated. It is probable that tigrolysis does not indicate serious injury to these centres, since it is sometimes found in cases that have not presented the slightest sensory or motor changes. It has been thought that these tigroid bodies are a reserve food supply for the ganglion cells, and that their destruction indicates increased metabolism. Vacuoles were also demonstrated in certain ganglion cells. In the grey matter circumscribed recent haemorrhages were an almost constant finding.

In two cases diffuse areas of degeneration were observed in the white substance of the cord, and in one case the posterior columns were entirely destroyed at all levels. In one case the column of Goll alone was affected. Secondary degeneration of the columns of the cord has been observed in neuritis due to other causes, such as ergotism and pellagra. Symmetrical and continuous degeneration of the entire column of Burdach was reported by Tuczek in a case of ergotism.

Gross alterations in the heart, chiefly hypertrophy or dilatation of the ventricles, were commonly found. Histologic changes were found in seven of the eleven cases, and consisted of a degeneration of the sarcoplasm, oedematous infiltration, increase of the interstitial substance, loss of striation and numerous foci of an inflammatory infiltration. In other words, he found the changes characteristic of acute myocarditis. One case is described as follows: "The heart shows very considerable histologic changes. In the musculature of the left ventricle are numerous moderately thick foci in which the muscle fibers have entirely vanished, their place being taken by a loose cellular granulation tissue. The muscular fibers become lost gradually and their pointed ends extend into these foci, which appear to be composed of spindle formed fibroblasts and capillary sprouts mixed with lymphoid cells, plasma cells and a few leucocytes. The muscle fibers surrounding these foci are rather small, their striation almost obliterated, and their nuclei are usually too elongated or are vesicular, and their chromatin is clumped."

Dürck does not regard the changes in the voluntary muscles which he and other authors have described as at all characteristic of beriberi, since all of these changes may be seen in other spinal or neurotic myopathies.

Tsunoda, in 1909, made a study of the changes in the nervous system in 12 cases of acute and four cases of chronic beriberi. His conclusions are briefly as follows: In the acute cases there was often no change in the central nervous system; only four of the 12 cases showed very slight changes. On the other hand, in the chronic cases the changes are practically constant. The cord and brain in acute cases often showed venous hyperaemia and oedema of subdural and subarachnoidal spaces. One case of acute kakke showed a bilateral ascending degeneration of the posterior columns of the cord, and in three other cases there was only simple nerve degeneration in both anterior and posterior roots. The remaining three cases were free from degeneration. At times tigrolysis of the cell bodies and pyknosis of nuclei were found in ganglion cells in posterior roots. In a few cases the ganglion cells of the anterior horn were also affected. In the first case the ascending degeneration was traced through the funiculus cuneatus and gracilis on to the pons. The vagus nucleus in a few cases showed slight degeneration of the nerve cells.

The changes in the nerve fibers of the posterior columns were first vacuolation and the formation of foam structure by fatty or hyaline degeneration of the medullary sheath, then splitting, clump formation or segmentation. In later stages a great part of the medulla was chemically altered and absorbed. The axis cylinders are part intact, and part were dissolved in the fluid medullary substance; sometimes they showed a coiled appearance or were fallen into fragments. Sometimes the nuclei of the neurilemma were swollen. A multiplication of these nuclei, such as is seen in inflammatory changes, was not observed.

In most cases leucocytes and round cells were found infiltrating the perineural tissue.

Brain. Venous hyperaemia of the membrances, anaemia and at times oedema of the brain, with slight increase in the cerebro-spinal fluid. Microscopic investigation showed nothing abnormal.

Peripheral Nerves. Showed more or less intense degeneration, *which did not correspond to the intensity of the clinical symptoms.* This finding agrees with the observations of Pekelharing and Winkler and Yamagiwa. *In acute cases* they showed most severe changes, but the cord seldom showed any alteration.

On the other hand, in chronic kakke there were great changes in the cord. Macroscopically there is truly no change, but microscopically the changes are apparent. In the four cases of chronic kakke I observed each time a degeneration and atrophy of the posterior columns at different levels, and also a degeneration and atrophy of the nerve fibers of both anterior and posterior roots. In all cases the posterior spinal ganglion was affected; the nerve cells showed atrophy, tigrolysis, pigmentation and pyknosis of the nuclei. The nerve cells of the anterior horn are similarly altered. The vagus nucleus showed slight degeneration in one case. The changes in the nerve fibers of the posterior column were as follows: Vacuolation, globulation or segmentation of the medullary substance, of which a great part was chemically altered and absorbed. Axis cylinders were either swollen or atrophied, with coiling, segmentation and solution. Leucocytes were usually absent from the perineural tissue. Neither macroscopic nor microscopic changes were found in the brain.

The peripheral nerves showed considerable change in all cases, like those described for acute kakke, but the changes were more advanced and intense, so that most fibers were destroyed. Scheube and Baelz have held that the changes in the nerves were inflammatory in character, but Tsunoda holds that there was no evidence of inflammation. All changes were degenerative in character or a regressive metamorphosis.

The above account contains the known facts with regard to the pathological anatomy of beriberi. It is evident that the essential changes fall into three groups, as follows:

1. Changes in the nervous system.
2. Changes in the heart.
3. Anasarca and effusions.

The relation of these changes to each other and to the cause of beriberi are still more or less a matter of speculation. This subject will be discussed in Chapter XV.

CHAPTER IV

THE SYMPTOMATOLOGY OF BERIBERI

As we have already seen, many of the older authors considered that the disease which we now call beriberi in reality consisted of two diseases, barbiers (dry beriberi) and beriberi (wet beriberi), but that since the time of Malcolmson (1835) it has been generally accepted that these are simply different manifestations of the same disease, beriberi.

But as there is no disease more variable than beriberi as regards its course, duration and termination, it has been customary in clinical descriptions to divide the disease into a number of forms or types, giving a picture of each. Thus Manson, though believing in the essential unity of the disease, describes the "dry," "wet" and mixed types. Castellani describes three types, the acute pernicious form, the typical form and the rudimentary form, in which the symptoms are so slight that the patient is indifferent to or unconscious of them. Scheube depicts four types, the rudimentary form, the atrophic form, the dropsical or moist form, the acute pernicious or cardiac form, and similar classifications have been used by other writers. Grimm describes two forms of beriberi, beriberi simplex, which, according to his belief, is caused by a single dose of the toxin, and beriberi multiplicatum or accumulatum, which is caused by repeated infections with the toxin. Yamagiwa distinguishes three forms, the cardiac form (acute), the nervous muscular form (subacute or chronic) and the renal form (wet beriberi). According to his theory beriberi is caused by a toxin which causes the arterioles to contract. The particular form of the disease depends upon whether the arterioles of the lungs, of the peripheral nerves and muscles or of the kidneys are chiefly affected.

A convulsive form and an adipose form have also been described. It is unusual for beriberi patients to have convulsions, but they may sometimes occur, in which case they are possibly caused by the oedema of the brain. The adipose form is probably non-existent. Thus we see that the number of types or forms described have been unnecessarily multiplied, partly in order to depict the variable and shifting picture of different cases, and partly in order to fit different theories as to its causation.

None of these descriptive classifications are strictly accurate. The case which apparently belongs in the rudimentary or undeveloped type may suddenly surprise us by developing cardiac symptoms and dying suddenly. Thus soldiers and prisoners have died while apparently in good condition and performing their usual duties. Again, cases of moderate severity belonging to the dry or wet types, who are under treatment in hospitals and apparently progressing favorably, may suddenly sit up in bed and die most unexpectedly of cardiac failure after a few minutes' struggle. This tendency to acute cardiac insufficiency may be said to occur occasionally in all types of the disease. The description of an acute pernicious or cardiac type can therefore hardly be justified.

The rudimentary form may remain in this incompletely developed condition for months or even years. Cases have been seen that have presented a little anaesthesia over the tibiae and a partial loss of reflexes for several years without material change in their condition.* On the other hand, this so-called rudimentary form may sometimes merely represent the onset of the disease in one of its more serious forms, so that it can hardly be considered to be a separate type of the disease.

Further, there is often no essential difference in the symptomatology or pathology of the dry or atrophic form and in the wet or dropsical form, except for the anasarca in the latter condition. The limbs of the patient suffering from "wet" beriberi may appear of normal size, or may even be swollen, yet examination after death may show that the muscles and nerves are equally atrophied in both cases. The general appearance of these two cases is so different as to justify describing a "dry" form and a "wet" form, and yet we must recognize that clinically the wet form is often simply the dry form with oedema superadded, and furthermore, that the wet form may become transposed into the dry form in certain cases by the simple process of dissipation of the marked oedema by means of increased urination, and that the dry form may at any time become wet.

This, however, might well be the case if in reality there were two diseases, dry beriberi and wet beriberi, which often coexist in varying degrees in the same patient. As will be seen in a later chapter, the writer is inclined to believe with the older authors that dry and wet beriberi are separate diseases. Yet, even if this is correct, it is also true that they are so constantly associated as to make it advisable to

* Such a history has been obtained from several mothers who have repeatedly lost their children from infantile beriberi.

consider both diseases together. Since, therefore, all divisions of the disease into types or forms are more or less questionable and misleading, we prefer to simply describe beriberi as one disease.

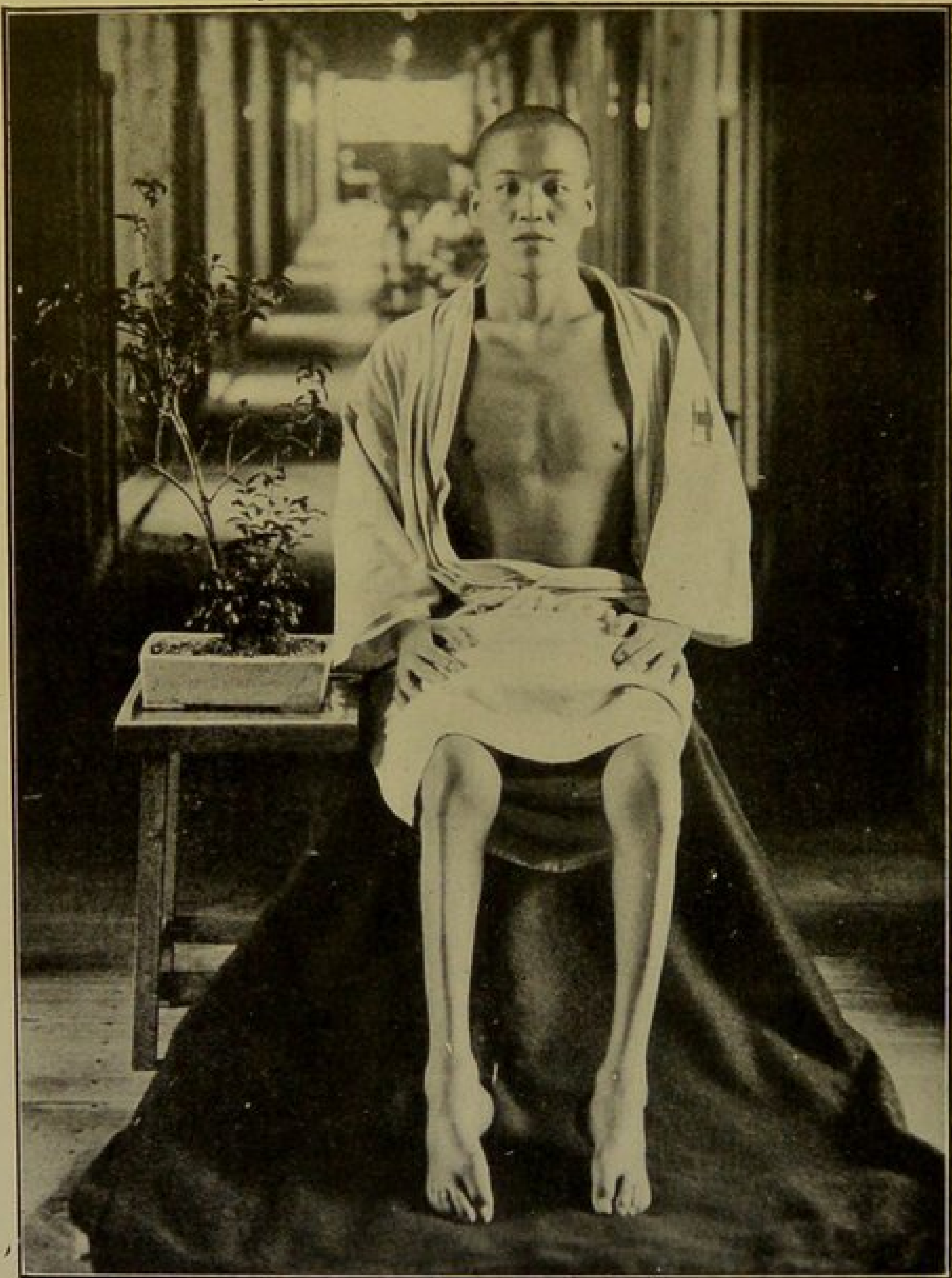

Figure 7. Dry beriberi, showing advanced atrophy of muscles of legs. [From Herzog, and plate lent through the courtesy of the Philippine Journal of Science.]

Beriberi frequently begins gradually, so that for several days or weeks the patient experiences an ill-defined malaise, associated with heaviness and weakness of the legs. In some cases there is a little fever, but this is by no means characteristic, and is quite possibly caused by a concomitant cold in the head, a slight attack of gastro enteritis or other similar complication. Because of this weakness of the legs there is an indisposition to walk far. The legs are stiff and numb, particularly in the calves. There may be a little oedema of the legs or face, and the patient is quite likely to complain of pain or oppression in the epigastrium and of palpitation of the heart. The patient may continue in this condition for months or even years, with periods of slight improvement or exacerbation of these symptoms, but without material change. Such cases have been called the rudimentary, incomplete or larval type of the disease. As a matter of fact, however, it is simply a very mild case of chronic beriberi, since it differs from the more serious cases solely in the mildness of the symptoms exhibited. Every grade of intensity of the disease may exist, some of these rudimentary cases showing nothing more than a trifling anaesthesia of the skin of the legs and a little muscular weakness. Should the disease become progressively worse, however, all these symptoms become accentuated, so that what was previously only a little numbness and weakness of the legs now becomes positive pain, especially if the affected muscles are squeezed. Anaesthesia becomes almost complete, the muscles shrink and waste away and the gait becomes markedly altered as the result of the muscular weakness. The legs are almost invariably affected first, but as the disease progresses the arms become involved in the same manner until in the severest cases the patient cannot perform the movements necessary to ordinary life, such as feeding and dressing himself. In this condition the patient lies on a bed, shrunken almost to a skeleton and quite helpless. This is the picture of the atrophic form or dry beriberi. (See figure 7.)

In other cases, while there is marked loss of power in the limbs and varying grades of anaesthesia, and other symptoms indicating that peripheral neuritis exists, the patient never becomes actually bedridden. Some of these cases may develop such marked general anasarca as to resemble an advanced form of kidney disease, but if the urine is examined it will usually be found to be normal in quality, though diminished in quantity. This corresponds to what is described as dropsical, wet or hydro-atrophic beriberi. (See figures 8 and 9.) In any of these cases the cardiac symptoms may be so slight as to be unnoticed, or they may be severe and may end in sudden death directly due to cardiac insufficiency.

In such cases the cardiac and pulmonary symptoms are so accentuated as to mask the rest of the clinical picture. There is probably

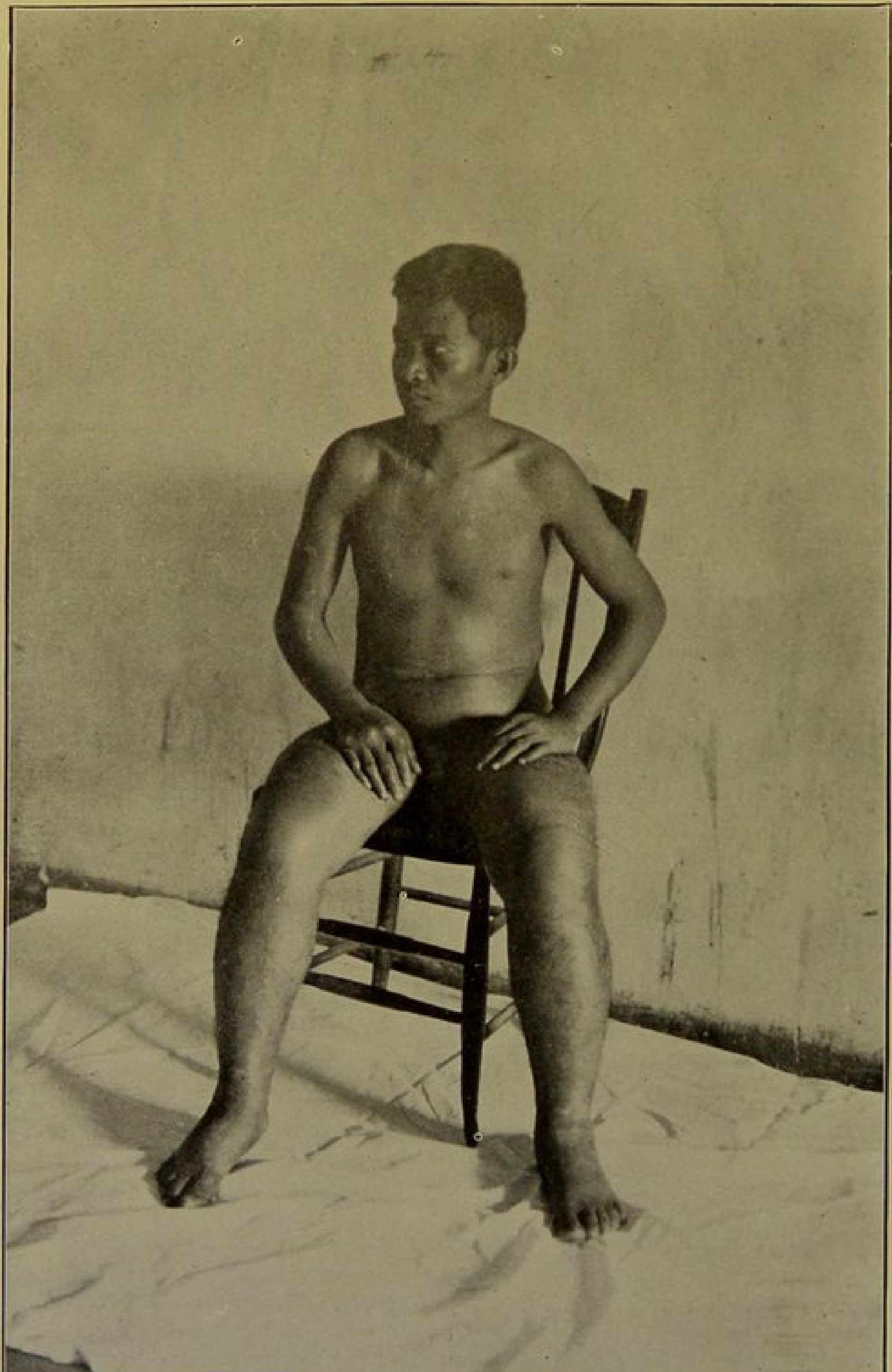

Figure 8. Acute wet beriberi. Great oedema of legs and feet. [From Herzog, plate lent through the courtesy of the Philippine Journal of Science.]

almost always some weakness of the muscles of the legs, loss of sensation, particularly over the tibiae, some pain in the affected muscles and a partial loss of the patellar reflexes, and frequently some oedema, but these symptoms may be overlooked because of the severe dyspnoea, palpitation and precordial distress. It is quite possible on theoretical grounds that these cases may exist without any sensory or motor disturbances in the limbs, and such cases have been reported. But it is believed that such cases are the exception, and that examination will

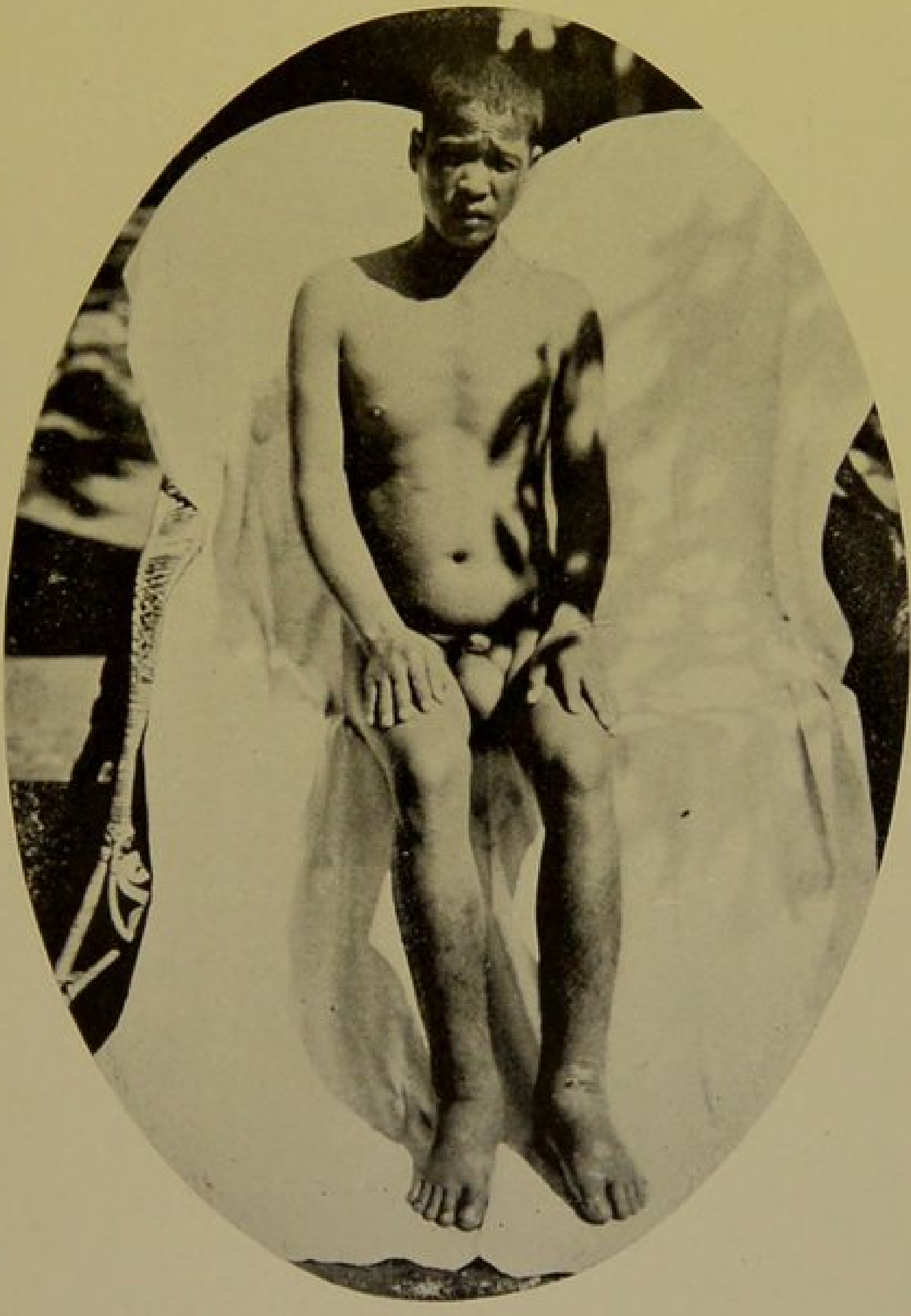

Figure 9. Chronic wet beriberi, showing oedema of legs and dorsum of foot. [From Herzog, plate lent through the courtesy of the Philippine Journal of Science.]

generally reveal some evidence of neuritis of the limbs. The dyspnoea, cardiac pain and the palpitation gradually or suddenly increase until the patient is evidently suffering from such a paroxysm that even the casual observer would recognize the fact that he is in extremis. Percussion and auscultation show that the right heart is dilated. The

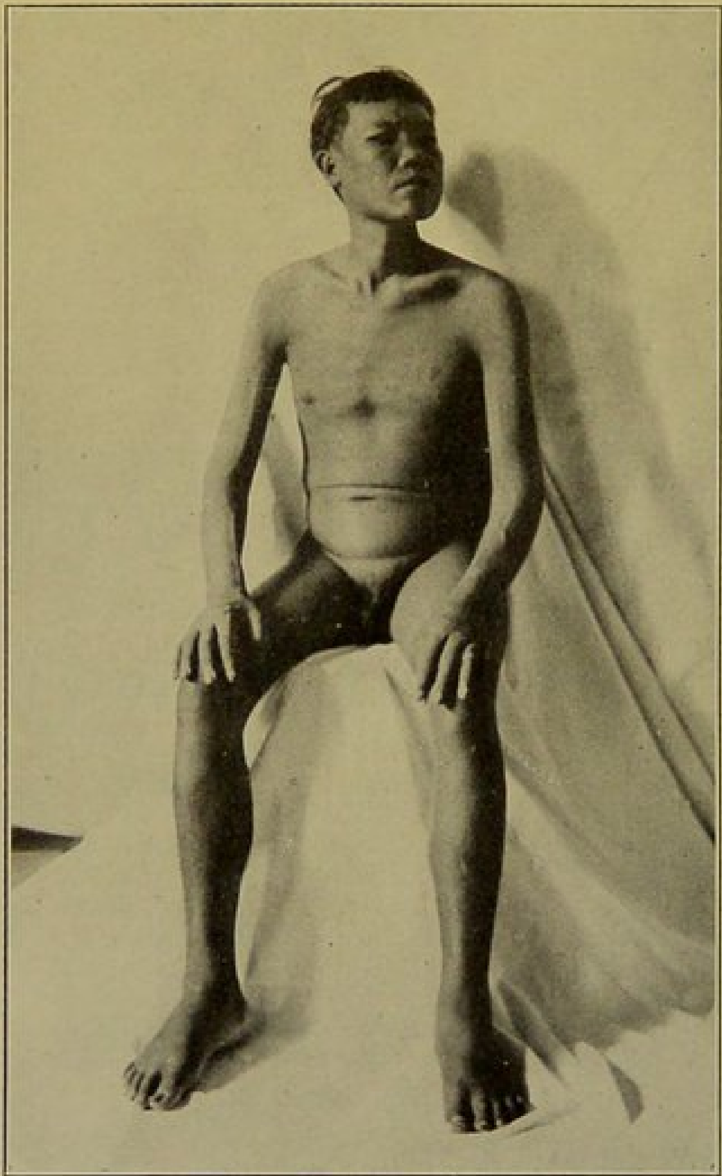

Figure 10. A case of so-called "mixed beriberi," showing atrophy of muscles of arms. Atrophy of muscles of legs partially masked by oedema.

pulse becomes small, the cervical vessels throb, the face becomes cyanosed, and the body becomes cold. Although gasping for breath and suffering the most intense precordial pain, consciousness is not lost until a few moments before death cuts the agony short. This is the usual termination of such a paroxysm. If the patient should recover from such an attack, or in those cases where such an acute paroxysm has not developed, vomiting may occur, the appetite is lost, the bowels may be constipated, the urine much diminished in amount and thirst may be added to the symptoms. But the dyspnoea and the cardiac insufficiency continue until in a few hours, a few days, or several weeks, another paroxysm occurs. These acute cardiac cases are almost always fatal, but fortunately comprise only a small proportion of the cases of beriberi. It should not be forgotten, however, that such an acute cardiac seizure is liable to occur in any case of beriberi at almost any time, and that this constitutes its main danger.

In those cases in which oedema occurs the amount and location of the oedema also varies greatly, in some cases being so slight as to be scarcely noticeable, and being limited to slight puffiness over the ankles or in the face. Between this condition and general anasarca all intermediate grades exist. In many cases in which this anasarca is pronounced the neuritic changes are slight or may be absent altogether.

The above description might lead the reader to suppose that, aside from the development of cardiac crises, the disease is quite chronic. This, indeed, is usually the method of onset, but cases which develop dropsy or paralysis very suddenly are by no means unknown. This sudden appearance of "wet" beriberi is particularly common in women during pregnancy or the puerperium, when it must be carefully distinguished from cases of renal insufficiency.

The fact that chronic cases may suddenly take on an acute aspect has been sufficiently emphasized. It should also be remembered that in certain instances the atrophic form of beriberi may be quite acute. Thus H. Wright records a case (Brit. Med. Journ., 1901, i, 1611) in which loss of power in the hands and feet appeared within fifteen days after the first symptom, consisting of slight numbness, was noticed, and the patient became paralyzed and died 23 days after the first symptoms appeared.

A most excellent conception of the disease is therefore gained by recognizing that beriberi is a composite of three main sets of symptoms:

1. The symptoms of peripheral neuritis.
2. Cardiac insufficiency.
3. A generalized tendency to oedema.

The type or variety of the disease as observed in a specific case depends simply upon the manner and intensity with which these sets of symptoms are blended together.

As the preceding description of the disease is necessarily incomplete, we shall endeavor to fill in the gaps by a discussion of the individual symptoms. Like alcoholic and diphtheritic neuritis, in beriberi there is a tendency for certain nerves to become involved rather than others, and the clinical picture of the disease will depend largely upon which set of nerves is involved to the greatest extent. There are certain symptoms commonly associated with peripheral neuritis affecting the nerves of the extremities, among which motor disturbances and sensory disturbances are most common.

Motor Disturbances. These are chiefly caused by degeneration and paralysis of the muscles as a direct result of the neuritis. The kind and degree of disturbance depend upon the muscles attacked and the extent of the involvement. All the muscles of a limb are not affected, a special predilection being shown for certain muscles. The extensors of the foot or those muscles supplied by the anterior tibial and peroneal nerves are usually the first to suffer, followed by the muscles of the calf, the extensors of the leg, the glutei, and flexors of the leg. When the arms become affected they are attacked in a similar order, the extensors of the hand being affected first. Finally, in the severe cases, the abdominal muscles, the intercostals, the diaphragm and the muscles of the larynx become affected. The sphincters apparently are never involved. The paralysis of these muscles is accompanied by prompt, rapid and extensive wasting, which is often readily apparent when not masked by oedema, and has caused these cases to be classed as "atrophic." All degrees of muscular paralysis are encountered, in the mild cases being so slight as to amount to little more than weariness on walking and diminution in strength as shown by the dynamometer, while in the severest cases the patient lies on his back completely paralyzed.

Gait. The gait of beriberi has been described as characteristic by several observers, and has been compared to the walk of a person emerging from the water with wet clothes on, or to the walk of a person in stiff clay. These descriptions are more or less fanciful, and it is probable that there is no characteristic gait, other than the gait that may be seen in any case of peripheral neuritis, and that this is more or less modified in each case, depending upon which muscles are attacked. In mild forms, where the extensors alone are involved and there is toe drop, the resultant effort to raise the foot sufficiently high, and to slap it down in order to avoid scraping the ground with the toe, may attract immediate attention to its peculiarity. But in more severe cases, where the flexors of the foot are also involved, the gait is little more than a shuffle.

Ataxia. It is generally stated that true ataxia does not occur in beriberi. It certainly is not usually present, although there may be marked instability. This is chiefly caused by muscular weakness and not by incoordination. However, in this connection it is interesting to note that Dürck found extensive degeneration in the columns of Goll and Burdach in one of his cases. With the cord so diseased, we should naturally expect to find true ataxia. The possibility of the coexistence of tabes dorsalis and beriberi in this case should not be overlooked, but it seems that true ataxia may possibly be found in exceptional cases where the degenerative process has chiefly affected the posterior columns.

Spasticity. A condition described by almost all observers is the spastic contraction of the affected muscles during convalescence, resulting in a gait resembling that of spastic spinal paralysis. This is interesting in connection with the exceedingly spastic gait observed in fowls that are recovering from polyneuritis gallinarum. The cause of this spasticity is obscure.

Contractions of the muscles, particularly of the calves, may occur, and may result in prolonged disability. Painful cramps, tonic convulsions and fibrillary muscular twitching have been observed in numerous cases.

Electrical Reactions. It is said that the response to both direct and indirect galvanic stimulation is diminished in the affected muscles, and the normal reaction returns very slowly during convalescence. The reaction to the faradic current is even more promptly lost, and returns still more slowly. Pekelharing and Winkler thought that this loss of electrical excitability was the earliest objective sign of beriberi, appearing before the ordinary sensory and motor disturbances, but other observers, such as Eijkmann and Glogner, have failed to find this condition even in advanced cases.

Reflexes. The deep or muscular reflexes are very generally diminished or lost, and such alteration in the patellar reflex is probably a very valuable sign of early or so-called rudimentary beriberi. The knee jerk may be completely lost in cases which at the time of examination present practically no other symptoms, and which cannot be diagnosed as beriberi at this time, but only after the appearance of other symptoms. This symptom, therefore, appears early and disappears very slowly months after convalescence is apparently complete. I have also seen cases in which the knee jerk in one leg was completely gone, while it was only slightly diminished in the other leg. On the other hand, exaggerated knee jerk has been reported by Pekelharing and Winkler, Grimm, Miura and others in the early stages of the disease. This symptom, which Grimm considers characteristic, appears very early, and is succeeded in about a week by the diminution of the reflex described above. Since it is only supposed to be present during the first week or so of the disease, and since natives of their own will rarely consult a physician so promptly, it may be that this temporary increase in the reflexes, while very common, is rarely observed for this reason. The superficial or skin reflexes are usually normal.

Sensory Disturbances. Anaesthesia. The sensory changes may precede or follow the motor disturbances, but are usually more or less concomitant. Chief and most constant among these is anaesthesia. I have seen a rough estimate made of the number of prisoners suffering from beriberi by simply testing for anaesthesia over the tibiae with a pin. In an institution where beriberi is prevalent it is susprising how many otherwise healthy individuals will show this anaesthesia, and careful search will almost always show other slight alterations showing that such patients truly have "rudimentary" beriberi, as mild chronic beriberi has been called. This anaesthesia may be partial or may be complete, so that a patient can be prodded until the blood runs without apparently being conscious that he was touched, but more often sensation is only diminished to a slight degree. In such cases also the response to the touch of a pin is generally very much delayed. The area of anaesthesia may be more or less sharply circumscribed or may be rather vague. It generally begins over the tibiae and spreads over the inner surface of the legs and calves and on the dorsum of the foot. The arms are affected later, as is the case with the motor paralysis, the fingers and extensor surfaces or forearm being the first to lose their sensitiveness. Later the trunk, neck and face may be attacked. Observers in Japan describe a circle of anaesthesia around the mouth. Perception of heat, cold and painful stimulation are all diminished in these anaesthetic areas.

Hyperaesthesia of the skin has been observed by Scheube, but is rarely seen. On the other hand, hyperaesthesia of the muscles is very common, being present to a greater or less degree in almost all cases. This pain is generally described as dull and aching, but it may also be sharp, cutting, dragging or even burning pain. This painful condition of the muscles is always accentuated by pressure, as a result of which the patient instinctively avoids having his limbs handled. The muscles most frequently affected are those of the calves, and later those of the forearm, but pain may also be present in the abdominal and other muscles of the body. The pain is worse at night and on damp, rainy days. Bentley says that girdle pain is sometimes seen, when the patient complains of a tightness in the abdomen around the loins. Pain in the calves and an indisposition to permit these muscles to be squeezed is quite a general symptom, and of practical importance in making a diagnosis.

Paraesthesia is also very common, and is manifested in many different ways. Thus some patients complain of a sensation of pins and needles or numbness, while others may describe formication or itching. Rubbing the skin gently may cause a sensation of heat; sensation is often delayed, and may be referred to a location quite different from the point of contact. Like other symptoms, these paraesthesias are observed more frequently in the legs, and may be increased on moist or cold days.

Vaso-motor Symptoms. The Heart. Cardiac symptoms are almost always present at some time during the disease in every case. Of these palpitation of the heart is most common and annoying. It may be constant or may appear after exercise or at night, and may be slight or it may be severe, and accompanied with such oppression and dyspnoea as to threaten impending death. Dull pains may also occur about the heart, with a sense of fullness in the epigastrium. It is hard to determine how much of this fullness is cardiac and how much is stomachic. This palpitation is usually the result of an actual increase in the action of the heart, which is accompanied by visible pulsation of the vessels of the neck and of the precordial and upper abdominal regions, although the amount of work performed by the heart may be diminished at these times, since the pulse is small and thready and the circulation poor. An examination of the heart at such times will usually show that the right auricle and ventricle are both enormously hypertrophied or dilated, probably both. This may also be observed in many cases in which the cardiac symptoms are not so prominent. The increased size may be readily demonstrated by percussion and by the downward and outward displacement of the apex beat, and it may also be inferred from the sounds of the heart, which are many times louder than normal. The second sound of the heart over the pulmonic area is particularly loud and sharp, and may be reduplicated. Murmurs may or may not be heard, and when present are usually systolic. They are not at all characteristic, and the enlargement and increased cardiac action is not due to any stenosis or insufficiency of the valves, since the post-mortem examination of these cases reveals a total absence of such conditions.

The pulse is variously described by different authors. After checking these descriptions by personal observation, it appears probable that there is no quality of the pulse which is distinctive of beriberi, but that it varies in different cases, and in the same case depending upon the condition of the heart. It is generally small and easily compressible, may even be thready, and is frequently irregular. It may sometimes be slowed, but is more often quite rapid, running from 100 in ordinary cases up to an absolutely uncountable pulse during severe cardiac seizures. Accompanying these circulatory disturbances are the symptoms we should expect, namely, general pallor, coldness of the extremities and a continual sensitiveness to cold in milder cases, while cyanosis of the face is apt to be particularly marked during cardiac seizures. Petechial haemorrhages under the skin and mucous membranes have been described a number of times as a post-mortem observation, but are rarely seen during life.

Fever. Beriberi is not a febrile disease. It occurs in some cases, never being very high or characteristic in any way. Bentley states that in none of his cases could an onset of acute symptoms have been foretold from the temperature chart. Scheube states that the fever is often accompanied by catarrhal symptoms. Since beriberi is a chronic disease, usually lasting for months or even years, there is every reason to suppose that its victims may occasionally suffer from mild or severe intercurrent infections, including colds, bronchitis, diarrhoeal diseases, etc., and that the temperature observed is due to the intercurrent infections, and is in no way the result of beriberi or characteristic of it.

Oedema and the serous effusions. One of the cardinal symptoms of beriberi is the pronounced tendency toward the accumulation of watery exudations or transudates. It is not seen in all cases, being absent in the so-called dry form, although some of these dry cases may have presented oedema during the earlier course of the disease. This tendency is manifested in subcutaneous accumulations or oedema, and as collections of fluid in the serous cavities, in the ventricles and meninges of the brain, and particularly in the fatal cases, as oedema of the lungs.

Oedema. This generally appears after the alterations in the peripheral nerves have become perceptible, but it is also in many cases a fairly early symptom. It frequently first appears on the dorsum of the feet and gradually extends up the leg. It may also appear on the backs of the hands, or in puffiness of the face. These are the commoner locations when the oedema is local, but there are many cases in which it is general, thereby masking the actual atrophy that has taken place, and these cases impress the casual observer as being plump and well fed. The oedema may progress beyond this stage until it is fully as intense as the most pronounced oedema ever seen in advanced nephritis, and involves every part of the body. We shall never entirely understand beriberi until we know the reason for these effusions in some cases and their absence in others.

Hydropericardium is the commonest of the effusions into the serous cavities. Thus, in 256 collected cases that have come to autopsy hydropericardium was present in 66 per cent. This effusion is hardly large enough in amount to cause much embarrassment in most cases. It is difficult to diagnose with certainty because of the enlargement of the right side of the heart which is so common.

Hydrothorax is not quite so common as hydropericardium, but is very serious when it does occur, since the amount of fluid is generally considerable, and constitutes a grave danger because the lungs are already overburdened and probably water-logged, and the hydrothorax may be the last straw to cause a pulmonary breakdown. It may be detected by the same signs as hydrothorax in any other condition, and should be promptly relieved by tapping.

Ascites. True ascites, or the accumulation of a sufficient quantity of fluid in the peritoneal cavity to cause distention or pressure, is quite rare, but hardly a case comes to autopsy that does not present some increase in the amount of peritoneal fluid.

Oedema of the Lungs is common in the so-called wet form, and is often the immediate cause of death. It is marked by cough, a watery sputum and increased dyspnoea and moist rales.

Oedema of the Meninges of the cord and brain may be observed at autopsy, but is extremely difficult to detect during life. The same is true of the hydrops of the ventricles found at autopsy. It is possible that the convulsions which are sometimes reported as occurring in beriberi cases are directly due to the pressure of these accumulations of fluid. Fortunately such hydrops, although probably generally present, since it is often found at autopsy, is not usually of sufficient amount to cause the symptoms of pressure.

The Blood. Observations on the blood have played quite a part in the study of the etiology of beriberi. Thus beriberi has been considered to be due to pernicious anaemia. The disease has been called acute anaemia of Ceylon or acute anaemic dropsy (ankylostomiasis?), and Sir Joseph Fayrer, in his article on beriberi in Quain's dictionary of medicine, says that in Europe pernicious anaemia is probably the same disease. Further observations, however, have shown that the red corpuscles are not noticeably diminished beyond the moderate amount that would be expected in any serious disease. The haemoglobin is likewise moderately, but not seriously, reduced.

Leucocytes. The results obtained by different observers vary. Thus, Bezancon and Labbe found that the percentage of the different white cells was normal. Takasu examined the blood of a number of cases in the hospital at Osaka, and found that the number of lymphocytes was increased and almost always exceeded the number of polymorphonuclear neutrophiles. The eosinophiles were not increased, being less than two per cent. Hunter and Koch, on the contrary, found an eosinophilia. They do not give the actual counts, but state that the eosinophiles are usually twice the usual number. Noc also found a relative increase in the eosinophiles, particularly in the wet form of the disease. However, of 20 prisoners that he observed for some time the eosinophile count fell from their usual 12 per cent to eight per cent when they contracted beriberi, and in another series the eosinophiles increased, when the patients were cured, from 11 per cent to 18 per cent. It seems probable that this eosinophilia was due in both instances to the presence of intestinal parasites. Brau claims to have proved that in undoubted cases of beriberi the mononuclear leucocytes exceed the polynuclear lymphocytes, and in severe cases an eosinophilia of four to six per cent exists. Saltet and Legrand, during an epidemic at Casablanca, found the mononuclears to be 40 to 45 per cent and the eosinophiles four to five per cent. Salanoue says there is no change in the blood picture in beriberi, and that the alleged eosinophilia is due to the presence of intestinal parasites. A. Leger studied the leucocytes in 31 cases in Madagascar, and found that in the beginning of the disease the polymorphonuclear neutrophiles were increased, but that during convalescence, or in chronic cases, that there was a more or less marked increase in lymphocytes. Eosinophilia was inconstant and associated with intestinal parasites. Mouzels found the leucocyte count to be normal. The proportion of eosinophiles was the same as observed in other natives infested with parasites. C. Mathis and M. Leger studied the leucocytes in 40 undoubted cases of beriberi. They conclude: (1) There is never an increase in polymorphonuclear neutrophiles. Out of forty counts they were normal six times (65 to 69 per cent), diminished 34 times (64 to 44.33 per cent). The average percentage was 57. (2) Lymphocytosis is obvious, and the number of lymphocytes sometimes exceeds the polymorphonuclear leucocytes. The average count was 36 per cent. (3) Large mononuclears varied from 1.66 to 11.33, with an average of four per cent. (4) The eosinophiles were appreciably reduced in number. They found the average in the forty cases to be 1.8 per cent, in spite of the fact that almost every case harbored some form of parasite. Mathis and Leger also studied the Arneth count in 17 of their cases, and found that there was a very pronounced shift to the right. The neutrophiles of the last two classes with four or five nuclei comprise 34 per cent of the total number, while in healthy individuals they found only 19 per cent in these classes. They conclude that it is difficult to draw any definite conclusions from this shift to the right except that it is permissible to believe that *beriberi is not an acute bacterial infection.*

In the interpretation of these results it should be borne in mind that Chamberlain and Vedder have found that there is a marked increase in the number of lymphocytes found in normal Filipinos over what is generally regarded as a normal count, and that normal white men living in the Philippines tend to approximate this condition. It is quite possible that this condition is general in tropical regions, and that the lymphocytosis observed by Mathis and Leger in beriberi was therefore more apparent than real. On the other hand Chamberlain and Vedder showed that the Arneth count of normal Filipinos was peculiar in that there was a very pronounced shift to the *left,* and that this condition was also slightly approximated by normal white men living in the Philippines. If this should be generally true in tropical countries it only accentuates the findings of Mathis and Leger that cases of beriberi show a shift to the *right.* It seems probable, therefore, that there is nothing characteristic in the differential leucocyte count in cases of beriberi, but that the Arneth count may be characterized by a shift to the right.

Chemical Alteration in the Blood. Manson states that the blood is said to be defective in alkalinity. Däubler found, in three patients who were convalescing from beriberi, that particles of fat were present in the blood, and these were supposed to be derived from the broken down fats of the diseased nerves. A decrease of albumen and an increase of the watery and mineral constituents of the blood has also been reported. It may be said, however, that little is known of chemical changes in the blood, and that what little is known is either unimportant or has not yet been properly co-related with the pathological process that is the cause of the disease.

The Digestive System. Digestive disturbances are common but are not characteristic. Bentley says the appetite is generally unaffected and remains good almost to the end. Manson says digestion is usually feeble. A full meal may cause distress from cardiac pressure. This is probably true in those cases where the cardiac symptoms preponderate, but in the majority of cases it appears that they are as willing to eat and as able to digest as patients suffering from any other disease. We naturally refrain from prescribing articles of diet that are notoriously difficult of digestion, and the amount of rice that they are accustomed to eat must be much curtailed, particularly if the polished variety is used. Otherwise there is little about the digestion that deserves comment. In some cases, however, vomiting occurs and is a serious symptom, since it usually indicates the onset of the disease in acute form, and in these cases the stomach must be most considerately treated. Diarrhoea and constipation both occur, but the latter is by far the commoner and most characteristic.

The Respiratory System. We have already referred to oedema of the lungs. Another important symptom that occurs more or less frequently is aphonia. This is usually only seen in advanced cases, and is probably due to paralysis of the muscles of the larynx which are supplied by the pneumogastric nerve. It is a very serious symptom and usually means impending death, either because it happens to be one of the last symptoms to develop as the disease progresses, or because such extensive involvement of the pneumogastric must necessarily incapacitate the heart, which it also innervates.

Urinary System. The autopsy frequently shows a more or less intense congestion of the kidneys, almost merging into inflammation. As a result we find that the quantity of urine is generally diminished, and in acute cases the urine may be completely suppressed for several days before death. Scheube reports that the specific gravity is diminished and that the secretion of urea, uric acid and phosphoric acid is also decreased. It has been noted that patients affected with the "wet form" may on occasions pass large quantities of urine, a process associated with the resorption of the dropsical effusions. The cause of this phenomenon is as obscure as the cause of the oedema and probably connected with it. Sugar is not found in the urine and albumen occurs only rarely and in small quantities, probably corresponding to those cases in which the congestion of the kidneys has changed to active inflammation.

Sexual organs present nothing of interest except that it has been reported that beriberic women cease to menstruate, and that this function returns after convalescence.

Differential Diagnosis. While beriberi is generally easily recognized, individual cases sometimes present great difficulties, especially when there is no oedema and the heart is little affected. Such cases resemble the common peripheral neuritides. The following distinctions may be of help in making the diagnosis:

1. ALCOHOLIC NEURITIS.	A history of alcoholism. General tremulousness and mental disturbances are common. The class of people who are rice eaters and subject to beriberi are seldom drinkers.
2. ARSENICAL NEURITIS.	A history of the medicinal use of arsenic, or of some occupation involving the use of arsenic. Many cases have occurred in beer drinkers. Symptoms of arsenical poisoning, including diarrhoea, abdominal pains, cutaneous pigmentation and puffiness of the eyelid may be present.
3. LEAD PALSY.	A history showing chronic lead poisoning. Blue line on the gums, colic, basiphilic degeneration of the red blood cells, the upper limbs are most frequently affected, and those muscles most used and fatigued are most commonly affected.
4. MALARIAL NEURITIS.	A history of repeated attacks of fever, with anaemia and possibly an enlarged spleen. Parasites may be found in the blood. This form of neuritis is quite rare.
5. HEART DISEASE.	Signs of valvular disease, albumen in the urine, no paralysis and no anaesthesia.
6. BRIGHT'S DISEASE.	Indicated by albumen and casts in the urine, no loss of sensation, of reflexes, or of power of movement.
7. ANKYLOSTOMIASIS.	Severe anaemia. Perverted appetite is common. No paralysis, loss of reflexes, or anaesthesia. A high degree of eosinophilia is common, and ova can always be found in the faeces.
8. LATHYRISM.	A history of eating pulse. Knee jerks are increased. No tenderness of muscles, no paralysis, and no anaesthesia.

Mortality in Beriberi. Statistics vary greatly in different localities, and in different epidemics in the same locality. In Japan Scheube observed an average mortality of 3.7 per cent. Van der Burg stated the mortality in the Dutch Indian Army (1884–1894) averaged 4.43 per cent. Da Silva Lima stated that the mortality in Brazil was from 50.8 per cent to 74.5 per cent. In the Marine Hospital of Tokio (1874–1878) 590 cases were treated of which 5.8 per cent died. In the police hospital in Yokohoma in 1871 there were 218 cases of which 5 per cent died. Wernich reported 132 cases with 7 deaths, or a mortality of 5.3 per cent. Anderson reported 402 cases of which 89 died, or a mortality of 22.1 per cent. It is therefore apparent that the mortality from beriberi may be trifling or it may equal that of the most fatal infectious diseases. Excluding cases from hospitals, where frequently only the most serious cases come for treatment, it is estimated that beriberi has an average mortality of 5 per cent.

PLATE I

A. J. E. Terzi del.

Bale & Danielsson, L[td] lith.

TRANSVERSE SECTION OF PADI (HUSK REMOVED.)

CHAPTER V

RICE AND ITS PREPARATION FOR FOOD

In order to understand the relation existing between the various kinds of rice and beriberi, it is quite essential to have an accurate conception of the structure and chemical constitution of the rice grain, of the different methods of preparing rice for food, and a clear understanding of the terms by which various rices have been designated by different writers.

The structure of the rice grain. A grain of rice, after removal of the husk, possesses three layers. The outer layer is very thin and has been called the pericarp or the "inner skin." The color of the pericarp varies in different species of rice from white to nearly black. The common varieties grown in the Philippines have either a yellowish white or a brick red pericarp. The middle layer has been called the sub-pericarpal or aleurone layer. It is considerably thicker than the pericarp and is composed of cells filled with aleurone and fat, and contains very few starch grains. Practically all of the fat and a great part of the albumen of the grain is confined to this middle layer. The third and innermost portion contains by far the greatest bulk of the grain, about which the two previous layers form a narrow rim or border. This innermost portion is composed of cells filled with starch granules. Although these layers have rather distinct outlines which can be readily perceived in sections, yet they are closely adherent to each other so that it is impossible to effect a perfect separation of these layers in the process of milling. Outside of the pericarp is the husk. Rice with the husk still on the grains is called "padi" or "paddy" by the Malays and "palay" by the Filipinos. (Plate IV, figure 4.) If rice grains are studied in sections,* these three layers may be clearly seen in the husked grain, and the fact that the two outside layers are almost completely lost in the steam milled rice will be observed. It will also be seen that sections of rice that has been parboiled or cured before milling also retains the greater part of these layers. (See plates I, II and III.)

* In order to study the histology of the rice grain, the following method is recommended by Fraser and Stanton:

Methods of preparing rice. 1. The Steam Mill. The following is a brief description of the details of the milling of rice as carried out in one of the largest of the English mills in Pangasinan province of the island of Luzon, P. I. (Figure 11.)

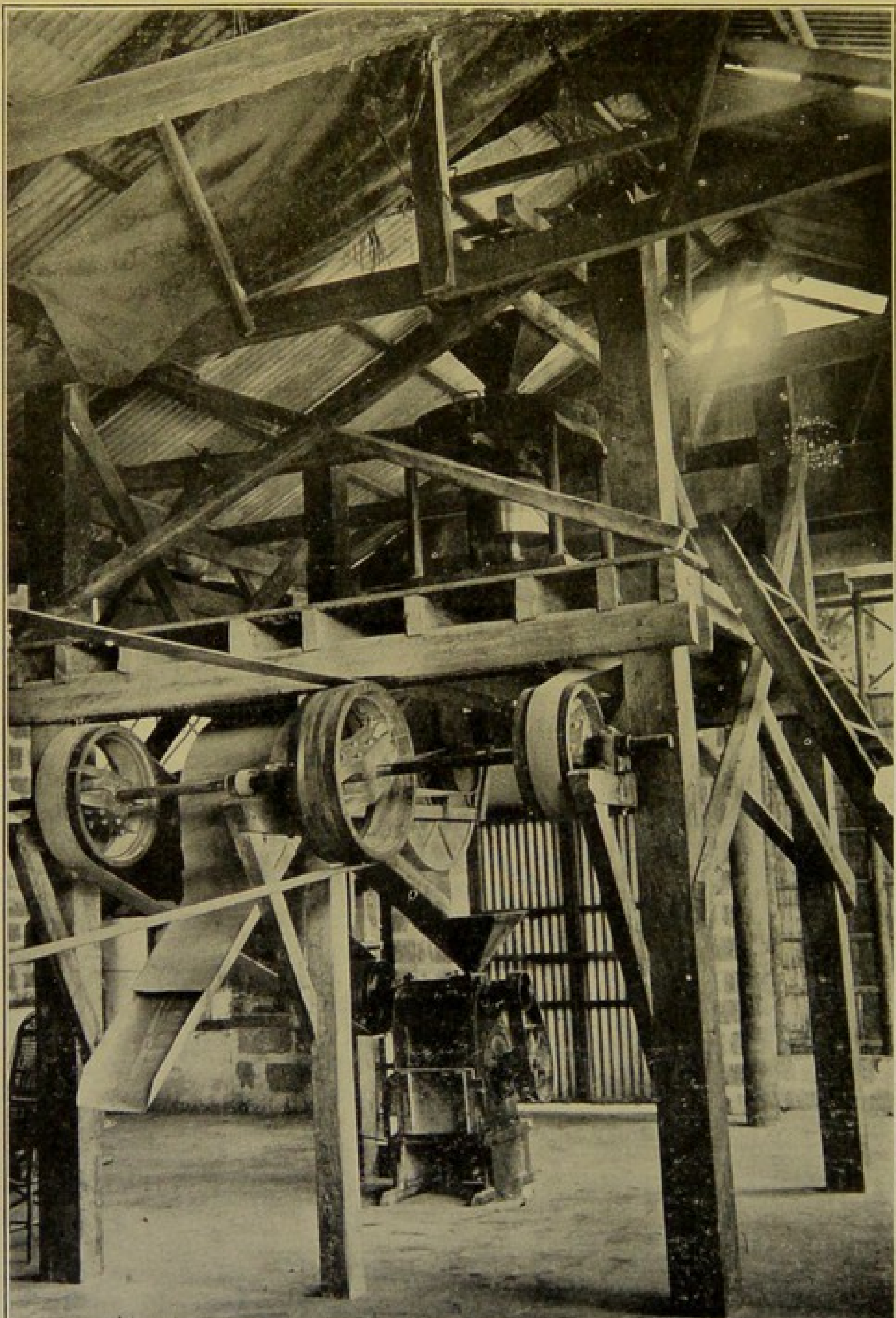

Figure 11. Interior of a steam rice mill operating in the Philippines.

The "palay," or unhusked grain, is husked between large horizontal revolving artificial stone discs, separated by a distance about equal to the length of a rice grain. The chaff is winnowed out and the husked grains separated from the unhusked by screening.

At this stage of the process only a very small part of the pericarp has been chipped off, and the grain as it comes from between the stones is called in Tagalog "pinaoa" or "pinawa." In the next process, "milling" is carried out by means of a vertical revolving conical artificial stone around which is a close fitting metal gauze case. Friction between the stone and the netting rubs off the pericarp and the aleurone layer, the degree of removal being dependent upon the distance between the netting and the stone, the speed of revolution and the length of time spent in the process. The dust escaping through the net consists of pulverized pericarp and aleurone layer, and is called "tiqui-tiqui" in the native dialect of the Philippines. It has also been called rice polishings and rice bran. In the so-called "highly milled" grades of rice, such as are commonly seen in the markets of the world, all of the pericarp and most of the aleurone layer have been removed by this process, leaving the central portion of the grain referred to above.

The last process in the treatment of rice in the mill is the polishing, which is carried on between a fixed wire screen and vertically revolving conical buffers covered with long-wooled sheep skin. This polishing process is not applied to all rices. It removes the tiqui-tiqui dust from the grain and produces a clean and shining grain.

At various stages in the process of preparing the rice it is winnowed and screened to remove dirt, dust and broken grains, and the commercial grade of the rice depends in part on the thoroughness of these steps, in part on the amount of pericarp left on the grain and in part upon the original quality of the "palay." This

The grains are softened for a month or so in a mucilage composed of

Gum acacia .... 4 parts.

Solution of carbolic acid (1-20) .... 6 parts.

The softened grains are freed from excess of mucilage and embedded in celloidin. The embedded grains are placed in alcohol (60 per cent) and after a few days are ready for cutting. The sections may be stained in anilin-gentian violet solution for from five to ten minutes after which they are freed from excess of stain and treated with Gram's iodine solution for one minute. The sections are then washed first in water and then in absolute alcohol as long as stain continues to come away. Finally they are cleared in anilin oil for five minutes and mounted in Canada balsam. The fat in the grain may be demonstrated by straining with osmic acid or Sudan III instead of the above method.

winnowing and screening, however, have no bearing upon the beriberi producing qualities of rice except for the following important consideration: According to general custom the best grade of rice is highly milled (i. e., pericarp and aleurone all removed), polished and cleaned with extreme care. The poorer grades are not milled, polished or cleaned with anything like the same care. It follows that the person who purchases rice in the open market, and desires the best grade, clean and free from bugs and weevils, will be obliged to purchase the highly milled and polished rice from which the outer layers are completely removed. From a dietetic standpoint he therefore purchases an inferior grade of rice at the highest price, and he is practically compelled to do so, because the undermilled rice from which these layers have not been removed is all of such inferior quality and so dirty that as a general thing even the poorest classes do not care to buy it. It will be seen later that this choice, highly milled rice is the rice which produces beriberi.

The native method of preparing rice in the Philippines. The palay, after it is harvested, is thrashed (figure 12), stored in a dry place and a sufficient quantity for the household is prepared every

Figure 12. Filipinos thrashing rice.

PLATE II

A. J. E. Terzi del. Bale & Danielsson, L^td lith.

TRANSVERSE SECTION WHITE (POLISHED) RICE

day. In husking the rice a wooden mortar is used, which is usually formed from the hollowed out trunk of a tree. The rice is placed in this mortar and pounded with a pestle. (Figures 13 and 14.) This latter is usually made of a smaller branch with the ends rounded

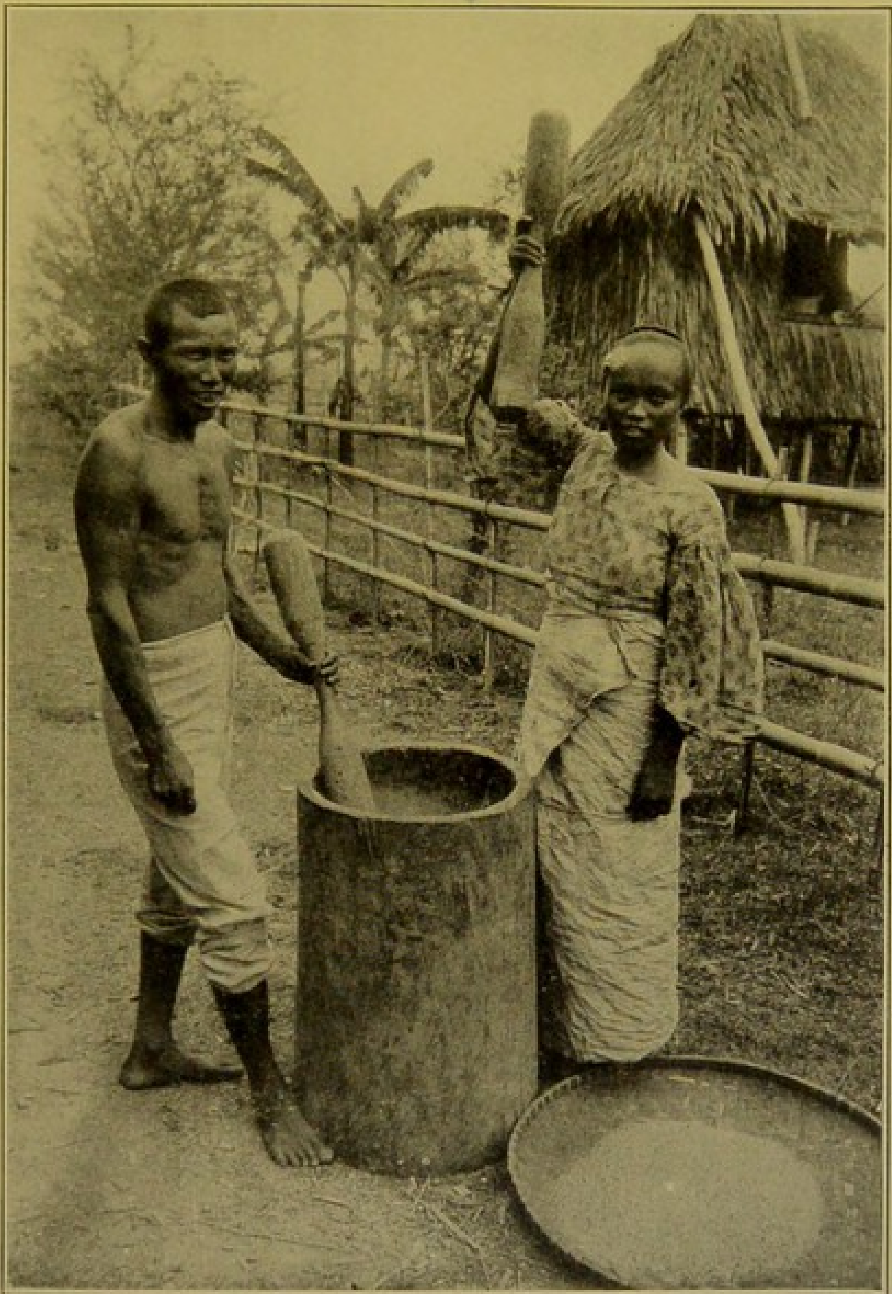

Figure 13. Native method of pounding rice in order to remove hulls. Tray for winnowing in the foreground.

off, and has a handle in the middle so that either end of the pestle can be used. This pestle is often quite heavy, and is raised slowly and allowed to fall into the mortar; the expenditure of energy is thereby curtailed, since because of the weight of the pestle it is not necessary to apply any great amount of force to the blow. After the hulls have been removed from the grain by this pounding it is placed on wide woven trays and the grain is tossed into the air. The rice falls back into the tray while the wind carries away the hulls. The natives acquire great skill in this manipulation, so that they rarely spill a

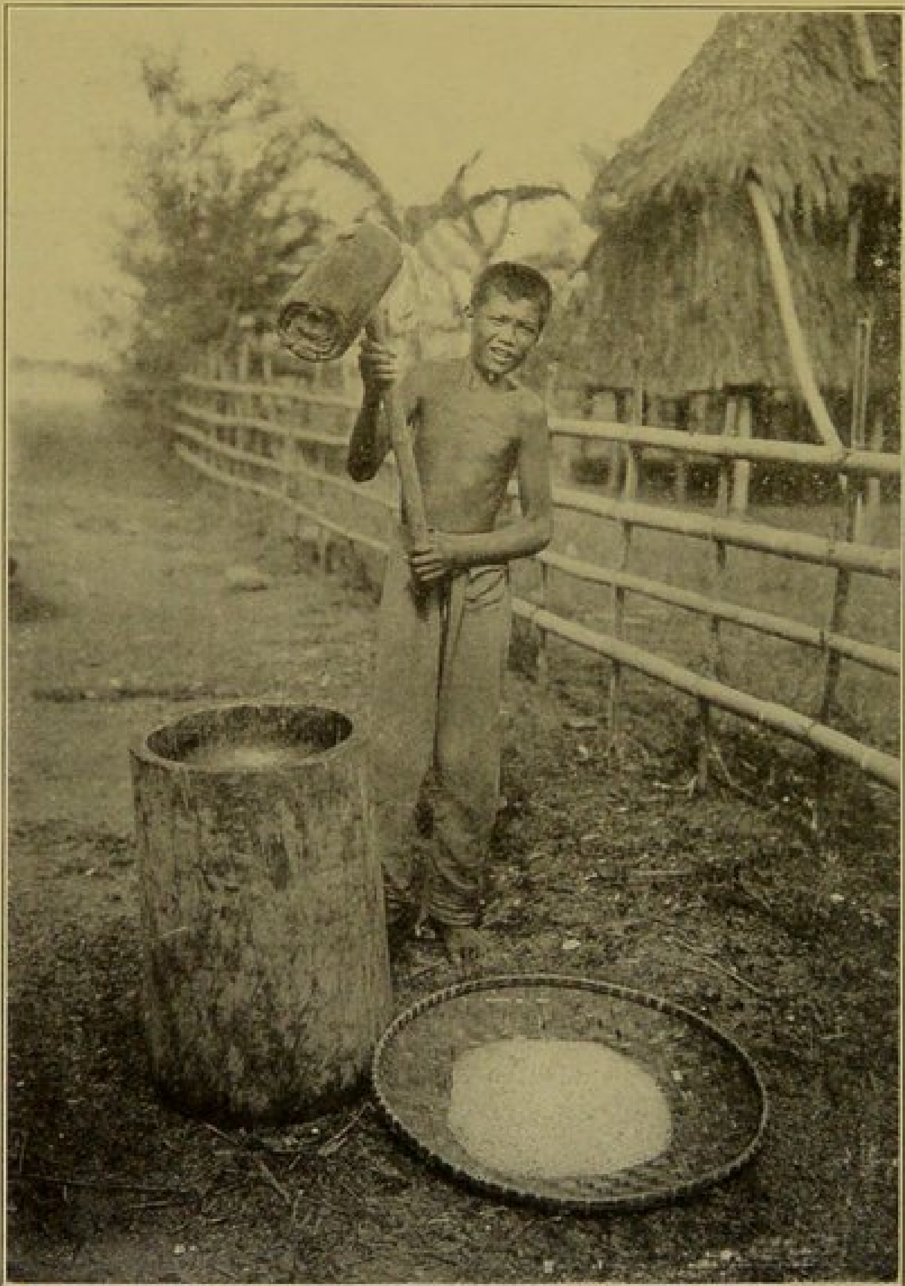

Figure 14. Another method of pounding rice.

grain of rice. This operation can be seen at almost any time in the native villages of the interior, and the dull sound of the mortar and pestle is very familiar to one who lives near such a village. Sometimes various kinds of fanning mills are used to separate the chaff from the grain. (Figures 15 and 16.) By means of this process the hulls are very thoroughly removed, but a large portion of the pericarp and aleurone layers remain on the rice. It is a well authenticated

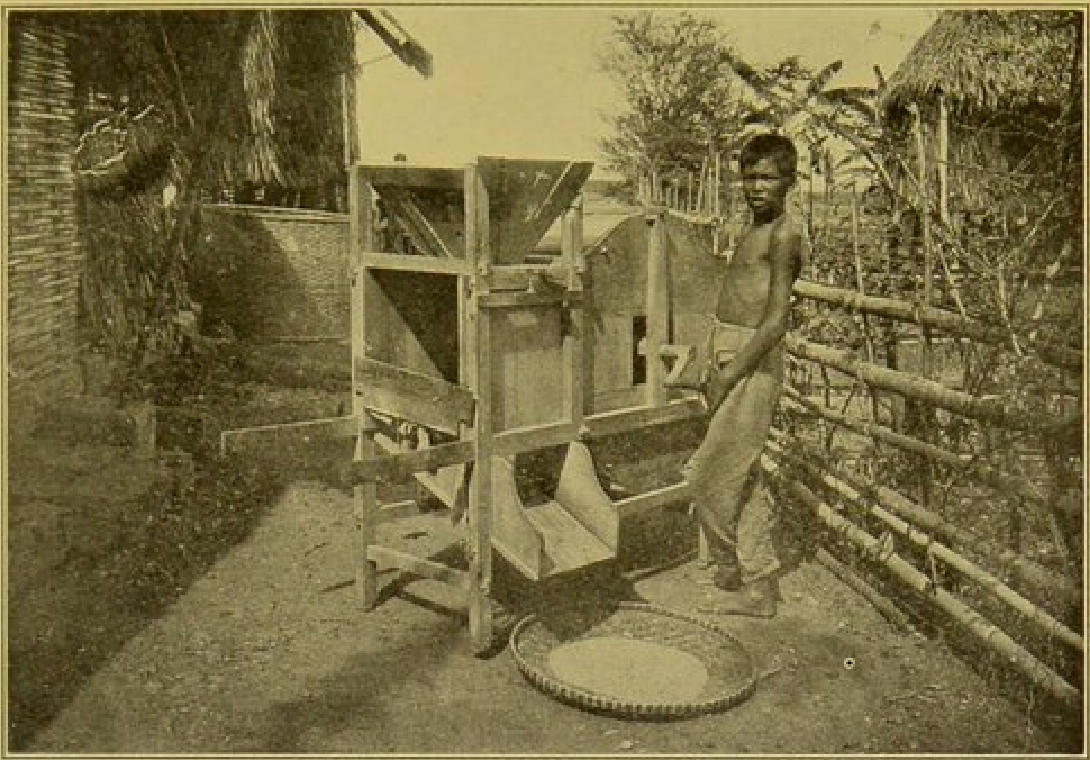

Figure 15. Filipino fanning mill for removing dirt and chaff from rice.

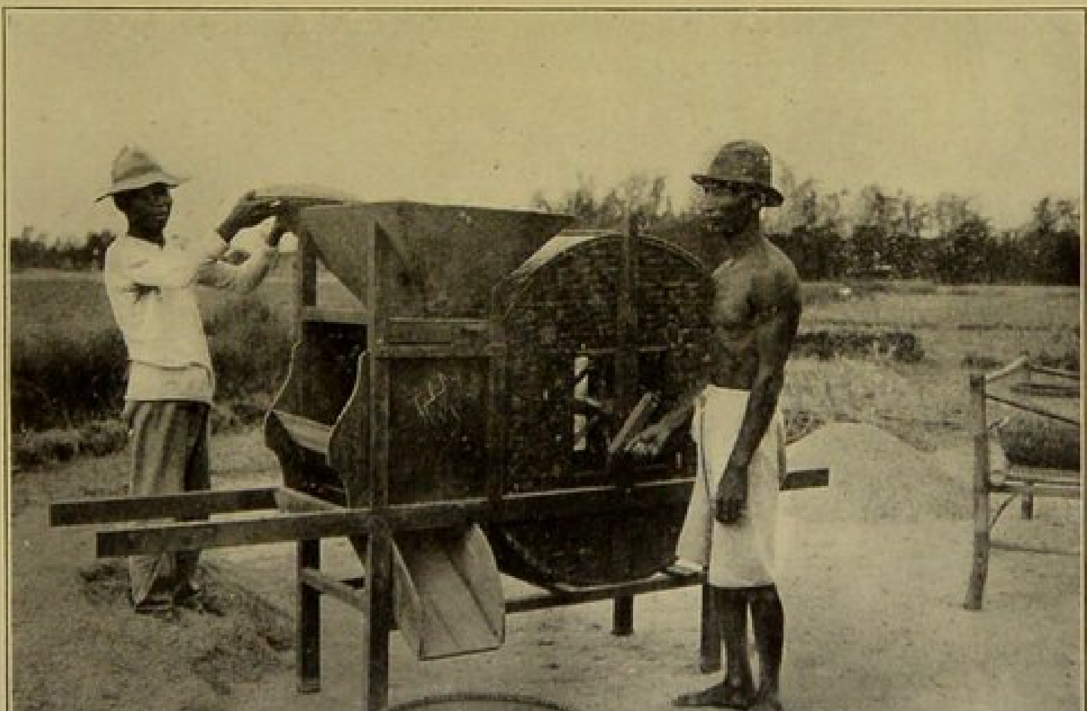

Figure 16. Another fanning mill in operation.

observation that the natives that live on this hand-pounded rice do not contract beriberi. Unfortunately the labor of preparing the rice in this way for daily use is considerable, and therefore as soon as the native becomes a little more affluent he at once discards this clumsy process, and if he is in a neighborhood where rice may be purchased he buys his daily supply from a tienda or shop where only the over-milled rice is for sale. He then becomes liable to beriberi. Thus in the interior, the poorest natives, who live on the land and pound their own rice, do not contract beriberi, while their more well-to-do neighbors who are able to purchase rice sometimes are affected. On the other hand, in the larger towns and cities where the natives never store and pound their own rice, but all, rich and poor, purchase it, the very poor are more liable to contract the disease because they are apt to live exclusively upon this over-milled rice, while the richer ones are usually exempt because they are able to purchase a more liberal diet. This fact is an illustration of the necessity of understanding the habits of a community before jumping to any conclusion as to their immunity from beriberi because of the financial status of the people. It also is the probable explanation of the observed fact that beriberi is most prevalent in cities along the coast and the banks of rivers. These are the localities that are reached by the world's commerce, and as a result highly milled rice is for sale, while in the interior it is often not obtainable.

Rice is prepared for cooking in this manner, or by similar primitive methods (figures 17, 18 and 19), by many of the natives in Malaysia and other Oriental countries. A modification of this method is very extensively used in Hongkong and other parts of China. Numerous rice mills in Hongkong consist of a long row of stone mortars over which heavy wooden hammers are suspended on an axle. A row of coolies stand between the handles of these hammers, at such an interval that each coolie operates two hammers, by standing first on the handle of one, thus elevating it, and then releasing it, allowing the hammer to fall into the mortar, while he steps with his other foot upon the handle of the hammer on the other side. The rice which is placed in the mortar is continuously pounded in this manner until it is sufficiently polished. It should be observed, however, that a white and highly milled rice can be and usually is produced by this method. Rice can be just as highly milled by any of these primitive methods as by steam milling, if the process be sufficiently prolonged. The native, in preparing rice for his own consumption, does not usually prolong the process beyond what is necessary to remove the hulls from the palay, because he is constitutionally opposed to any more labor than is necessary. In Hongkong, however, the owner of the rice mill desires to produce a white rice to compete in the general

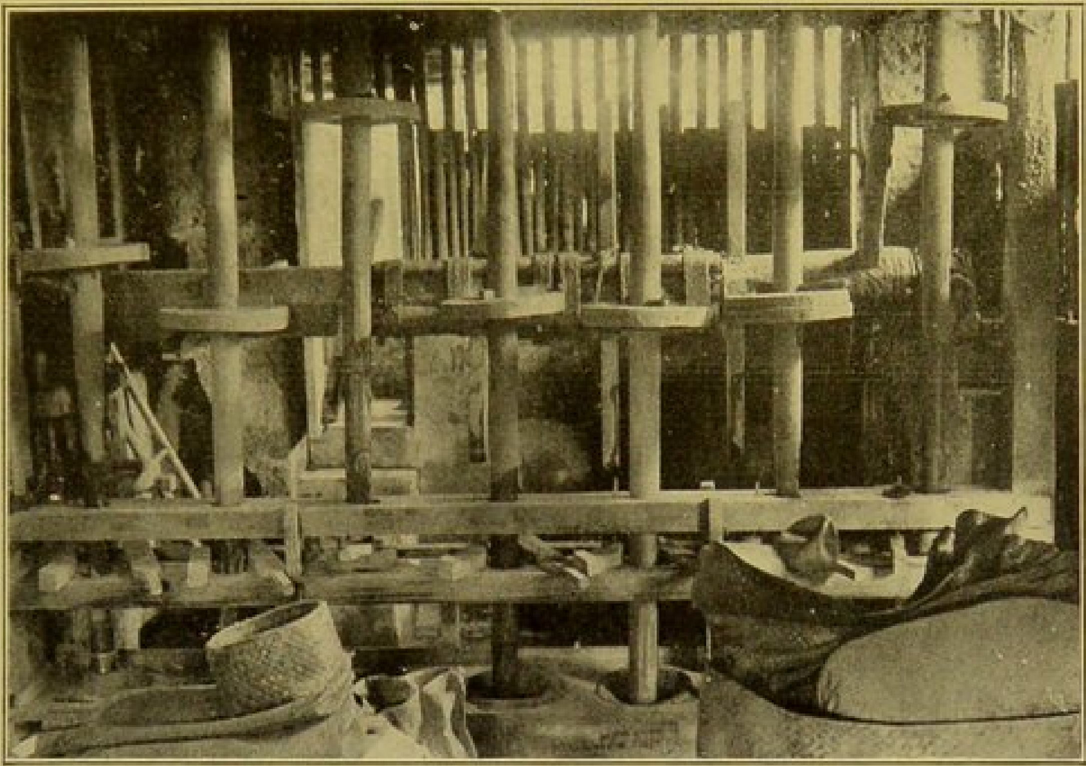

Figure 17. Interior of a primitive rice mill operated by water power.

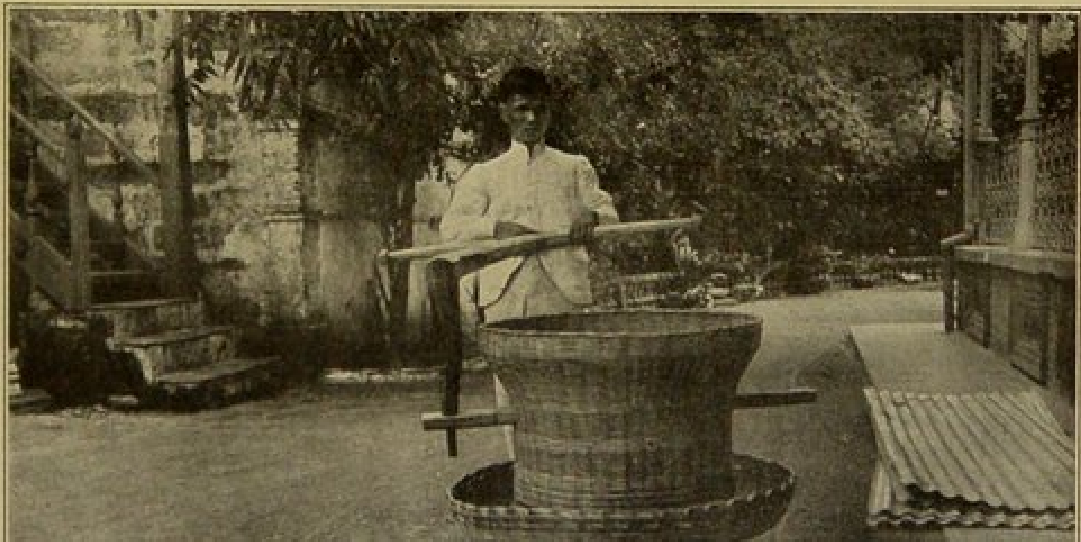

Figure 18. A Filipino hand power rice mill.

market, and merely uses the method described above because coolie labor is cheaper than steam.

An important variation in the method described is the preparation of "cured" or "parboiled" rice, which is used by large numbers of natives of India and Malaysia.

Figure 19. A Filipino millers' plant and machinery.

The preparation of "cured" or "parboiled" rice. The grain is soaked in water for 24 to 48 hours, the water is then run off and the grain is transferred to cylinders which are lightly covered, and steam is passed through the contents for five or ten minutes. The grain is then exposed in open paved courts and sun dried. The result of this treatment is that the husk is more readily detached than is the case with the untreated grain, while the pericarp and aleurone layers are rendered tough, resistant and much less easily removed from the kernel. In the milling therefore the husk is removed, but, since by no process can such rice be made to appear white, the milling is much less thorough than is the case with rice that has not been "cured." The rice that has been prepared in this manner generally has a peculiar disagreeable odor caused by the preliminary soaking in cold water.

PLATE III

A. J. E. Terzi del.

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TRANSVERSE SECTION PARBOILED (UNPOLISHED) RICE

This can be and sometimes is avoided by soaking the grain for a shorter time in hot water in place of cold water. The objectionable odor has prevented the extensive use of cured rice, although it undoubtedly prevents beriberi. However, now that we know that undermilled rice produces exactly the same result, there appears to be no longer any necessity for the use of cured rice, with its complicated preparation and its objectionable smell and taste.

Chemical constitution and dietary value of rice. With regard to Indian rices, Church says: "The analyses which have been made of a large number of samples of cleaned rice give figures which are wonderfully accordant, considering the great differences in the appearance of the specimens and the very diverse conditions under which they have been grown. The fiber and adventitious earth are sometimes rather high from the imperfect cleaning of the grain, but the nitrogenous constituents or albumenoids ocillate within narrow limits. Probably nine samples out of ten will be found to contain not less than seven per cent and not more than eight." According to Church the average composition of Indian rice is as follows:

Water	12.8
Albumenoids	7.3
Fat	0.6
Starch	78.3
Fiber	0.4
Ash	0.6

Wiley's figures* representing the composition of polished rice are as follows:

Moisture	12.4
Proteids	7.5
Ether extract	0.4
Crude fiber	0.4
Starch	78.8
Ash	0.5

The food value of an undermilled rice is considerably higher. Thus, Balland found that decorticated or milled rices from many localities showed an average composition varying between the extremes quoted below:

	Water.	Proteids.	Fat.	Amyloids.	Fiber.	Ash.
Maximum	16.00	8.82	0.75	81.35	0.42	0.58
Minimum	10.20	5.50	0.15	75.60	0.18	0.42

* Quoted from Harrington "Practical Hygiene."

While crude or undermilled rices contained a higher percentage of nitrogenous and fatty substances and ash, the limits being as follows:

	Water.	Proteids.	Fat.	Amyloids.	Fiber.	Ash.
Maximum	13.30	9.05	2.50	75.60	2.38	2.20
Minimum	11.20	6.18	1.85	73.85	0.93	1.20

The difference between these two sets of analyses represents what is lost in the milling process.

Fraser and Stanton have also furnished analyses of different rices, showing their varying food value, as follows:

	Protein.	Fat.	Carbo-hydrate.	Ash.	Moisture.
Unpolished rice	9.0	1.65	77.52	1.08	12.75
Polished rice	7.7	0.25	77.23	0.52	14.30
Parboiled rice	7.8	0.50	76.88	0.82	14.00
Malay rice*	7.3	0.63	77.19	0.88	14.00

* Malay rice is the term Fraser and Stanton used to indicate hand pounded rice.

Moreover, these authors state, The miller estimates that from 40 parts of padi there are produced 25 parts of rice and five parts of polishing; about 12 per cent of the grain is thus lost in the polishing. An actual weighing of some thousands of grains of unpolished and polished rice from the same lot of padi showed that the loss was about 10 per cent. The 10 to 12 per cent of the total weight of the grain thus lost in the milling process consists of the two outside layers, which contain the greatest part of the fat and proteid of the grain. Thus C. A. Browne of the Louisiana Experiment Station found, in 1904, that while raw rice afforded 9.88 per cent of proteids, the rice polishing contained from 17.76 to 24.4 per cent proteids and 14.0 to 21.0 per cent fat. The polished rice ready for sale contained only 6.56 per cent of proteids. From these different sets of figures it is shown conclusively that almost all the fat and a large part of the proteid elements are removed from rice in the process of milling.

Loss of food constituents in cooking. Hooper* performed a series of experiments to determine the amount of this loss. Four kinds of rice were used. Twenty grains of analyzed rice were placed in 110 cubic centimeters of water and boiled for half an hour, until

* Agricultural Ledger, 1908-09, No. 5. Calcutta Government Press, 1909.

properly swollen and soft. The water was thrown away and the boiled rices were dried and analyzed. He found that the boiling removed more than half of the fat, over eight per cent of the albumenoids, nearly eight per cent of the carbohydrates and 17.6 per cent of the ash. This method of cooking is the one usually employed in the United States, and it is apparent that a large part of the food value of the rice is thereby lost. Orientals, however, do not cook rice in this way. They place the rice in a pot, barely cover it with water, and allow it to cook over a slow fire. As the rice swells it absorbs the water, so that there is never any water left to throw away, and the rice as eaten is dry and comparatively firm. But while they do not lose any of the food value of the rice in this method of cooking, they always lose a considerable portion of the rice itself, which sticks to the pot and burns, and is never eaten.

Descriptive terms applied to different kinds of rice. "White rice," "scoured rice," and "polished rice," are terms often used as synonymous with "highly milled rice" by various writers on the subject. On the other hand "unpolished rice" and "red rice" are terms frequently applied to those rices that retain a considerable amount of the pericarp and aleurone layers. The hand-pounded rice used by the natives has sometimes been designated as "country rice" or "Malay rice." It seems clear that the use of all these terms must necessarily lead to confusion, because so many different standards are being used as a basis of comparison. The use of the terms "white rice" and "red rice" are especially undesirable, since it leads to confusion between the milling process and the color of the grain. A "white rice" is not necessarily a "highly milled rice," since those rices having a white pericarp are white before they are milled. Nor is "red rice" synonymous with "undermilled rice," since the pericarp of rice is not always or even usually red. The terms "country rice" and "Malay rice" attempt to designate the kind of milling from the locality, a method which may be correct in general, since country rice is generally hand pounded and undermilled, but may be incorrect in certain instances.

Since the main point to be established in describing a rice with regard to its relation to beriberi depends upon the amount of pericarpal layers left on the grain, it will be clearer and simpler to use only the following terms:

1. Undermilled rice. A rice retaining a large share of the pericarp and aleurone layers.

2. Highly milled rice. A rice that has been almost entirely or entirely deprived of those layers.

Phosphorus pentoxide as an indicator of the amount of pericarp left on a given rice. It has been found that the phosphorus of the rice grain is chiefly contained in the pericarp and aleurone layers. Thus analyses of rice polishings from Philippine rices have shown a phosphorus pentoxide content of 2.58 per cent to 5.61 per cent, while analyses of the rice remaining after removal of the polishings averaged 0.255 per cent phosphorus pentoxide.

Fraser and Stanton found that

1. Polished white rice of the kind commercially known as Siam rice yields on an average 0.26 per cent phosphorus pentoxide, and is the variety usually associated with severe outbreaks of beriberi.

2. Polished white rice of the kind commercially known as Rangoon rice yields on an average 0.328 per cent of phosphorus pentoxide, and the incidence of beriberi is less on this kind of rice than the former.

3. Malay rice yields on an average 0.38 per cent of phosphorus pentoxide, and the incidence of beriberi is still less on this kind of rice.

4. Parboiled rice yields on an average 0.41 per cent or over of phosphorus pentoxide, and beriberi does not occur when this kind of rice is eaten.

5. Unpolished rice yields an average of 0.54 per cent of phosphorus pentoxide, and can never produce beriberi.

6. An unpolished rice yielding 0.56 per cent of phosphorus pentoxide was polished in the ordinary way and the polished or white rice yielded only 0.26 per cent.

7. None of the rices connected with outbreaks of beriberi yielded more than 0.26 per cent of phosphorus pentoxide. The rices substituted for these, and which were effective in preventing the continuance of the outbreaks, yielded not less than 0.40 per cent of that substance.

After considerable practical experience based upon these observations Fraser and Stanton believe that a rice which contains over 0.4 per cent of phosphorus pentoxide will not cause beriberi, while one with less than that amount is unsafe if the rice forms the principal article of diet. It is not claimed that the lack of phosphorus is the cause of beriberi; in fact, as we shall show in another place, it is clear that this is not the case, but it does seem established that the per cent of phosphorus pentoxide is a fairly reliable *indicator* of the beriberi producing power of a given rice, simply because this estimation gives a very accurate idea as to how much of the pericarp is left on the rice. It is quite possible that the estimation of other chemical substances contained almost exclusively in the pericarp and aleurone layers would prove fully as reliable as phosphorus as indicators of

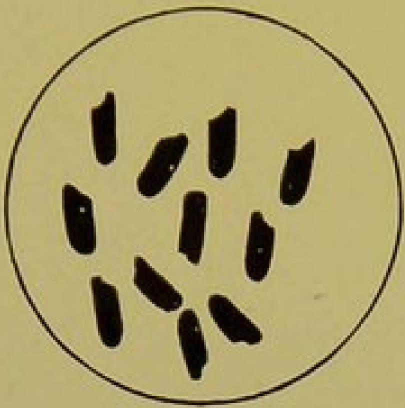

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 1. A highly milled or polished rice stained by Grams iodine solution. The starch, being completely exposed, stains uniformly a dark blue. This rice will produce beriberi.

FIG. 2. An undermilled rice stained in the same way. The unstained areas show where the adherent pericarp has protected the starch from the action of the iodine. This rice will probably not produce beriberi.

FIG. 3. A sample of undermilled rice that contains still more pericarp. The use of this rice will surely prevent the development of beriberi.

FIG. 4. The unhusked grain or "palay." When the husks are removed by hand pounding, a rice like Fig. 3 or Fig. 2 is produced.

the safety of a given rice. But, since the estimation of phosphorus pentoxide has been very generally employed as an indicator of the safety of rices, and since it is a comparatively simple and an accurate chemical procedure, it is probably the best *chemical* indicator at our disposal. However, it should be borne in mind that it is possible that the phosphorus content of a rice may depend upon the amount of phosphorus in the soil. It is quite conceivable that rices may be found that have been grown in a soil poor in phosphorus that are nevertheless rich in the protective substances, while on the other hand a rice grown in a soil rich in phosphorus, or when phosphates have been used as fertilizers, might be quite rich in phosphorus, although being deficient in the protective substances. No such instances are on record, but in view of the possibility it is well that it should be clearly understood that the estimation of phosphorus pentoxide is an *indicator* which has in the past proved reliable, but is not necessarily infallible.

A simpler method of determining whether a given sample of rice has sufficient pericarp left on the grain to render it a safe article of diet for oriental races, is a careful macroscopic examination of the grains. This can probably be done with more ease and certainty after the rice is stained with Gram's iodine solution. When treated in this way, and then washed and dried, the pericarp will be gray, while the parts denuded of pericarp will permit the starch to take the characteristic deep blue color. In any highly milled rice the grains will practically all be dark blue and almost black. The appearance of a highly milled rice, and of undermilled rices when treated in this manner, is illustrated in plate IV, figures 1, 2 and 3. That this method is of practical value is shown by the fact that for over a year the undermilled rice used by the Philippine scouts has been selected by this method, without a single analysis of phosphorus pentoxide being made. During this period beriberi has continued to be absent from these native troops. The method has the advantages of being simpler and vastly less time consuming than a chemical analysis, and of being an equally accurate method of determining the amount of pericarp left on the grain. It suffers from the disadvantage of being a matter of judgment rather than a fixed standard, such as is afforded by a phosphorus estimation, but a little experience will enable anyone to acquire the necessary judgment. A few days spent in studying different rices will afford sufficient education on this point to enable the observer to almost predict what the phosphorus pentoxide estimation of a given rice will be, and to enable him to declare with certainty that a certain rice will or will not prevent beriberi when used as a staple article of diet.

CHAPTER VI

THE ETIOLOGY OF BERIBERI

Is Beriberi a Specific Disease?

Introduction. Having dealt with the symptomatology and pathology of beriberi, it is now desired to make a study of the etiology of this disease which may be as conclusive and convincing as possible. In order to attain this object it is essential that the more important theories that have been advanced in the past be discussed critically, and at more or less length. But such a voluminous literature has been produced on this subject that it is absolutely impossible to discuss fully every contribution within the limits of space assigned to this book, so that an attempt must necessarily be made to be as brief as is consistent with a clear review of the subject. The reader who desires to go more fully into any part of the subject is referred to the literature which we have collected in another place.

To avoid confusion, it has seemed necessary to make some attempt to classify the various theories that will be discussed. The following analysis will conduce to a logical discussion of the subject:

CLASSIFICATION OF THEORIES OF THE CAUSATION OF BERIBERI

I. Theories regarding beriberi not as a specific disease, but as a group of diseases, each one having a specific cause.
  1. Dürck, H.
  2. Luce, H.
  3. Nocht, B.

II. Theories regarding beriberi as a specific disease.
  1. Beriberi caused by physical agencies.
  2. Beriberi an intoxication.
    (1) Inorganic, without the agency of microorganisms.
      A. Arsenical poisoning (Ross).
      B. Oxalate poisoning (Treutlein, Maurer).
      C. Carbon dioxide poisoning (Ashmead).

(2) Organic, without microorganisms or caused by hypothetical microorganisms.
  A. Absorption of a toxin produced by some free living germ outside the body (Manson).
  B. Toxin produced in food outside the body.
    (a) Ichthyotoxismus (Grimm, Miura).
    (b) Sitotoxismus.
      Lathryism.
      Rice (Vorderman, Braddon, Yamagiwa, Van Dieren).
  C. An auto-intoxication (Dürck).

3. Beriberi an infection.
  (1) By animal parasites.
    A. Protozoa.
      (a) Plasmodium in blood (Glogner).
      (b) Protozoa in urine (Hewlett and Korte).
      (c) Haematozoa in blood (Fajardo, Voorthuis).
    B. Nemathelminthae.
      (e) Trichiuris trichiura (Erni, Kynsey).
      (b) Anchylostoma duodenale (Noc, Kynsey).
  (2) By vegetable parasites.
    A. Bacteria.
      (a) Cocci in the alimentary canal, etc. (Dangerfield).
      (b) Diplococcus in urine (Tsuzuki).
      (c) Diplococcus from blood, urine and organs post mortem (Okata and Kokubo).
      (d) Four kinds of cocci (Musso and Morelli).
      (e) Cocci in blood and air (Pekelharing and Winkler).
      (f) Bacilli and cocci (Lacerda).
      (g) Bacillus (Taylor).
      (h) Bacillus (Rost).
      (i) Bacillus (Ogata).
      (j) Three kinds of bacilli (Nepveu).
      (k) Bacillus (Eecke).
      (l) Bacillus in alimentary canal (Hamilton Wright).
    B. Fungi. Mouldy rice (Hose).

4. Beriberi due to some deficiency in the food.
  (1) Deficient fat (Bremaud, Laurent).
  (2) Nitrogen starvation (Takaki).
  (3) Deficient vegetables combined with an infection (Fales).
  (4) Deficiency in organic phosphorus (Schaumann).

(5) Deficiency of some as yet unknown substance not phosphorus (Fraser and Stanton, Chamberlain and Vedder, Shiga, Funk, etc.).

Is beriberi a specific disease? A disease condition may be said to be a symptom complex when it is not a disease *per se,* but a group of symptoms which may occur in several diseases. Dropsy is an example of a symptom complex. A condition such as diabetes, which always presents a clear-cut clinical picture, but does not necessarily have a specific cause (while diabetes is generally caused by disease of the pancreas, there is evidence that it may be caused at other times by disease of the liver or brain), may be called a clinical entity. A specific disease not only has a definite clinical entity, but it also has a specific cause, i. e., typhoid fever.

It is proper that theories regarding beriberi not as a specific disease, but as a group of diseases each having a specific cause, should be discussed first, since we should not waste time and effort in the endeavor to discover a single cause for this disease if in reality it is not a specific disease. Several authors have stood sponsor for the statement that beriberi is not a specific disease, and we will first examine the evidence on which they base this assertion.

Dürck, in 1905, said: "In more recent times the conception has been advanced that a disease whose clinical picture is as complicated as beriberi, perhaps has no single cause, and that the clinical and anatomical phenomena which to-day, for lack of better information, we call beriberi or kakke can perhaps be attributed to different causes; that it may occasionally result as a sequel of an antecedent case of malaria or dysentery, or that it may sometimes originate through a definite intestinal infection, and at other times through the absorption of toxic products of a nonorganized nature."

It is evident that this statement is merely a conjecture or a guess at the truth, and contains no evidence that requires refutation. The clinical picture and anatomical findings in beriberi are no more complicated or variegated than are the lesions of syphilis or tuberculosis. The mere fact that a disease is complicated and does not always run a regular or classical course, affords by itself absolutely no good ground for assuming that it is not a specific disease.

Again in 1908 Dürck mentions a number of the different theories as to etiology formulated by other observers, and concludes that since there is so much confusion, a single specific etiologic agent of beriberi does not exist. "Beriberi is a collective name, a symptom complex that under different conditions could be brought about by different agents. The South American beriberi is not the same as the Japanese kakke and the Malaysian beriberi. Perhaps it is similar to Nocht's ship beriberi or Italian pellagra, or to the many forms of European polyneuritis which Oppenheim has shown to be similar and whose pathology is identical." "Our peripheral nervous system under different external conditions and different injurious alimentary, toxic, or infectious influences reacts with the same degeneration process, whose course, intensity and extension correspond to the intensity and quality of the injurious agency, but whose essence is ever the same."

Again it is apparent that Dürck has made very broad and sweeping statements without furnishing one iota of evidence in their support. The only basis for his conclusions is that there have been so many different theories as to the causation of beriberi. But it by no means follows that all of these theories are correct; indeed we hope to demonstrate that most of them are absurd. Dürck's conclusion that beriberi is not a single disease is therefore, so far as we can judge by the evidence he furnishes, founded solely on his inability to examine critically the various theories as to the etiology and to reject those that are incorrect.

Luce has frequently been quoted as stating that beriberi is not a specific disease but a group of diseases. Luce's actual statement is as follows: "That beriberi, in spite of the fact that it is a clinical entity, has not a single cause but a complex etiology in which several endogenous and exogenous factors co-operate. The sum of the causes of the disease is the sum of all the injurious agencies which are inherent in the geographical ethnical individuality, and have their roots in the hygienic and social conditions of Japan." It should be stated that Luce is here speaking of beriberi in Japan, where he studied it, but he says that he sees no reason why his arguments should not apply to other nationalities that are afflicted by beriberi.

It is clear therefore that Luce accepts beriberi as a clinical entity, but believes that its causation cannot be attributed to any single factor. The facts which have led Luce to this belief may be stated briefly as follows: He first reviews the evidence which convinces him that beriberi is not an infectious disease. He then states that the pathological anatomy of the disease demonstrates clearly that the chronic and acute changes in the nerve muscular system are of a secondary nature, and that it is readily conceivable that these changes in the nervous system may be caused by a great number of products that might result from pathological metabolism, or as the result of various intoxications.

The objection to this conception is that beriberi is not simply a polyneuritis, but is a complex disease in which polyneuritis is associated with a diseased heart, with a tendency to generalized oedema, and other pathological manifestations. It is this fact that distinguishes it clinically from the various kinds of polyneuritis seen in Europe and the United States.

Luce then proceeds to the consideration of the various exogenous and endogenous agencies which he believes play a part in the causation of beriberi. He discusses at considerable length the bad sanitation of Japan, particularly in the large cities. The drinking water used is always bad. A proper system for disposal of wastes is practically non-existent, so that the ground water is all infected, and this latter is used for drinking purposes or contaminates the pure water supplied through bamboo tubes in which it is usually conducted to the consumer. He mentions the habit of using human excreta as fertilizer, and believes that all of these unhygienic conditions play their part in the production of beriberi through the various intoxications and infectious diseases that are produced thereby. He next mentions the unsanitary dwellings. They lack foundation and the ground air reaches them freely. The walls of the rooms are thin, so that they afford no protection against the cold, while the rooms themselves are too small, and are overcrowded. They are completely closed at night, ventilation is entirely lacking, and the only method of heating them is the ubiquitous charcoal stove or hibachi. Also in Japan there are great changes of temperature during the day and the light cotton clothing worn is quite inadequate to protect the body from these changes. These conditions are seriously advanced as causes of beriberi.

In reply to such arguments it is only necessary to state that the Esquimaux probably live in much more unsanitary conditions than the Japanese, but do not have beriberi. Indeed it is not necessary to go so far afield as the Esquimaux. All the large cities in Europe and the United States have thousands of poverty-stricken people in their slums, who daily live in infinitely worse surroundings with regard to housing, exposure to cold, lack of ventilation, deprivation of food, etc., than the Japanese, yet they never contract beriberi.

On the other hand, men living under very good sanitary conditions, with the exception of the food, have contracted beriberi in many instances. This was notably true of the beriberi in Bilibid prison, Manila. (Fales.)

Luce then considers the food of the Japanese, mentions its great lack of nitrogenous and fatty constituents, and the great bulk of a purely vegetable diet, but concludes that since the Japanese have been well nourished on this food for hundreds of years, and since Scheube, Baelz, Kellner and others have shown that from a physiological standpoint this food is sufficient, that this unbalanced diet cannot be a direct cause of beriberi, but is only one of the contributing causes along with the other unhygienic conditions mentioned. The fallacy of this reasoning consists: 1. In ignoring the variations in the food of different individuals. Two individuals seldom eat precisely the same food, and the important distinction between the different kinds of rice used is entirely overlooked. 2. In assuming that a diet is physiologically sufficient, because it contains a sufficiency of fats, carbohydrates and proteids, and because many individuals living on it appear plump and well fed. There are other most important chemical constituents in food, but the importance of these substances has long been overlooked, particularly in the case of beriberi, whose incubation period is now known to be long (at least ninety days), during which time the victim may appear well nourished.

Luce mentions the numerous intestinal parasites of the Japanese as a possible cause of beriberi, and then proceeds to a consideration which he considers as of great etiological significance, namely the habitual sitting posture of the Japanese. As is well known, the peroneal, tibial and sciatic nerves are usually the first nerves affected, and the ones in which the most advanced degeneration is commonly found. He attributes this to the habitual squatting habits of the Japanese, who never sit on chairs, but rest the body on the heels with the knees tightly flexed, thereby continually compressing the nerves and blood vessels of the legs. This results in a chronic traumatism of the nerves which is a serious etiological factor in the development of the disease. It hardly seems necessary to treat this suggestion seriously, but perhaps it would be well to mention that no such chronic traumatism of the nerves as a result of this sitting posture has ever been demonstrated. That this method of seating themselves is almost universal among all peoples of the Orient, many of whom, such as the Tamils in the Malay States, to quote only one example, never have beriberi. And that compression of the vessels and nerves of the legs is also quite common among western peoples who sit in chairs, as is evidenced by the very common sensation of a leg that has "gone to sleep," yet we never consider that we are thereby inducing an attack of beriberi.

We are therefore forced to the conclusion that the belief of Luce that the disease beriberi is a clinical entity yet has many causes is supported by evidence that will not bear criticism.

Nocht merely suggests that beriberi may not be a specific disease, but may be a group of diseases, with different etiology. It may be like dysentery, in which disease similar symptoms are produced by the action of entirely different organisms. Nocht is led to make this suggestion because he regards the infectious origin of beriberi as proven in certain cases, while the fact that it is a disease of metabolism is equally proven in other cases, and he can explain this discrepancy only on the supposition that these are different diseases presenting a similar symptom complex. This reasoning would be correct were his premises granted, but his belief that the infectious origin of beriberi is proven in certain cases rests on very flimsy evidence. This evidence is given in the following translation of his own words: "Very weighty proof of the infectious nature of the disease has been furnished in recent times. First, the undoubted introduction of the disease by colored laborers into countries previously free from it, and its spread from them to the surrounding people, such as the introduction of the disease in the Fiji Islands by Japanese in 1894, and in New Caledonia by Annamites in 1891. Especially interesting is the beriberi introduced in 1900 into Diego Garcia, an island of the Chagos group, where the disease had not existed previously. Among the workers who wandered from the Comores by way of Mauritius were five cases of beriberi. After several months the nurse who took charge of these patients in the hospital was first taken with the disease, and later a number of other people, including a woman. This woman died and the child that she left behind was adopted by the wife of the manager of the oil factory in which the people worked. Three weeks after the child was taken into the household of the manager it sickened and died. At the same time the woman of the house, who had acted as foster mother to the child, contracted beriberi *and died after several weeks. She had never been in contact with the workers but only with the child.* (Italics ours.) Further Manson considers Travers' cases very convincing. In Pudoh Gaol, at Kuala Lumpur, beriberi broke out, and the sick and a portion of the healthy were then taken to a neighboring jail. The disease stopped, but its incidence in the first prison remained the same. The inmates of both prisons received the same food from the same kitchen. Manson further states that in a prison in Singapore, only the men and not the women were attacked, although both received the same food."

This is all the evidence that Nocht gives in his article to demonstrate the infectious nature of beriberi, and since he is the only one of the observers quoted in this chapter who have given specific instances, it will be well to investigate them.

1. The introduction of the disease into Fiji by Japanese in 1894. Fortunately this epidemic has been investigated by Braddon, and the following is quoted direct from his book:

"In the Fiji Islands, prior to the event now to be described, beriberi had never been known. The aborigines — Polynesians — use for their staple food *taro* (yams), also corn (maize) and other vegetables, and they eat much fish. European and other settlers eat bread made from wheat flour as elsewhere.

"In 1894 a number of Japanese were imported into Fiji to work on sugar estates. They were picked coolies, and in good health when they left Japan, and on the journey. On their arrival at Fiji they were divided into two bands. One, consisting of fifty coolies, was sent to work on a certain estate. The dietary was liberal, including meat or fresh fish to the amount of one-half pound per diem, besides two pounds of rice and a variety of condiments.

"Nevertheless, within two months of the arrival of the coolies on the island, beriberi broke out, and in all 42 cases occurred. Eight of these patients died; 34 were returned to Japan suffering from the disease, the remaining eight healthy coolies accompanying them. The other batch of immigrants — 205 in number — were sent to a sugar estate in another part of the island. They had a similar dietary. Within a month beriberi broke out among them.

"The cases steadily increased, and by the end of six months 226 out of the 250 were affected; 69 died. The survivors — 181 in number — many still affected with beriberi, were sent back to Japan."

I have been favored by Dr. Glanvill Corney, the present Chief Medical Officer of Fiji, with some further interesting particulars relative to these ill-fated Japanese.

Thus, the quarters occupied by them "were newly built specially for them to occupy on arrival; and it was a condition of their contract that for the first six months' residence all their rations should be imported from Japan. Later, however, they were given rice which came from Calcutta, and was of the common stock issued to the Indian coolies and native laborers on the same company's plantations * * * The Japs did not work in the same field batches as the Indian coolies or Fijians.

"There are no Chinese coolies in Fiji. But after working hours there was absolutely no bar, except social differences, between the Japs and all other nationalities on the estates or in the surrounding native villages, and it was an everyday occurrence for them to stroll around together. * * *

"The rice imported from Calcutta was ordinary Ballam rice, such as we use in Fiji year after year.

"No person in Fiji has had beriberi except the Japs, who came on the occasion referred to, and, in 1904, a couple of newly-arrived Chinese merchants' employees. These two men never went to either of the districts where the Japanese were located in 1895–1896."

"Here was an epidemy, the cause of which, were it an infection, was at once virulent and active enough, and placed under apparently perfect conditions for spread. Its victims were many and severely stricken; they were in constant intercourse from the earliest to the last stages of their malady with classes of natives whom experience elsewhere has shown to be peculiarly susceptible. For Indians have suffered severely in Malayan gaols, and Polynesians are the very class of natives whom Hagen claims to have succumbed to beriberi in New Caledonia through mere chance and quite brief contact.

"Yet the disease did not spread. It was confined to those who were rice-eaters, and among these to the eaters of one particular sort.

"The immunity of those rice-eaters who were fed on Ballam rice during this epidemy is also a fact of very great importance, the significance of which will appear later on.

"Such instances as the above have been multiplied in almost all parts of the world wherever parties of the indefatigable nation have settled. Like the Nessian shirt, their use of a certain sort of rice, wherever they have gone, has been an inalienable secret factor leading to destruction."

Such evidence, if it does not prove the dietary origin of the beriberi on Fiji, at least seems to throw very grave doubt upon its infectious origin.

2. The introduction of beriberi into New Caledonia by Annamites in 1891. Again we quote from Braddon, as follows:

"Epidemics in New Caledonia. — The islands called by this name were adopted by the French as a penal settlement in 1859.

"There were 21,630 convicts (*forcats transportees*) conveyed thither between this date and November 28, 1896, after which no more were sent. Of these, 1,713 only were 'natives' — African, Asiatics or Polynesians — the rest were European.

"In addition to the convicts, after 1885 there were sent there annually several hundred *relegues* — banished recidivists.

"From 1880 onwards there was thus an average European population in these islands of over 8,000 persons.

"The climate, a mild and equable one, permitted them manual labor. They were fed on the same sort of food stuffs as in Europe.

"The mortality was, though high, not severe. During the 33 years 7,222 of the convicts — about one-third — had died.

"Kermorgant, from whose interesting account these particulars are taken, states that the principal causes of death were: Diarrhoea and dysentery, over a quarter; tuberculosis, enterica, about one-tenth of all deaths, each; chest troubles and anaemia, each about five per cent of the deaths. There was no malaria.

"Beriberi is not mentioned, and it must be presumed did not occur. It is, in fact, stated by Grall, Vincent and Poree that before the event to be described this disease had never been known in the islands. Here, then, was a population of non-rice-eating Europeans, living otherwise (as convicts) not under the best hygienic conditions, among whom beriberi had been, from 1858 to 1891 at least, unknown.

"In the latter year were introduced into the islands some 800 Annamites and Tonkinese, convicts from Cochin China.

"These men were fed almost exclusively on rice. Beriberi broke out among them immediately after their arrival. Two hundred were severely — all perhaps slightly — attacked, and 70 died. At the height of the epidemy these people were distributed from the quarantine island, where they had hitherto been kept, among several stations. There was thus opportunity given for the malady — were it infectious — to spread. But no Europeans were attacked.

"In 1892, 600 healthy Japanese, recruited as laborers, were brought to the same settlements. They, too, were fed almost wholly on rice. They, also, shortly after arrival, got very severe beriberi. Two-thirds are recorded as having been attacked, and there were many deaths.

"But again the disease remained entirely confined to the rice eaters. Not a single European acquired it." *

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* Arch. de Med. Nav., t. lxiii., Nos. 2, 3, 4, pp. 134, 187, 260, February-April, 1895; also Hagen, *Rev. Med. de l' Est. t. xxv.*, No. 2, p. 42, January 15, 1893. It was from a consideration of facts connected with the epidemy among the Tonkinese that Hagen, against most authorities and all the facts, announced beriberi to be contagious. Certain Polynesian labourers under Hagen's own care developed, after the out-break among the Tonkinese, symptoms resembling beriberi, and diagnosed by Hagen and Keiffer, the chief local medical officer, to be beriberi. There had been opportunity of infection between the two classes. Without discussing the likehood, always highly probable, that both these lots of labourers had shared the same sort of food, Hagen concludes that his coolies must have incurred the

It is plain, therefore, that the infectious nature of the disease is not proven by this instance. On the contrary, it also is evidence favoring the dietary origin of beriberi.

3. Beriberi introduced in 1900 into Diego Garcia. There are very serious objections to be brought against Nocht's statements with regard to this epidemic, and to the conclusion drawn, that it was spread by infection. In the first place, Nocht states that the foster mother who adopted the child "contracted beriberi and died after several weeks. She had never been in contact with the workers, but only with the child." All that is known of this epidemic is derived from the report of Bolton, who was not present himself at the time of the epidemic, but received all his information from the manager of the oil factory where the cases occurred. However, Bolton says: "*Mrs. de Cailla (the foster mother), who had been most untiring in the care of the sick, nearly fell a victim to the disease. She had undoubted symptoms of it.*" This statement is flatly contradictory to Nocht's account. Bolton himself thought the disease was spread by infection, but this is improbable, according to his own evidence. Eight men and one woman with beriberi landed at Diego Garcia from Mauritius, July 27, 1900. One died on August 6, 1900, and the next case did not die until January, 1901. The hospital attendant to whom Nocht refers was not affected until March 27, 1901, *which was a matter of eight months after the disease was first introduced.* No other case occurred among the inhabitants during this time, with the exception of the cases that were introduced, for Bolton says: "Up to now (March 27, 1901) the disease had been limited to the Joanna gang" (the laborers from Mauritius). Furthermore, there never were more than three or four cases among all the inhabitants of the island at any time, although these infected laborers mingled freely with the rest of the population during these eight months and subsequently. This does not look much like the spread of an infectious disease. Still further, although Bolton thought that diet was eliminated from this epidemic, this was in reality far from correct. Bolton says: "The men of Diego have every chance of nourishing themselves well, and they take advantage of the facilities offered them. It is true that the Joanna gang were Mohammedans, and as such did not eat pork, but they had every facility for obtaining fowls, eggs, sea birds and vegetables of all kinds, and limes are given to the men with a very free hand." Rice was, however, used as a staple article of diet, and it will be noted that Bolton says that the

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disease by direct contagion. He does not even mention the fact — which, however, Legrand and Burot supply (*Maladies des Marins*, etc., 1896, —. 86, footnote) — that the Polynesians in question were like all who then got (or get) beriberi, being also fed almost wholly upon rice.

men had every facility for obtaining a variety of food, but he does not state that they were furnished with a proper ration, nor does he give any evidence to show that the men actually affected with the disease availed themselves of the facilities and obtained a proper diet. It is much more probable from what we know of the Oriental under these circumstances that they ate the rice which was furnished them and saved their money and their time by not obtaining a varied diet. At any rate, in the absence of conclusive evidence as to the exact food eaten by the persons affected, and with the positive evidence which we have that beriberi is produced by an improper diet, some of which evidence is quoted by Nocht himself, it is plain that it is unjustifiable to regard the infectious nature of this epidemic on Diego Garcia as proven.

4. Travers' observations in Pudoh Gaol. With regard to Travers' observation, Braddon has also shown very clearly that it was faulty for the following reason: When Travers took his party from the old jail to the new he took chiefly short-time prisoners to the new jail, leaving the long-time prisoners in the old jail. Now Fraser and Stanton have shown conclusively that it requires about 90 days on an exclusive diet of polished rice to produce beriberi. In accordance with this observation is the recorded fact that beriberi was very rare in short-time prisoners and very common in the long-time prisoners at Pudoh Gaol. So that in Travers' observation, although two parties of prisoners were kept for eight months at different jails on the same food, it happened that most of the long sentences were kept in the first and most of the short sentences in the second jail. Beriberi was only observed in the jail where the former were confined. Travers, not having taken this factor into his reckoning, esteemed both parties equally circumstanced, and was therefore led into the mistaken belief that since the food supplied to both was the same, it could play no part in determining the different incidence of beriberi.

Sambon (Brit. Med. Journ., 1902, ii, 835), also criticising Travers' experiment, says: "I fail to see how Doctor Travers' observations can sweep away the enormous amount of evidence brought forward against rice, not only by Saneyoshi in his admirable report on the experience of the army and navy of Japan, but by the great majority of physicians of all times who studied the disease in China, Japan, the Dutch Indies and Brazil. *I will just point out that the rice used in Doctor Travers' experiments, though supplied by the same contractor, was not the same in both jails, because it was bought from several Penang merchants, who themselves collected it from many districts in separate bags.*"

5. With regard to Manson's alleged statement that in a prison at Singapore only the men and not the women were attacked, although both received the same food, it appears that this also is wrongly quoted. What Manson actually said (Brit. Med. Journ., 1902, ii, 831) is as follows: "Two institutions placed side by side, as for example the male and female prisons in Singapore, with identical *piped water supplies* (italics ours), one, the male, is attacked with beriberi; the other, the female, is exempt." Manson made absolutely no reference to the food used in this particular instance.

It will thus be seen that none of the evidence upon which Nocht bases his belief in the infectious origin of beriberi will stand criticism. This being the case, his whole argument as to the existence of two classes of beriberi, one of infectious origin and one of dietary origin, falls to the ground.

It must be emphasized that this discussion has no reference to the question as to whether dry and wet beriberi are possibly two diseases. The authors quoted, like almost all modern writers, have accepted dry and wet beriberi as forms of the same disease, but have decided that this one disease has various causes. It is clear that this position cannot be sustained by the evidence which they present.

We shall therefore proceed with the investigation of the etiology of beriberi, for the present assuming that it is a single specific disease, in the absence of definite evidence to the contrary.

CHAPTER VII

THE ETIOLOGY OF BERIBERI, CONTINUED

Is Beriberi an Intoxication?

According to the classification we have adopted, the first of the theories which accepted beriberi as a specific disease attributed its causation to physical agencies. It will be seen by consulting the chapter on the history of beriberi that this was the explanation of several of the old Chinese writers. Bontius also attributed the disease to a cold humor and sudden chilling of the body. According to Castellani, "the older writers, like Davy, considered that it was brought about by some unusual state of the atmosphere, but they said, honestly, that this was merely a cloak for their ignorance of the true cause." In general, it may be said of these statements that they were made in the pre-scientific days of medicine, and are supported by no evidence that we would to-day consider, with the exception of the fact that these older writers noticed that beriberi was more prevalent during certain seasons of the year. This point will be discussed later, and it will be sufficient to state here that weather *per se* probably has no influence on the incidence of beriberi. The theory that beriberi is to be attributed to physical agencies is therefore only of historical interest.

The theory, however, that beriberi is caused by an intoxication must be fully discussed and given careful consideration, since many have believed that this was the true explanation of the disease, and some investigators are still adherents of this theory. We come first to the consideration of the possibility that beriberi is caused by an intoxication with some inorganic substance. Ross' theory of arsenical poisoning is one of the most important of this class of hypotheses.

The Arsenic Theory. Ross was struck by the fact that the symptoms of beriberi are very similar to those shown by patients observed in England in 1900 suffering with chronic arsenical poisoning. In investigating this theory he reported a case of beriberi resembling these cases of arsenical poisoning, and Professor Dixon Mann analyzed a lock of hair from this patient and found a considerable amount of arsenic, although no arsenic had been administered as medicine. Ross then procured twenty samples of hair from beriberi patients from the

Penang General Hospital, which were also analyzed by Mann, who found arsenic in six out of the twenty samples. The positive samples were nearly all from recent cases and the negative ones from old cases. Ross concludes: "The probability is very strong that the Penang beriberi is arsenical, especially when we know that the people there largely work in tin manufactories and are brought closely into contact with arsenic." In a subsequent report he obtained eight further samples of hair from beriberi cases at the Singapore Asylum, and analyses showed arsenic in the hair from three recent cases and none in the five samples from older cases. Ross therefore concludes: "Whatever the truth may ultimately prove to be, the analyses which Professor Dixon Mann has made seem to suggest that the arsenic, after producing the characteristic neuritis, has gradually disappeared from the hair in some manner, or has perhaps been cut away as convalescence has advanced."

In disposing of this theory, it is sufficient to state that arsenic has been claimed by some authors to be a normal constituent of the human body, and there are also many circumstances under which it may be absorbed in small quantities. Manson stated in 1902 that Doctor Preston Maxwell had lately sent him some samples of Chinese tobacco to which arsenic had been intentionally added, with the object of giving it a peculiar and much relished garlicky flavor. This is only one of the many possible ways in which small quantities of arsenic might find an entrance to the bodies of some beriberics. Ross did not find arsenic present in all of his cases, and the theory that it disappears as convalescence advances is a mere assumption. The occurrence of slight traces of arsenic in the hair of a few beriberics can hardly be an argument that it is the cause of the disease. Herzog, in testing the validity of this theory, caused ten samples of hair from beriberi patients to be analyzed, with the result that arsenic was found to be absent in all ten cases. It appears quite certain, therefore, that the presence of small quantities of arsenic in the hair of beriberics is purely accidental, and stands in no causal relation to the disease.

The Oxalate Theory. Maurer, in 1903, distinguished between an asphyxiated and a neuritic type of beriberi. He thought that both forms were caused by an intoxication with the products formed in the intestine from the fermentation of rice. The starch of the rice is changed to sugar, and the bacteria and moulds in the intestine change the sugar into various acids. He believed the neuritic form of beriberi was caused when oxalic acid was produced from the sugar, while the asphyxiated form was the result of intoxication by other acids. Maurer attempted to prove this theory by feeding experiments on fowls, and Treutlein performed similar experiments in 1906. None of these experiments were conclusive, however. Neuritis was only produced in several cases out of a large number of experimental fowls, and these instances were open to criticism. Thus Eijkman, in 1907, criticised these experiments as follows:

"Maurer and Treutlein believe they have shown experimentally that the polyneuritis produced in fowls by rice is caused by oxalic acid poisoning. They both proved my observation that nourishment on polished rice caused degeneration of the peripheral nerves of fowls, and further that these manifestations were lacking in starving animals. The disease also appeared on mixed feeding (20 to 40 grams rice, and wheat 20 grams), but not when they were fed on wheat alone. One should now expect that the experiments with oxalic acid should have been conducted with complete exclusion of rice diet, but this was not the case. Maurer describes only a single one of these experiments, in which a young hen was fed first with cooked rice and glycerin and subsequently on polished rice and oxalic acid, and was attacked by the disease. Treutlein fed, also with positive result, oxalic acid or its sodium salt in rice flour balls, and gave as additional food both rice and wheat. The possibility that only the rice and not the oxalic acid is responsible for the disease does not appear to be excluded. Further, Treutlein believes to have found that lime containing food (egg shells) delays the disease, and in larger amounts can even prevent it. But because of the variable stage of incubation of the disease the lengthening of this period is not very striking evidence, and Treutlein's experiments are by no means conclusive. His hens 38 and 39, fed on rice, wheat and 0.8 gram egg shells, were taken with the disease in 16 and 28 days, respectively. Furthermore, in the cases where protection was afforded, since the fowls were fed on both wheat and egg shells in addition to the rice, it is just as likely that the protection they received was due to the wheat as to the egg shells.

"I, myself, had previously found that the mixture of chalk with rice did not act as a prophylactic. Since Treutlein's communication I have repeated this experiment with egg shells, and have found that the addition of 12 per cent egg shells (six to eight grams per day) to polished rice does not hinder or delay the development of the disease. *I have also repeated the experiments with oxalic acid and its sodium salt on animals fed exclusively on wheat. The animals have all died sooner or later, but without the clinical or anatomical evidences of polyneuritis.* I consider, therefore, that the opinion that polyneuritis of fowls is an oxalic acid poisoning is disproved."

Maurer replied to this criticism, but it is clear that he himself did not regard his theory as proven. (See Appendix, page 386.) In 1909 Maurer wrote a long paper giving a more complete account of his experiments, and elaborating his theory as to the causation of beriberi. In the course of this paper he says: "I do not to-day consider my original conception that oxalic acid is the cause of the nerve degeneration of beriberi, as correct. I lean rather to the opinion that the poison which produces the degeneration in nerves and muscles is another product of starch; a bacterial product, or more probably an intermediate product of digestion, which is absorbed unchanged through the intestinal wall into the lymph and blood circulation, or which passes through the injured mucous membrane of an atonic intestine."

It will be seen, therefore, that Maurer himself has abandoned his oxalic theory.

The theory that he substitutes, namely, that beriberi is caused by some unknown product formed from the decomposition of starch in the intestine, is pure speculation, and is manifestly incorrect for the following reason: We may feed a man or a fowl unlimited quantities of starch or rice, but if we add a sufficiency of other food, or even of rice polishings, the man or the fowl remains in good health. Manifestly, were the disease a toxaemia from decomposed starch or rice, the man or fowl would suffer from this toxaemia, provided he ingests large quantities of starch or rice, even although he does eat some other food with it. But this is not the case, and we are asked to believe in a toxaemia which can only be produced when the diet is polished rice alone, and which is not produced when rice polishings are added to the food. Such a theory is untenable.

Ashmead's Carbonic Acid Theory. The theory that beriberi is due to carbonic acid poisoning has been fathered by Ashmead and advanced by him in a number of publications from 1893 to 1901. So far as is known this theory has never been adopted by any other observer, and does not therefore deserve extended notice. (See Appendix, page 387.)

The absurdity of the idea that beriberi can be caused by carbonic acid poisoning is sufficiently evident without extended argument. In the first place, carbon dioxide in small quantities is probably not a poison. The choke damp in mines, which is composed almost wholly of this gas, kills not by its poisonous action, but because of the deficiency of oxygen which exists in such an atmosphere. The statement is made by competent authorities that atmospheres badly vitiated by overcrowding are deleterious, not because of carbon dioxide present so much as because of the numerous organic matters that are also present in such an air. But however this may be, we cannot consider carbon dioxide the cause of beriberi, because of the innumerable instances in which beriberi has been acquired although ventilation has been perfect. One cannot suppose that the thousands of Japanese soldiers in Manchuria who contracted beriberi during the Russo-Japanese war, and who must have lived chiefly in the open air, were poisoned with carbon dioxide. The Russian army, living in the same country under similar conditions, had no beriberi. Still more satisfying is our experience with the 5,000 Scouts (Filipino troops) who have lived under the same conditions and in the same kind of barracks as American troops. These Scouts were certainly not poisoned with carbon dioxide or any other atmospheric poison, and their sanitation has been directly supervised by United States army surgeons, yet until recently they have had approximately 600 cases of beriberi annually, while the American troops were unaffected by this disease. Such examples could be multiplied indefinitely were it not a waste of ammunition.

Ashmead's statement that the food *supplied* to those who escaped and those who were attacked was identical, is probably correct, but it does not follow that the food *actually eaten* was the same in both cases. This error is inherent in all observations which detail the rations supplied, but ignore the fact that all men sitting at the same table do not necessarily eat the same food.

The Miasm Theory. This has been proposed in various forms by numerous observers. Anderson, in 1877, thought beriberi was due to a gas which originated in the ground and arose from it and was absorbed by the respiratory organs. Neeb, in 1887, thought beriberi a specific disease of coast countries, caused by cosmo-telluric influences producing miasm that was absorbed by the body. Turner, in 1895, apparently adopted Manson's theory, and considered the disease to be due to the absorption of a poison which is produced by a micro-organism outside the body. Turner thought that this organism can live in sand, ballast, water, etc., and produces the disease particularly in men that have been weakened by fever, hard work, sudden climatic changes or diseases of some other kind. But Manson is the strongest advocate of the miasm theory.

Manson's Theory. The quotations which follow were taken from an article written by Manson in 1902 because he there states his theory most clearly; but he still adhered to this theory in the 1907 edition of his text book on tropical diseases, although it is possible that he may now have changed his mind.* But although Manson has to our knowledge never definitely renounced his theory, he is by no means dogmatic in asserting it. He says: "I hold that this neuritis is (a) produced by a toxin, (b) the product of a germ operating in, (c) some culture medium, (d) located outside the human body. Further, I hold that (e) the said toxin enters the body neither in (f) food nor in (g) water, and am therefore forced to conclude that it is introduced (h) through the skin or (i) that it is inhaled. I may be all wrong in this view; to-morrow some new fact may upset it. But for the present this is the result of my study of other men's work and of my own observations."

His argument for this theory is as follows:

(a) Beriberi is produced by a toxin. (1) "The analogy of many, possibly with the exception of leprosy, of all known forms of peripheral neuritis encourages this view." This is undoubtedly true, but analogy, while instructive, is not evidence, as is shown by the exception in the case of leprosy. (2) It is now generally recognized that the most important measure in the management of a case of beriberi is the removal of the patient from the place in which he sickened. If this is done at a stage of the disease sufficiently early the symptoms begin to mend, and he almost invariably recovers. On the other hand, his mates left in the endemic spot will continue to be ill for months, and many of them will likely die. On this and similar experiences I argue that the cause of beriberi cannot be a germ living and multiplying in the body of the patient, for if it were such the patient, when he left the endemic spot, would still carry the germ with him, and the disease it produces would continue until immunity was acquired. We cannot get rid of a germ by leaving the place where it was acquired, but we can get rid of a toxin in this way.

The facts on which this argument is based are undoubtedly partly correct. It has happened so many times that patients have recovered after removal from the *circumstances* under which they were taken ill, that no one can doubt the fact. But in these cases the food was also changed, and the benefit is to be ascribed to the change of food and not to the change of place. On the other hand, there are many instances in which the patients have remained in the place where they sickened, but have had a proper change made in their food, and have recovered just as marvelously. As such instances I would cite the epidemic of beriberi in Bilibid prison, Manila, P. I., reported by Fales. The cure of beriberi in the lepers on the island of Culion, P. I., and the cure of

* See discussion on beriberi in Transactions of the Society of Tropical Medicine and Hygiene, 1911, v. 85.

infantile beriberi reported by Chamberlain and Vedder. In each of these cases beriberi was cured by a simple change in the diet, without removing the patients from their surroundings or changing any other condition in which they lived.

This is all the evidence that Manson produces to show that beriberi is a toxaemia, and it is very inconclusive. Since the whole structure of his theory is built upon this foundation, it must now fall. But it will be instructive to follow his further reasoning. The evidence is reviewed which convinces Manson that beriberi cannot be an infectious disease. Since we agree entirely on this point, which is discussed at great length in a subsequent chapter, we pass on to the next step in the theory.

(b) **The toxin of beriberi is produced by a living germ.** He says: " The proof of this lies in the circumstance that the disease can be introduced into virgin country and there spread. That is to say, the cause can multiply. Spontaneous multiplication is a property peculiar to living things. Therefore the originating agent of the toxin of beriberi is a living thing — a germ." This is a very pretty syllogism, and I can see no escape from the deduction so long as we consider the disease to be a toxaemia. This we have already discredited. It is interesting to note, however, that the very cases which Manson cites to prove the spread of beriberi in a virgin country are the three which we have already criticised at some length (Chapter VI), namely, the introduction of beriberi into Fiji, into New Caledonia and into Diego Garcia. We then saw that in all of these cases the bulk of the evidence pointed to the dietary origin of the disease.

(c) The toxin producing germ operates in some culture medium. This need not be discussed, since the proposition is self-evident.

(d) The culture medium is located outside the human body. Given that beriberi is produced by a toxin, and that there is no germ in the bodies of beriberics, it follows that the culture medium must be outside the human body.

(e) The toxin of beriberi does not enter the human body in food. Manson thinks that all question of the toxin entering with the food is effectually disproved by Travers' experiment at Pudoh jail. This is all the evidence Manson adduces on this point, and it is the weakest point in his theory. He discards altogether the tremendous sanitary advance made when beriberi was eliminated from the Japanese navy by a simple change of ration, and all the evidence accumulated by Eijkman, Vorderman, Braddon, Yamagiwa and others implicating rice as the cause of beriberi, and we will see later how positive and convincing this evidence is. He pinned his faith absolutely upon one man's single experiment and in the face of the fact, which Manson himself pointed out, that Travers' experiment had a purely negative result. We have already (Chapter VI) shown clearly the fallacy in Travers' experiment.

(f) The toxin of beriberi is not conveyed in drinking water. "This is easily proved. Two institutions placed side by side, as for example the male and female prisons in Singapore, with identical piped water supplies; one, the male, is attacked with beriberi; the other, the female, is exempt."

"We must conclude, therefore, that the virus of the disease is conveyed to man either by the air or through the skin by contact, or by means of some insect or other animal which inserts it under the skin, or by a combination of these ways." *"So far, unfortunately, we have nothing to show either what the toxin is nor what the germ that produces it is, nor what the precise nidus in which it is produced is, nor the way by which it gains access to the body."* In other words, this theory is based entirely on deductive reasoning. Manson's greatest successes have been along this line of reasoning, by which he deduced that the carrier of filariasis and malaria must be a nocturnal biting insert, and so incriminated the mosquito. But his beriberi theory is based upon an uncertain premise, and without absolute certainty in our premises there is nothing so deceptive as deductive reasoning.

Icthyotoxismus (Grimm, Miura). The opinion that beriberi is caused by fish poisoning has been attributed to Grimm. But while Grimm's articles indicate this as a possibility, they do not seriously advance this theory. Indeed, in 1890, Grimm wrote that "against the theory of fish poisoning is the fact that the Aino, the original inhabitant of Hokkaido (Japan), never has beriberi, although he is a fish eater par excellence." Again, in 1898, he writes: "Experience in Japan has given us certain hints on prophylaxis, although the nature of the virus is unknown." "Many things indicate that the beriberi poison has some relationship with sea animals; other things indicate that after proper preparation and cooking these sea animals are harmless."

Miura, however, not only advances the fish poisoning theory seriously, but he incriminates a certain family, the Scomberidae, for he says: "According to my investigations kakke is surely caused by an intoxication resulting from the use of certain kinds of fish, particularly the Scomberidae." It will be interesting to see how he arrived at this conclusion, and his argument may be systematized and criticised as follows:

1. Miura believes kakke is a toxaemia, because the pathology and symptomatalogy are similar to that of known intoxications. This is reasoning from analogy again. Analogy is valuable in suggesting a hypothesis, but the proof of the hypothesis or theory must be substantiated by other facts. But Miura is satisfied that the case for an intoxication is demonstrated and proceeds.

2. Beriberi is associated with food, as is proven by Takaki's experience in eradicating beriberi from the Japanese navy, and many other similar observations. We heartily agree with Miura on this point. One case which he cites is so illuminating that it is quoted further. Miura says in the penitentiaries in Japan, where the food is properly supervised, there are practically no cases of beriberi among the prisoners, although the attendants and physicians often have it. Prisoners who are admitted with beriberi promptly get well. Sanitary conditions were investigated and found to have no bearing on the disease. The food of the prisoners consists principally of vegetables. Beef is served very rarely, and sometimes dried herrings or salted salmon. No fresh fish is used because it is difficult to obtain in large quantities and expensive. *No pure rice is used, but a mixture of four parts rice and six parts barley* (italics ours). This diet is very poor in nitrogen, and therefore it is apparent that lack of nitrogen is not the cause of beriberi. Miura sarcastically remarks: "The momentous fact that these prisoners do not have beriberi is a great wonder which we may attribute to the barley used in the diet, if we are satisfied with an easy explanation." It is a pity Miura did not investigate the easy explanation further, because it happens to be the correct one. The officers and attendants in the prison used a highly milled rice as the staple article of diet and developed beriberi, while the prisoners who were forced to eat six parts of barley to each four parts of rice were protected. The Japanese sailors at Port Arthur during the Russo-Japanese war used a similar mixture of barley and rice, and were protected from beriberi, although the Japanese soldiers, living under similar conditions, but on a straight rice ration, were badly attacked by the malady. However, Miura proceeds:

"If we compare the food supplied these prisoners and the new ration in the navy, only one factor coexists, and that is the exclusion of certain kinds of fish from the food in both cases." Miura made a slight mistake here. He forgot to mention that olive oil, molasses candy, oysters and a large number of other edibles were not present in either ration, and that therefore, on similar reasoning, all these articles of diet must cause beriberi. Further he says: "Europeans and Americans, who seldom or never have kakke, eat little fish, while statistics show that of the natives, soldiers, sailors, students and hand workers are especially predisposed to kakke. These are exactly the people who eat the most fish, and are therefore the most exposed to the poison. Certainly it is true that kakke is prevalent near the border of the sea, and that here more fish are eaten." All of Miura's evidence is of this type. It is apparent that such arguments are merely suggestive, and really prove nothing. In a subsequent article he summarized his arguments as follows:

1. Kakke appears regularly in March and disappears in September. This coincides with the season when certain Scomberidae are in the market.

2. The men of the Imperial Japanese Navy and the prisoners in the penitentiaries, who eat no Scomberidae, do not have kakke.

3. The soldiers eat largely of fish, principally the cheap Scomberidae. The same is true of students and laborers. These persons are the ones which furnish the majority of cases of kakke.

4. I know several families who are accustomed to use Scomberidae and are afflicted with kakke.

5. There are several large cities in Japan on the sea which have no kakke. On investigation it appears that Scomberidae are only seldom seen there.

6. In Tokio, where the mortality from kakke is high, Scomberidae are very numerous, cheap and much eaten.

Finally he inculpates the following varieties of Scomberidae:

Pelamys orientalis, Schlegel.
Thynnus albacora, Lowe.
Scomber saba, Bleek.
Caranx hippos, Linn.
Cybium niphonium, Cuv. et Val.
Seriola quinqueradiata, Schlegel.

But he also states in this same article: *"I unfortunately know of no positive cases where kakke resulted from the suspected kinds of fish"* (italics ours). It is apparent that no real proof is here adduced. We will only state in refutation that fish is eaten in many places where beriberi is not prevalent. Moreover, beriberi has occurred many times when fish was not a part of the diet. In the experiment carried out by H. Wright at Pudoh jail in Selangor in 1901–1902, during a particular 11 months no fish of any kind was permitted to enter the jail, and yet numerous cases of beriberi continued to occur among the inmates. Fish was rarely included in the ration of the Philippine

Scouts except as canned salmon, which is also eaten frequently by Americans and Europeans. Yet the Scouts were very subject to beriberi.

Lathyrism. The theory that beriberi is a form of lathyrism has been advanced. However, while there is a slight similarity between the symptomatology and pathology of beriberi and lathyrism, no one at the present time seriously considers the two diseases as the same. And if we should grant that beriberi is a form of lathyrism, this does not prove that beriberi is an intoxication, since there is no proof that lathyrism is an intoxication.

Lathyrism is generally considered to be an intoxication from eating the seeds of Lathyrus sativus, but as a matter of fact we have no actual knowledge that this is true. Indeed, we know far less of the causation of this disease than of beriberi. No poisonous substance has been isolated from the pulses that are supposed to cause the disease, and even the precise species concerned is not finally determined.

Allbutt writes: "It is said that foreign seeds, such as a species of Ervum, mixed accidentally with the pulse may do the mischief; or, again, the Lathyrus purpureus or Lathyrus clymenum may be the offending ingredient. On the whole it seems most likely that the Lathyrus sativus or cicera, or both, are concerned in the evil. An exclusive or almost exclusive diet on the chick pea, and wretched conditions of life, seem to be accessory causes."

It is quite evident, therefore, that so far as we know lathyrism also may be caused by the deficiency existing in an exclusive diet of chick peas instead of being a toxaemia. We do not desire to speculate on this subject, but to point out that even if beriberi were a form of lathyrism, which with our present knowledge does not seem at all likely, this would afford absolutely no evidence that beriberi is an intoxication, but would only push the problem back one step further.

Intoxication by spoiled rice. A large number of observers have connected beriberi with the consumption of rice, but many of them have believed that it was only caused by rice which had spoiled or had deteriorated in some way, and we will now investigate the evidence produced by these latter.

Eijkman was one of the earliest and most important of these observers, but his later work has led him to abandon the intoxication theory.

Van Dieren, in 1897, tried to show by statistical evidence that beriberi is a disease like ergotism, but caused by poisoning from the use of rice. But while Van Dieren's evidence goes far toward incriminating rice, it affords no proof that the disease is an intoxication. The following is one of the cases quoted by Van Dieren as indicating that beriberi is caused by bad rice: A ship, the Blommerdaal, had a crew consisting almost entirely of natives. For about two years the crew received an excellent ration, including live cattle and other fresh provisions, and they had no beriberi during this time. However, in April, 1885, a new ration was provided, consisting chiefly of rice, dried fish and cocoanut oil. After a few weeks on this diet a case of beriberi appeared, and this one was followed in about ten days by eight more cases. The captain then decided to feed the natives like Europeans. As a result of this change in diet all the cases recovered and no new cases occurred. Later the men were again placed on the rice and fish ration, and beriberi again appeared. But in the next voyage of the same ship, when there was a good supply of fresh food, not a single case of beriberi occurred. Here was an instance where beriberi appeared and disappeared with the changes in the ration, and Van Dieren is quite correct in incriminating the rice. But it will be evident to the reader that a diet consisting chiefly of rice, with a little fish and cocoanut oil, could have been at fault through its deficiency, quite as well as from a toxaemia.

Sakaki showed by statistics that the kakke season corresponded to the season when badly preserved rice from certain provinces (Echigo and Akito) appeared in the market and was commonly bought. But he affords no direct evidence that this badly preserved rice was actually toxic. Indeed, Sakaki stated that he had made attempts to isolate this toxin, but had not yet succeeded.

Yamagiwa (1889) reasons that beriberi is connected with the diet because: 1. Kakke has disappeared in the Japanese navy as a result of change of food, which is now like European food. 2. In Tokio they have learned to use as daily food barley, either pure or mixed with rice, as a prophylactic during the kakke season. Those using this remain free from kakke. 3. All Europeans who adhere to the use of European food remain free from kakke. 4. Among the Japanese there are some who at home in the summer suffer from kakke, but while absent in Europe remain free from it. Removal of beriberic sucklings from the breast of the affected mother is the best treatment for this illness.

Yamagiwa thinks that beriberi is a toxaemia because: 1. Hirota and Miyaka so described it. 2. Komoto and Komo have found central scotomata in beriberics that correspond to those found in other intoxications. 3. Sakaki has proven statistically that the kakke season corresponds to the season when badly preserved rice appears in the market and is commonly bought. 4. Eijkman in Batavia believes polyneuritis gallinarum to be an intoxication. 5. In kakke bodies we see no infectious spleen and no circumscribed focal necroses, as in many infectious diseases. 6. The contraction of fine arterial branches of the large and small circulations can be accounted for most easily by the conception that it is a reaction to a particular poison. 7. Kakke patients frequently get better by changing their location. 8. Purges, like magnesium sulphate, are very efficacious in kakke. 9. The fulminating form is very similar to acute poisoning, and the chronic paralyses are very similar to those from lead, arsenic and alcohol.

Yamagiwa concludes that "Kakke or beriberi is an intoxication caused by the daily use of a kind of cooked rice as the staple of diet, the toxin from which causes the contraction of the small arterial branches of the pulmonary and general circulations. This in turn produces hypertrophy and dilitation of the heart, local anaemia of the skin, mucous membranes, peripheral nerves, skeletal muscles and kidneys, followed by degenerative changes in those organs."

The conception that infantile beriberi is a toxaemia is dealt with in the chapter on that disease. For the rest it is sufficient to state that there is neither a conclusive argument nor satisfactory evidence that beriberi is a toxaemia in any of the reasons advanced by Yamagiwa for that belief. He himself says: "Direct proof of this conception has not been furnished, but this appears to be the most probable explanation."

Hose (1901) is another observer who concluded on insufficient evidence that beriberi is a toxaemia. He says: "By a process of elimination I arrived at the conclusion that the principal cause of beriberi in Borneo is the consumption of mouldy rice. The disease is much more prevalent among men than women. It is frequently contracted, as in my own case, on a journey in the jungles of the interior." "The women in Borneo, who very rarely leave the villages for any length of time, live mainly on freshly husked rice, while the men are frequently absent in the interior on rubber collecting expeditions for several months at a time. They carry their rice with them in bags, and after a time it becomes mouldy from the damp climate."

"I further noticed that the outbreaks of the disease in the Baram district of Sarawak are more noticeable in the months of April, May and June, immediately after the period when the northeast monsoon has made it impracticable for ships or native craft to enter the Baram river. To meet the local requirements, large quantities of rice are imported before the monsoon period. Probably the rice has been in bags for some weeks or months before it reaches Baram, and after being kept in bags for a further period it becomes mouldy."

"I have a strong impression that the incidence of beriberi is distinctly heavier in those tropical or sub-tropical countries which import rice than in those which supply sufficient on the spot to meet all local demands. Naturally the opportunity for deterioration in transport is greater when rice is imported from a distance."

Hose believes he has found a fungoid growth on rice that had been stored for some time, but states: "I have observed apparently identical fungoid or mould-like growths upon maize, sago flour and even on dried fish, so that any of these articles of diet might convey the disease."

Here again a toxaemia is by no means the only possible explanation of the observed facts. The men, when they live in the village on rice freshly husked by hand, which is never entirely freed from pericarp, do not suffer from any deficiency. But when they go for months into the interior they carry in bags *highly milled rice* furnished them by the contractor, and eat little else. They therefore suffer from a deficiency of the elements contained in the pericarp and aleurone layers, and develop beriberi. Again, Hose says the beriberi in the Baram district coincides with the period when large shipments of rice are imported. Now, imported rice is always a highly milled rice. This was the reason for the incidence of beriberi in April, May and June, and not the fact that this rice was stale or spoiled. Again we see a toxin theory born without direct evidence of a toxin in rice, and without any evidence which cannot be satisfactorily explained in another way without the assumption of a toxin.

Uchermann, in 1904, gave the results of the investigation of the committee appointed by the Norwegian government. He considers beriberi a multiple neuritis caused by toxic substances in spoiled vegetable and animal food, so that a vegetable form or Asiatic beriberi, and an animal form or ship beriberi are to be distinguished. This point of view is discussed in the consideration of ship beriberi, to which the reader is referred.

M. Miura studied the epidemic of beriberi among the Japanese troops in Manchuria during the Russo-Japanese war and published his conclusions in 1906. He found that during the first year of the war beriberi was much more severe and widespread than during the second year. All the provisions used by the troops for the first year came from Japan, but during the second year they were obtained in Manchuria. He therefore concludes that the food from Japan contained the toxin or the organism capable of producing a toxin. This by no means necessarily follows, however.

Takaki explained this circumstance as follows: "Unfortunately, during the Chino-Japanese and Russo-Japanese wars, owing to circumstances, only rice was given to the men as the principal food, and consequently cases of beriberi increased greatly. But in the later period of the Russo-Japanese war, when we began to give the men barley with rice, and increased the quantity of meat, beriberi decreased rapidly with this change of diet."

We now come to the consideration of the evidence which Braddon brought to this theory in his book on the cause and prevention of beriberi, published in 1907.

Braddon bases his rice poison hypothesis on the following argument: If this theory is the correct explanation, it becomes predicable in every epidemy of beriberi that —

1. Those whom it attacks should be rice eaters.

2. It should not attack those who do not eat rice.

3. Among rice eaters its incidence should vary with the sort or quality of the rice eaten.

4. Among eaters of any sort of rice which the event shows is or may be poisonous to some, other things being equal, the case incidence (or number of persons attacked) and the case mortality (the severity of incidence upon individuals attacked) should vary directly with the quantity of rice eaten.

(a) Absolutely.

(b) Relatively to the quantity of other articles composing the diet, as a poison taken alone will often produce a severe or more rapid effect than the same or even a larger dose of it taken together with other food.

5. The course of the disease in those affected should not tend, or tend little, to recovery, and the number of persons attacked, when all are not affected simultaneously, should persistingly increase so long as they continue to use the same rice which they ate when it was acquired, and conversely should tend to recovery when the noxious rice is discontinued.

Braddon states that these five deductions "are such as could obviously be made from no other premises than those of the rice theory as it has been formulated here" (i. e., the rice poison hypothesis). He also states: "For the logical proof of any theory it is necessary to show not only that all the inferences which can properly be made from it are verifiable, so far as they can be put to the test of experience, but also that some at least of the facts which constitute that experience are incapable of explanation on any other theory." However, all the facts that Braddon advances as proving his theory can not only be explained by the theory of a deficiency in the food, but can be actually better explained by the latter theory. Let us take up the points of Braddon's theory one by one.

Braddon presents very convincing evidence to show that in epidemics of beriberi, and in places where it is endemic, rice eaters only are attacked, while those who eat no rice escape. We believe he proves this point with the following important reservation which he himself makes in another place. Thus he states: "It is to be observed here that rice is postulated only as being the *common* or *usual*, but not as a *necessary* habitat or medium for conveying the poison. Beriberi, as the result of the operation of the same or a similar agent in other articles of food or other cereals, may very well occur under circumstances in which rice could not play a part."

Braddon here admits that beriberi can occur among people who live on a diet which never includes rice. For example, certain races who live chiefly on sago and fish. Therefore rice *per se,* or a toxin which can only be produced in rice, cannot be the cause of beriberi. Braddon avoids this difficulty by the supposition that his toxin or a similar toxin can be produced in other farinaceous articles of diet, such as sago. Now, while this supposition is a possibility, it is far more probable that the defect in rice, sago and some other farinaceous food used as a staple article of diet consists in the dietary deficiency existing in this class of food rather than in its toxicity. It will be useless to dwell upon this point at the present stage of our discussion, since we cannot decide in favor of the two competing theories on a *probability.* But the point should be remembered when we show later, not only that the alleged toxin in rice, sago, etc., is hypothetical, but that it cannot be extracted from these foods.

Braddon then gives in great detail evidence that proves that the incidence of beriberi varies with the sort of rice consumed. He demonstrates this point so conclusively that I do not see how any one can question the fact. After showing that the users of red rice (undermilled rice, see Appendix, page 389) and cured rice never have beriberi, that those who store their own rice and prepare it freshly from day to day almost never have beriberi, and that those who use the white stale rice are exceedingly subject to beriberi, he draws the following deductions: (1) That the users of red rice are protected from beriberi because the red rice, having its pericarp, is protected from the action of the saprophyte that forms the hypothetical toxin. (2) That the users of cured rice are protected from beriberi because the rice has been sterilized by boiling, and the formation of a toxin thereby prevented. (3) Those who store their rice as padi and husk and prepare it daily are protected because the unhusked grain is protected from the action of the hypothetical organism, and the rice, after it is husked, is eaten before this toxin can be formed. (4) Those who consume stale white rice are subject to beriberi because this grain, being deprived of its covering, is subject to the action of this hypothetical organism, and especially when stale is apt to produce beriberi.

The fact that the users of red and cured rices are exempt, while the users of the white rice are liable to beriberi, can be as well explained by a theory which does not demand a hypothetical organism producing a hypothetical toxin. Eaters of red rice are protected because it retains the pericarp and aleurone layers, which contain certain substances necessary to life. These substances are lacking in a white or highly milled rice which is deprived of these layers. Cured rice also contains these layers, for the reason that the process of curing renders these layers so adherent to the underlying grain that they cannot be entirely removed. The protection secured by the eaters of cured rice and red rice may therefore be due to the retention of these layers with their included necessary food substances. Those people who pound out their own rice from day to day also secure protection, because by this method the aleurone layer and pericarp are seldom completely removed.

This deficiency theory explains the facts better than does the toxin theory, because experience has shown that hand-pounded rice or any undermilled rice can be stored for long periods of time and yet does not produce beriberi when it is finally consumed. This has been our experience in feeding the Philippine Scouts on an undermilled rice which has necessarily been stored for several months before its final consumption.* Now, while undermilled rices retain much of their pericarp, it is by no means retained intact. The starchy center of the grain is exposed in many places, and there is no reason why the hypothetical organism could not attack these unprotected portions of the grain and produce the hypothetical toxin, if Braddon's theory were correct. But this does not occur, and it therefore seems much more probable that these rices afford protection by reason of some substance or substances contained in the surface layers.

* Experiments have shown that an undermilled rice may be kept for over a year, under most adverse circumstances of weather and exposure, but that it will still prevent polyneuritis gallinarum when fed to fowls even although it is mouldy and quite unfit for human consumption. (Vedder and Williams.)

With regard to the proposition that the incidence and even the mortality of beriberi should vary directly with the quantity, absolute or relative, of rice eaten, Braddon himself says: "Owing to the fact that the assumed poison in rice which produces disease has not yet been identified, precise evidence on this point is not obtainable." "But if it were possible to place two different sections of a population otherwise all equally susceptible to beriberi for sufficiently prolonged periods upon a diet composed chiefly of the same uncured rice, but in quantities which should, for whatever reason, always be unequal either absolutely or relatively or both, for the two classes, then the result would afford some measure of the direct effect which quantity of rice eaten has upon the incidence of the disease." Braddon then proceeds to quote a number of instances where such conditions have obtained, and he shows that in many of them the incidence of beriberi has varied both absolutely and relatively to the amount of rice consumed.

But cannot this incidence of beriberi be explained by the theory of a deficiency in the food just as readily as by the toxin theory? I think we may assume that since the size of the stomach is more or less definite, and since a man eats until the stomach is filled, or until a feeling of satiety is produced, that the larger the quantity of rice eaten, the smaller will be the amount of other food eaten with the rice. Now, if this rice is deficient in some substance which may be supplied in other articles of food, it follows that those eating the largest quantities of rice, and therefore the smallest quantities of other food, will be the first to experience the effects of this deficiency. In other words, the incidence of beriberi will generally be proportionate to the quantity, absolute or relative, of rice eaten. Moreover, where conditions are reversed Braddon's theory fails, while the deficiency theory fits the facts. If men are fed on polished rice alone or chiefly, but in small amounts, in other words if they are underfed, it should take much longer to produce the disease, because a smaller amount of toxin is being ingested. This is not the case if other food is excluded. The underfed man succumbs to beriberi more quickly than the man who eats larger quantities of rice.

Again, were beriberi a toxaemia caused by the absorption of a toxin produced in this stale white rice, the disease should occur among people using this rice even though they also eat other articles of food. This is not the case, however. The evidence is clear that beriberi is not acquired, *no matter if considerable stale white rice is eaten*, provided a sufficient quantity of other proper food is also consumed. Europeans eat daily the same white rice that produces beriberi among the natives, yet they do not contract the disease. This is generally conceded. In the Philippines, officers and their families and native servants have consumed for many years large quantities of white highly milled rice. Thus a certain family, including native servants, for years has used 100 pounds of white rice every month, and this instance is no unusual exception. The identical rice obtained by the same commissary and from the same contractor was furnished the Scouts (native troops). The Scouts averaged about 600 cases of beriberi a year, while beriberi was unknown among the officers and their families and native servants using the same rice. This does not accord with a toxin hypothesis. If the rice were toxic surely Europeans or Americans using the same rice should develop beriberi even though they do eat other food.

Finally Braddon presents much evidence to show that beriberi will persist as long as the same rice is used and will disappear when this is discontinued. It is clear that if beriberi is really caused by a deficiency existing in highly milled rice, it will persist as long as this rice is used and will disappear when an undermilled or cured rice is substituted.

We have thus taken every one of the five points upon which Braddon founds his theory, and have shown that an intoxication is not a necessary deduction in a single one of them. His theory is not, therefore, logically proven, judging by the standard which he himself sets.

Braddon indeed briefly considers the deprivation theory, but dismisses it in a single paragraph, as follows: "But, apart from the difficulty of conceiving that white rice and many other articles of food thus not only normally share, but also are liable periodically to lack a given principle, without which they are practically rendered poisonous when consumed, the objection seems to the writer insuperable against the privatory theory that *fresh rice is never toxic.* It never produces beriberi, in however large a quantity consumed, and with however little of other adjuncts it may be taken. But to explain the irregularity of occurrence of beriberi in communities whose diets were continuously the same, it had to be assumed that some quality in their food was periodically lacking. The fact that in fresh rice the quality is never lacking seems a proof therefore that it cannot be to any such periodic absence of any principle from their food that its subjects acquire beriberi." Braddon therefore completely dismisses the deprivation theory for the sole reason that he believes that fresh rice is never toxic.

The statement that fresh rice is never toxic is believed to be an error. At any rate it is a negative statement and one that Braddon cannot possibly prove. It is difficult to disprove this statement for the reason that it requires ninety days on a diet of highly milled rice to produce beriberi in man, and it is therefore apparent that it will be exceedingly difficult to obtain cases of beriberi in which the rice used has not been stored for at least short periods of several months. However, it has been shown that polyneuritis gallinarum can be produced in fowls by using white or highly milled rice which is absolutely fresh, and so many instances of beriberi in man are on record in which the rice used was absolutely above suspicion as to its excellent quality and condition, that it is difficult to believe that decomposition of the rice plays any part in the production of beriberi. It seems evident, therefore, that Braddon had insufficient grounds for discarding the deprivation theory.

Braddon is probably the most important adherent of the theory that beriberi is caused by a toxin produced in certain kinds of rice. But while this theory of a toxaemia cannot be held to be proven, it should be stated that Braddon's book is one of the most important contributions that has ever been made to the subject of beriberi. It contains in readable form so much evidence on the vexed question, and proves so conclusively that beriberi is usually caused by the use of certain kinds of rice, that it is hardly possible to form an intelligent opinion on the merits of the controversy as to the etiology of beriberi without a careful perusal of his book. I believe it is impossible for anybody to read his book and consider critically and without prejudice the evidence that he presents without being convinced. 1. That a diet consisting chiefly of certain kinds of rice will produce beriberi; 2. That the use of parboiled or cured rice will prevent beriberi; 3. That people who do not subsist chiefly on rice or some equivalent farinaceous food do not have beriberi. If these three points are correct, it is clear that the etiology of beriberi is definitely connected with the use of certain kinds of rice. Moreover, Braddon's book focussed attention on the rice question and led to much of the advance which has been made in recent years.

Kohlbrugge believes that rice is subject to the action of a group of bacilli which he has isolated and named Bacillus Oryzae, and that the fermentation products of these bacteria cause beriberi. He states that he has produced beriberi in fowls in four or five days by feeding polished rice mixed with agar cultures of these bacteria isolated from rice. However, he did not demonstrate the existence of nerve degeneration in the fowls, and from what we know of beriberi and polyneuritis gallinarum it seems impossible that he could produce this disease in four or five days. It is most probable therefore that his fowls died of some toxaemia or infection, and not from beriberi.

Moreover, Shiga in endeavoring to test the validity of the intoxication theory performed the following experiment: He fermented an undermilled rice in the incubator for about a week and fed fowls on this fermented material, but they remained healthy for two hundred days, when the experiment was discontinued. Chamberlain, Vedder and Williams repeated this experiment with the same result, and also fed fowls on a highly milled rice, fermented in a similar way. These fowls did not develop neuritis any sooner than fowls fed on the same rice when perfectly fresh and dry. These experiments seem to completely disprove Kohlbrugge's theory.

Mott and Halliburton performed an experiment which has led some to believe in the existence of a poison in the blood of beriberics. They injected blood taken from an acute case of beriberi into a cat and found a fall of blood pressure, with dilatation of the vessels of the stomach, intestines and liver, as well as general venous engorgement, and they also noted dilatation of the right side of the heart and microscopical haemorrhage into the liver. However, it must be borne in mind that the normal blood from one species is distinctly toxic to individuals of another species, and this possibility is by no means excluded in the work of Mott and Halliburton. Shiga later performed similar and also many other experiments. He injected kakke serum into rabbits and guinea pigs, both subcutaneously and intraperitoneally, and injected normal human serum into other animals as controls. The kakke serum was no more toxic than the normal serum. Experiments undertaken to show a lack of complement in kakke serum such as Ehrlich and Morgenroth found in the serum of dogs that had been poisoned by phosphorus, were also negative. There was no difference between kakke serum and normal serum with regard to cleavage by hydrogen peroxide. Attempts to demonstrate a toxin or an abnormal substance in the urine or the milk of kakke women by means of cleavage with hydrogen peroxide were undertaken but were negative. Similar attempts to prove the existence of a toxin by determination of the freezing point of kakke serum were also negative. Shiga's experiments were continued for two years, but none of them were positive or gave any support to the theory of intoxication.

Adachi claimed to have isolated a toxin from rice which exercised a marked action upon the heart of the lower animals. But his method of obtaining the toxin was as follows: Cooked and wet rice was mixed with takadiastase, and allowed to stand until it was greatly fermented. He then filtered the resultant liquid and evaporated it. The residue was taken up with absolute alcohol, the alcohol again evaporated and the final residue dissolved in Ringers' solution in the proportion of 1–50. It would seem from such a method that a poison might possibly be extracted from any food. The rice was mixed with takadiastase *and bacteria,* and allowed to ferment and putrify before extracting the poison. Good meat has been known to develop toxins under such circumstances.

Inagaki and Nemori found that the milk of beriberic mothers had the property, when placed in contact with the heart of the frog, of diminishing its contractions or of paralyzing the heart in diastole. This action they believe to be due to a toxin. However, experiments of this kind are not satisfactory. Distilled water or various salt solutions poured on the frog's heart might have a similar effect.

Guerrero and Gavieres performed similar experiments and found "that the milk of a beriberic woman, who has a beriberic child, kills the frog's heart within less than 30 minutes in 71 out of 100 cases. This reaction is not, however, constant; 29 per cent of the cases exceed 30 but not 60 minutes; only one of the cases examined by us reached 55 minutes. On the other hand, this proportion is reversed in the case of non-beriberic women with non-beriberic children, because here only 36 per cent do not exceed 30 minutes, while 64 per cent live beyond 60 minutes." From this very inconclusive evidence the authors believe the conclusion is justified that the milk of beriberic women contains a toxic substance.

It is evident that there may have been many other factors concerned in the action of the milk besides a toxin. Loeb and others have shown that certain well-known inorganic salts stimulate cell activity while others are inhibitive in action. The action of these different milks on the frog's heart could be easily explained on this basis without assuming the presence of a toxin. Moreover, Chamberlain and Vedder had already shown that children suffering from infantile beriberi may continue to nurse their mothers and recover promptly if they are given in addition an extract of rice polishings. This could hardly be the case if the milk contained a toxin.

If beriberi were caused by a toxin in the food it should be possible to extract this toxin. The extraction of both organic and inorganic poisons from food substances is a very simple chemical feat, although it may be difficult in the case of the more complex ptomaines to isolate them in chemical purity. We do not demand this, but it is believed to be fair to demand evidence that the incriminated food is injurious because of a contained poison. All of such attempts have failed signally. We have already mentioned Sakaki's failure to obtain a toxin from rice.

Fraser and Stanton have performed most elaborate experiments to determine the existence of such a poisonous principle. White rice was macerated and extracted with alcohol acidulated with acetic acid. The alcoholic extracts were concentrated in vacuo and freed from alcohol by exposure in evaporating basins at moderate heat. The extracts were examined and treated in every way possible for the isolation of poisons, but although numerous examinations and experiments were made, a poison or poisons were never isolated.

Inoculation experiments were performed on guinea pigs, rabbits and monkeys with various substances isolated from white rice, but yielded no satisfactory result. Feeding experiments were then performed as follows:

1. Finely ground white rice was macerated for four days with 94 per cent alcohol, and then percolated. The rice was then removed, freed from alcohol by expression and dried in the sun. Five fowls were fed on the exhausted rice, and three developed polyneuritis within five weeks.

2. The same was repeated, using hot alcohol and extracting in a large Soxhlet apparatus for twenty hours. The alcohol was then expressed and the rice dried in the sun. Four fowls were fed on this exhausted rice and two developed polyneuritis.

3. The alcoholic extract was condensed by distillation in vacuo and entirely freed from alcohol by exposure in shallow basins at low temperature. The alcohol free extract was emulsified in distilled water and two fowls fed on cured rice received daily an emulsion of the extract representing that obtained from 100 grams of white rice. The experiment was continued for 51 days, and both fowls gained in weight and showed no signs of any disease. These experiments prove that no alcohol soluble poison was contained in white rice.

But in order to control these experiments cured rices were treated by methods precisely similar to those just described. Fowls were then fed on the cured rice after exhaustion by alcohol. Cases of neuritis appeared. But when, on the other hand, fowls were fed on white rice (supposedly toxic) with the addition of the alcoholic extract from cured rice all remained healthy. These experiments indicate that white rice is not toxic, since no toxin can be extracted and since it does not produce injury when combined with the substances extracted by alcohol from cured rice or rice polishings. They have been repeated so many times by so many different observers with the same results that there cannot be the slightest question as to their accuracy.

Various observers who have thought from the pathology of the disease, or for other reasons, that beriberi is a toxaemia, but who have recognized the futility of all attempts to demonstrate a toxin, have fallen back upon that asylum of ignorance, auto-intoxication. There undoubtedly is such a pathological condition as auto-intoxication, but our exact knowledge of it is extremely limited. It is most unscientific to refer all diseases of whose causation we are ignorant to this category, and in the present state of our knowledge such a classification of disease is purely tentative. If beriberi were an auto-intoxication the blood of beriberics should be toxic, and experiments have failed to substantiate this point. Moreover, beriberi is an epidemic disease which is quite contrary to the theory of auto-intoxication. Epidemics of auto-intoxication, whatever this may be, do not occur.

It would be possible to go on in this way and analyze the work of every investigator who has advocated the intoxication hypothesis, but it would be too tiresome. Braddon's work is the best, and its weakness has been exposed.

We will therefore conclude this discussion. A beriberic toxin has never been discovered in spite of earnest efforts to find such a poison. No facts have been observed which cannot be explained by the deficiency theory as well as or better than by the toxin theory. No advocate of the intoxication theory has furnished direct proof of its truth. Indeed there is absolutely no foundation on which to base an intoxication theory, and we will therefore dismiss it from further consideration.

CHAPTER VIII

THE ETIOLOGY OF BERIBERI, CONTINUED

Is Beriberi an Infection?

In order to determine whether we are to consider beriberi an infectious disease we will first examine the evidence offered by the principal advocates of this theory and see whether any of it affords convincing proof that beriberi is an infection.

Several observers have described protozoa, which they believed were the causes of beriberi. Glogner examined the blood from splenic punctures and found a peculiar organism in 63 out of 98 beriberic cases. This organism was round or oval, extra globular, richly pigmented, and the younger forms were actively motile. They possessed a development similar to that of the malarial parasite. Indeed, Glogner at first believed that they were of malarial origin, but as he studied them further he was led to believe that this was not the case because, "1. Even the youngest forms are pigmented and the pigmentation is heavier than in malarial parasites. 2. The pigmentation possesses a characteristic form. 3. They are entirely extra globular. 4. They are found in splenic blood and not in the peripheral blood." Glogner concludes: "According to my observations the cause of beriberi, like the multiple neuritis of Europe, is of complex origin, but in malarial countries I believe the principal cause is the splenic parasite and the malarial plasmodium. Further investigations must show whether this is also the cause in other countries, like Japan and Brazil."

It seems quite possible that Glogner's parasite was some form of the malarial organism. In the first place many of his cases had enlargement of the spleen and slight fever. This is characteristic of malaria, but not of beriberi. Moreover, Glogner describes several cases in which malaria plasmodia were found and which he thought also had beriberi, but in which, after administration of quinine, both the fever and the symptoms of beriberi had disappeared.

The points which Glogner cites are by no means sufficient to prove that these protozoan organisms were not of malarial origin, and finally Glogner himself says: "I know very well that a direct scientific proof of their etiological significance is not yet furnished. Two things are necessary for such proof. First, that the organism should be found in all cases of beriberi, and secondly that they should be recovered and the same pathological condition produced by their inoculation. With regard to the last point experimental evidence is lacking." Glogner has recently abandoned this theory.

Fajardo also found a haematozoan in the blood and internal organs of beriberics which he believed had not been described. It produced a pigment and the single phases of development were similar to that of the plasmodium of malaria. It was an intracorpuscular parasite and there is no evidence to show that it was not of a malarial origin, while the description and figures furnished would lead to the belief that they were malarial parasites.

Voorthuis found plasmodia resembling the malarial plasmodium in his beriberic patients in Sumatra. Since he states that the disease usually began with several days' fever and that the spleen was enlarged in many cases, it seems probable that malaria existed as a complication in the cases of beriberi Voorthuis studied.

Some of the older authors thought that beriberi was a disease of malarial origin, but this supposition is not seriously considered at the present day.* Malaria is often present in regions where there is no beriberi, and *vice versa*. Many epidemics of beriberi have been noted on ships a long distance from the land, where no malaria was present, and finally the plasmodium malariae is only seldom found in beriberic cases, where it is evidently a complication.

Hewlett and Korte, in 1907, observed a disease in monkeys resembling beriberi and found that their urine contained some highly refractile cells which were possibly of a protozoan origin. They then examined the urine of beriberi cases and found small refractile spherical bodies two to three microns in diameter with a thick capsule and hyaline contents. Other cells were also found, twenty microns in diameter, globular and containing a cytoplasm studded with refractile granules and having a single nucleus. A third form of cells was also present, thirty microns in diameter, with a thick capsule, and containing a finely granular oval nucleus with a rounded nucleolus. They suggest that these cells are either peculiar degenerate cells or are possibly protozoa.

They fed monkeys with beriberic urine, but the experiments were inconclusive, and they do not mention the diet upon which these monkeys were subsisted.

* Glogner now maintains that beriberi is a secondary affection, and that a relationship exists between it and an earlier malaria. So far as I am aware, Glogner is alone in this view.

As a result of these observations the authors merely suggest that beriberi may be a protozoan infection, and that the urine may convey this infection. Several other observers have found protozoa in the blood and have attributed more or less significance to them, but these findings in no case coincide with each other, nor have they ever been confirmed, nor has any real connection between any of these protozoa and beriberi ever been proven.

Some of the common nematode parasites have also been implicated. Thus Kynsey, in a report on anaemia, or beriberi of Ceylon, was quite certain that certain forms of beriberi were due to anchylostomiasis. He contended that the so-called wet form of beriberi should be subdivided into two classes: 1. Cases due to malarial poisoning characterized by extreme debility, impoverishment of the blood and enlargement of the spleen, sometimes followed by dropsy and more rarely palsy. 2. Cases caused by the presence in the intestinal canal of parasites, mainly of anchylostomum duodenale, but possibly of trichocephalus dispar.

Kynsey, however, was apparently not dealing with true beriberi. As we have stated in another place, there is no beriberi at present in Ceylon and there is good reason for supposing that most of the cases previously so diagnosed were cases of anchylostomiasis. Kynsey in fact showed that the so-called beriberi of Ceylon was in reality anchylostomiasis and not beriberi, although he did not reach that conclusion himself.* But no one at the present time would consider

* The grounds for supposing that a large proportion of cases of beriberi were caused by anchylostomiasis are as follows according to Dr. Kynsey:

"Both (anchylostomiasis and beriberi) are most prevalent in the tropics but may and do develop beyond these regions; both prevail most extensively in seasons characterized by a high degree of atmospheric moisture and temperature; both are prevalent on the sea coast and along the banks of great rivers, dampness, wetness or swampiness being the characteristics of the soil, but there is no connection with malaria. The areas or centres where both prevail are often narrowly circumscribed, while adjoining districts with the same climatic influence escape. Both attack bodies of men collected together under bad hygienic conditions, and those of strong physique are equally liable to be attacked with the weak, but those living on innutritious food, or food not corresponding to the metabolisms and blood making, or the needs of the body, such as rice and fish, suffer the most severely. Both are due to the use of bad drinking water, and both recover if the anaemia has not advanced too far, on leaving the focus of the disease and changing the mode of living, particularly by the use of nutritious blood forming food. Both attack at all ages, but adults and males are more frequently affected than females or very young children. In both predisposition increases with length of time spent at the focus of the disease, and a residence of some months is necessary before the disease is developed; and as regards race, the natives suffer more than the Europeans, but the latter, living under the same conditions as the natives, suffer equally. In both the anchylostomum duodenale is found." "Neither is communicable from person to person. In both anthelmintic remedies give relief or cure, and in both sudden death so prominently alluded to in old descriptions and by Professor Maclean is appallingly frequent."

these intestinal parasites as the cause of beriberi. A large proportion of the native population in some localities are infested with anchylostomum duodenale, so that the fact that many beriberics may harbor these parasites ceases to be of importance.*

A large number of investigators have isolated bacteria from cases of beriberi and have claimed that these organisms are the cause of beriberi. But there is absolutely no agreement between these investigators, since practically all of them incriminate different organisms.

Nepveu in 1898 found in the tissues of beriberic cases that had been preserved and sent from Senegal, three different kinds of bacilli, and believed that they were specific for beriberi on this slight evidence although no cultures or experimental investigations were made.

Lacerda isolated a bacillus in 1883 from blood of beriberics, and thought it was the same bacillus subsequently found by Ogata.

Taylor also believed he had found a bacillus that was the cause of beriberi. He obtained it from blood and urine of beriberics and also in canal water and washings from rice. Ogata, however, criticised his work, saying that Taylor worked with peptone gelatine sterilized at 115°F. and was convinced that all lower organisms were killed at this temperature.

Ogata in 1885 found in the blood of beriberics a spore bearing bacillus somewhat resembling anthrax. The organism was cultivated readily, and Ogata believed that it produced the symptoms of beriberi in rats, mice, rabbits and monkeys. Ogata used blood obtained by

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* Certain other authors, notably Giles (1880) and Erni (1886), have maintained that beriberi is a form of anchylostomiasis. In 1894 Walker, in a communication to the Eighth International Congress of Hygiene at Budapest, found as the result of examining the stools of 927 beriberics from Sandakaw, North Borneo, that 85.5 per cent of the cases were infested with anchylostomes. He remarks that the parasite is infrequent among the native population and concludes that although not the true cause of beriberi, anchylostomiasis may be a predisposing cause of some importance.

Noc in Cochin China (Ann. Inst. Past. 1908, p. 896) studied the relation of Necator Americanus and beriberi. In the first series of 77 beriberics he found 74 carriers of anchylostomes, and in a second series of 211 cases he found 197 carriers. He concludes that this remarkable frequency of Necator Americanus in Asiastics bears a relation to the appearance of symptoms of beriberi, and may play concurrently with poverty of food, a very important role in the production of this disease.

Mathis and Leger, however, observed a number of beriberi cases at Hanoi and investigated the prevalence of anchylostomiasis. Thus out of 55 adult beriberics, anchylostomes were found 31 times or 56.36 per cent. However, they also found that adults who did not suffer from beriberi were infected in 52.28 per cent, and that in certain places, *i. e.*, the prison of Hadong, which has never been a focus of beriberi, the percentage was much higher. Thus out of 55 prisoners 36 were carriers, a percentage of 65.65 per cent. Also according to unpublished notes of Dr. Seguin this latter found 18 carriers out of 30 beriberics, or a percentage of 60.0, while of 431 non-beriberics 59.16 per cent were carriers.

Thus contrary to the findings of Noc in Cochin China the proportion of anchylostomiasis in Tonkin is the same in beriberics and in those inhabitants who do not suffer from this malady.

puncturing the finger which was previously cleaned and sterilized with two per cent carbolic acid. He only obtained a pure culture five times, his other tubes being sterile or contaminated by a mixed growth. The animals inoculated with this organism died in from a few hours to a few days, and there was nothing characteristic of beriberi in the autopsies although the bacteria were recovered in practically all cases.

Rost (1900) investigated different rice liquors used in large quantities by coolies of Rangoon and discovered in them a peculiar micro-organism. It was an angular diplo-bacillus and a spore-bearer. He also found the same organism in damp rice, in the blood of beriberics, in cerebro-spinal fluid and in the serous exudate from the sheath of the sciatic nerve of beriberic cadavers. He cultivated the organism and produced beriberi-like symptoms in fowls with the cultures and also with beriberic heart blood and cerebro-spinal fluid. He was convinced that this organism was the cause of beriberi. The fatal defect in his experiment was the fact that the diet given his fowls is not mentioned, and we now know that beriberi-like symptoms can be produced in fowls by an improper diet alone.

Pekelharing and Winkler made cultures from 80 cases of beriberi. They found no bacteria in 65 cases, bacilli of different kinds in three cases and a number of different kinds of cocci in the remaining cases. Their results therefore were not uniform and their methods were faulty. Even they consider the bacilli to be contaminations. Of twelve experiments conducted with one of the cocci isolated, nine were positive in that degeneration of certain nerves was found. This, however, may be seen in several infections. They disregarded the fact that the other pathological changes of beriberi were not found in the inoculated animals and also laid little stress on the symptoms of the animals experimented on, of which two developed abscesses, two peritonitis and one purulent pleurisy.

Pekelharing and Winkler concluded that these cocci were the cause of beriberi, but while their work received considerable attention at the time and has been widely quoted, it is now generally discredited.*

Somewhat similar to the findings of Pekelharing and Winkler are those of Van Eecke, who incriminated three species of cocci and a bacillus, and Musso and Morelli, who found four kinds of cocci. It is highly improbable that any disease is caused by four different organisms working together and most probable that all of these organisms were contaminations for reasons that will be discussed later.

Hamilton Wright (1901–1902) elaborated what is, in many respects, the most attractive theory of beriberi that has ever been proposed.

* A more detailed account of this work may be found on page 390 of the Appendix.

Wright believes the disease is due to a specific bacillus. If taken into the intestinal canal, this bacillus multiplies in the stomach and duodenum and produces a local injury, while at the same time it produces a toxin which is absorbed, and causes the injury to the peripheral nerves, which ultimately leads to bilateral symmetrical atrophy. The organism leaves the patient in the feces. The incubation period is seven to twenty days. In this stage the primary effect is a considerable gastro-duodenitis, which is commonly considered as an independent indigestion, with loss of appetite, belching and slight rise of temperature. Nervous disturbances come later and gradually. The patellar reflex is either diminished or abolished. In acute cases, paresis of lower extremities, arms and hands, comes on quickly. Autopsy of such an early case shows: Recent haemorrhagic inflammation in the vicinity of the pylorus and duodenum. Punctiform bleeding spots on summit of the folds and tumefaction of the first row of mesenteric glands. The microscopic picture is characterized by necrosis of the superficial mucus membrane in which is found a bacillus of constant morphology. This penetrates to the limit of the mucus membrane. In one case this organism was found among other microorganisms in the various organs.

In accordance with this theory Wright proposed the following classification of beriberi:

1. Acute pernicious. Onset sudden, almost always die.

2. Acute beriberi. Onset more quiet but distinct symptoms of gastro-duodenal irritation.

3. Subacute beriberi. Onset insidious. Symptoms of gastro-doudenitis may not be complained of or be readily demonstrable and paralyses slight.

4. Beriberi residual paralysis, or the disease as it persists after the gastro-duodenitis has cleared up.

Wright thought that this attractive theory fitted all the facts, and for many years it was the most generally accepted of the various beriberi theories. Unfortunately, however, a careful examination shows that it cannot be substantiated. The gastro-duodenitis which Wright considered the primary lesion of beriberi is frequently found in the chronic cases. It is, in fact, not a true inflammation, but is a chronic passive congestion, and may be found in any cases, acute or chronic, in which dilatation of the heart has occurred with resultant chronic passive congestion of all of the abdominal viscera including stomach, intestines, liver, spleen and kidneys. Other investigators have failed to find the bacillus described by Wright in this lesion, or any other bacteria for that matter. Van Dudgeon (1906) questioned the specificity of the bacillus obtained by Wright, since it was not pathogenic for mice or guinea pigs and did not agglutinate with serum of beriberics in dilution of one to twenty.

Wright also believed that he had succeeded in producing beriberi in monkeys by confining them in cells that had been inhabited by beriberic prisoners. The food of these monkeys was bananas, sugar cane and pineapples which were first rubbed on the floor to pick up the specific organism. The cells were not cleaned and Durham describes the result as "nauseatingly filthy." Durham severely criticises Wright's claim of having produced beriberi in these monkeys. Under the circumstances described, it is no wonder they were sick, and he says the neuritis in Wright's monkeys was due to septic infection from old chronic ulcers. Indeed, the monkeys in Wright's possession, but not confined in cells and not exposed to any presumable beriberic influence, were similarly diseased and at autopsy showed extensive nerve degeneration. Durham also gave the contents of the gastro-intestinal tract of beriberics to monkeys by mouth with *negative* results. Thus Wright's theory is seen to fail at every point.

Wright, in studying beriberi in Kuala Lumpur gaol, believed he had positively eliminated diet as a factor in the causation of the disease because the food was sterilized before delivery to the prisoners. The fallacy of this is obvious. Sterilization of food might exclude the possibility that an infection was conveyed in the diet, but it could not exclude the possibility of the existence of a deficiency. As a matter of fact rice was a staple article of diet, and it has been shown that the neuritis-preventing vitamines contained in foods are destroyed by sterilization. The diet used by Wright could therefore hardly have been improved on as a producer of beriberi.

In September, 1905, Okata and Kokubo published a preliminary report on their investigations and described a coccus which they believed to be the cause of beriberi. They examined the blood of 129 patients. In 65 cases they found this coccus in stained preparations and cultures. In 34 cases both were negative, while in 11 cases microscopical examination was positive and the cultures negative and in 19 cases microscopical examination was negative and cultures positive. They also succeeded in isolating this coccus from the urine of beriberi cases.

The authors, however, bring no evidence that this coccus is the cause of beriberi aside from the fact that they recovered it from a considerable proportion of the patients examined. Their method, which was simply to puncture the skin and use the flowing blood for smears and cultures, is open to the criticism that accidental contamination from the skin was very probable. And finally Herzog made a detailed study of this coccus. He obtained cultures of this organism from Okata and Kokubo and while in Japan studied their methods. On returning to the Philippines he endeavored to obtain this organism from cases of beriberi and for this purpose made blood cultures from the median cephalic vein in 52 cases of beriberi. In 33 of these cases the cultures remained permanently sterile, and in none of the others was the Okata-Kokubo organism found. He also made cultures from the internal organs in a number of post-mortem examinations and still failed to find this organism, and moreover he failed to find any organism in any of his cases which could be considered as the cause of beriberi. He also inoculated animals with the Okata-Kokubo coccus, using for this purpose 24 monkeys, 24 guinea pigs, 24 rabbits and 21 rats. Some of these animals were kept under observation for one month and some for two months. Not a single animal developed beriberi; all but seven rats were alive and well at end of period of observation, and of the seven rats, none of them, when autopsied, showed lesions in any way due to the Okata-Kokubo coccus. Herzog concludes: "Our animal experiments and blood examinations appear to indicate very strongly that none of the claims brought forward for the discovery of a specific microorganism, for the disease can be looked upon as substantiated."

Dangerfield isolated a micrococcus from a number of beriberi cases, and claims that it was present in the blood obtained from a puncture of the toe, in the stomach contents, feces, sputum and even at times in the urine and vaginal secretion. It was isolated in pure culture and its cultural characteristics described. He also performed a number of experiments on animals to determine the pathogenicity of this coccus, and concluded from these experiments that beriberi was caused by it. A consideration of his experiments, however, will show plainly how inconclusive they were. Experiment VI was as follows:

"EXPERIMENT VI A. January 15, 1902. A fowl and a rabbit. The fowl was plucked over the entire anterior surface of the body and under the wings; the rabbit was deprived of hair over all the thorax and abdomen, and they were then vigorously rubbed with beriberic excrements. The operation was repeated Jan. 23, 1902, Jan. 31, 1902, and Feb. 8, 1902, that is to say, three times within an eight-day interval.

"RESULT. At the end of a month the fowl was greatly emaciated and the rabbit died on the thirty-fifth day.

"EXPERIMENT VI B. January 16, 1902. A guinea pig and a pigeon were inoculated with a solution of sputum and mucus obtained from the posterior pharynx of a recent beriberic, and suspended in pure sterile water. Ten cubic centimeters of this mixture was inoculated into the peritoneum of the guinea pig and into the cellular tissue of the interscapular region of the pigeon.

"January 20th. The guinea pig died in the night and the pigeon has a large painful tumor at the point of inoculation.

"January 31st. The pigeon can no longer stand on its feet, is oppressed, and pinching of the feet provokes no reaction. It no longer takes nourishment.

"February 2d. The pigeon died during the day, stretched out on its side.

"EXPERIMENT VI C. Two rats fed with grain sprinkled with beriberic products (mucus vomit and vomited food).

"These animals presented diarrhoea during the first days and died at the end of February of the same year.

"CONCLUSION. Beriberi is directly transmissible from man to animals by the pathological products."

Can anything be more absurd than this conclusion? Absolutely no evidence is given that any of these animals died of beriberi. Indeed, it is quite apparent that some of them died of plain infection, notably the guinea pig whose peritoneal cavity was insulted with ten cubic centimeters of sputum and who died in four days, and the pigeon who presented a large painful tumor at the site of inoculation.

In other experiments rice contaminated with cultures of the coccus was fed to animals and seven out of ten died, but again there is no satisfactory evidence that they died of beriberi.

A further circumstance which throws still further doubt upon Dangerfield's coccus is his own statement that: "These same bacteria which have given us certain results in the colonies seem to act differently in France. Is it necessary to blame the climate which has attenuated these bacteria or even destroyed the virulence of the germs and taken away all pathogenic action; as it acts marvellously upon beriberic sufferers curing them rapidly? We are driven to believe this after the minute precautions which have been taken in carrying these germs to Europe." It is very strange indeed that these cocci which were so pathogenic in Reunion should have totally lost all pathogenicity in Paris.

Dangerfield also thought he had eliminated a rice diet as a cause of beriberi. In several experiments he fed 13 fowls on polished rice for several months in order to determine the effect of the food alone. None of these fowls developed polyneuritis, and he therefore concludes that rice by itself does not give rise to polyneuritis gallinarum. But in these experiments Dangerfield used rices from different provinces, including Madagascar, Patna (India), Saigon, Rangoon, he only tested each variety of rice with two birds, and he does not state clearly that all of these rices were highly milled. It seems probable, therefore, that some of the rices used may not have been sufficiently highly milled to produce the disease, and in any case too small a number of fowls were tested on each rice, since it is by no means uncommon to find one or more birds out of a group of four that do not develop neuritis for several months, even on a diet of most highly milled rice. This experiment must be discounted not only because of this error, but because it has now been conclusively shown by a long series of investigators that nothing is more certain than the fact that a considerable proportion of fowls fed on an exclusive diet of highly milled rice will develop polyneuritis.

Finally, Dangerfield's coccus has never been found by other observers and his results totally lack confirmation.

Durham performed a number of experiments with the view of producing a disease similar to beriberi in monkeys, guinea pigs and rabbits. His experiments included feeding of dry fish and rice, injection of serum from beriberi cases, the administration by mouth of the contents of the gastro-intestinal tract of beriberi cases, the administration of dust from infected localities, inoculation from throat to throat, and attempts to convey infection by bedbug bites. All of these experiments were negative, yet Durham believed that the disease was infectious chiefly because of the difficulty in explaining the occurrence of the disease by any of the dietary hypotheses in vogue at that time. He isolated a streptococcus from the mucus of the throat of beriberics which he thought was of some importance in the production of the disease, but even he did not regard this as proven.

Dubruel (1905) thought beriberi an infectious disease caused by a microorganism contained in hulled rice. The bacteria cause in man and experimental animals a disease of the alimentary tract. The germs penetrate into the circulation and elaborate a toxin which destroys the spinal nerves and certain organs, while the cranial nerves are exempt. This toxin does not produce an ascending neuritis so much as a disseminated form. The germ is very resistant to heat and can easily withstand for a long time temperature of 100°, but it is quite sensitive to light in which it quickly loses its virulence. This is another speculative theory. Dubruel did not succeed in demonstrating this organism.

Tsuzuki in 1906 isolated a diplococcus from the urine of beriberic cases which agglutinated with the serum of beriberics in dilution of one to fifty. He described the cultural characteristics of this organism and concluded that he had discovered the true cause of beriberi because: 1. It is contained in the urine of beriberics and not in the urine of healthy individuals or of those suffering from other diseases. 2. It is specifically agglutinated by serum of beriberics, but not by serum of healthy individuals or those suffering from other diseases. 3. It is contained in stools and intestines of beriberics. 4. It can produce phenomena in experimental animals which are identical with beriberi in man. 5. It produces a poison which causes symptoms and pathological conditions in animals identical with beriberi in man.

1. Tsuzuki examined the urine of 65 beriberics and about the same number of healthy and patients suffering from other diseases. He found the diplococcus in 18 beriberics or 27.7 per cent, while the urine of the healthy individuals and those suffering from other diseases were all negative. This is suggestive, but the percentage of positive findings was so small that his conclusion that this diplococcus is contained in the urine of beriberics does not appear to be justified. Moreover, in subsequent observations published in 1908, he found this organism still less frequently in the beriberic urines examined.

2. With regard to the agglutination, he tested the serum of 106 beriberics with this coccus with a positive result in 103 cases in 1 to 50 dilution. As controls he tested the serum of 12 healthy individuals, 8 typhoid cases and 1 dysentery case. None of these were positive in dilution 1 to 50, but in dilution of 1 to 20, four healthy and four typhoid sera gave a positive reaction. This evidence does not appear sufficient to justify his conclusion that his coccus is not agglutinated by other sera. Moreover he used the macroscopic method, mixing one cubic certimeter of a bouillon culture with one cubic centimeter of diluted serum, and kept his tubes for 24 hours in the incubator before reading them. A test performed in this way might be inaccurate because of the profuse growth that would result after 24 hours in the incubator.

3. He found the diplococcus twenty-two times out of thirty-eight cases in the stools of beriberics, but apparently did not look for it in normal stools.

4. With regard to the phenomena produced in animals by the

kakke coccus and its toxin, Tsuzuki obtained different results depending on the size of the dose employed. With a very large dose, the experimental animals developed what is described as a cardiac form of beriberi. There was no paralysis and the animals died in 4 to 12 hours. With lesser doses a paralytic condition developed and the animal died in 4 to 7 days. The autopsy findings were by no means convincing, since the lesions found were not typical of beriberi and especially since no attempt was made to demonstrate degeneration of the nerves. The entire description of the symptoms and pathology of these animals suggests an acute poisoning rather than the production of beriberi.

Tsuzuki himself has now admitted the error of this work, has abandoned the infectious theory and has become an advocate of the theory that beriberi is caused by a deficiency in the food

Salanoue (1906), working in Hanoi, found that blood exudates and the pulp of different organs of beriberics were harmless when inoculated into animals. But the emulsion of a piece of pneumogastric inoculated under the dura mater or in the pectoral muscle of pigeons produced in these animals a progressive paralysis of the feet and wings. He isolated a diplococcus that was pathogenic for rabbits, mice, guinea pigs and monkeys when introduced introperitoneally, intracranially or into the trachea. The animals succumbed rapidly after injection of the cultures, and at the autopsy the manifestations of acute beriberi were thought to be found. These included vaso motor paralysis, congestion of all the internal organs, degeneration of the myocardium, pericardial and peritoneal effusions. These phenomena, however, could all have been caused by an acute septic process. The fowls and monkeys on the other hand developed the disease in a chronic form with polyneuritis resembling dry beriberi in man. This would be very important were it not for the fact that no mention whatever is made as to the diet given these experimental animals, but because of this omission nothing can be regarded as proven.

None of the organisms described by these and other investigators can be regarded as the demonstrated cause of beriberi. The evidence is insufficient in every case.

Many authors have expressed opinions that beriberi is infectious, but without incriminating any particular organism or producing any proof. Thus Van der Scheer thinks that beriberi is due to the influence of microorganisms, and believes that insects and cockroaches may distribute it.

Schubert (1906) considered beriberi an infectious disease that could be spread by insects, like malaria. On the contrary he thinks ship beriberi is an intoxication with decomposed fish.

Van Gorkom is of the opinion that beriberi is an infectious disease whose cause is taken in with the food and spread through human feces on the ground, in rooms, jails, ships, etc. He believes there is an acute feverish stage of infection with local disease of stomach and intestinal mucous membrane. This is practically Wright's hypothesis.

Jeanselme (1907) thought beriberi an infectious disease that attacked particularly weakened individuals. The disease may be manifested in two ways, either by a slight feverish condition, or by an attack of polyneuritis. The causal organism localizes itself in a part of mucus membrane of the digestive tract (in the throat or in the intestine) and there elaborates the toxin which produces the neuritis. Jeanselme, however, admitted that "direct contagion from man to man has never been capable of demonstration."

This class of authors may be typified by Scheube, who is one of the most important adherents of the infectious theory because one of the most frequently quoted, although he says: "The nature of the virus of the disease is still unknown. My personal opinion is that the microorganisms hitherto found in the blood and tissues of beriberi patients by various observers, are not the specific excitants." His reasons for claiming that beriberi is an infectious disease are as follows:

1. "Strong, well-nourished young persons are most frequently attacked by beriberi, and are particularly liable to the severest form of the disease."

2. "Beriberi has not only its definite geographical region of distribution, but even in beriberi countries it does not occur everywhere, being mostly confined to certain narrow, sharply limited districts." As we observed above, the disease rages principally in tropical and sub-tropical districts. Within this region of distribution it occurs by predilection on the sea coast, along the banks of large rivers and on the contiguous plains. It is less frequent in the interior, and still less so in mountainous regions, although even these are not quite free from the disease, as proved by its occurrence in Indian hill stations; in Fort de Koch in Sumatra (which is the garrison at the greatest altitude in the Dutch Indies); in the Japanese province of Thinano, etc. Beriberi is, moreover, principally a disease of large towns, usually the low-lying parts of the city being principally attacked. Occasionally certain centres and certain buildings are specially at-

tacked, particularly jails, barracks and hospitals, and sometimes the disease is even confined to certain spaces and stories of these buildings.

3. "The seasons of the year, or rather the conditions of the weather occasioned by the seasons, exhibit a certain influence on the appearance of the disease; the maximum of the frequency of the disease occurs during that season which is first of all distinguished by great moisture, and secondly by a high temperature liable to many variations."

4. "During recent decades beriberi has attained a considerable distribution in tropical countries as in Java, Japan, and Brazil, without any change of food having taken place amongst the people, so that this reason cannot be made answerable for its appearance. In Atjeh, where the disease now rages severely, it was unknown before it was annexed to Holland." "By all these facts it is strikingly proved that the actual and essential cause of disease cannot be sought in defective or scanty nutrition. Famine has existed in all possible forms, at all times, and on every portion of the surface of the globe without ever having caused the development of beriberi as a sequence."

This is the whole case for the infectious theory, according to Scheube, and which he claims is sufficient proof of its truth. It is surprising that Scheube should have come to such a conclusion based on such evidence. The same kind and an equal volume of evidence was used for many years to prove that malaria was caused by a miasm. If we examine in detail each of his arguments it can be shown that in some cases his facts are incorrect, and in others, instead of proving the infectious theory, the facts are equally strong arguments in favor of the theory of a deficiency in the food.

1. Strong, well-nourished young persons are most frequently attacked by the disease.

It is possibly true that young adults are most frequently attacked, but that they are strong and well nourished is not granted. It by no means follows that an individual is strong and well nourished because he *appears* to be. It is a well known fact that many Chinese and Japanese coolies are exceedingly muscular and perform hard labor, and *appear* well nourished although they live on an almost exclusive diet of polished rice and a little fish. That such individuals are actually well nourished cannot be believed by anyone who accepts the standards of the physiologists with regard to a balanced diet. That beriberi develops among such people, instead of proving the disease infectious, merely shows that their appearance was deceitful and that they were in fact very badly nourished.

It must be remembered that Fraser and Stanton have shown that it requires ninety days on an exclusive diet of polished rice to produce beriberi. Now it is quite possible that the men in this experiment appeared well nourished and were capable of performing their usual labor for several months on this diet, although the fact was that they were badly nourished and were on the point of developing beriberi as a direct result of this faulty diet.

2. Even in beriberic countries the disease does not appear everywhere, but is mostly confined to certain sharply limited districts. It occurs by predilection on the sea coast, along the banks of large rivers and is less frequent in the interior, and is principally a disease of large towns.

These facts, instead of proving the infectious theory, may all be explained as follows: In all rice-eating countries the people in the interior are accustomed to prepare their own rice for consumption, in some cases by "curing," in others by storing the grain unhusked and husking it themselves in mortars as needed or by means of other primitive devices. The grain prepared in this way retains sufficient of the pericarp to prevent beriberi. The people of large towns along the sea coast and rivers on the other hand do not do this by very reason of their location, but are engaged in commercial pursuits and purchase their rice. The rice furnished through the regular channels of the rice trade is practically all milled and polished by machinery, the nutritious and neuritis-preventing pericarp is removed, and the variety of rice which it has been demonstrated will produce beriberi is the kind which is easy of access to and undoubtedly purchased by the people of towns, river banks and the population of the coast.

A certain percentage of those who live almost exclusively on this rice will develop beriberi to a mathematical certainty. Certain buildings, jails, barracks and hospitals develop the disease for similar dietary reasons, as shown by the fact that when the proper change is made in their diet, i. e., the substitution of undermilled rice for polished rice, or the addition of some leguminous vegetables to the ration, the beriberi disappears. The facts in several such instances will be given more fully when discussing the evidence in favor of the so-called rice theory.

3. The seasons of the year or the conditions of the weather affect the disease, its maximum of frequency occurring during the season distinguished by great moisture and heat.

It is surprising that this seasonal variation should be accepted as evidence proving that the disease is an infection. According to this line of reasoning, neuralgia and the condition known as chronic rheumatism must be infectious because they are more prevalent during cold, damp seasons. It is quite possible that the conditions of the weather during the beriberi season in the tropics so affect metabolism as to render the disease more prevalent at this time, and it seems equally possible that the variety of rice consumed during this season may be different from that used during the rest of the year.

As is well known, the warm rainy season, or time of greatest prevalence of beriberi, is exactly the time when it is the universal practise to plant the rice in these countries. Because of habitual improvidence or other reasons it is quite likely to be true that the supply of rice remaining from the last harvest becomes exhausted at about this time, and that the people dependent upon this staple are obliged to purchase rice to tide them over until the new harvest. In which case they would almost certainly purchase the white, polished and beriberi-producing variety, because this is the kind of rice invariably found in the market and usually the most highly esteemed. This is not advanced as a proof, for the evidence that this is the truth is insufficient, but it is merely suggested as one of the possible explanations of the seasonal occurrence of beriberi, and to show that this seasonal prevalence cannot in any way be regarded as a proof of the infectious nature of the disease.

4. During recent decades beriberi has attained a considerable distribution in tropical countries such as Java, Japan, and Brazil, without any change in the food of the people.

The statement that there has been no change in the food of these people is a negative proposition, and like many other negative statements is difficult to prove and dangerous to make. It is undoubtedly true that the same staple articles of food in all tropical countries, i. e., rice and fish, have been consumed for generations or even centuries. But there is also little doubt that the variety of rice used has undergone changes at different times. The last few decades, during which beriberi is noticed to have increased, are the very ones when, owing to the advancement of these people and their gradual assimilation by European governments, the use of machinery has become more generalized. Undoubtedly there are many more rice mills now than existed twenty or thirty years ago, and the consumption of polished rice instead of the hand-milled article is much more general now than was the case then.

Finally Scheube states that: "It is certain that a *rice diet* cannot be considered as the cause of the disease, for beriberi occurs in regions where rice is not eaten, as in Brazil, and in the Moluccas and in the Lingga Archipelago, where the population live on sago, fish and game, and where the disease was observed in Europeans who at that time had never eaten rice." In reply to this objection it cannot be too strongly emphasized that we do not accuse rice *per se* as the cause of beriberi. The cause of this disease is a deficiency in the diet. This deficiency most often exists as the result of using polished rice as the staple article of food, but sago will answer the purpose equally well. Both sago and rice consist chiefly of starch and the neuritis-preventing substance would undoubtedly be deficient in such a diet as sago, fish and game.

Scheube's statement that beriberi must be an infectious disease cannot therefore be accepted.

On the other hand there are a large number of investigations recorded which render it exceedingly difficult to believe that the disease is infectious. Thus Ellis, working at Singapore in 1898 with abundant material, made a number of blood examinations to verify Pekelharing and Winkler's claims. He completely failed to find any organism in the blood, and cultures made from the spleen, stomach, nerves and other organs at post-mortem examinations were likewise negative.

Stanley examined the blood in thirty cases of beriberi occurring in Shanghai. In each instance one cubic centimeter of blood was collected under aseptic precautions from the median cephalic vein, and inoculated into various culture media. In all 150 cultures were made. All the tubes except two remained sterile. These developed staphylococcus pyogenes aureus and micrococcus tetragenus. He also injected one cubic centimeter of blood from beriberi cases into each of six rabbits. These animal experiments and others in which mouldy rice was employed were completely negative. Stanley concludes that the blood in beriberi is sterile and that the organisms found by Pekelharing and Winkler do not stand in any causal relationship to the disease. His experiments to determine whether a specific toxin was present in rice were also negative.

Tetamore, in an epidemic in Pangasinan, made bacteriological examination of blood in 35 cases. The results in general were negative, but in a few cases micrococci were found which were not regarded as specific.

Baelz and Scheube have made careful investigations, but have failed to find any organism. Robert Koch investigated the blood of recent cases of beriberi in New Guinea and failed to find any specific parasites.

Hunter and Koch performed an elaborate series of experiments in Hongkong in 1905. They first made a large number of blood cultures and came to the following conclusions:

"The results of these experiments show more or less clearly that microorganisms of the common type are absent from the blood during an attack of beriberi. The repeated sterile result after inoculating bouillon and agar tubes with appreciable quantities of freshly flowing blood, demonstrate more or less clearly the non-bacteriemic nature of the disease. The findings of other workers who have pinned their faith in the microorganismal nature of the disease must, as a result of our investigations, be looked upon in a different light. The prevention of contamination is a difficult matter even in the hands of an expert, and the description of the presence of micro-cocci and bacteria of several kinds must be regarded as the result of defective technique in the methods applied for the determination of this important question."

Hunter and Koch then tried to convey beriberi experimentally from man to animals, using a large number of different animals and many methods of experimentation, including feeding the animals beriberic blood, spleen, gastro-duodenal mucosa, brain substance and cerebro-spinal fluid, and also performing inoculation experiments with these substances. Their conclusions are as follows:

1. "It has been found impossible to convey beriberi to any of the animals used for the experiments.

2. "Monkeys have been used extensively and experimented upon in a great variety of ways, including that recommended by Hamilton Wright. In no instance has any of them exhibited the slightest trace of beriberi infection.

3. "The pigs used for the experiments showed signs of lameness, etc., and a condition simulating beriberi was once or twice reproduced. The animals, however, were frequently subjected to somewhat rough handling by the attendants, and this, coupled with the continued observation of their progress, and the result of post-mortem examination, leads us to the conclusion that a condition of true beriberi never existed.

4. "In regard to the other animals, viz., sheep, calves, rabbits, fowls, etc., notwithstanding vigorous experimental efforts, we have been unable to obtain from them the slightest evidence of beriberi infection.

5. "As a result of our extensive experiments *it would appear that transference of beriberi infection from man to animals is impossible.*

It may be possible that animals contract the disease through other channels. This, however, we doubt.

6. "These experimental researches, negative though they may be, possess in our opinion great value as they practically prove in opposition to Hamilton Wright and others that *in beriberi we are not dealing with an infectious disease, but with one of an entirely different etiology.*"

Braddon also made blood cultures. He tested the blood of twenty-three persons, and all the tubes proved to be sterile. Sixteen were typical beriberics and seven controls. Repetition of the experiment on another series of twenty-five cases taken at different stages of the malady, making anaerobic subcultures, had the same result. Braddon was therefore convinced that there is not to be found any coccus or bacterium in the blood of beriberics at any stage of the disorder which will grow upon ordinary media.

De Haan and Grijns, in order to determine the existence of antigen and antibodies in beriberi and polyneuritis of fowls, have used the method of deviation of the complement. In all the experiments the haemolytic tests have been prepared in the usual manner. The authors have used three acute cases, one chronic case with hydropericardium and one case that had just been cured.

On the hypothesis that the serum of the patient that had just been cured should contain antibodies, they endeavored to demonstrate their presence, using as antigen (a) extract of erythrocytes from the same patient; (b) pericardial fluid from the case with hydropericardium. In all their experiments there was no deviation of the complement. The same negative result was obtained when they used the serum from the cured case or the three acute cases to furnish the antibodies.

In testing polyneuritis of fowls the serum of sick fowls treated with katjang-idjo served as antibody. For antigen they used extracts of liver, spleen and nerves, blood and diluted serum of sick fowls. They never obtained any deviation of the complement.

As a result of these experiments in which they were unable to demonstrate the presence of beriberic or neuritic antibodies or antigens, they are not in favor of the infectious theory of the disease.

Similar experiments were performed by Shiga with the same result.

A poison, whether endogenous or exogenous, of bacterial origin should be capable of demonstration by means of immunity reactions either directly or indirectly. To determine this point Shiga undertook experiments in complement binding. For antigen he used the contents of the small intestine of three kakke cases obtained at autopsy, ten times diluted with salt solution and shaken for two hours, after which it was centrifuged and bacteria and sediment removed. This experiment was negative, no difference being found between the kakke serum and the control sera (from normal men, typhoid and diphtheria cases). The same negative result was obtained using an extract of a number of different kinds of bacteria isolated from the intestine of beriberi bodies as antigen.

A rabbit was injected with 10, 20 and 35 cubic centimeters of serum from a fatal case of acute kakke at intervals of five days. Fifteen days after the last injection the animal was bled. Complement deviation experiments were undertaken with this rabbit's serum, using kakke serum, healthy serum and serum from cases of other diseases. No differences were found to exist between these sera.

Finally I have been authoritatively informed that Fraser and Stanton, in the course of their work on beriberi, performed a large number of human experiments, in which they tried by every conceivable method, including insect transmission, to infect healthy individuals from beriberi patients. These experiments were all negative, but were unfortunately suppressed by the Government for political reasons.

We may conclude, therefore, that since none of the organisms advanced by different investigators has been shown to be the cause of beriberi, that since direct transmission of the disease from man to man, or man to animals, has never been proven, but that on the contrary all attempts to do so have failed; and since these investigations have been continued by different workers over a period of many years, *we are justified in believing that beriberi is not an infectious disease.*

CHAPTER IX

THE ETIOLOGY OF BERIBERI, CONTINUED

Beriberi Is Caused by the Deprivation of Some Substance Which Is Deficient in Certain Kinds of Food.

The idea that beriberi is caused by some deficiency in the food is not new, but has been advanced with more or less evidence for a number of years. Thus as early as 1859, Pop explained the occurrence of the disease in the navy of the Dutch Indies on this basis. In 1863 Von Kappen observed that, among the Chinese working in the mines of Banka, those who received an ample diet were protected from beriberi, while those who had become anaemic as a result of insufficient nourishment were attacked. Overbeck de Meijer wrote in 1864: "If beriberi appears among the crew of a ship, this is always the result of an exclusive diet of salt fish, and if the troops on military expeditions in certain parts of the Dutch Indies are supplied exclusively with the food used by the natives, they will almost invariably be attacked by beriberi." Van Leent in 1867 came to a similar conclusion saying: "The principal cause of beriberi is a diet that is too uniform, insufficient and of bad quality. The organism, deprived of those elements that are indispensable for blood formation and nutrition, becomes impoverished little by little." Stendijk (1871) stated that beriberi appears on ships when the food becomes deficient or is spoiled. Westhof (1879) blamed the bad food (rice and dried fish) on the transports of the Dutch Indian service and Schutte (1879) claimed to have observed beriberi in the prisons of Parimaribo as a result of a diet of rice, salt fish and cooked green bananas. Wernich (1878) says: "Kakke is a chronic constitutional disease of blood formation and of the vascular system. Rice, used exclusively as a diet is particularly responsible for its appearance, not as has been supposed because the rice was spoiled, but because on account of its large mass the power of assimilation for other kinds of food is reduced, and in spite of its quantity, it is not capable of furnishing proper nourishment and materials for blood formation. Even when albuminous constituents are added in the form of fish and bean cheese, these only partially make up the deficiency. Fat in a digestible form is almost entirely lacking in the Japanese food."

Van Leent continued his observations, and in 1880 published a paper in which he concludes: "The fault in the food, which I regard as the all important cause of the diseased condition of beriberi, consists in a deficiency of proteids and fat." The observations which he relates in support of this view are of the greatest importance, and afford a proof that beriberi is dependent in some way upon the diet eaten. Thus Van Leent showed that prior to 1874 the ration furnished the native crews of the Dutch East Indian fleet was as follows:

Articles.	Grams.	Proteid.	Fat.	Carbohydrates.
Rice	1,000	75	0	800
Meat	300	54	20	0
Total	1,300	129	20	800

During the same period the ration of the European crew was much better, and consisted of the following components:

Articles.	Grams.	Proteid.	Fat.	Carbohydrates.
Bread	400	30	0	184
Rice	500	38	0	400
Meat	400	72	25	0
Lard	75	0	75	0
Butter	35	0	35	0
Beans, peas and potatoes	300	40	0	150
Total	1,710	180	135	734

Beriberi was exceedingly common among the natives and was rare among the Europeans, the rates being as follows:

Year.	Nationality.	Strength.	Cases of beriberi.	Cases per 1000.
1870	Europeans	2,259	14	4.7
	Natives	967	194	206.2
1871	Europeans	2,483	6	2.4
	Natives	831	206	247.0
1872	Europeans	2,326	19	8.1
	Natives	770	199	260.0
1873	Europeans	2,744	24	8.8
	Natives	762	460	603.7

Since the Europeans and natives were on the same boats and living under similar circumstances a relation between their respective diets and the amount of beriberi they suffered from is at least suggested. In 1874, therefore, the native sailors were given the same ration as the Europeans. The number of beriberi cases fell very greatly. Van Leent says specifically that: "Beyond the radical alteration in the food of the native crews, all other circumstances remained exactly the same as before." This evidence was still further strengthened by another circumstance. In 1875 a part of the fleet was ordered to New Guinea and the Celebes and reverted to the old native ration, while the remainder of the fleet stayed at Atjeh on the more liberal ration. The detached ships on the poor ration suffered severely from beriberi while there was little or no beriberi on the ships at Atjeh. In the few exceptions that occurred, an official inspection made by Van Leent developed the additional fact that the affected sailors had not drawn the European ration which was then optional, but had preferred the native diet. In the future, therefore, the improved or European ration was made compulsory and beriberi then disappeared. As Van Leent said in 1880: "Beriberi has almost entirely disappeared from our warships in India."

Bremaud in 1889 thought beriberi a dyscrasia of alimentary origin, being due to the deficiency, partial or complete, or fatty ingredients in the food, and occurring in hot climates much in the same way as scurvy occurs in temperate regions when there is deprivation of meat and fresh vegetables. Bremaud based his opinion on several observations of which the first was as follows: The penitentiary on the island of Poulo-Condore, containing about 1,000 prisoners, was so healthy that it was almost considered a sanitarium. This state of affairs continued for several years when the commandant was changed, and this new official altered the diet of the prisoners so that it consisted only of rice and salt. Beriberi promptly appeared and the mortality was heavy. An inquiry brought about an improvement of the diet, pork was introduced as a staple ingredient, and the epidemic immediately ceased. The second epidemic, which Bremaud witnessed, occurred on a ship in which one portion of the crew who used lard were protected while the Mohammedans, who did not use lard, were affected.

Later in 1899 Laurent, of the French government service in Siam, receiving his inspiration from Bremaud, tested this fat theory in two epidemics. The first at Chantauboun, concerned a party of 260 native soldiers. One hundred and forty were bachelors. Of these, 100 used only their service rations, and 47 of them developed beriberi, a percentage of 47. Forty boarded out, paying extra for their food, and only three of these were attacked or a percentage of seven and a half. One hundred and twenty were married, of whom two were attacked, a percentage of one and two-thirds. Among the 120 wives there were no attacks. Laurent found no difference among these groups except in their food. The married suffered equally with the others from exposure and had similar houses and water. It is also probable that they had less food since it was shared with their families, but it was more oily, like the food generally used by the natives. The soldiers did not like the beef supplied them, as it was not fat enough. Doctor Laurent prevailed on the local commandant to alter the soldiers' ration. Hitherto each man had been in receipt of 12 meals of fresh beef and two of preserved beef per week, but under the new order he drew 11 meals of pork *with fresh vegetables,* and only three of fresh beef. The epidemic which had lasted for a month, and was increasing in severity, suddenly ceased, and did not reappear, the same alimentary modifications being kept in force.

The second epidemic, observed by Laurent at Poulo-Condore was much longer and more serious since in a year it had made upward of 360 victims. It ceased in the same sudden fashion from the moment the fat containing regimen was given to the individuals still in health, after which not a single fresh attack manifested itself among them. Doctor Laurent, however, is careful to add that he does not attribute the causation of beriberi exclusively to the deprivation of fat. Many factors must be considered, but in his opinion absence of suitable food is undoubtedly the principal one.

It is now certain that beriberi is not caused by a lack of fat. Epidemics have been observed in which there was an ample sufficiency of fat in the diet, and the experimental work on fowls shows conclusively that addition of fat will not prevent polyneuritis gallinarum. Moreover it is apparent that Laurent overlooked the influence of the fresh vegetables added to the diet. But these observations certainly indicate that diet is at least a main factor in the causation of beriberi. It must be noticed that in all of these epidemics rice constituted the main staple article of diet.

Rice also became more directly implicated as time progressed. Thus, in 1889, Smyth noted that during an expedition that had just been made in the Soudan, the Madras sappers and miners on service there suffered severly from beriberi, while not a single case occurred in any other arm of the service. These Madras troops were the only ones present with whom rice formed the staple article of diet. The rice was of fair quality and used constantly by the European officers without any bad effect. This latter observation should be noted, for if it be granted that the rice was at fault it could hardly be because of its toxicity, otherwise we should have expected some cases among the Europeans.

Of much greater importance, however, were the observations of Vorderman. This investigator studied beriberi in the prisons of Java and Madura in 1895–96, and found, after analyzing statistics from 279,623 prisoners: 1. That out of 51 prisons in which polished rice was eaten, 36 or 70.6 per cent developed beriberi in the proportion of one case to each 39 prisoners. 2. That out of 37 prisons with undermilled rice as the staple food, one or 2.7 per cent developed beriberi in the proportion of one case to 10,000 prisoners. 3. That out of 13 prisons using a mixture of these two rices as a staple diet, six or 46.1 per cent developed beriberi with one case to 416 prisoners.

Vorderman also found that in the jail at Tolong, where the principal food had always consisted of polished rice, that the per cent of sick reached 5.8. On July 1, 1895, undermilled rice was substituted, and the figures for disease then fell to nothing, although all other factors remained the same. Thus Vorderman showed not only that there was a causal relation between rice and beriberi, but that the disease could be prevented by the use of undermilled rice. This is the greatest advance that had been made in the study of beriberi up to this time, but unfortunately like the work of Eijkman and Takaki it did not receive the attention it deserved.

The epidemic at Lingayen, P. I. Another interesting observation reported about this time (1902) was that of Captain Littlefield, an assistant surgeon in the U. S. Volunteers, who reported an epidemic that occurred in the jail at Lingayen, Pangasinan, P. I. His account is substantially as follows:

Since the establishment of this prison until February 1st of this year the native prisoners have been supplied with Chinese white rice. During this time beriberi has been markedly endemic in the prison. The number of deaths have averaged five monthly, while the number of new cases monthly averaged 20. When prisoners reported sick with beriberi they were removed from the prison to a building about one-half mile from the hospital, the upper story of the building being used for a hospital. The difference between conditions existing at the beriberi hospital and the prison being only the higher elevation of the former. The diet supply was the same at both places. Many of the cases at the beriberi hospital continued to grow worse and died. The majority of those who did recover did so after a very long illness and many of them suffered from numerous relapses. During the month of January there were 35 cases in the hospital and as many who were slightly affected at the prison. The sanitary conditions were excellent. In the civil prison, not more than one-quarter of a mile distant, there were confined a large number of natives, the sanitary conditions not being as satisfactory as those of the military prison. They were more crowded in poorer buildings. In this civil prison there were no beriberi cases, the only difference existing in favor of the civil prison being that the ration was purchased in the open market. At the beginning of February of this year, upon the recommendation of the prison surgeon, the use of the Chinese white rice supplied by the commissary was discontinued and native rice from the open market purchased in its place. Since that time no new cases of beriberi have developed and no death has occurred. Of the 29 cases remaining in hospital on the last of January, 16 have been returned to duty, eight released greatly improved and five remain also greatly improved and still improving. The mild cases in the prison have all recovered. This marked change occurred in the space of one month, the only apparent difference existing during this period and in the previous times being that of the rice supply. From these facts it would seem that the cause of beriberi in this prison has been brought about by the use of the Chinese rice, white variety.

Fales made an important contribution to the subject by reporting an epidemic of 5,448 cases with 229 deaths in Bilibid prison, Manila, P. I., 1901–1902. At that time the prison contained about 2,000 prisoners. Previous to the epidemic, which began in December, 1901, there had been but few cases of beriberi in the prison. At this time the ration was changed and almost at once the epidemic commenced with great severity and continued throughout the year in spite of all methods taken for its suppression along the lines of general sanitation and disinfection. Thus the entire prison and everything coming in contact with the sick were disinfected without result in reducing the cases. In July, August and September the prisoners' hands and dishes were scrubbed and disinfected in a 1-1000 solution of bichloride of mercury before eating to test Hamilton Wright's theory of transmission. This also was useless. Overcrowding had no effect, because: 1. During the time of the epidemic certain buildings which were the most crowded showed no greater proportion of beriberi cases. 2. Beriberi cases did not lessen when crowding was diminished. 3. About two years after the epidemic had ceased, when the prison contained over 4,000 prisoners instead of 2,000 and was crowded far beyond its capacity, there was no increase of beriberi, although the disease was endemic at the time. The disease appeared in all parts of the prison simultaneously. Hospital attendants did not contract the disease, and prisoners who worked in the kitchen seldom were attacked.

On October 20, 1902, the ration was again changed for the better and the beriberi ceased. The relation of the beriberi to the change in rations and the nutritive values of the two rations are shown in the following tables:

RATION FOR CONVICTS AT BILIBID FROM DECEMBER 1, 1901, TO OCTOBER, 1902.

4,300 cases of beriberi occurred in this period.

Ration.		Proximate principles in grams.					
Components.	Amounts in grams.	Non-proteid nitrogen.	Albuminates.	Proteid nitrogen.	Fats.	Starches.	Salts.
Sugar	28.35	....	....	....	....	27.35	0.14
Bread	151.20	0.38	12.09	1.55	2.26	74.39	1.96
Rice	453.60	0.09	35.43	5.58	3.12	377.40	2.26
Beef	226.80	0.27	48.52	7.49	11.77	....	3.62
Potatoes	85.05	0.34	1.13	0.18	0.09	11.90	0.50
Onions	28.35	0.28	....	0.09	....	....	....
Pepper	0.50	....	....	....	....	....	....
Vinegar	10.00	....	....	....	....	....	....
Salt	18.00	....	....	....	....	....	18.00
Ginger root	28.35	....	....	....	....	....	....
Total	....	1.36	97.17	14.89	17.24	491.04	26.48

Total vegetable amids, calculated as asparagin, 5.84 grams.

RATION FOR CONVICTS AT BILIBID INTRODUCED IN OCTOBER, 1902.

Beriberi disappeared after this change.

Ration.		Proximate principles in grams.					
Components.	Amounts in grams.	Non-proteid nitrogen.	Albuminates.	Proteid nitrogen.	Fats.	Starches.	Salts.
Sugar	28.35	....	....	....	....	27.35	0.14
Bread	302.40	0.76	24.18	3.11	4.53	148.78	3.93
Rice	255.15	0.05	17.71	2.78	1.56	188.70	1.13
Beef	226.80	0.27	48.52	7.49	11.77	....	3.62
Dried fish	56.70	0.15	7.08	0.97	0.85	....	0.28
Potatoes	119.07	0.48	2.38	0.37	0.14	25.00	1.19
Onions	102.06	1.00	1.84	0.29	0.50	5.90	0.70
Pepper	0.50	....	....	....	....	....	....
Vinegar	10.00	....	....	....	....	....	....
Salt	18.00	....	....	....	....	....	18.00
Ginger root	28.35	....	....	....	....	....	....
Total	....	2.71	101.71	15.01	19.35	395.73	29.99

Total vegetable amids, calculated as asparagin, 12.26 grams.

SHOWING THE MONTHLY NUMBER OF CASES OF BERIBERI WITH DEATHS IN BILIBID PRISON, MANILA, P. I.

Year.	Month.	Cases.	Deaths.
1901	November	2	0
Ration changed.			
1901	December	52	2
1902	January	169	12
1902	February	1,087	16
1902	March	576	15
1902	April	327	15
1902	May	310	19
1902	June	451	17
1902	July	233	33
1902	August	571	24
1902	September	522	31
Ration again changed October 20th.			
1902	October	579	34
1902	November	476	8
1902	December	89	3
1903	January 1–15	4	0
Total		5,448	229

It seems clear in this case that the appearance and disappearance of the epidemic were coincident with changes in the ration. Moreover, the change made simply reduced the consumption of rice by one-half, doubled the consumption of bread and increased the allowance of potatoes and onions.

Beriberi and the Diet in the Japanese Navy. The experience of the Japanese navy in eradicating beriberi by a change of diet is classical. The following is Takaki's account in abbreviated form:

The first time I heard of the fearful nature of beriberi was 44 years ago. At that time guards were despatched by several Daimios to Kyoto to act as protectors of the imperial palace, and my father, being one of them, stayed there for over a year. On his return he told me of the disease called beriberi which killed many of these men. *They attributed the cause to food, and called the provision box the beriberi box.*

I entered the Navy in 1872, and what at once attracted my notice was the large number of beriberi patients and the numerous deaths resulting from it, and I turned my full effort towards finding its cause and treatment. In pursuing this purpose I met with many difficulties and passed through years of hard work. By May, 1875, I had seen several hundred beriberi cases at the Naval Hospital. In the summer several acute cases appeared daily. Often five or six cases had to be treated at the same time, and attending officers had to work hard both day and night. At that time the beriberi patients constituted three-fourths of the whole number of patients. Treatment was general, and there was no definite opinion as regards the food. In order to be better prepared for studying the subject I went to England in 1875, and after five years' study returned to Japan in 1880. The general conditions on my return were exactly the same as before I went to England, and with subsequent increase of sailors more beriberi cases appeared. At times we found the hospital too small and had to use neighboring temples. I feared if these conditions continued our navy would be of no use in time of need. While studying the disease I noticed the following facts: 1. Beriberi occurred mostly from the end of spring to summer, but it was not limited to the warm season, sometimes occurring during the severe cold winter. 2. The occurrence of the disease varied in different ships, barracks, etc. 3. Even on the same ship it appeared in some stations and not in others, and was never certain. 4. It occurred from time to time without regard to the state of quarters or clothing. 5. Although clothing, food and quarters were not quite the same in all stations, yet they were almost similar. 6. Sailors, soldiers, policemen, students and shop boys suffered most. The upper class rarely became affected. 7. The people living in the same place suffered unequally; that is, some suffered and others did not. 8. Although it occurred mostly in large cities, yet it sometimes appeared in the smaller town as well.

In 1882 three warships were sent to Chemulpo. They stayed there only 40 days, but owing to the shortness of hands, caused by the prevalence of beriberi, the officers felt unfit for battle. For example, in one of the ships 195 out of 330 were down with beriberi. In 1883 I examined the hygienic conditions of ships, barracks, schools, etc., belonging to the navy. I found that although working hours, clothing, dwelling houses, etc., were similar everywhere, yet in food there was a great deal of difference. I now asked the head of each department to send me in reports describing in detail the food eaten on three different days. From this I discovered *that the nitrogenous substances contained in the food were not sufficient to maintain nitrogen metabolism, but that the food contained too much carbohydrate.* Physiologists estimate that a man requires 310 grams of carbon and 20 grams of nitrogen, i. e., nitrogen should be to carbon as one is to 15.5. The food taken by our sailors contained one part of nitrogen to 17-32 parts of carbon. *And finally, the greater the difference in these proportions the more beriberi occurred, and the lesser the difference the less beriberi occurred.* Thus I came to think that beriberi is caused by the disproportion of nitrogenous and non-nitrogenous elements in food. That is, that the amount of the nitrogenous food was insufficient and that of the non-nitrogenous food excessive.

I therefore desired to change the old dietary system, but the change proposed was thought too radical, and met great opposition. My opinion finally prevailed, and the new ration was introduced in 1884. The ration as finally issued cost more than double the old ration. Shortly before it was adopted I asked for an investigation on the cause of the unprecedented amount of beriberi on the training ship Riujo. This ship carried 276 men, and during a cruise of 272 days from Japan to Honolulu, via New Zealand and Valparaiso, 169 cases of beriberi occurred, with 25 deaths. After a very extensive investigation by a committee, who asked over 10,000 questions, 10 reports were compiled, dealing with the following subjects: (1) patients, (2) clothing, (3) bedding, (4) food, (5) drink, (6) housing, (7) labor, (8) rest, (9) voyage, (10) anchorage, (11) weather and climate, and (12) conclusion. It will therefore be seen that all phases of the situation received consideration. The diet on this ship contained a proportion of nitrogen to carbon rising from one to 28 for the sailors to one to 20 for the officers.

After considerable opposition, authority was obtained in 1884 for another ship, the Tsukuba, to perform the same trip, but with the improved dietary in which the nitrogen was so increased that it bore a relation to the carbon of one to 16. In the course of 287 days' voyage four cadets and ten men were attacked by beriberi, and on investigation it was found that all of these individuals had refused to eat certain parts of the ration provided, such as condensed milk and meat. When the good report of the experimental voyage of the Tsukuba became known, all opposition to the reformed ration was withdrawn, and it at once went into general effect, subject to occasional modifications which occurred by law in 1890, 1898 and 1900.

Beriberi in the Japanese Army. Takaki said, in 1906, the health of our army has been gradually improving in late years, but beriberi is not yet eradicated as it is in the navy. The fact that the introduction of barley into the prison diet had almost eradicated beriberi suggested this to the military authorities. It was first tried in the divisions of Nagoya and Osaka, and the rates for beriberi dropped in these localities, although it remained high for other divisions of the army.* Thereafter barley was generally used throughout the army,

*Except Hiroshima, where Takaki says the price of food is less than in other places and more and better food is supplied there.

and the rates for beriberi fell greatly, although it was never completely eradicated, as was the case in the navy.

Saneyoshi also gives a good account of this great hygienic advance. His account is as follows: Until 1883 the Japanese navy suffered severely from beriberi both at sea and on shore. Cases occurred even during voyages to America, Australia and other countries, and in such numbers that the disease interfered with the service of the ships. After a study of the question, Takaki, the Inspector General, proposed an improvement in the ration. The daily allowance for the ration was 18 sen, and while it differed in various places, yet its nutritive value was always too low, containing about 622 grams of carbohydrate, 15 grams of fat and 109 grams of proteid, as compared with Voit's standard of 500 grams of carbohydrate, 50 grams of fat and 118 grams of proteid for average work. Now if the ration is compared with Voit's standard for a man performing hard labor, namely, 500 grams carbohydrate, 100 grams of fat and 145 grams of albumen, it will be seen that there is a great deficit in the ration. The ration of the Japanese navy was thus inferior to that used by other powers, but the sanitary conditions in the Japanese navy were in no manner inferior to the conditions obtaining in other navies. Exercise and work in the Japanese navy were the same as in the English navy. The crews have the same kind of sleeping quarters and hammocks. Many of the Japanese ships were purchased in England, America or other countries of Europe, and were constructed after modern designs. Beriberi has never broken out in ships of the European navies when sent to the Orient and exposed to the same climatic conditions, and performing the same work in similar ships. It seemed most probable, therefore, that the cause of the disease was to be found in the food. In February, 1884, therefore, the ration was changed, and the following substituted:

Component.	Grams.	Component.	Grams.	Component.	Grams.
Rice	648	Sugar	75	Wheat flour	75
Bread	600	Fat	15	Kidney beans	45
Biscuit	490	Salt	8	Vegetables	75
Fish	150	Meat	300	Shoyu sauce	60
Milk	45	Miso (beans)	50	Sake	90
Tea	....	Vinegar	....		

The nutritive value of this ration is 775 grams of carbohydrates, 43 grams of fat and 196 grams of proteid. In 1884 there was some difficulty in applying this ration, but even in that year there was a great diminution in the number of cases of beriberi. After this ration was in universal use beriberi disappeared almost entirely, as shown in the following table:

Year.	Total force.	Cases of beriberi.	Per cent. of cases.
1878	4,528	1,458	32.80
1879	5,081	1,978	38.93
1880	4,956	1,725	34.81
1881	4,641	1,165	25.06
1882	4,769	1,929	40.45
1883	5,346	1,236	23.12
Average	4,887	1,586	32.45
After the improvement in the ration the figures are as follows:			
1884	5,638	718	12.74
1885	6,918	41	0.59
1886	8,475	3	0.04
1887	9,106	0	0.00
1888	9,184	0	0.00
1889	8,954	3	0.03
1890	9,112	4	0.04
1891	10,223	1	0.01
1892	9,747	3	0.03
1893	9,322	1	0.01
1894	11,003	29	0.26
1895	13,006	17	0.13
1896	13,033	11	0.08
1897	14,964	22	0.14
1898	18,426	16	0.08

A minute investigation was made of those cases which still continued to occur after 1884, and it was found that these beriberics were individuals who did not like meat or bread, and ate rice almost exclusively, so that these cases further proved the intimate relationship of beriberi with the food. Again, the daily ration in the prisons of the Japanese Empire for a number of years consisted of 750 grams of rice, with a daily allowance of a sen or a sen and a half to buy other food. On this diet numerous cases of beriberi occurred. In 1875 the prisoners began to receive a mixture of rice and barley, and in June, 1881, a law was passed providing that the food of all prisons should consist of barley and rice in the proportion of six to four. Since that time beriberi has appeared only on rare occasions. A similar result was obtained in the army. The daily ration in the army was formerly 900 grams of rice, with six sen for other food. Cases of beriberi from 1882 to 1884 are as follows:

Year.	Total force.	Cases of beriberi.	Per cent. of cases.
1882	39,975	7,966	19.9
1883	38,717	7,128	18.4
1884	36,483	9,643	26.7

At Osaka the military authorities became convinced of the good results obtained by the introduction of barley in the food of the prisoners, and they instituted the same reform among the soldiers in 1885, and the number of beriberi cases fell *below ten for each thousand.* Barley was then given in several barracks, and to-day it is generally used in the army, where cases of beriberi have become rare. As the result of these observations, Saneyoshi was firmly convinced that the origin of beriberi was intimately connected with a certain kind of diet.

It should be observed in this connection that barley has been found to prevent polyneuritis from developing in fowls. It is therefore apparent that barley contains some essential principle which prevents the development of beriberi in man and polyneuritis in fowls, and this constitutes a strong argument in favor of the hypothesis that beriberi is due to the deficiency of some essential substance in the food.

These astonishing results have never received sufficient attention. The statements of Takaki and Saneyoshi were at once assailed by the adherents of the infection theory. The latter claimed: 1. That other sanitary reforms introduced at this time were responsible for the disappearance of beriberi. 2. That the disappearance of beriberi was post instead of propter with regard to the change. With regard to the first objection, it is distinctly disposed of by the accounts of Takaki and Saneyoshi. No other changes worth mentioning were made, and such measures as had been previously taken were of no avail. The beriberi still continued until the change in the ration was made.

Color was added to this charge by the fact that when the beriberi disappeared, the deaths from all other diseases dropped at the same time. However, this fact was sufficiently explained by Takaki. Monthly weights of each person in the Japanese navy were taken for many years, and these showed conclusively that for ten years after the new ration was introduced there was a gradual increase in the weight of the personnel, amounting to an average of eight pounds per person. The number of general diseases decreased gradually coincidently with the yearly increase in weight. It is evident, therefore, that previous to the introduction of the new ration in 1884 the personnel of the navy was underfed and suffered more severely from general diseases than was the case when the men were well fed. This is only what would have been expected. No abrupt cessation of general disease at all comparable to the eradication of beriberi was observed.

As for the second objection, Baelz and Scheube stated that beriberi disappeared in all the barracks of the army and navy simultaneously, although the improved diet was not introduced simultaneously. This, however, is not correct. The disappearance of beriberi in the prisons began from 1875 to 1883, while the disease was at its height in the navy and army. The adoption of the improved ration in the navy in 1884 reduced the disease to nothing while the disease was unchecked in the army. And when barley was introduced into the ration of the army, the beriberi was reduced in those divisions that used the barley while the rates for other divisions remained unchanged. These facts are altogether too striking and follow too uniformly the changes in diet to be post instead of propter. This fallacy is one against which we must always be on guard, and yet it is certain that the only way in which it is possible to reason from cause to effect is to observe whether the same effect always follows a certain cause. This is exactly what happened in the Japanese experience. The diet was improved in a number of separate instances, and each time the improvement in beriberi rates became noticeable at once. Moreover, this experience in Japan has now been reinforced by similar observations made in all parts of the world, some of which will be related later.

But while beriberi was reduced in the Japanese army it was not eradicated, and later, during the two wars in which the army was engaged, the army suffered more from beriberi than from any other one disease. Why should this have been true if the real cause had been found? It was probably because Takaki's results were not generally accepted even in Japan, and while he had sufficient influence to maintain his reform in the navy, of which he was an officer, he was unable to continue it in the army. Takaki himself says, "Unfortunately during the Chino-Japanese and Russo-Japanese wars, owing to circumstances, only rice was given to the men as the principal food, and consequently cases of beriberi increased greatly. But in the later period of the Russo-Japanese war, when we began to give the men barley with rice, and increased the quantity of meat, beriberi decreased rapidly with this change of diet." Another illustration of the influence of diet upon the health of the men is shown by the fact that there was not one case of beriberi among the sailors of the naval brigade during the siege of Port Arthur, although there were a large number of cases of beriberi in the army, living among the sailors and under exactly the same conditions. But the sailors differed from the soldiers in one respect, in that they were supplied with one pound of meat, 10 *ounces of barley* and 20 ounces of rice per day, while the soldiers were supplied with five ounces of meat and 30 ounces of rice.

We may now ask why were these wonderful results in the Japanese navy so generally disregarded. The answer is probably to be found in the fact that Takaki's theoretical explanation of this great sanitary improvement was erroneous, and that this error was readily demonstrable. Takaki believed that beriberi was caused by nitrogen starvation, and as he said, the greater the deficiency in nitrogen in the ration the more beriberi, and vice versa. But while this may have been true in Japan it is not always true, and probably was true in Japan because a deficiency of nitrogen in the rations of the Japanese was merely an indicator of the fact that the diet consisted too exclusively of *rice*. Instances were promptly related in various parts of the world where beriberi was prevalent, although there was ample nitrogenous food in the ration, and conversely many cases can be cited where the nitrogen has been reduced below the proper limit without the production of beriberi. As evidence of the latter, it is apparent that there are thousands of poor laborers in Europe and America who perpetually suffer a greater deficiency of nitrogenous food than was the case with the Japanese sailors, yet who never have beriberi. Indeed, as Braddon pointed out, this theory was not supported by Takaki's own figures, as shown by the following table:

	Proteid, grams.	Fat, grams.	Carbohydrate, grams.
The old diet contained	109.9	15.8	622.0
The new diet contained	196.0	43.0	775.0

"Without contesting that the first ration was inferior, or that the latter was a great improvement, can it be contended that there was serious nitrogen starvation on the old diet?" In answer to this question, we may refer to Chittenden's experiments, in which he found that a man could maintain nitrogen metabolism even while performing hard work on a proteid intake of only 60 grams.

We are forced, therefore, to the conclusion that Takaki's theory of nitrogen starvation is untenable, but let us not on that account discard all his valuable experience, as has been done for so many years. *There can be not a shadow of a doubt that beriberi was reduced in the Japanese navy as a result of a change of diet.* This change consisted in a reduction of the amount of rice consumed and an increase of meat, fish, vegetables, including beans, and the addition of milk and flour. Rice, however, still continued to be used to the extent of 648 grams.

Clearly, the disease was not produced by the toxicity of the rice, for if this were true it could hardly be eradicated by a mere reduction from 782 grams to 648 grams. The disease must, therefore, have been caused by the deficiency of some substance, not nitrogen, which was supplied in the articles added to the new ration. Granted that the disease was of dietary origin, and not infectious, this conclusion necessarily follows, unless there was an intoxication by some other article of food than rice. This is not seriously considered by anyone.

Other literature dating before 1907, tending to show the connection between a rice diet and beriberi, could be quoted, but it is not considered desirable to do so for the reason that, while these references are important, most of them have been collected and analyzed by Braddon. As we have seen from the references already quoted, there had been for many years good reason for believing that beriberi was of dietary origin, and even that it was connected with the use of rice, but this evidence did not receive much credence prior to 1907, and the theory that the disease was infectious, continued to hold the first place. Manson's place infection theory and Hamilton Wright's ingenious speculation concerning an infectious duodenitis were most generally accepted at this time. Braddon had formulated and published his theory that beriberi was caused by eating stale white rice which had become toxic as early as 1901, but it received little attention at that time. Governmental officials were opposed to any such theory, the profession at large was not convinced, and some individuals openly scoffed.

Thus W. Gilmore Ellis wrote in 1903, "That beriberi is a place disease, that the soil and buildings are infected, and that people dwelling there are liable to absorb the poison, whatever it is; that this poison, absorbed in sufficient quantities, is the cause of beriberi, *and this opinion I have never seen reason to change.*" Hartigan in a short letter to the British Medical Journal in the same year emphasized this opinion and said that to attribute beriberi to rice was absurd. That it had just as much to do with beriberi "as eating fish had to do with leprosy or chewing tiger's flesh with the production of courage."

But in 1907 Braddon published his book, "The Cause and Prevention of Beriberi," and all this was changed. The attention of the world was attracted to Braddon's theory, and while there was still plenty of opposition it was compelled to be respectful. This great work of Braddon was not based on experimental work of his own, so much as on wide observation and reading, as a result of which he brought together in logical order such a mass of evidence that it became impossible to doubt the importance of rice in the production of beriberi. It would be futile to attempt to present this evidence here because of its great volume. And even were it possible it would not be desirable, because every one interested in the subject of beriberi should read Braddon's book. In this book Braddon proved: 1. That beriberi attacks those that are rice eaters and does not attack those who do not eat rice.* 2. That among rice eaters its incidence varies with the sort of rice eaten. Those eating white, polished or over-milled rice are subject to the disease, while those eating hand-pounded rice or cured rice never suffer from beriberi. Braddon, indeed, thought he proved that beriberi was an intoxication due to a fungus growing in the decorticated rice. This part of his views is sufficiently disposed of in Chapter VII. The rejection of this part of Braddon's hypothesis does not, however, diminish the importance of his communication, which alone turned the attention of the world seriously toward rice. Nothing but the contribution of a master mind could have accomplished this result in a world so blind as to ignore the results Takaki had recorded some years earlier (1893).

One of the first converts to Braddon's view was W. Gilmore Ellis, who stated so positively in 1903 that beriberi was a place infection, and the following account taken from his article published in 1909 loses nothing from this fact:

"Beriberi, endemic since the opening of the Singapore Lunatic Asylum in 1887, broke out in an appalling manner early in 1896 and resisted all endeavors to combat its ravages until towards the end of 1901 when I began to experiment with Bengal (cured) rice. In these earlier experiments carried on throughout the years 1902 and 1903 some of the patients were given a diet with cured rice and some with uncured rice for varying periods, and, watching the results, it appeared that there was something in Braddon's theory. In 1904 all patients were kept on cured rice until October 16th without a case of beriberi occurring; upon this date a change was made to uncured rice with the result that we had 15 cases in December with one death. Throughout 1905 several changes were made from cured rice to uncured rice and back again. These experiments so increased my belief in the theory that in 1906 we ran the first eleven months of the year on cured rice and without a single case of beriberi. This result decided me to make one last and systematic trial of the two varieties of rice, and I deter-

* With certain exceptions such as cases of ship beriberi referred to elsewhere and the beriberi occurring among natives of those countries where a similar starchy food is used as the staple article of diet.

mined that for a year or longer all patients should be placed alternately four months on a diet containing cured rice and four months on uncured rice. Our full native diet consists of rice, one and one-half pounds; meat, four ounces; fish, four ounces, vegetables, assorted, six ounces; salt, one-half ounce; onions, one-half ounce; garlic, one-eighth ounce, and lard, one-half ounce daily. This trial was carried out with the exception that the second and third spells of four months on uncured rice were cut short on account of the rapid manner in which patients from all parts of the asylum succumbed to beriberi. I am happy to say that on cured rice we have had no recurrence of the disease for over a year. A return will never be made to the uncured grain."

Even more striking were the results obtained by Fletcher, who determined to test the truth of Braddon's theory, and who published his conclusions in 1909. Beriberi was prevalent in the Kuala Lumpur lunatic asylum. During the year 1905, 94 of the 219 lunatics treated in the asylum were affected, and 27 died from the disease. During 1906, therefore, half of the patients were placed on a diet of cured rice, while the other half remained on the diet of uncured rice, which all the lunatics had been eating previous to this experiment. These lunatics were housed in two exactly similar buildings on opposite sides of a quadrangle, surrounded by a high wall. On December 5, 1905, all the lunatics at that time in the hospital were drawn up in the dining shed and numbered off. The odd numbers were sent to the east ward and supplied with uncured rice; the even numbers were sent to the west ward and given cured rice. The full ration was as follows:

Fresh meat, four ounces four times a week.
Fresh fish, five and one-half ounces twice a week.
Salt fish, five and one-half ounces once a week.
Vegetables, eight ounces daily.
Cocoanut oil, two-third ounce daily.
Rice, twenty-eight ounces daily.

Both varieties of rice were of excellent quality, and were cooked the same way by the same cook. All lunatics drank the same water. At the end of the half year the batch in the east ward was sent to the west ward, and *vice versa* in order to eliminate place infection. The result of this experiment was that out of 124 inmates fed on uncured rice 34 suffered from beriberi and 18 died, whereas among 123 patients fed on cured rice there were only two cases of beriberi, both of whom suffered from the disease on admission, and no deaths. During 1907 the observation was continued on the same lines. During this year

136 patients received uncured rice. Of these patients 28 suffered from beriberi, four of whom had the disease on admission. One hundred and thirty-one patients were treated on cured rice. Four had beriberi on admission, but none developed the disease in the asylum. Thus the net result for the two years was as follows: Two hundred and nineteen of the patients admitted to the asylum were put on a diet containing cured rice. None of these patients developed beriberi. On the other hand, 226 patients received uncured rice and 65 cases of beriberi occurred in this group. Many of these patients in both groups were only in the asylum for a short time. If these cases are excluded the discrepancy between the two groups is more marked. Thus, excluding all patients who were in the asylum less than 28 days there were 154 patients fed on cured rice, none of whom developed beriberi, and 153 patients fed on uncured rice, of whom 65 developed beriberi in the asylum. The possibility of place infection is excluded. The whole asylum had been a hotbed of beriberi, and should have been thoroughly impregnated, yet the disease was confined to the east ward of the hospital, where uncured rice was served, and did not appear in the west ward, where cured rice was served. But in June the patients were transferred, thus changing the domicile of each group, while their food remained the same as before. If the disease were a place infection the patients transposed to the east ward should have developed the disease. This, however, was not the case. On the other hand, the disease followed the uncured rice and broke out in the hitherto healthy west ward. Contagion may be excluded because patients were allowed to associate with each other, and lunatics suffering from beriberi were admitted to both groups during the course of the year. Moreover, 26 patients suffering from beriberi were transferred from the uncured rice group to the cured rice ward, yet none of the latter developed the disease. The result of feeding persons actually suffering from beriberi was also observed, and the net result of the two years' observations on this point are as follows: Thirty-six patients actually suffering from beriberi and fed on uncured rice, of whom 24 died (66.66 per cent). Thirty patients suffering from beriberi were fed on cured rice, of whom three died (10 per cent). Fletcher concluded: " That the cause of beriberi is to be sought for in the diet, and that white polished rice, although of the best quality, is a cause of beriberi, acting either by some poison which it contains, or by a starvation due to some defect in the nutritive value of such rice."

Fletcher's own statement as to his attitude of mind when he started this experiment is interesting, and shows that actual trial converted another sceptic. Fletcher wrote: "In an experiment of this nature the personal factor always comes into question. It may, therefore, not be out of place to state that at the commencement of the experiment the opinion was held by myself that rice was neither directly nor indirectly the cause of beriberi. It was fully expected that the patients on Bengal (cured) rice would suffer from beriberi to the same extent as those who remained on the Siamese variety (uncured), and that the result of the experiment would be a refutation of the rice theory. With this in view, precautions were taken to provide separate utensils, plates, etc., for each set of patients in order that the upholders of the rice theory might not be able to point to any possibility of contamination of the Bengal rice with the poison that is supposed to be present in uncured rice. Contrary to expectation, the result of the experiment, so far as it goes, is to prove the truth of Doctor Braddon's contention that uncured rice is the cause of beriberi."

Fraser and Stanton's Experiment. In 1907–1908, Doctors Fraser and Stanton, acting on Braddon's suggestion, determined once for all to determine the truth as to the part played by rice in the production of beriberi. The experiment as they performed it was understood to be a crucial test. The investigators took 300 Javanese laborers into a virgin jungle, where they occupied new and sanitary quarters. After excluding the existence of beriberi by a careful examination of each person, they were divided into two parties of equal numbers. One party received polished rice as the staple article of diet, while the other party received cured rice. In three months beriberi appeared among the members of the party receiving white rice. When a certain number of cases had been noted, polished rice was discontinued, and thereafter no cases occurred. No sign of the disease appeared among the party receiving cured rice. *The conditions were then reversed.* The party hitherto on parboiled rice were given white rice, and after a somewhat longer interval beriberi broke out in this group also. *This outbreak also ceased on discontinuing the issue of white rice.* Again no sign of the disease appeared among the control party receiving parboiled rice. Place infection and communicability were excluded by transferring individuals suffering from beriberi from one group to the other from time to time. The conclusions drawn by Fraser and Stanton from this experiment may be found on page 394 of the Appendix. Such an experiment should be conclusive, because it was carefully controlled. The disease could not have been infectious, because the men were well at the begining of the experiment, and the earliest case to develop beriberi only appeared after 89 days. Since the experiment was conducted in a virgin forest and new buildings, there were only two possibilities of infection, one that the men were infected at the beginning of the experiment before removal to the forest, the other that the food supplied was infected. But it is improbable that the incubation period of the disease should be 90 days if it were infectious, and it is also impossible to explain why all the cases were limited to the party receiving polished rice, and why, no matter how the patients and the diets were changed about, *the beriberi always followed the polished rice.* It seems quite clearly shown by any one of these three experiments that beriberi will be produced on a diet of polished rice, and can be prevented by a diet of parboiled or cured rice. And there is not one iota of evidence to the contrary. Each one who has performed this experiment has been convinced of the truth of this statement. We shall now pass on to another series of experiments, which not only confirm the previous evidence that beriberi is due to a too exclusive diet of polished rice, but will show that it can also be prevented by the addition of katjang idjo (Phaseolus radiatus) to the ration.

Grijns, in 1901, had found that polyneuritis gallinarum could be prevented by adding katjang idjo to the diet of polished rice. Hulshoff Pol therefore determined to test the effect of this legume as a preventive and curative agent in beriberi. He first fed 150 grams daily to 31 patients who had suffered a long time from beriberi. These patients all improved, but still suffered from paralyses. As a result of this experiment he came to the conclusion that there is a distinction between beriberi itself and its effects, i. e., the degeneration of the nerves and the resultant paralyses; that the disease was curable through the administration of katjang idjo, but that the resultant paralyses could only be cured through the slow processes of regeneration. He also found that this legume exerted a marked diuretic effect on the cases suffering with pronounced anasarca, and that the oedema disappeared very rapidly, although the katjang idjo apparently had no diuretic effect on healthy people or on cases of oedema from other diseases than beriberi. It will be seen in the chapter on infantile beriberi that exactly the same result was obtained by Chamberlain and Vedder after administering an extract of rice polishings to infants who suffered from anasarca as a result of beriberi. These facts were confirmed by Wuller in 1906 and Kiewiet de Jonge in 1907. Even more satisfactory and convincing were the experiments conducted by Hulshoff Pol to test the prophylactic action of katjang idjo. A good opportunity for the test was found in an insane asylum containing 300 inmates who were housed in 12 pavilions. The inmates in pavilions 1, 5 and 9 received daily 150 grams of katjang idjo instead of one meal of rice. The inmates of pavilions 2, 6 and 10 received daily 300 grams of different kinds of vegetables in addition to the usual amount. These were served partly raw and partly cooked. The inmates of pavilions 3, 7 and 11 served as controls and received only the accustomed ration. The inmates of pavilions 4, 8 and 12 also received the accustomed ration and nothing else, but the pavilions were thoroughly disinfected with a three per cent solution of carbolic soap. The result of this experiment was as follows, after it had been continued for nine months

Pavilions.	Number inmates.	Cases of beriberi.
1, 5 and 9 receiving katjang idjo	78	1
2, 6 and 10 receiving extra vegetables	86	16
3, 7 and 11 controls	78	33
4, 8 and 12 were disinfected	58	19

This experiment is very interesting, not only as showing the result of administration of katjang idjo, but also as showing the effect of the fresh vegetables. As we will see later, some vegetables possess the power of preventing beriberi, while others are absolutely devoid of this property. The result, therefore, is exactly what might have been expected. That is, since it is probable that a part of the fresh vegetables given possessed this power, while others did not, the inmates receiving fresh vegetables, therefore, had less beriberi than the controls, but more than the inmates receiving katjang idjo, which possesses this power to a high degree. However, the evidence in favor of katjang idjo is much stronger than this. In order to test the place hypothesis the diets in the pavilions was reversed. Pavilions 2 and 7 were given katjang idjo, while the legumen was stopped in pavilions 1 and 5. No change was made in the food of pavilions 3, 4, 6 and 8, in which no beans were given in the first test. This experiment lasted from May, 1902, until February, 1904, or 21 months. The result of this experiment was that pavilions 2 and 7 had no beriberi, although cases of beriberi developed in pavilions 1, 3, 4, 5, 6 and 8. Not satisfied with this very positive experiment, it was continued by van Hengel during the absence of Hulshoff Pol for five months longer, at the end of which time he was convinced of the value of katjang idjo and discontinued the experiment. The disease at this time had assumed so serious a character that all the patients were given katjang idjo. The result of these experiments, which lasted over three years, may be tabulated as follows:

	Number of beriberi cases.
PAVILION 1.	
May to July, 1901, rice alone	5
August, 1901, to April, 1902, rice and beans	0
May, 1902, to January, 1904, rice alone	10
February to June, 1904, rice alone	12
PAVILION 2.	
May to July, 1901, rice alone	4
August, 1901 to July, 1902, rice alone	5
August, 1902 to January, 1904, rice and beans	0
February to June, 1904, rice alone	9
PAVILION 3.	
May, 1901 to June, 1904, rice alone	2·
PAVILION 4.	
May, 1901, to June, 1904, rice alone	26
PAVILION 5.	
May to July, 1901, rice alone	3
August, 1901, to May, 1902, rice and beans	0
June, 1902, to June, 1904, rice alone	20
PAVILION 6.	
May, 1901 to June 1904, rice alone	42
PAVILION 7.	
May to July, 1901, rice alone	3
August, 1901, to May, 1902, rice alone	18
June, 1902 to January, 1904, rice and beans	0
February, 1904, to June, 1904, rice alone	6

That is, during over three years while the experiment lasted there was no case of beriberi in the pavilions in which rice and katjang idjo were given, while in the pavilions in which rice alone was given 211 cases of beriberi have occurred in the same time. This experiment can hardly fail to convince anyone: 1. That a diet containing too large an amount of overmilled rice will produce beriberi. 2. That the disease can be prevented by the addition of katjang idjo to the diet. 3. That beriberi must be due to some deficiency in the diet, since it is hardly conceivable that if the rice were toxic that the disease could be prevented simply by the addition of another vegetable to the diet. If we administer an amount of arsenic or other known poison sufficient to produce an intoxication, we do not expect that these effects will be counteracted in the least by the administration of beans or any other food. Hulshoff Pol then conducted a similar experiment to determine whether Zea Mais (corn) would exert a similar influence on beriberi when combined with a diet of polished rice, but this experiment showed that corn conferred no protection against beriberi, neither was it capable of curing beriberi.

The next step was to determine whether a decoction of katjang idjo would contain the essential principle of these beans, and he demonstrated, by treating 18 beriberi patients with this decoction, that the decoction contained this essential element. Next the decoction was purified by precipitating with liquor plumbi subacetatis. The yellow precipitate so obtained was filtered off, washed with water and treated with hydrogen sulphide to remove the lead. After the lead sulphide was filtered off a yellow, strongly acid fluid remained. He then treated four beriberi cases with this purified decoction, selecting cases of wet beriberi for the trial. All four cases recovered or improved. Extensive oedema disappeared in a week in one case, in two weeks in a second case, and in three weeks in the other two cases.

Hulshoff Pol then took a quantity of this purified decoction and evaporated it to dryness, and obtained from the decoction from one kilo of beans about 100 milligrams of crystals. These crystals, which were still probably not entirely purified, were analyzed chemically and found to apparently belong to the vegetable acids. It should be noted that this same decoction of katjang idjo also cured polyneuritis gallinarum when administered to fowls suffering from that disease, and also prevented the disease from developing in birds fed on polished rice. As will be seen later, this and similar facts constitute evidence of the strongest kind for the belief that beriberi in man and polyneuritis gallinarum in fowls are essentially the same condition.

The next great step in advance was made through the demonstration that undermilled rice, i. e., rice containing the pericarpal layers, was just as efficacious in preventing beriberi as cured rice.

We have already seen the important evidence which Vorderman had obtained some years earlier on this point, which was now further verified by a large number of independent observers. It would be impossible to detail all of these instances, but the following are quoted at length as being quite sufficient to prove this point:

1. Fraser and Stanton's experiments on fowls.
2. Highet's experience in Siam.
3. Evidence from civil institutions in the Philippines furnished by Doctor Heiser.
4. Evidence from Poulo-Condore furnished by Theze.

After Fraser and Stanton showed so conclusively that cured rice would prevent beriberi, they endeavored to discover the reason for this fact. They first attempted to extract the hypothetical poison from white or polished rice, but these experiments were negative; no toxin could be demonstrated. They then extracted cured rice in a similar way, and found that rice so extracted lost its protective power, but that the extract removed was capable of preventing polyneuritis gallinarum. They then demonstrated that fowls could be fed on polished rice without developing polyneuritis if a certain quantity of rice polishings were administered daily. As a result of these experiments they concluded: (1) Beriberi is a disorder of metabolism, and, as it occurs in this country, is associated with a diet in which white rice is the principal constituent. (2) White rice as produced in the mills here commonly makes default in respect of some substance or substances essential for the maintenance of the normal metabolism of nerve tissues. These substances exist in adequate amount in the original grain, and in superabundant amount in the polishings from white rice. (3) The prevention of beriberi in this country will be achieved by substituting for the ordinary white rice, a rice in which the polishing process has been omitted or carried out to a minimal extent. It will be seen that these experiments corroborate the work of Eijkman and Vorderman, which had previously received so little consideration.

2. **Evidence from Siam.** (1) In 1910 Dr. H. Campbell Highet read a paper before the first meeting of the Far Eastern Association of Tropical Medicine, of which the following is a condensed account:

Beriberi is now common at Bangkok, although it has not always been so. In fact, the only reliable records go back no further than 1890, when an epidemic broke out in the central jail. Even after this date beriberi was unknown to the general practitioner and even to the hospital physician until 1900. However, in August, 1900, the first case was admitted to the police hospital, and since 1901 beriberi has become one of the ordinary diseases seen in that hospital. There are no reliable data for the civilian population, but the collected statistics of the hospitals, the army, the navy and the police from 1901–1909 show that there have been 22,670 cases of beriberi, with 1,063 deaths. My experience in Bangkok leads me to confirm absolutely the opinion first expressed by Braddon, and lately confirmed by Fraser and Stanton, that beriberi is closely associated with the consumption of white, steam-milled rice. The opinion is based on the following observations:

(1) Beriberi was unknown in Bangkok until white rice began to be retailed locally. For over ten years prior to the first outbreak in the jail white rice was prepared in one or two steam mills in Bangkok, but the whole of this was exported to Europe. One of the first large institutions to be supplied with white rice was the new jail, with the result that an epidemic of beriberi appeared. When the change was made to hand-milled rice beriberi died down, and has not reappeared

since the prison authorities have continued to supply this hand-milled rice. During the 90's many mills were erected and large quantities of white rice were thrown upon the local market. This was the result of the abolition of slavery in Siam, after which the price of labor went up, and steam-milled rice could be produced more cheaply than the hand-milled article. By the year 1900 most of the old hand mills had stopped working, and the people began to suffer from beriberi. The first case was admitted to hospital in this year.

(2) Experience in the insane asylum. In 1900 white rice was substituted for hand-milled rice, and beriberi soon appeared. During the nine years white rice was used beriberi increased in virulence, and 783 patients died of this disease. In February, 1908, cured and hand-milled rice was introduced. Since that time not a new case of beriberi has developed in those patients using this kind of rice, and it is now a year since it was first issued. No other alterations in diet or in hygienic surroundings were made in the asylum.

(3) The reformatory school at Koh Si Chang. This was started March 5, 1908. There were no cases of beriberi until steam-milled rice was sent from Bangkok. Beriberi then appeared. After February, 1909, hand-ground rice or cured rice was used, and since then not a single case of beriberi has occurred.

(4) Jails near Bangkok. In four of these jails fresh hand-milled rice is supplied, and in these beriberi is a distinct rarety. In two other jails steam-milled rice is supplied, and beriberi is frequent.

(5) Police school in Bangkok. Four hundred conscripts were admitted to this school in January, 1909. White rice was supplied by a contractor and was always of good quality. Within a fortnight after using this rice beriberi broke out, and at the end of a month 353 out of the 400 conscripts contracted the disease. On April 31 a second batch of about 400 were admitted, and they were given fresh hand-milled rice. Since then, nearly a year ago, over a thousand men have passed through the school, and only a few cases (14) have been detected, and these men were probably suffering from beriberi when admitted.

(6) Geographic distribution of disease in Siam. In the province of Bangkok, 1,700 square miles in extent, beriberi clings to the banks of the Menam river and to the banks of the large navigable canals which join this river to adjacent streams. This is because the river and the canals are the principal means of transport, and along these white rice from Bangkok is freely sold. Back from the banks, where communication is difficult, the cultivators mill their own rice, and invariably escape beriberi.

The whole idea of prevention, then, would seem to be that rice, however milled, which retains a considerable proportion of the pericarp does not cause beriberi, but the removal of the outer layers of the grain takes away a prophylactic agent. With regard to parboiled rice, it is clear that its prophylactic powers are not due to any sterilization during the process of parboiling, but to the retention of a considerable proportion of the oil-bearing layers of the seed. The practical method of combating beriberi is therefore to encourage the consumption of undermilled rice.

Further evidence recently secured from Siam appears in the Journal of Tropical Medicine and Hygiene, August 15, 1912, as follows:

Nearly two years ago there was a good deal of beriberi amongst the customs guard at the different stations along the river. The use of polished rice was discontinued, and the only kind supplied was the undermilled variety, known as No. IV Siam, in which a large part of the phosphorus is retained. This is milled by the Borneo Company, Limited, to meet the demand that has arisen as a consequence of the accepted medical view with regard to beriberi. During this period the cases of beriberi averaged barely one a month.

From last December the use of white polished rice was again resumed, owing to the Borneo Company, Limited, ceasing to mill. Last month beriberi again began to be noticeably present amongst the guards, and in one station containing just over 200 men there were 19 cases last month. The loss involved in having a growing number of men on the invalid list is very considerable.

3. **Evidence from Civil Institutions in the Philippine Islands.** The Culion leper colony. Doctor Heiser states that since the opening of the Culion leper colony in 1906 rice has been the staple article of diet, and it was customary to use either Saigon rice No. 2 or local polished rice. Beriberi was more or less continuously present until February, 1910. By substituting mongos and meat for rice it was always possible to reduce the number of beriberi cases, but the disease was never completely eradicated. It was found later that this failure was probably due to the fact that many of the lepers preferred to deny themselves food rather than eat mongos.

In February, 1910, the use of unpolished rice was made compulsory for all inmates of the Culion leper colony. The total number of deaths and the deaths from beriberi before and after this introduction of unpolished rice are shown in the following table:

Before the use of unpolished rice, 1909. Average population, 1,537.			After the use of unpolished rice, 1910. Average population, 1,952.		
Month.	Total deaths.	Deaths beriberi.	Month.	Total deaths.	Deaths beriberi.
February	39	14	February	66	20
March	54	15	March	36	0
April	52	17	April	29	0
May	47	15	May	22	0
June	48	8	June	27	0
July	57	9	July	15	0
August	61	9	August	24	0
September	65	21	September	12	0
October	43	4	October	13	0
November	80	30	November	15	0
December	188	69	December	58	0
January	164	98	January	52	0
Total	898	309	Total	369	20

From this table it will be seen that beriberi was eradicated from the Culion leper colony by the use of unpolished rice in place of the polished rice previously used. Moreover, beriberi did not reappear during 1911 while unpolished rice continued to be used. However, in 1912, owing to the scarcity of rice in the Philippine Islands, some difficulty was encountered in obtaining unpolished rice for Culion, and a quantity of polished rice was purchased and issued. The issue of this rice began November, 1911, and beriberi reappeared January, 1912. During the latter part of February, 1912, large quantities of mongos were used, and about the middle of March, 1912, unpolished or partially polished rice was reintroduced. A decrease in the number of beriberi deaths began during the latter part of March. The influence of the varieties of rice on the death rate in 1912 is shown in the following table:

Month.	Total deaths.	Deaths from beriberi.
January	35	2
February	86	36
March	92	60
April	25	3
May	29	6
June	38	2
July	22	1

An investigation of the deaths which are reported from beriberi, from April to July, reveals the fact that all of them were either chronic cases that were contracted during January or February and did not die until some months later, or they were cases in persons who came to the colony with the disease.

This experience at Culion affords as clear a demonstration of the influence of polished rice on the production of beriberi as it is possible to obtain. Moreover, the evidence obtainable from all other governmental institutions confirms the experience at Culion. Thus Doctor Heiser again says, prior to May, 1910, beriberi was very common throughout the Philippines in jails, lighthouse stations, charitable institutions, on government vessels and among the Filipino troops of the United States army. An investigation has shown that it was the invariable practise to use polished rice as the staple article of diet in all of the places mentioned. In May, 1910, an executive order was issued by the Governor General of the Philippine Islands prohibiting the use of polished rice in all public civil institutions. Since August, 1910, only two cases of beriberi in the above places have come to my attention. One of these was among the crew of the steamer Rizal. An inspection of the ship's stores showed that the crew's rice was of the white polished variety. The other case occurred in a prisoner in the Tacloban jail. The physician in charge reported that it had not been possible to purchase unpolished rice at Tacloban, and for that reason polished rice was being used. However, in 1912, during the rice shortage before referred to, polished rice was issued to a number of governmental institutions, and beriberi again appeared in these places. As in Culion, the beriberi again disappeared after the use of unpolished rice was resumed.

At the Hospicio San Jose, which is an asylum for insane, orphans and aged of over 700 inmates, beriberi has been constantly present at least during the past ten years. Since June, 1910, unpolished rice has been used, and a few weeks afterward beriberi disappeared, and since then no further cases have been reported.

4. Similar and convincing evidence was furnished in a paper written by Theze in 1910. According to this author the penitentiary at Poulo-Condore has been a focus of beriberi for a long time. In 1906 this disease caused nine-tenths of the total number of deaths (116 out of 130). In the epidemic of 1906 the substitution of rice incompletely decorticated for the completely decorticated rice previously used produced remarkable results, after disinfection of the quarters and intestinal disinfection had failed. This method applied toward the middle of August stopped the epidemic short, and those already sick rapidly recovered, so that after the 22nd of August there was not another death. Consideration of the ration leads the author

to the belief that the disease was due to a lack of phosphate in the food. Contagion did not play any role.

STATISTICS AT POULO-CONDORE.

Year.	Number of prisoners.	Per cent of deaths from beriberi.
1901	295	27.45
1902	375	13.60
1903	489	57.46
1904	534	7.67
1905	511	46.57
1906, Jan. 1 to Aug. 15	363	31.99
1906, Aug. 15 to Dec. 31	249	0.00
1907	703	0.00
1908	909	0.00

A note added to this report by the editor of the Ann. d' Hygiene et de Med. Col. gives the interesting results obtained at a prison at Saigon. Decorticated rice was excluded from the diet in November, 1903, by M. Grall, the inspector general:

Years.	Average number of prisoners.	Deaths from beriberi.	
1899	615	80	
1900	628	78	
1901	507	92	
1902	464	85	
1903	584	76	
1904	746	3	Entered the prison sick.
1905	779	6	
1906	860	15	
1907	762	5	

These facts led Breaudat and Denier to use rice polishings as a preventive and curative agent. As we have seen, this had already been done in the case of fowls. These authors concluded that rice polishings did not cause any digestive disturbance, and that, given in a prophylactic dose of 40 grams a day, it clearly exerted a protective influence. Used as a curative dose on natives already suffering with beriberi, and without making any change in their ordinary diet, it was fully as efficacious as modern methods of treatment combined with a European dietary.

Another important advance was the demonstration that the ordinary white bean will prevent beriberi.

Evidence from the Philippine Scouts.* The following account is partly derived from the paper of Major W. P. Chamberlain, who first described the eradication of beriberi from the Scouts. The United States army board for the study of tropical diseases was influenced by all this work, and proceeded to investigate the diet actually eaten in 18 companies of Filipino Scouts.

The components of the ration for the Philippine Scouts prior to 1910 are shown in the following table:

Filipino ration, Army Regulations, 1908, paragraph 1220.

Component articles.	Quantities.	Substitute articles.	Quantities.
		Bacon	8 ounces
Beef, fresh	12 ounces	Canned meat	8 ounces
		Fish, canned	12 ounces
		Fish, fresh	12 ounces
Flour	8 ounces	Hard bread	8 ounces
Baking powder, when in field and ovens are not available	32 ounces		
Rice	20 ounces		
Potatoes	8 ounces	Onions	8 ounces
Coffee, roasted and ground	1 ounce		
Sugar	2 ounces		
Vinegar	.08 gill		
Salt	.64 ounce		
Pepper, black	.02 ounce		

It by no means follows, however, that this was the food always actually eaten by any one company for several reasons. During active campaigning the ration was frequently reduced to rice and canned salmon. Again, some Scout companies were stationed in remote districts, where it was impossible to obtain ice, and therefore fresh beef could only be obtained on rare occasions (once or twice a month), while during the remainder of the time the meat component was substituted by fish or bacon. And in addition to these circumstances the regulations provided that "savings" could be made on several articles of the ration, and the money value of these savings could be applied to purchase other articles of the ration, or supplies from the market, for the purpose of adding variety to the mess. And finally the money value of articles so saved could be added to the company fund and be spent for entirely different purposes. As a result of the information obtained with regard to the food actually eaten, the board (then consisting of Captains Phalen and Kilbourne) on September 30, 1909, recommended the following changes in the ration issued these Scouts:

* The organization known as the "Philippine Scouts" consists of approximately 5,000 Filipino enlisted men serving as infantry. The commissioned officers are Americans. This organization is under the control of and supported by the War Department of the United States, and is scattered in small garrisons throughout the Archipelago.

1. That the daily amount of rice used per man be limited to 16 ounces instead of the 20 ounces at present supplied.

2. That Filipino No. 2 rice (undermilled) be substituted for choice Saigon rice (overmilled).

3. That 1.6 ounces of beans be added to the ration.

4. That the issue of canned tomatoes be authorized in place of an equal quantity of potatoes, but not to exceed 20 per cent of the total issue.

5. That onions be issued on the same terms as tomatoes instead of allowing them to be substituted for all the potatoes.

6. That no savings be permitted upon the fresh beef and potatoes or their substitutive articles.

The first and third recommendations and that part of the sixth recommendation relating to the saving of fresh beef were made effective by an order issued November 3, 1909, and the Subsistence Department purchased Filipino No. 2 rice to replace the polished Saigon rice. None of this undermilled rice was issued for use until about August.

The authorities in Washington had independently taken a similar action, and in March, 1910, issued an order modifying the Scout dietary. The components of the ration thus prescribed are as follows:

FILIPINO RATION, GENERAL ORDERS NO. 24, WAR DEPARTMENT, 1910.

Component articles.	Quantities.	Substitute articles.	Quantities.
Beef, fresh	12 ounces	Bacon	8 ounces
		Canned meat	8 ounces
		Fish, canned	12 ounces
		Fish, fresh	12 ounces
Flour	8 ounces	Hard bread	8 ounces
Baking powder, when in field and ovens are not available	.32 ounces		
Rice, Filipino No. 2	16 ounces	Rice, Saigon (when Filipino No. 2 can not be obtained).	
Mongos	4 ounces		
Camotes*	8 ounces		
Coffee, roasted and ground	.5 ounce		
Ginger root	.5 ounce		
Sugar	2 ounces		
Vinegar	.08 gill		
Salt	.64 ounce		
Pepper, black	.02 ounce		

* The camote is a vegetable allied to the sweet potato. The mongo or katjang idjo (Phaseolus radiatus Linn.) is allied to the bean. "Filipino No. 2" as the term is used in this ration means an undermilled rice.

The board had no knowledge of this new ration prior to the promulgation of the order in the Philippine Islands. It will be seen, however, that the order carried out in spirit the three most important recommendations of the board in that an undermilled rice (Filipino No. 2) is prescribed in the amount of 16 ounces daily, and mongos (equivalent to beans) are added to the ration in lieu of the four ounces of rice taken away.

The subsistence department at once proceeded to obtain mongos and camotes, but in order to use up the large supply of Saigon rice on hand a delay occurred in the issue of Filipino No. 2 rice. From a careful study of the records it was possible to set a date before which none of the articles could have become part of the diet, and a period during which they must have been gradually going into use.

None of the Filipino No. 2 rice could by any possibility have been in use prior to July 15, 1910, and but little could have been issued at any time in July. In August the issue became more general, and probably all Scout companies were supplied by the last of August or the first part of September.

The first consignments of mongos and camotes were shipped simultaneously, and none left Manila until May 20, 1910. Under the most favorable conditions of unloading and prompt issue one Scout command (three companies) might have put mongos and camotes into use as early as May 21, but probably did not. No other Scouts could possibly have been using these camotes and mongos before May 25, even granting that they were issued at once on arrival at the station. About half of the Scouts could not have received any mongos and camotes until well into June. The issue to the last of the posts was not completed till the first part of July.

The first shipments of ginger root occurred at the same time as those of camotes and mongos. In some of the Mindanao posts ginger root was received about ten days sooner than camotes and mongoes, but not, however, before the last two or three days of May. The importance of fixing these dates will be appreciated when the beriberi statistics for 1910 are considered.

For many reasons the new Filipino ration, as ordered by General Orders No. 24, caused dissatisfaction among the troops and in the subsistence department. The Filipino No. 2 rice, in addition to being undermilled, contained many unhusked kernels and much broken grain and dirt, and furthermore was thought to become infested with worms and insects more readily than did polished rice. The camotes did not keep well, and neither they nor the mongos could always be obtained in sufficient quantities in the island markets. Therefore some had to be imported. The ginger root was not acceptable to the Scout as a partial substitute for coffee. Neither mongos nor camotes met with favor as constant articles of diet. This order was, therefore, revoked by the War Department on November 7, 1910, and the ration reverted to its original status. There was, however, so much Filipino No. 2 rice on hand in the depots that its issue and use continued until June, 1911. On this date the ration was finally prescribed, and remained practically the same as the old Filipino ration, except that undermilled rice was ordered and Scout organizations were required to use the entire allowance of meat and not more than 16 ounces of rice per day, and 1.6 ounces of beans per ration had to be consumed. It will thus be seen that after November, 1911, there was a period of at least five months when the ration was exactly the same as the old ration which produced so much beriberi, except that undermilled rice was issued, and that after June, 1911, it was the same ration except that both undermilled rice and beans were compulsory. This has continued in effect until the present time.

The admission rates of the Scouts from beriberi are shown in the two following tables:

Calendar year.	Mean strength Surgeon General's office.	Admissions		Deaths.		Discharges for disability.	
		Number.	Rate per 1,000.	Number.	Rate per 1,000.	Number.	Rate per 1,000.
1902	4,826	598	123.92	29	6.01	2	0.41
1903	4,789	614	128,21	22	4.59	5	1.04
1904	4,610	334	74.62	7	1.52	6	1.30
1905	4,732	170	35.93	6	1.21	1	0.21
1906	4,759	176	36.98	9	1.79	6	1.19
1907	4,679	115	24.58	6	1.28	3	0.54
1908	5,085	618*	121.54	7	1.35	13	2.50
1909	5,369	558	103.93	12	2.17	33	5.96
1910	5,422	50	10.00	2	0.36	3	0.55
1911	5,389	2	0.37	1	0.18	0	0.00
1912	5,463	3	0.55	0	0.00	0	0.00

Admissions for beriberi by months, calendar years 1908 to 1912:

Year.	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Total.
1908	14	34	102	23	51	33	55	39	63	59	88	63	624*
1909	138	89	96	88	38	24	28	36	7	27	22	11	604
1910	19	8	12	3	4	1	0	2	0	0	0	1	50
1911	1	0	0	0	0	0	0	1	0	0	0	0	2
1912	1	0	1	0	0	1	0	0	0	0	0	0	3

* The discrepancy between the total admissions in the two tables is due to the fact that the first table is compiled from the reports of the Surgeon General of the Army and the second table from records in the office of the Chief Surgeon, Philippines Division. In the former only one admission is recorded for each case, while in the latter a new admission is recorded if the patient is transferred from one hospital to another.

From these tables it will be seen that there was a great reduction in the amount of beriberi in the year 1910. This reduction is most significant when it is considered that all the sanitary conditions remained unchanged with the exception of the diet.

The following table will be found useful in determining to what components of the ration this improvement was due:

BERIBERI ADMISSIONS BY MONTHS, CALENDAR YEARS 1910, 1911 AND 1912, AND INFLUENCE ACTING THEREON.

	1910.											
	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.
Admissions	19	8	12	3	4	1	0	2	0	0	0	1
No. 2 rice								—	—	—	—	—
Camotes					—	—	—	—	—	—	—	—
Mongos					—	—	—	—	—	—	—	—
Ginger root					—	—	—	—	—	—	—	—
Reduction and legume	—	—	—	—	—	—	—	—	—	—	—	—

	1911.											
	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.
Admissions	1	0	0	0	0	0	0	1	0	0	0	0
No. 2 rice	—	—	—	—	—	—	—	—	—	—	—	—
Camotes												
Mongos												
Ginger root												
Reduction and legume							—	—	—	—	—	—

	1912.											
	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.
Admissions	1	0	1	0	0	1	0	0	0	0	0	0
No. 2 rice	—	—	—	—	—	—	—	—	—	—	—	—
Camotes												
Mongos												
Ginger root												
Reduction and legume	—	—	—	—	—	—	—	—	—	—	—	—

From this it will be seen that 39, or 80 per cent, of the admissions occurring in 1910 appeared during the first three months of the year, when the changes in the ration had been in effect but a short time. It should also be noted that some decrease in admissions began in the last quarter of 1909. This is ascribed to the fact that just prior to that time members of the board had visited many Scout posts and had advised the limitation of the daily consumption of rice and the more liberal use of other components of the ration instead of economizing for the purpose of making cash savings.

It is not believed that camotes and ginger root were of any importance in effecting this improvement, and it is obvious that undermilled rice could have had nothing to do with the great decrease in beriberi admissions which occurred prior to August, 1910.

It therefore appears that the great reduction in beriberi from January to August, 1910, was due to the reduction in the quantity of rice consumed and the substitution, in lieu of the rice taken away, of a leguminous vegetable, either beans or mongos. From September to December, 1910, undermilled rice probably contributed an important share in the continuance of good results.

On the other hand, in 1911, from January to June, the undermilled rice was the only factor in operation that differed from the old beriberi-producing ration. During all these months there was only one case of beriberi. Since it has been repeatedly shown that the incubation period of beriberi is about three months, we have here a certain demonstration that beriberi can be prevented simply by the use of undermilled rice.

From July, 1911, to the present date, April, 1913, both undermilled rice and beans have been supplied, while the ration has otherwise been practically the old beriberi producing diet. Beriberi has not reappeared during this time. Sporadic cases only have occurred, and investigation shows that these cases have been due to the fact that these individuals have refused to eat the beans and undermilled rice. (See Appendix, page 395.)

We are able to state with certainty that there have been no sanitary improvements among the Scouts, other than the dietetic, which could account for this lowered incidence of beriberi. There was no sudden decrease in the admission rates for other diseases during 1910 and 1911 when beriberi disappeared. Thus the average monthly admissions for all diseases was 420.5 in 1908, 393.9 in 1909, 341.5 in 1910, 349.7 in 1911, and 316.2 in 1912. Since beriberi was causing an average monthly admission of 50 in 1908 and 1909, it is evident that the main decrease in the years 1910 and 1911 is due to the disappearance of beriberi.

The reduction in beriberi among the Scouts in 1910 was not coincident with a decrease of beriberi in the general population. On the contrary, beriberi is on the increase throughout the islands generally as may be seen by consulting the statistics for the Philippines given in the chapter on prevalence of beriberi.

The eradication of beriberi from the Philippine Scouts constitutes a sanitary achievement fully as striking as the eradication of that disease from the Japanese navy, while the facts show clearly that beriberi can be eliminated from natives subsisting on rice as a main staple of diet, either by issuing an undermilled rice or by supplying a proportion of beans. It is obviously surer and, therefore, preferable to combine these two methods.

Reviewing this evidence supplied by different investigators, we find that beriberi can be prevented by the use of (1) cured rice, (2) undermilled rice, (3) barley, (4) mongos, (5) beans, (6) other vegetables (Fales).

It seems quite apparent that this fact that beriberi can be prevented by the use of an *undermilled* rice, and also by the addition of various other articles of food to a diet whose staple is polished rice, is quite incompatible with Braddon's toxin theory. Undermilled rice has not been sterilized by parboiling. The starch of the grain is not protected from the action of the supposititious fungus, since in removing the husks the pericarpal layers are removed from many portions of the grain. Hardly any undermilled rice grains contain the whole pericarp, and in most undermilled rice the starch is greatly exposed to the air and to the action of any organism that could attack a polished rice. Undermilled rice is, therefore, simply a polished rice plus the food value of the adherent fragments of the pericarpal layers.

In view of all this evidence obtained from so many different countries, we may regard it as proven that beriberi is of dietary origin, and that since it can be prevented by the addition of rice polishings, or beans or mongos or extracts of these articles to the ration, the disease must be due to some deficiency existing in a diet whose main staple is rice. However, since many in Manila and elsewhere were still sceptical, Strong and Crowell decided to perform a further experiment which should determine definitely whether beriberi is an infectious disease or is due to a disturbance of metabolism caused by the prolonged use of polished rice as a staple article of diet. This experiment was accordingly conducted in 1912 in Bilibid prison upon subjects who were entirely isolated. Twenty-nine volunteers were divided into four groups, which were entirely separated by stone walls. These groups ate separately and under guard so that it was impossible for any interchange of food to occur. All of these men received exactly the same diet except with regard to the kind of rice.

Group 1 received white rice and extract of rice polishings and special diet.

Group 2 received white rice and special diet.

Group 3 received red rice and special diet.

Group 4 received white rice and special diet.

The results of these experiments were as follows:

Group 1. Two men out of six developed early symptoms of beriberi.

Group 2. Four men out of six developed beriberi.

Group 3. Two men out of six developed some symptoms of beriberi.

Group 4. Four men out of 11 developed beriberi.

Strong and Crowell concluded, It is evident from our experiments that beriberi may be produced by the prolonged consumption of a diet in which white rice constitutes the staple article. Of the 17 individuals fed upon such a diet, eight developed beriberi, and the stage of the disease was well advanced before the close of the experiment, while one man died of beriberi. It is evident that beriberi among the individuals comprising our experiment was produced only by means of the diet, and that the disease has, therefore, a true dietetic causation. It is further evident that beriberi develops owing to the absence of some substance or substances in the diet necessary for the normal physiological processes of the body. Such a substance or substances are evidently present in red rice and in rice polishings, and also in small amount in the extract of rice polishings, and when these articles are added to what would appear to be an otherwise physiologically proper diet, they usually prevent the development of the disease. It is also evident from our experiments that the disease is certainly not an infectious one in the sense in which we usually employ this term.

Strong's and Crowell's conclusion that beriberi will be produced by a diet of overmilled rice appears to be amply justified. However, the experiment was not as satisfactory as it might have been, because early symptoms of beriberi appeared in the groups receiving red or undermilled rice and extract of rice polishings.*

* This failure to protect completely by these diets may, however, be explained. The red rice which was used possibly did not contain sufficient pericarp to afford complete protection. It is by no means easy to obtain a rice sufficiently undermilled, and in our efforts to obtain such a rice for the Philippine Scouts there has been a constant struggle to prevent the millers who furnish this rice from carrying the milling process too far. The failure to completely protect the group receiving extract of rice polishings in addition to the polished rice may be explained even more satisfactorily. Strong and Crowell extracted each 5 kilos of polishings, with 14 liters of 95 per cent alcohol, in three successive macerations of 24 hours each, using

The theory that beriberi is caused by a lack of phosphorus in the food. Schaumann has maintained, in a long series of important contributions, that beriberi is caused by the deficiency of organically combined phosphorus in the food. Schaumann found that diets that produced peripheral neuritis were invariably poor in phosphorus, and that substances like rice polishings, katjang idjo, etc., which prevent the development of polyneuritis, are rich in phosphorus. That almost invariably the smaller the percentage of phosphorus in a diet the greater was its influence in producing beriberi. It will be seen that this observation corresponds to the work of Fraser and Stanton, who found that the percentage of phorphorus was an indicator of the beriberi producing power of a given rice. Unlike these latter investigators, however, Schaumann jumped to the conclusion that the lack of phosphorus was the cause of beriberi, although he had no direct proof of this view. Indeed, all of his feeding experiments with phosphorus compounds (phytin, nucleins, etc.) were negative. Schaumann first thought that the active principle containing phosphorus was nucleic acid. Feeding experiments with nucleic acid conducted by several investigators failed completely. Schaumann then shifted his ground and maintained that the essential principle was phosphorus in some organic combination. This was shown to be improbable by Chamberlain and Vedder, who showed that the alcoholic extract of rice polishings, which was highly protective, contained less than one-thousandth of the total amount of phosphorus in the original rice polishings. Thus this extract contained 0.0016 per cent of phosphorus pentoxide, while rice polishings contain from 2 to 5 per cent phosphorus pentoxide. Later Funk showed that fowls suffering from polyneuritis gallinarum could be cured by the administration of an organic base which he extracted from the rice polishings, which contained absolutely no phosphorus.

These results seem to absolutely exclude the possibility that beriberi is caused by a deficiency of phosphorus *per se,* although it cannot be denied that a deficiency in phosphorus may cause serious disturb-

6 liters the first day, and for the second and third days 4 liters each. I have found by long experience with this method that the neuritis-preventing substance is only very slightly soluble in 95 per cent alcohol, and that much larger quantities of alcohol than those used by Strong and Crowell are essential if a complete extraction is to be made. Thus, in my work, I now use 30 liters of alcohol to extract each 5 kilos of polishings (15 liters the first day and 7½ liters on both second and third days). I have also found that even when using this large quantity of alcohol that the polishings are not completely extracted, because the polishings extracted in this manner will still protect fowls from polyneuritis. It is apparent, therefore, that the men receiving this extract of rice polishing as prepared by Strong and Crowell were only partially protected because the extract only contained a part of the neuritis-preventing substance from the polishings.

ance of metabolism, and that when this deficiency coexists with a deficiency of the true neuritis-preventing substance, the clinical picture of beriberi may be to some extent influenced thereby.

We have already shown in criticising the intoxication theory that proof of the existence of a toxin could not be demonstrated. It is clear that the final proof of the deficiency theory must equally depend upon the isolation of the substance which is deficient, and the prevention and cure of beriberi by means of this substance in a chemically pure state. This evidence will be presented in the following chapter.

It will now be worth while to examine some of the objections that have been urged from time to time against the theory that beriberi is due to a dietary deficiency. Many of the older authors make observations of this character. These are mostly only of historical interest at the present time, but it will be worth while to examine a few of them. Thus Anderson said of Japan, "That the coolie class who live more exclusively on rice than the soldiers, sailors or traders, yet suffer less than these latter from beriberi." Exactly what should occur if the poor coolies used hand-pounded rice because it was cheaper while soldiers and sailors were supplied with overmilled rice because it was supposed to be better.

MacLeod did not believe the disease was due to poverty of living, or to any dietary condition whatever, because well-fed Mohammedan butchers accustomed to generous living were equally seized. This is a very general observation. He gives absolutely no details as to what these well-fed Mohammedan butchers actually ate. If the facts were known they probably ate chiefly polished rice.

Simmons of Yokohama has observed that those who are able to afford good and abundant food are liable to beriberi, but remarks that rice is badly tolerated by the stomach of the beriberic and appears to aggravate the symptoms. The argument that people in well-to-do circumstances sometimes have beriberi is often made and is probably true. In these cases, if the truth were known, we should probably find that the individuals affected have, through preference or because of indigestion or other reasons, lived chiefly on rice. The fact that a person is well to do or even rich is not a proof that he eats a balanced diet, although it is probably true that the majority of them do, and that is the reason why beriberi is much less common among the well to do.

Rupert does not consider diet the cause of beriberi on the ground that, if it were, the disease should be much more prevalent than it is, because the native often eats little except rice and fish and yet does not get beriberi. Rupert made his observation before any account was taken of what kind of rice the native used. It is only in certain localities that the native uses *polished rice*, and in these areas beriberi is not uncommon but quite the contrary.

Weintraub denies that diet is the cause, because the diet of day laborers in the Indian archipelago is all rice, fish and fruit, while the native soldiers have rice and bacon and only occasionally salt or dried fish. The native convicts have a scanty flesh diet, yet we see beriberi common in soldiers and convicts and rare in natives. He concludes that the diet theory is futile. Yet now that we know of the distinction between polished and unpolished rice, this is exactly what we should expect if the day laborers were living on hand-pounded rice while the soldiers and convicts were being supplied with the polished article.

More definite objections that have been raised in recent years are the following:

1. It has been thought that the dietary hypothesis does not explain the tendency of the disease to occur in epidemics. A little consideration, however, will show that this theory fully accounts for epidemics. We have only to suppose that a change is made in the food supply of a school, jail or other institution resulting in the use of a beriberi producing diet. Now, since the average incubation period is about three months, it follows that nothing will happen for about that length of time. When, however, this period has elapsed a few cases of beriberi will begin to appear. These will be those individuals least able to endure the deficiency. As the days go by, more and more individuals will succumb, and when the time has passed at which the great majority can no longer endure the lack of the necessary substance in the food, the cases of beriberi appear in large numbers. Later, when all the individuals of ordinary resistance have succumbed, the "epidemic" gradually decreases in severity as only here and there a case appears among those individuals who possess much greater resistance to the unfavorable condition than the majority of their fellows; and finally a certain percentage will always remain who never develop the disease. These individuals apparently possess some pecularity of excretion or metabolism, as a result of which they do not suffer from the deficiency of the neuritis-preventing principle as ordinary individuals do. Similarly every individual does not appear to be equally susceptible to scurvy when a large number of people are fed on a diet favorable to the development of that disease. We have here an explanation for the gradual rise in the number of cases, the great severity with which the disease rages for a time, and the gradual abatement of the disease

if unsupplied with fresh material. It is exceedingly similar to the progress of an epidemic of infectious disease, but this fact by no means proves that the disease is infectious or offers any real objection to the acceptance of the dietary hypothesis. But it may be answered, this is a very plausible explanation of epidemics of beriberi in a jail, or hospital or institution where the diet is the same for all, and where all would, therefore, be equally liable to suffer from a deficiency if it existed. But how about epidemics of beriberi among the people at large who select and buy their food according to individual preference? It may be answered that these epidemics undoubtedly occur as the result of some economic condition which results in suddenly changing the food of a large part of the population. It has already been shown how the abolition of slavery in Siam was followed by a large increase in the rice mills, and that thereafter a large part of the population purchased overmilled rice in place of the hand-milled or undermilled rice to which they had been accustomed, and that an epidemic of beriberi followed.

Another interesting case in which the facts are given is the epidemic of beriberi affecting Manila in 1882. The circumstances of this epidemic are given by Königer as follows:

From August to October, 1882, Manila was visited by a severe cholera epidemic which found there a fertile soil and carried off between 15,000 and 20,000 victims. (The population of Manila was estimated at 400,000.) A panic occurred among the native as well as among the European population, because cholera had not been present since 1865 and the mortality was more than 75 per cent. After the epidemic had subsided, on October 20, a terrible typhoon visited the city and province and destroyed all the suburban houses built of light material. As a consequence, almost the whole native population of Manila and its surroundings was without shelter. Nor was it possible to rebuild the destroyed houses and huts, since, following the typhoon a flood occurred and all the lower parts of the city and province were under water for several weeks. By this time, while the cholera epidemic was still smoldering, a new disease, which killed its victims in a few days or weeks, was noticed among the inhabitants. The native and Spanish physicians did not recognize the malady and the terror of the population increased. In some cases the disease was connected with a swelling of the glands and it, therefore, was believed by some to be a variety of bubonic plague.

As soon as I saw the first cases I had no doubt that I was dealing with a particularly malignant epidemic of beriberi, of which I had seen some cases in Japan. The epidemic rapidly spread in the province of Manila and along the coast to the neighboring territories. It remained stationary during November and December, and gradually decreased during January. When I left Manila, during the middle of March, the epidemic had very much decreased, and there were also still present a number of sporadic cases of cholera.

The probable explanation of this epidemic of beriberi is as follows: There was an epidemic of cholera and the people were in terror. As a result they ceased using fresh fruits and vegetables, and ate nothing except what could be boiled, naturally chiefly rice. But most of these people were eating hand-pounded or undermilled rice, and were therefore protected from beriberi. Then came the typhoon and the flood, which swept away houses and the accumulated supplies of rice. Thereafter the people were compelled to purchase their rice in the open market, and many of them bought white or overmilled rice. Since they were impoverished and subsisted almost entirely upon this rice, after the incubation period had elapsed they all succumbed to beriberi at about the same time. Very similar circumstances would undoubtedly explain all the epidemics of beriberi that have occurred in the past, and should be sought for to explain any that may occur in the future.

2. In the past objection has been raised against the dietary hypothesis because various observers have seen the development of beriberi in institutions where the ration was believed to be absolutely satisfactory, and even considerably above the diet obtained by the average native. Many such instances will not bear critical inspection.

Thus Doctor Rowell (see Bentley, page 10), when he was the Principal Civil Medical Officer of Straits Settlements, made a report to the government, dated June 14, 1880, with regard to an outbreak of beriberi in the prison at Singapore, in the course of which he says: "I feel assured that the dietary *per se* cannot be credited with having been a factor in the causation of the disease. It is a prison diet, but it is one which is liberal, sufficiently nutritious and varied. *The nitrogenous element is certainly deficient in it* (italics ours). It is the same diet which is in use in the gaols of the sister settlements of Penang and Malacca, and is that which the native female prisoners have had, and who fatten on it. It is the same as the prisoners have had who have been sent to the Civil Prison for treatment, and is a diet unquestionably better than the mass of prisoners, previous to entering the gaol, enjoy outside, and in liberality will vie with that of almost any of the gaols in India. It is, moreover, a dietary on which two-thirds of the prisoners gain weight, and some largely so * * *. The history and progress of the outbreak, too, have shown conclusively that the diet has been a cypher in its production."

This is absolutely characteristic of the arguments that have been made in the past, and are still being made, to refute the proposition that beriberi is due to a deficiency in diet. It is quoted at length because of this fact, and because in this case the facts obtainable completely contradict Rowell's statements. He himself says: The nitrogenous element is certainly deficient. Now let us see this much-vaunted ration. It is as follows: Rice, one pound and 14 ounces. Fresh beef, six ounces, twice a week to Malays, or fresh pork, six ounces, twice a week to Chinese. Fresh fish twice a week to all, six ounces. Salt fish, four ounces, three times a week. Vegetables, six ounces daily. Oil or lard, one-half ounce daily. Curry, one-half ounce daily. Salt, one-half ounce daily. It appears, therefore, that the prisoners received six ounces of fresh meat twice a week, six ounces of fresh fish twice a week and salt fish three times a week, with nearly two pounds of polished rice daily. This is an insufficient allowance of meat for a properly balanced dietary, though it may be true that it is as much as natives are accustomed to get when they provide for themselves. It is not stated of what the daily six ounces of vegetables consisted. Some vegetables, such as onions, are absolutely devoid of power to prevent beriberi, as we have shown in our fowl experiments. It is also possible that many natives in the prisons never actually consumed these vegetables, even though they may have been provided in the ration. In that case their diet would have been rice with a little fish. Exactly what we have found time and again is the diet best calculated to produce beriberi.

But the interest in this case is greatly increased when we learn that five years later Doctor Rowell, finding that the disease never disappeared, though at times varying in intensity, introduced a change in the diet with the most satisfactory results. He largely increased the amount of nitrogen and decreased the carbohydrates by adding wheat flour and a kind of black bean, while decreasing the allowance of rice. The results were excellent. The cases of beriberi became fewer and soon ceased altogether, the general sick rate was diminished, and those already in hospital with beriberi were soon discharged cured. This improvement was permanent, and the disease did not reappear. Doctor Rowell considered that though the former diet had nothing perhaps to do with the actual or direct causation of the affection, yet its poverty in nitrogenous elements did undoubtedly predispose the blood of the prisoners to the reception of the poison.

This may have been a reasonable deduction in 1885, but it is now unreasonable, because this is no longer an isolated case. The same beneficent results have been secured in every instance in which the rice has been reduced and the nitrogenous foods increased, and since the disease can invariably be prevented in this manner we must now believe that a deficient dietary is the real cause of the disease.

It is by no means uncommon to find similar instances in the literature where beriberi developed in spite of the fact that the patients had received what was supposed to be a fairly well-balanced ration containing rice as the staple article of diet. This observation is still urged as an insuperable objection to the theory that beriberi is caused by a rice diet. But Vedder has shown that fowls will develop polyneuritis when fed on a diet containing a sufficiency of all the alimentary principles, provided no one of the ingredients of this diet contains the neuritis-preventing substance. Vedder and Clark have shown that when fowls are fed on polished rice, and are daily given in addition 10 grams of various food stuffs, such as meat or potatoes, the fowls nevertheless develop neuritis, but after a more or less prolonged incubation period. They thus clearly showed that most articles of diet contain only small amounts of the protective substance, and that when even moderate quantities of many foods are added to a staple of rice the deficiency in the neuritis-preventing substance still exists. These experiments completely dispose of the objection so often raised against the deficiency theory, that men who eat various quantities of other food in addition to a staple of rice may nevertheless develop beriberi.

3. Adverse experimental evidence. Travers' experiments conducted at Kuala Lumpur have often been quoted as disproving the dietary hypothesis. There are two jails in that city, one of which was the seat of an extensive and persistent epidemic of beriberi, while the other remained healthy. Travers caused the rice supplied to the prisoners in the healthy jail to be taken from the same stock of grain and to be cooked in the same vessels as that supplied to the prisoners in the beriberi-stricken jail. The prisoners in the healthy jail remained healthy, and the prisoners in the beriberi jail continued to develop beriberi. Braddon has clearly exposed the fallacy of this experiment. It has been shown that it requires three months on a polished rice diet to produce beriberi. Now it happened that the healthy jail in Travers' experiments contained only short-term prisoners, while the beriberic jail had the long-term prisoners. The prisoners in the former jail did not develop beriberi because they did not remain there long enough. Travers, who did not take this factor into consideration, believed both

parties were similarly circumstanced, and therefore believed, erroneously, that, the food supplied to both being the same, it could play no part in determining the different incidence of beriberi.

H. Wright performed a similar experiment, and came to a similar conclusion, which has also been often quoted against the dietary causation of beriberi. Wright gave the same diet to two separate parties confined in the same jail, but made the same mistake of overlooking the fact that part of them were short-term and part long-term prisoners, and hence were not similarly circumstanced.

This evident error disposes of the only important experimental evidence that has ever been urged against the dietary hypothesis.

4. Observations indicating that beriberi may appear on a diet of unpolished rice:

(1) Breaudat reported the following instance to the Far Eastern Association of Tropical Medicine in 1912: "There are in the island of Culaogieng (Indo-chine) two large settlements, almost adjacent and under the same management. One, only for women, is a nunnery, with a novitiate, an orphanage or a day nursery, a hospital and a maternity, containing all together 500 or 600 Anamites. The other settlement, for men, is separated from the former only by a five-feet-wide ditch, and contains between 100 and 150 inhabitants. In the first settlement the rice has always been polished by hand every day. Not a single case of beriberi has ever been reported. On the other side, on the contrary, the rice used to be polished every 10 or 12 days and kept in large quantities in big wooden boxes. Beriberi made its appearance every year during the rainy season, with an average of 60 to 90 cases. The pupils had to be sent home three times during a period of a few years. In 1909 I strongly advised the manager to use the daily polishing of rice, and not a single case occurred since that time. Therefore I come to the conclusion that even hand-polished rice, if 10 or 12 days old, may produce beriberi."

The incidence of beriberi in these two settlements might easily be explained in an entirely different way. Hand-milled rice does not usually produce beriberi because it is almost always incompletely polished. However, if the process is sufficiently prolonged, a polished rice may be produced which will cause beriberi. In the first community, where beriberi did not occur, the rice was pounded as it was needed from day to day, and was incompletely polished. The second community was evidently more careful in providing the rice supply, since it was polished in quantities every 10 days and stored. It may well have been that this rice was more thoroughly polished. A white rice has always been more highly esteemed, and it seems quite probable that a community that prepared its rice for 10 days in advance would require a white rice, and would prolong the polishing process to a point where beriberi would result. I have kept unpolished rice such as is furnished to the Philippine Scouts for one year in an open tin. At the end of this time the rice was mouldy and unfit for human food. Yet when fed to fowls it did not produce polyneuritis gallinarum. Moreover, unpolished rice that has been mixed with water and allowed to ferment in the incubator for four or five days still retains its protective quality when fed to fowls. It therefore appears most probable that the beriberi produced in the case described by Breaudat was really caused by a rice that was too highly milled, in spite of the fact that the milling had been done by hand.

(2) Shibayama says: "Upon the basis of the theory of the connection of rice with the etiology of beriberi, a freshly husked, but not polished, rice was used in some of the mines on Banka Island, but the result was in evident contradiction to the theory.

"In 1908, 1,195 cases of beriberi developed in the Blinjoe, one of the mining districts. Mine No. 3 was especially unfortunate, for 166 out of 410 workmen contracted the disease, and mine No. 4 developed 118 cases among 390. No. 5 had 400 workmen, and 97 of these were ill with beriberi. On the other hand, the remaining mines showed but few cases. For two years the workmen had received unpolished, fresh rice, not only in mines Nos. 3, 4 and 5, but also in No. 11, in which latter 49 out of 300 workmen contracted the disease. On the other hand, the laborers in the remainder always had polished and old rice. It may further be stated, according to Hulshoff Pol, that the workmen in all the mines received 150 grams kadjang idjo beans, together with dried fish and fresh vegetables, daily. The result of our observations, therefore, was as follows:

"1. Even if the workmen in the mines receive 150 grams of kadjang idjo regularly every day, nevertheless beriberi occurs among them.

"2. Even if the laborers are given a diet of fresh, unpolished rice, nevertheless they develop more cases of beriberi than those in the other mines where they receive polished and older Java rice.

"I therefore could not find the assumption to be confirmed that unpolished rice, which has the same composition as parboiled rice, could prevent beriberi."

These statements are utterly at variance with all the evidence thus far quoted. If Shibayama's facts were correct they would form a serious objection to the acceptance of the belief that beriberi can be always prevented by the use of unpolished rice.

I therefore wrote to Doctor de Vogel, the chief of the civil medical service of Java, requesting information as to whether the facts stated by Shibayama were correct. Doctor de Vogel very kindly had the subject investigated very thoroughly. His letter in reply and the enclosed reports are very illuminating and are as follows:

BATAVIA, *February* 4, 1913.

DEAR DR. VEDDER:

In reply to your favor of October 25th a. p. I send you herewith copies of different letters and a map, containing several curves, relative to rice and beriberi, and a letter of Dr. Grijns, the Director of the Medical Laboratory, dated January 12th past on the same subject.

As I wished to inform you as completely as possible, it was a long time before I got all the data about the beriberi at Blinjoe.

You will see that the hypothesis that beriberi is caused by nourishment with unpolished rice has not lost in the least of its strength by the alarming publications of Dr. Shibayama.

It seems that his investigation on the subject in Banka was not thorough, and that he took the data of Dr. Rost van Tonningen without any criticism.

As you will see from the letter of the acting Resident of Banka, dated Muntok, September 24, 1912, with the list of figures joined to it, the results of the feeding on unpolished rice in the mining district of Koba are very satisfactory indeed.

Yours truly,
(Signed) DE VOGEL,
Chief of the Civil Med.

The letter of Dr. Grijns referred to above is as follows:

WELTEVREDEN, *January* 12, 1913.

DEAR SIR:

Dr. de Vogel requested me to give you an explanation for the Japanese beriberi investigation subcommittee's statement, that in Banka experiments with unpolished rice proved this to be devoid of any protective property against beriberi.

The Japanese committee (Shibayama, Miyamoto and Tsuzuki) stayed in Banka about ten days, two at Muntok and eight at Blinjoe. Therefore we may assume that the committee got its information chiefly from Dr. Rost van Tonningen, surgeon to the tinworks at Blinjoe.

Now Dr. Rost van Tonningen, on August, 1909, presented to the

Government a report on this subject, a translation of which will be forwarded with the present. There he concludes "the nourishment with unpolished rice had not the least effect."

Dr. Muschaert, his predecessor, held the opposite opinion, as he wrote me in a personal letter, he did not conceive why we took so much trouble with katjang idjoo, while unpolished rice had already been shown to prevent beriberi in the prisons.

I have studied the report of Dr. Rost van Tonningen, and found that in those mines where unpolished rice has been given, the new-comers (Sinkahs) at the commencement of the experiment were lodged in separate sheds and fed on polished rice. Dr. R., however, has added all the men of every mine and those suffering from beriberi also. Therefore his results are quite unreliable.

I segregated from his report those groups of Sinkahs in which it is stated what kind of rice they ate, and at what time some of them contracted beriberi. Where there is no evidence whether the cases of beriberi occurred before or after a change in diet, the observation is eliminated.

Therefore I dropped from mine 3 the newcomers on 30–1 and 5–6; from mine 4 those of 14–6; from mine 5 those of 3–4; mine 11 wholly; from mine 14 those of 30–1; from mine 25 those of 30–1. Amongst the arrivals on July 12 and 17, in mine 3, two contracted beriberi before unpolished rice was given. Also one of the arrivals on July 17 in mine 4. These three cases are withdrawn from the statistics.

With the rest I combined the following table, wherefrom it may be seen that in Sinkahs at Blinjoe fed on polished rice beriberi was 24 times more frequent than in those fed on unpolished. (See Table, page 195.)

A later report from the Governor of Banka deals with an experiment in the mine district Koba, where unpolished rice was afforded, whilst in the other mines polished was given. In the preceding years Koba held the record for beriberi in Banka. The year unpolished rice was given only two cases occurred. The relief set in in the same week the unpolished rice had been introduced. Doctor de Vogel will have the Governor's and Dr. Rost van Tonningen's report translated and sent to you.

You may see from this how difficult it is to get correct information even when you go to the spot, if you do not understand the local languages and you have no time to meet the several authorities and study the thing at your leisure.

As to the supply of katjang idjoo, information has been received that the beans were cooked with the rice to a thick porridge and given in the morning. Coolies get a large quantum in their mess and every one takes as much as he likes. In the two remaining meals rice without katjang is given. As to the amount of katjang idjoo that was provided pro man and pro die I am not quite sure, as Dr. Muschaert wrote me, it was 150 grams, while the Department informed me that it was 7.9 thail or 0.08 K. G. Dr. Hulshoff Pol and Dr. Kiewiet de Jonge used 0.25 K. G. daily in their experiments at the lunatic asylum in Buitenzorg. The average quantity of rice for a coolie is 1 pikol = 62 K. G. a month, which will be sufficient for himself and his family if he has one. As it is a general observation that katjang idjoo is very soon disliked when given daily, you may easily conceive that the coolies never will eat all the katjang that is provided, because they have plenty of other rice, and therefore the katjang idjoo prophylaxis is insufficient.

I hope my information will have persuaded you that the observations in Banka are not in the least contradictory to those of others; they have only been misunderstood by Dr. Rost van Tonningen, and so the Japanese committee has been falsely informed.

Such facts are very unhappy as they contribute to discredit a theory which could have already spared thousands of men, if it had been adopted generally some years ago.

Yours sincerely,

(Sgd.) G. GRIJNS,

Director of Medical Laboratory.

The letter from the acting resident of Banka with regard to the influence of unpolished rice upon the miners in the district Koba is as follows:

MUNTOK, *September* 24, 1912.

In your letter of August 16, 1912, you asked for circumstantial information with regard to the influence of the distribution of unpolished rice to the miners in the district Koba on the development of beriberi among the workmen.

In reply I invite your attention to annexe I, showing the number of cases of beriberi which occurred monthly among the tin laborers of the different districts during the period, March, 1910, till July, 1912.

Please notice that only since February 1, 1912, unpolished rice was given to the miners in the district of Koba. In order to be able to compare the district mutually and the different years of exploitation with one another as to the frequency of beriberi, it is necessary to state how many cases of beriberi occurred per 100 men of the mean strength. Annexe II shows the mean strength of the miners in the different districts at Banka during the two latest years of exploitation and the first five months of the current year of exploitation.

Statistics of Beriberi in Sinkahs at Blinjoe, Furnished by Dr. Grijns.

Mine.	Date of arrival.	Ate polished rice.			Ate unpolished rice.		
		Number arrived.	Contracted beriberi.	Percentage.	Number arrived.	Contracted beriberi.	Percentage.
1..........	14-6	30	10	33	....	....	....
2..........	12-7	20	3	15	....	....	....
	17-7	15	5	33	....	....	....
3..........	3-4	20	8	40	....	....	....
	12-7	....	....	....	39	1	2.5
	17-7	....	....	....	19	0	0
	9-8	....	....	....	48	0	0
4..........	12-7	17	2	11	15	0	0
	17-7	....	....	....	19	1	5
	9-8	....	....	....	48	0	0
5..........	31-1	15	0	0	....	....	....
	12-7	17	0	0	....	....	....
	17-7	....	....	....	20	2	10
	9-9	....	....	....	48	0	0
14..........	28-6	96	52	54	....	....	....
25..........	12-7	15	11	73	....	....	....
	17-7	15	8	53	....	....	....
	28-8	10	0	0	....	....	....
26..........	6-6	123	54	40.7	....	....	....
	17-7	15	8	53	....	....	....
	28-9	18	0	0	....	....	....
		426	161	38	258	4	1.6

The figures mentioned in the annexes I and II will enable you to settle the number of cases of beriberi that occurred yearly per 100 men of the mean strength. The results of these calculations are mentioned in annexe III.

The figures of this annexe III show that during the current year (1912) the miners of the district Koba were the least contaminated by beriberi, while during the two preceding years these workmen suffered considerably from this disease.

This change for the better succeeded, as shown by annexe I, to the furnishing of unpolished rice in February, 1912. It seems very probable that the occurrence of this improvement must be explained in this way: That the supply of unpolished rice prevented beriberi.

This result makes me believe it advisable not only to continue this experiment, but to extend it.

The Act. Resident of Banka,

Chief of the Tinworks.

(Sgd.) R. I. BOERS.

Annexe I. Number of Beriberi Cases Occurring Monthly in the Different Districts Among the Tin Miners.

Period.	Tobo-ali.	Mun-tok.	Dje-baes.	Soengei liat.	Panhel-pinang.	Soengei-slan.	Koba.	Blin-joe.	Total.
March, 1910....	3	24	21	85	11	28	68	35	275
April..........	1	25	5	60	14	9	7	35	156
May..........	1	3	0	32	10	22	6	6	80
June..........	1	1	1	19	3	6	5	7	43
July..........	1	0	0	20	2	9	3	8	43
August........	2	1	0	2	3	9	4	2	23
September......	3	5	3	3	2	20	5	6	47
October........	2	6	2	12	23	33	2	7	87
November......	2	4	0	27	24	15	11	3	86
December......	3	2	0	25	11	1	9	9	60
January, 1911...	3	4	5	59	20	11	7	10	119
February.......	7	7	1	23	59	8	5	6	116
Total 1910–1911	29	82	38	367	182	171	132	134	1,135
March, 1911....	17	23	0	121	30	37	26	5	259
April..........	11	3	5	65	28	12	4	11	139
May..........	4	1	2	26	5	2	3	4	47
June..........	0	2	1	12	2	14	1	0	32
July..........	0	2	2	4	7	4	3	2	24
August........	1	0	0	3	0	0	2	1	7
September......	0	0	0	4	1	0	4	1	10
October........	1	0	1	6	0	0	1	0	9
November......	0	0	2	10	7	2	5	0	26
December......	0	0	2	10	5	4	4	0	25
January, 1912...	0	1	15	19	16	5	8	0	64
February.......	0	1	2	24	3	9	1	8	48
Total 1911–1912	34	33	32	304	104	89	62	32	690
March, 1912....	5	1	9	58	15	17	1	23	129
April..........	5	2	0	38	32	18	0	29	124
May..........	0	1	3	16	16	15	0	1	52
June..........	0	0	0	3	2	0	1	1	7
July..........	0	1	0	0	2	4	0	0	7
Total 5 months 1912–1913....	10	5	12	115	67	54	2	54	319

Annexe II. Number of Miners in the Several Tin Mines.

Year of exploitation.	Tobo-ali.	Mun-tok.	Dje-baes.	Blin-joe.	Sonegei-liat.	Panhe-pinang.	Soengei-slan.	Koba.	Total.
1910–1911....	1,202	1,707	1,936	4,115	4,932	3,217	1,450	1,256	19,823
1911–1912....	1,505	1,773	1,893	4,352	5,416	3,357	1,537	1,459	21,292
5 months 1912	1,600	1,603	1,719	4,253	4,978	3,392	1,502	1,354	20,399

Annexe III. Number of Beriberi Cases (Per Cent of Mean Strength) Occurring Yearly in the Different Districts.

Year of exploitation.	Tobo-ali.	Mun-tok.	Dje-baes.	Blin-joe-	Soengei liat.	Panhel-pinang.	Soengei-slan.	Koba.	Average.
1910–1911....	2.41	4.80	1.96	3.25	7.44	5.63	11.70	10.5	5.72
1911–1912....	2.25	1.86	1.74	0.73	5.61	3.09	5.79	4.2	3.24
1912–1913 (5 months)	1.50	0.75	1.69	3.06	5.54	4.75	8.66	0.37	3.76

These letters, with statistics, indicate that Shibayama misinterpreted the facts with regard to beriberi on the island of Banka, and that these facts, so far from indicating that unpolished rice and katjang idjo are of no prophylactic value, on the contrary are strong corroborative evidence of the value of both of these food stuffs.

Before deciding in any given case that unpolished rice has not prevented beriberi, several things must be taken into consideration. Many contractors, through ignorance or through disregard of all considerations except their own gain, persist in furnishing most highly milled and polished rices instead of the undermilled rice demanded. This has repeatedly occurred in the Philippines, and only eternal vigilance will prevent this error. Again, some individuals often refuse to eat unpolished rice. For these reasons, when investigating cases of beriberi it is always most important to be absolutely certain that the unpolished rice *was actually eaten.* I have investigated a number of such alleged cases, and have always found that for one reason or another the rice actually eaten was highly milled or polished.

As to the katjang idjo, we have also found from the experience in Culion and with the Philippine Scouts, that most natives do not care for katjang idjo, at any rate as a steady diet, and will often go hungry rather than eat them.

The report of Jenissen with regard to beriberi on Billiton, an island adjacent to Banka, further corroborates the evidence just quoted with regard to Banka. Jenissen investigated the epidemics of beriberi which have occurred among the workers in the tin mines of Billiton since 1870. The food prior to 1908 consisted of rice, fresh and dried fish, pork, vegetables, peas, beans, and katjang idjo. While beriberi was more or less constantly present, its incidence varied greatly.

Thus from 1875–1876 beriberi was on the increase.
1877–1883 there was a decrease in the amount of beriberi.
1883–1884 another increase.
1885–1886 followed by an increase in these years.
1887–1892 another epidemic during these years.
1893–1894 the disease fell to its usual limits.
1904 a marked epidemic.
1905–1907 followed by a fall.
1908 another epidemic.

This peculiar occurrence of beriberi in waves or epidemics has been frequently noticed in regions where beriberi is endemic, and has been used as a strong argument favoring the infectious nature of the disease. Jenissen, however, found that in Billiton *these epidemics* *were coincident with the immigration of large numbers of Chinese.* Most of these coolies come from regions of China where there has been famine, or where the country is impoverished. The ones who are already living well in China do not leave that country. After the arrival of these half-starved coolies in the mines of Billiton they eat enormous quantities of polished rice and easily develop beriberi.

From this account of Jenissen we have therefore obtained an understanding of one cause of the occurrence of beriberi in epidemic form.

(3) Braddock, in a recent communication, says: "I have had an extensive experience with beriberi, and never saw it except when the rice used for food had been stored in a damp place; when care was taken to store the rice in a dry place there was no beriberi." Braddock's experience with beriberi was probably acquired in Siam, where he served for some years in an official position. His experience is directly at variance with the careful observations of Highet, which have just been presented, and also with the experiment which we have just quoted, in which it was shown that undermilled rice that had been stored for one year in a damp place still retained its protective action.

It would take too long to mention each author who has criticised the dietary hypothesis, and most of these criticisms consist of arguments that have already been fully answered. None of these criticisms will bear investigation. On the contrary we have presented ample evidence to prove that beriberi is caused by the deficiency of some substance in the food, and we will now present the experiments that have been performed to ascertain the nature of this deficiency.

CHAPTER X

THE ETIOLOGY OF BERIBERI, CONTINUED

Polyneuritis Gallinarum

The experiments that have been performed for the purpose of ascertaining the chemical nature of the substance whose deficiency in food produces beriberi, have, for the most part, been performed on fowls because of the susceptibility of these animals to a peculiar disease called polyneuritis gallinarum. But, in order to show the application of these experiments to human beriberi, it will be necessary for us to determine whether polyneuritis gallinarum is the same disease as beriberi. This question can only be settled by a study of the symptomatology, pathology and etiology of polyneuritis gallinarum, and this subject will now be presented as briefly as is consistent with a satisfactory answer to our query.

Historical. Eijkman first observed this disease in Batavia, Java, and made his first report on the subject as early as 1890, following this with numerous other communications. Eijkman's attention was first directed to this condition from the fact that a few cases occurred spontaneously in the laboratory chicken coop, and developed in fowls that had been fed cooked rice, while fowls that were fed on kitchen scraps, or were given the same cooked rice, but were left loose so that they could pick up other food, were never attacked. This fact, and the peculiar nature of the paralysis, excited his curiosity and led to a most exhaustive study of the disease. Eijkman's results were received with much scepticism, and his actual observations were discredited. Thus it was claimed that his experiments were conducted in a locality and at a time when the disease was prevalent, and that if he had prolonged his experiments over a greater time the neuritis in his fowls would have ceased to appear when the infection in the locality disappeared. That his experiments were not properly conducted; that neuritis was not observed in all fowls subjected to the same diet, etc. Those who rejected Eijkman's results apparently never thought of repeating the very simple experiments, for if they had done so they would have been convinced of the accuracy of Eijkman's work. It is unnecessary now to answer their criticisms for the simple reason that Eijkman's results have been confirmed and amplified by a series of workers in different parts of the world, and his actual observations have been established beyond doubt, although some of his earlier theoretical deductions cannot now be admitted.

Grijns was one of the first to repeat Eijkman's work, making his first contribution to the subject in 1900. He also continued his observations over a series of years, but his work did not become very generally known. Hulshoff Pol continued similar experiments, publishing results in 1904 and later. The experiments of Fraser and Stanton, published from 1909–1911, gave a great impetus to the study of this interesting disease. Schaumann made a valuable contribution in 1910, Shiga and Kusama another in 1911, and the United States Army Board for the Study of Tropical Diseases as they exist in the Philippines started experiments on fowls in 1910, and has steadily continued this work until the present time. (See Appendix, page 397.) The results obtained by these and other investigators will be presented in the following discussion.

Symptomatology. The symptomatology of polyneuritis gallinarum has been described by a number of writers, and for purposes of comparison it will be well to take a glance at several of these descriptions. Eijkman said the disease appears after an incubation period of from three to four weeks, during which the fowls become emaciated. The beginning of the disease may be recognized by an unsteady gait and inability of the fowl to reach his perch, and the disturbances of motility increase rapidly both in intensity and extent. The fowl stands with legs bent at the knees, and when it attempts to run it sinks down or falls over. Finally it remains lying on one side, and in its attempts to right itself the paralysis of the wings is apparent. Paralysis of the body muscles quickly follows, and in a few days the bird has become so helpless that it cannot eat or drink. Swallowing motions can be made, but the bird cannot raise or lower the head to take food. Then symptoms appear that depend on paralysis of the respiratory muscles, and the bird becomes dyspnoeic; the breathing is slowed, the beak opened, the comb and skin become cyanotic, and the neck is bent back. The fowl falls into a stupor with the eyes closed and the body temperature sinks about a degree below normal. The bird dies in acute cases after two or three days of illness, and almost always after a few days longer. Death is the rule if the food is not changed. If this is done soon enough a gradual improvement sets in, but complete recovery only occurs after several months.

Maurer described polyneuritis as follows: When fowls are fed on cooked rice, they eat considerable amounts at first (120–160 grams or one-tenth of their body weight daily). Soon, however, they lose their appetite and thereafter eat only small amounts, an average quantity of 40–60 grams being consumed daily. After a short time the fowl appears ill and sits in a bunched up attitude, with ruffled feathers and a blue comb. This initial stage may last from four to six weeks or longer, and is sometimes more and sometimes less prominent. As these symptoms increase in severity the bird becomes very thin, the wings droop and it becomes comatose. It sits in the cage with closed eyes and does not move from the spot, although sometimes when the cage is opened, the fowl wakes quickly from this lethargy and runs to and fro. After from 30–40 days from the beginning of the experiment, paralyses appear in most of the birds. Often these appear very suddenly, but usually these paralyses may be anticipated for several days. First a slight uncertainty of gait is noticeable, and the bird falls when it attempts to fly. This uncertainty becomes more and more manifest both in walking and standing, and soon the bird cannot arise on its feet at all, but sits on its heels or lies on its side, and the paralysis extends rapidly to the rest of the body so that the bird is completely helpless. Leg, wing and neck muscles are paralyzed and the bird is unable to raise its head or take nourishment. The crop cannot empty itself. Breathing is long and deep. Death occurs two to five days after the paralysis has set in. Sometimes the bird may recover if given proper food, but often they die in spite of this. The disease does not always run this course. In certain birds the paralysis occurs sooner, and a few birds may be fed exclusively on polished rice for months without injury. Many birds remain in the initial stage, and die of weakness without any paralysis having occurred. Fowls fed on cooked rice may therefore be divided in four groups, depending upon the way in which they react to this food.

1. The birds become sick after a four to six weeks' incubation period, and develop the characteristic paralyses.

2. They develop paralysis very rapidly without any incubation period.

3. This group show only the symptoms of the incubation period or of asphyxia.

4. This group may remain well for a long time.

The following brief account of the disease is taken from the paper of Shiga and Kusama: The beginning of the disease may be recognized by an uncertain gait; running and flying become irregular. The fowl stands with legs straddled because of weakness, and the joints of the knee become bent. When they do walk they stagger and fall forward. The paralysis progresses rapidly, and the wings hang down on both sides of the body until they touch the ground. If the bird is now laid upon its back, it cannot get up again. The comb is usually cyanotic, and slight oedema may be seen about the feet. The toes curve inwards because of paralysis of the extensors. At the same time there is hypoaesthesia of the legs, and the birds show only slight reaction to strong stimulation. Breathing becomes more or less dyspnoeic, the neck is bent backward and the head is drawn in. After a few days the symptoms increase in severity, and the birds become comatose, the eyes are closed, the temperature falls, and they die. The disease lasts as a rule from three to seven days. From the beginning of exclusive rice feeding until the appearance of the first symptoms is usually from 20 to 30 days for fowls, and about the same time for doves which develop the disease even more regularly.

Vedder and Clark have described the symptomatology of polyneuritis gallinarum as follows:

Incubation Period. Observers agree that when fowls are fed exclusively on polished rice, the symptoms of polyneuritis appear in from 20–30 days. We have a record of 124 fowls in which the conditions of the experiment were such as to permit an accurate observation of the period of incubation. The average incubation period of the disease in these fowls was 26.86 days. The shortest incubation period observed was 17 days, but a number of cases occurred in 18 and 19 days. On the other hand in a number of cases the disease only appeared after 40 days. These fowls were all fed on polished rice. However, if fowls are fed on a diet of polished rice, but receive in addition small amounts of other food stuffs, or an amount of extract of rice polishings which is insufficient to afford complete protection, they suffer from the disease in its typical form, but only after a greatly prolonged incubation period. Thus some of our fowls on such a diet have developed neuritis after 90 days' feeding, and Eijkman records a case where neuritis appeared only after a year's feeding.

Percentage of Fowls Affected. Of 211 fowls on an exclusive diet of polished rice, 154 or 73 per cent have developed polyneuritis, while 57 or 27 per cent have not showed any symptoms of the disease. The experiments from which this observation is made were only prolonged for 60 days. It is, of course, probable that a higher percentage of fowls would have succumbed if the experiments had been prolonged for a longer period.

Course of the Disease. A typical case of the disease may be described as follows: Careful observation during the incubation period will reveal nothing abnormal, except that the fowl may be noticed standing bunched up with ruffled feathers and the comb may become blue. The first symptom noticed will usually be a weakness of the legs, so that the fowl is unable to walk well, and as he steps there is a tendency for the joint formed by the tibio-tarsus and the tarso-metatarsus to give way allowing the fowl to sink to the ground. (Figure 20.) This is due to beginning paralysis of the extensor

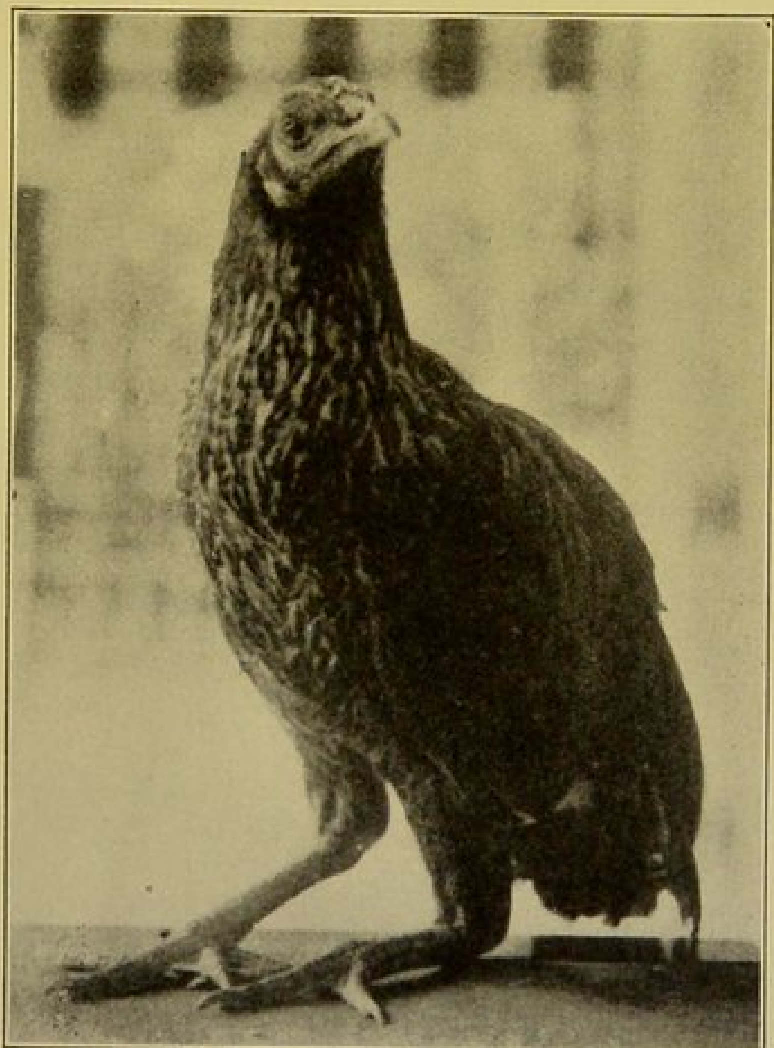

Figure 20. Very early stage of polyneuritis. [From Fraser and Stanton.]

muscles of the leg which it will be remembered are the first muscles to be affected in men suffering from beriberi. A peculiarity in the gait may be recognized before the legs become completely paralyzed. This is a tendency to raise the feet high in the air and thrust forward with them as though the fowl were attempting to brush away something from in front of it. This high stepping gait has never been seen in any other condition affecting fowls except polyneuritis. The fowl may show a tendency to teeter forward on its toes, and may stumble when hurried. From the time when paralysis first appears the disease progresses with great rapidity and, as a rule, by the next day the fowl will be no longer able to stand. The position assumed by the bird in this condition is very characteristic. Usually it sits quite still upon its flexed tarso-metatarsus (Figures 21, 22), but occasionally a bird of

Figure 21. An early or mild case of polyneuritis. [From Fraser and Stanton.]

more vigor will still attempt to walk about the cage. However, as the extensor muscles are completely paralyzed, it cannot walk upon its feet, but shuffles along upon its flexed tarso-metatarsus. The paralysis now extends rapidly cephalad affecting the muscles of the wings, the neck and the body, usually in the order named. As a result the bird is soon unable to sit up, but lies upon its side. (Figure 23.) There seems, however, to be a general weakness or debility associated with this paralysis. At any rate, the fowl becomes prostrated rather more rapidly than one would expect as a result of mere muscular paralysis. Most of the fowls affected in this way die very promptly, and it is by no means unusual to find the bird dead within two or three days after the first onset of the disease. Some fowls last longer, but almost none survive a week after the paralysis has set in.

Figure 22. Polyneuritis, showing a more advanced stage of paralysis. [From Fraser and Stanton.]

Wing Drop. Many of the birds present this symptom, which consists in inability to hold the wings in the accustomed position close to the body. They droop in some cases until the wing feathers trail on the ground. This symptom, which is probably due to the paralysis of the wing muscles referred to above, does not occur in all cases and comes on later than the leg symptom. It will be remembered that beriberi in man almost always commences by affecting the muscles of the legs, and if the arms are affected this is almost always during a later stage of the disease.

Spasticity. This occurs in rare instances during the development of the disease, but more often during recovery. A fowl that has developed this spastic gait, stands and walks with the knees stiff, leaning forward on tips of the toes so that the ball of the foot scarcely touches the ground. In the effort to maintain its balance, short rapid steps are taken as though the body were so far forward that the feet have to hurry to keep up. During walking the feet frequently strike together and when the spasticity is severe, the fowl topples forward as the result of this interference of the legs.

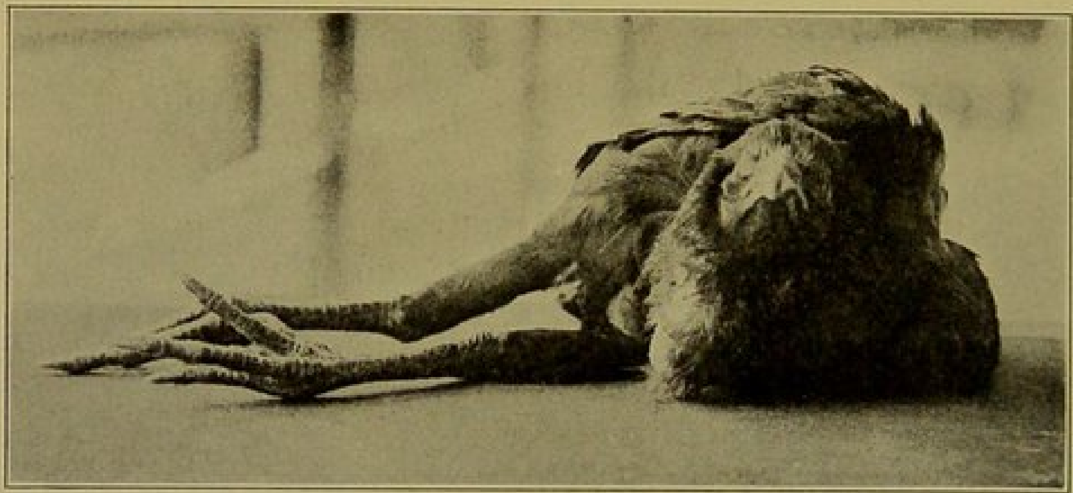

Figure 23. A severe or advanced case of polyneuritis showing complete paralysis of the legs. [From Fraser and Stanton.]

Retraction of the Head. This is a frequent symptom in the later stage of the disease. The anterior groups of muscles in the neck become paralyzed and the continued action of the posterior groups retracts the head far backward. This overbalances the fowl so that it is unable to sit upon its paralyzed legs. If a fowl in this condition is placed upon its legs in a squatting position, it makes several spasmodic efforts to retain its equilibrium, and finally topples over backward. Such a fowl is unable to rise without help. (Figure 24.)

Dysphagia. After the fowl becomes so paralyzed that it is unable to arise, dysphagia almost always sets in. The fowl appears to be totally unable to swallow normally, and if water or medicines are administered they run out of the mouth when the bird is laid down unless care is exercised to prevent this. It is always very easy to choke such a bird by attempting to revive it by hand feeding.

Respiration. The respiration of the fowl suffering from an advanced stage of the disease is slower and deeper than normal. As the bird lies on its side, its abdomen may be observed to expand and contract slowly, almost like a pair of bellows.

Sensory Symptoms. It is somewhat difficult to obtain accurate information with regard to the sensory changes. But by tapping, pinching and pricking the legs, and comparing the reaction with that obtained in normal fowls, it is apparent that sensation is much reduced in the legs of birds suffering from polyneuritis, and it is believed that this loss of sensation precedes slightly the motor paralysis. It is possible that the peculiar high stepping gait described above may be the result of sensory disturbance.

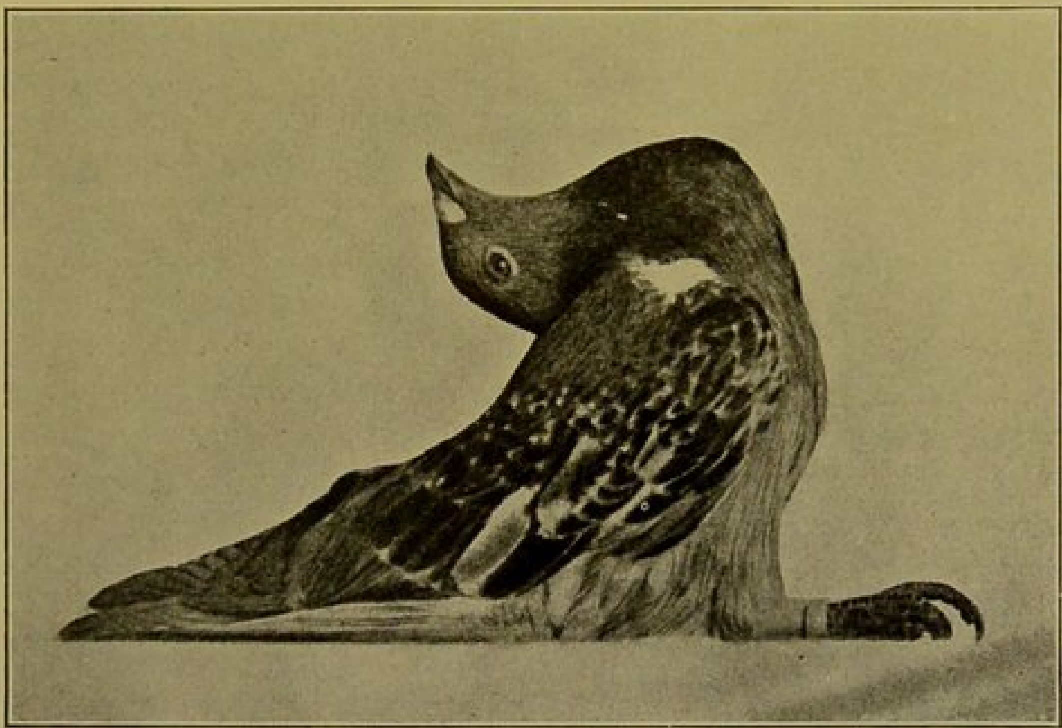

Figure 24. Pigeon affected by polyneuritis, showing characteristic position due to paralysis of legs and retraction of neck. [From Schaumann.]

Loss of Weight. Progressive loss of weight was an almost constant symptom. Thus of 20 fowls fed on polished rice, whose weights were carefully recorded, the average weight at the beginning of the experiment was 3.15 pounds. The average weight of these same fowls, taken on the date when the first symptoms of polyneuritis appeared, was 2.45 pounds. This represents an average loss of 0.7 pound or 22 per cent of their original body weight. A few fowls, however, developed neuritis although they lost comparatively little weight. Thus one fowl whose original weight was three pounds one ounce developed neuritis after a loss of only three ounces, and several fowls lost only five ounces.

This loss of weight is such a constant observation, that the view has been held that polyneuritis of fowls is simply the result of inanition which is expressed by this loss of weight. That this is not the case is shown by the fact that fowls fed on polished rice, but protected by an extract of rice polishings, also lose weight, but do not develop neuritis. Thus 25 fowls fed in this way, of an average original weight of 3.08 pounds, weighed 2.68 pounds at the conclusion of the experiments which lasted 90 days. They thus lost an average of 0.4 pound or 13 per cent of their original weight as compared with 22 per cent lost by the fowls on the same diet, but which received no protection. However, several fowls in this group ended the experiment with no loss of weight, and one or two fowls actually gained a few ounces.

While the disease as described above appears to be the usual form, yet a certain percentage of cases present marked variations.

Fulminating Cases. Some of the cases are even more rapid in their course and for lack of a better name may be called fulminating cases. During the incubation period they may lose considerable weight and may appear to be in poor health, but they rarely show any paralysis of the legs. They will be seen in this condition on one day, and the next day will be found lying on the side completely prostrated, often with the neck retracted and exhibiting the characteristic breathing already described. Death follows in a few hours. The course of the disease in these cases is therefore much more rapid, and is marked by much greater muscular wasting and general prostration than usual.

In a still smaller percentage of cases, paralysis of the legs occurs suddenly as already described, but the bird remains in good general health. The comb is red, the appetite remains good, and the fowls lose little weight. We have had several fowls that lived in this paralyzed state but in otherwise good health for a month while still subsisting on polished rice.

Treatment. Fowls affected with any of these forms of polyneuritis can rarely be saved by feeding an ordinary mixed diet. Almost all die in spite of efforts to save them by hand feeding. But if they are given an extract of rice polishings,* the majority of them can be saved. A great difference, however, has been observed in the manner in which fowls respond to this treatment. Thus birds affected with the form of the disease described as fulminating have been observed that appeared at the last gasp, but recovered almost completely after the administration of this extract, so that they were able to walk about

* See Appendix, page 400.

within a few days. This result has not been obtained with fowls suffering from marked paralysis. If birds of this latter group are given this extract, they improve in general health, but the paralysis remains, and it is usually only after several months of treatment that they recover complete control of their legs.

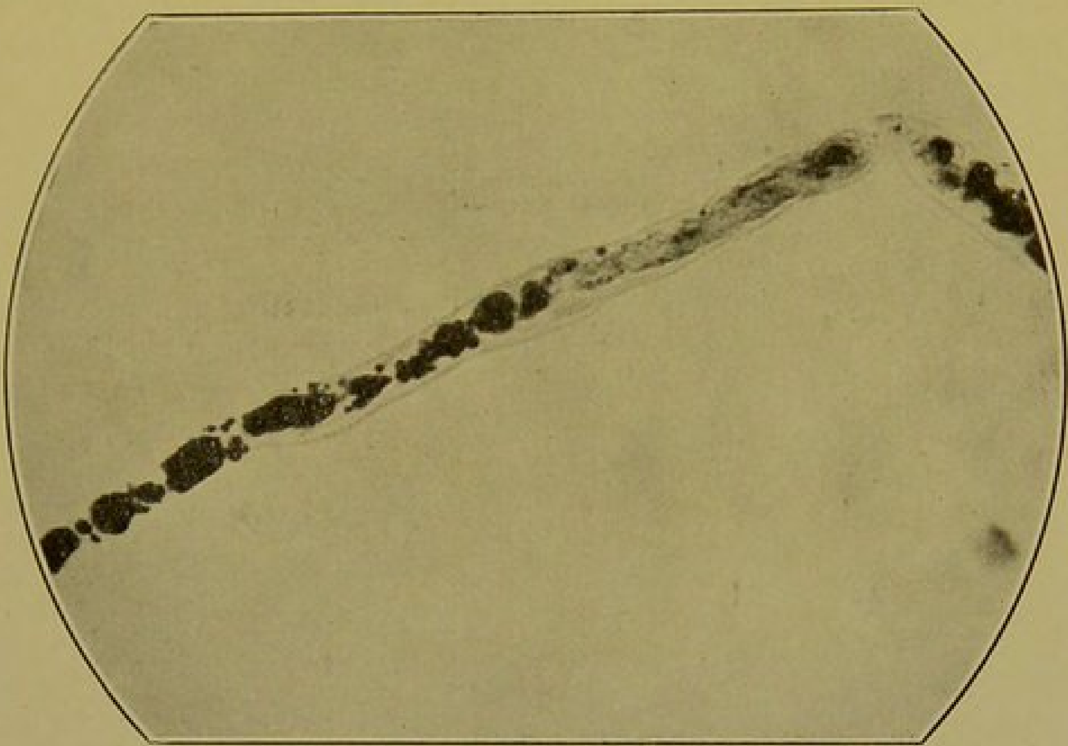

Figure 25. Fiber from sciatic nerve of fowl suffering from polyneuritis (Marchi method), showing advanced degeneration. [From Vedder and Clark and plate lent through the courtesy of the Philippine Journal of Science.]

The relation between the amount of polished rice eaten and the development of neuritis. It has been generally observed that the great majority of the fowls fed on polished rice usually lose their appetites after about a week on this diet, and thereafter eat only small amounts of rice. There are always a few fowls, however, which eat greedily up to the very last, and will eat far greater amounts than the usual ration allowed (120 grams). Several deductions have been drawn from this fact with regard to the development of neuritis. Some observers have thought that those fowls that have eaten well throughout the experiment have been protected from the development of the disease by this increased consumption of rice and have therefore been inclined to regard polyneuritis as the result of simple inanition. On the other hand, other observers have thought that those fowls that ate the most rice developed the disease soonest and have regarded this as an argument in favor of the theory that polyneuritis is caused by some toxin contained in the polished rice. We have observed fowls that always ate well, and yet developed neuritis sooner than usual, but we have also observed other fowls that ate large quantities of rice throughout the experiment but whose incubation period was longer than normal. Again some of the fowls that have eaten poorly have developed neuritis promptly, while others have not developed the disease at all. It is believed, therefore, that the amount of rice eaten has little

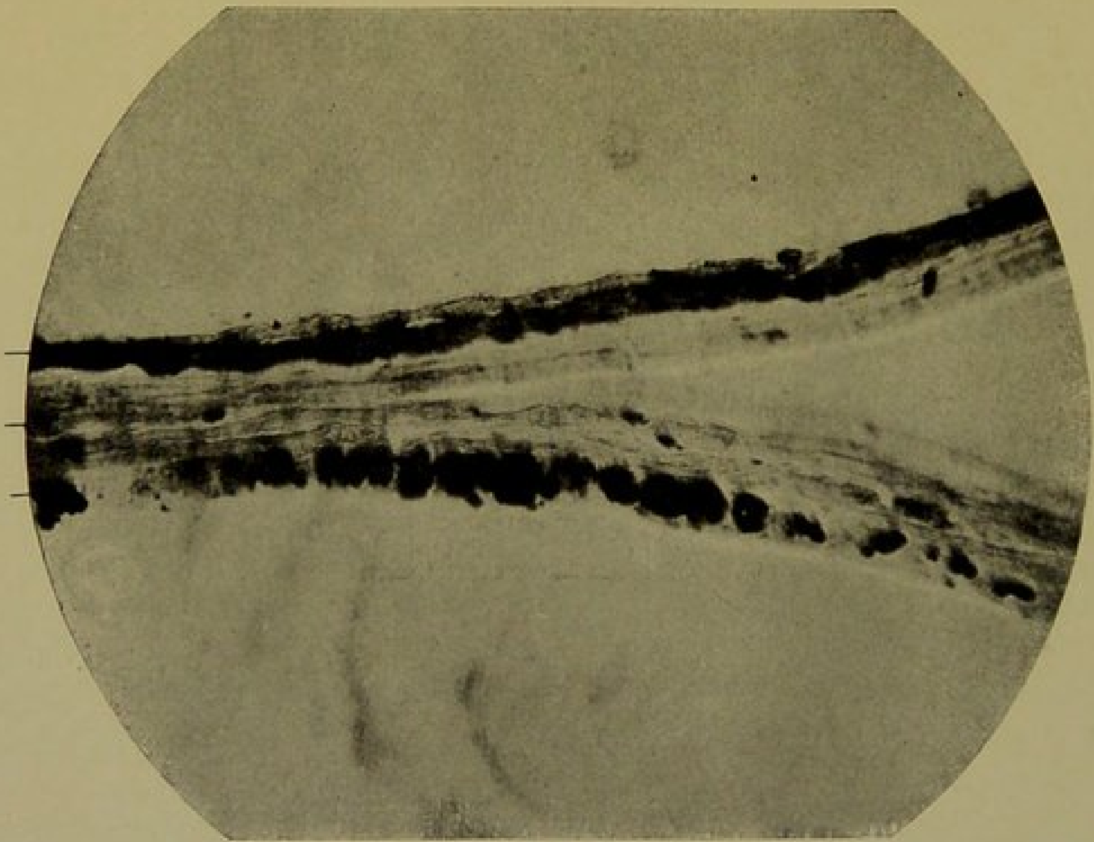

Figure 26. Teased preparation of sciatic nerve of a fowl suffering with polyneuritis gallinarum (Marchi method), showing three different stages of degeneration. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

to do with the development of the disease, which depends rather on the idiosyncrasy of the fowl with regard to the amount of neuritis-preventing substance required.

As a result of these observations Vedder and Clark think that there are three types of polyneuritis gallinarum:

1. A form in which the symptoms of neuritis and those of general prostration are combined. This is the usual form.

2. A form in which there is pronounced neuritis, but the fowl remains in good general health.

3. A form described above as fulminating cases, in which the symptoms of neuritis are absent, but in which great general prostration results in death.

Pathology of Polyneuritis Gallinarum. Eijkman stated that with few exceptions there were no gross changes found at autopsy. Emaciation was the rule. Hydropericardium was found quite frequently, and there was also rather more fluid beneath the skin, par-

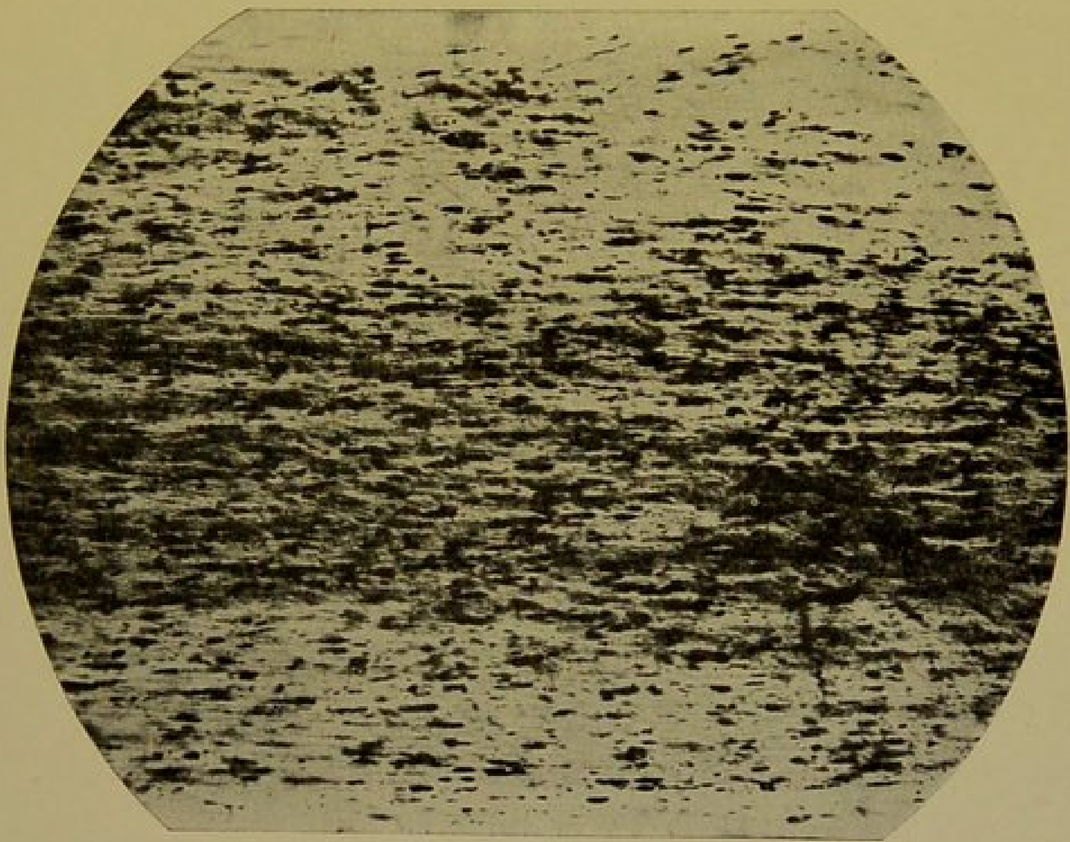

Figure 27. Teased preparation (Marchi method) of the vagus of a fowl suffering from polyneuritis, showing relatively advanced degeneration. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

ticularly of the lower extremities, than normal. The main and constant finding was a polyneuritis with degeneration of the peripheral nerves, and degeneration and atrophy of the ganglion cells in the anterior horn of the cord was demonstrated in some of the cases. The affection of the peripheral nerves was most severe, involving both the sensory and motor fibers, and affording a picture of non-inflammatory atrophic degeneration such as is shown in nerves after cutting, particularly in the part separated from the centre. There were also certain degenerative and atrophic changes in the spinal roots, and the muscles innervated by the affected nerves were likewise degenerated.

Shiga and Kusama also investigated the pathology of this disease, and found that a high degree of atrophy was the rule. Fat was practically always entirely absent, and the muscles were wasted and of a damp, pale appearance. There was no abnormal fluid in the abdominal and thoracic cavities, but the pericardial fluid was greatly increased. Thus 10 cubic centimeters were obtained from one hen, and three cubic centimeters from a dove, but this fluid was normal in appear-

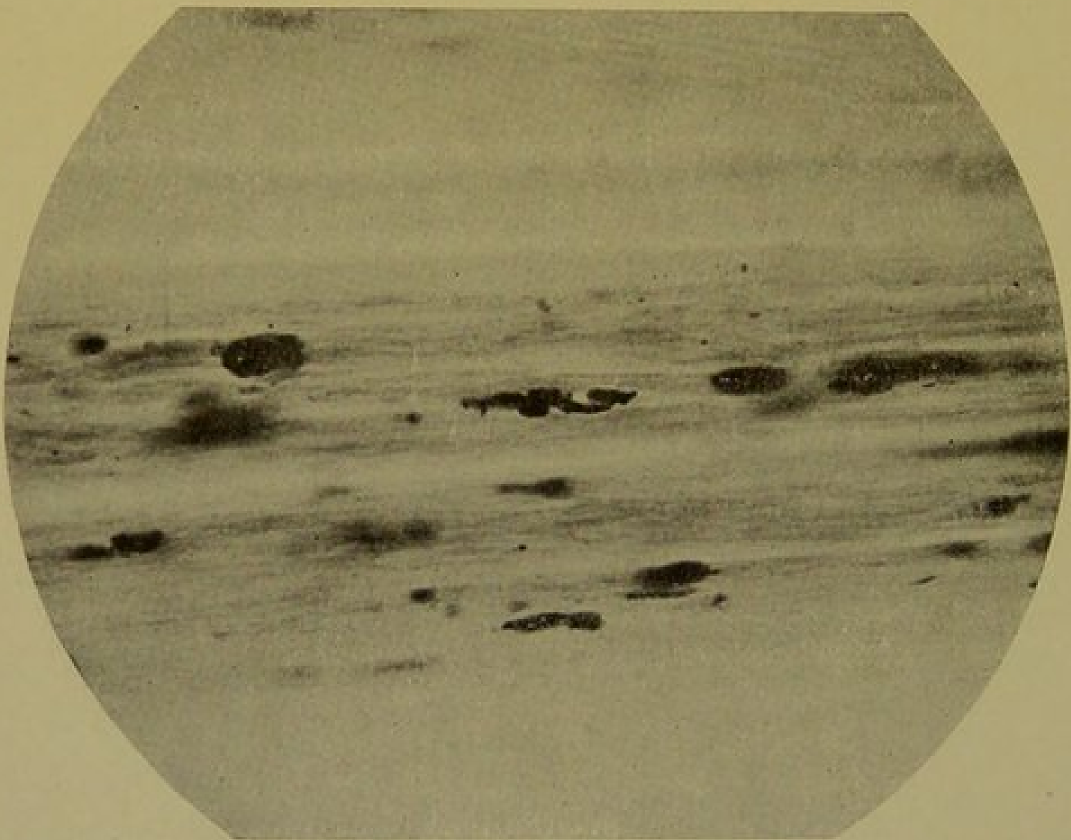

Figure 28. A high power magnification of an area of the nerve shown in Figure 27. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

ance and composition. In most cases there was slight anasarca of the lower extremities. The heart was of the usual size and of a good color and consistency, but the right heart was greatly distended with fluid blood or clots. There was no change of importance in the lungs, spleen, kidneys or liver beyond slight atrophy and venous congestion. The mucous membrane of the intestine was atrophic and thin, and showed more or less considerable venous congestion, especially in the duodenum and rectum. The brain and spinal cord were normal with the exception of a considerably reduced consistency of the brain. The microscopic changes in the peripheral nerves were striking. In longitudinal and cross sections stained by the Marchi method, the medullary sheath was found to be reduced to a collection of black globular masses, so that in the badly degenerated fibers the sheath of Schwann was completely altered. The axis cylinder usually showed no change, but in fibers that were markedly degenerated, the axis cylinder showed swellings and segmentation. The epi-and endoneurium were entirely free from any proliferative processes or round cell infiltration. Thus the peripheral nerves showed no inflammatory change, but a simple

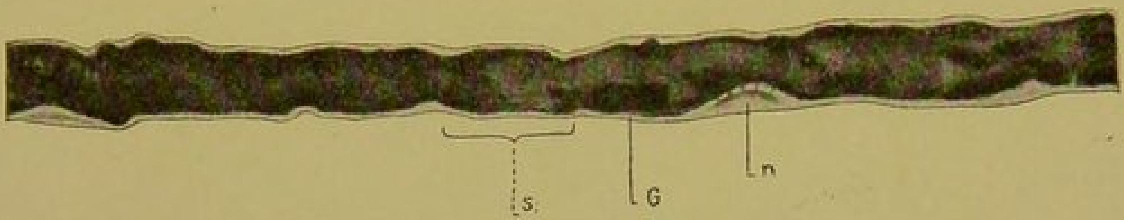

Figure 29. Drawing of a nerve fiber to show early stage of myelin degeneration (Marchi method). Diffuse blackening, tendency to segmentation (s); (n) is nucleus of neurilemma sheath. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

degenerative process. This process was most intense in the nerves of the lower extremities, and Shiga and Kusama thought that in the same nerve, the peripheral and finer branches were more involved than the main stem.

Spinal cord. In the white substance, single fibers were degenerated without any particular localization. The ganglion cells of the anterior horn showed simple atrophy and chromatolysis.

The heart muscle was usually fragmented. This change had also been found by Sakaki. Shiga and Kusama therefore found in both fowls and doves suffering from polyneuritis gallinarum, general atrophy, congestion of intestines, spleen, liver and kidneys, hydropericardium, sometimes anasarca, and on histological examination, a simple degeneration in the peripheral nerves and cord, and fragmentation of the heart and skeletal muscles.

Vedder and Clark confirmed most of these findings, and greatly extended our knowledge of the degenerative changes in the nervous system in polyneuritis gallinarum. They described the degenerative changes found in the peripheral nerves, including the vagus, in the nerve roots and in the fiber tracts of the cord, and even in the brain. Changes in the nerve cells of the cord and dorsal root ganglia were also found. The nature and extent of the changes found by these authors is shown in figures 25–36 and plate V. They were, however, unable to confirm the belief that degeneration begins earlier and is more advanced in the peripheral rami, since careful counts of the number of degenerated fibers in such rami, and in the main trunk of the nerve, showed that the number of degenerated fibers in both was about the same. Nor did they find oedema or pericardial effusions in any of the fowls autopsied. The summary of the findings of these investigators may be found on page 400 of the Appendix.

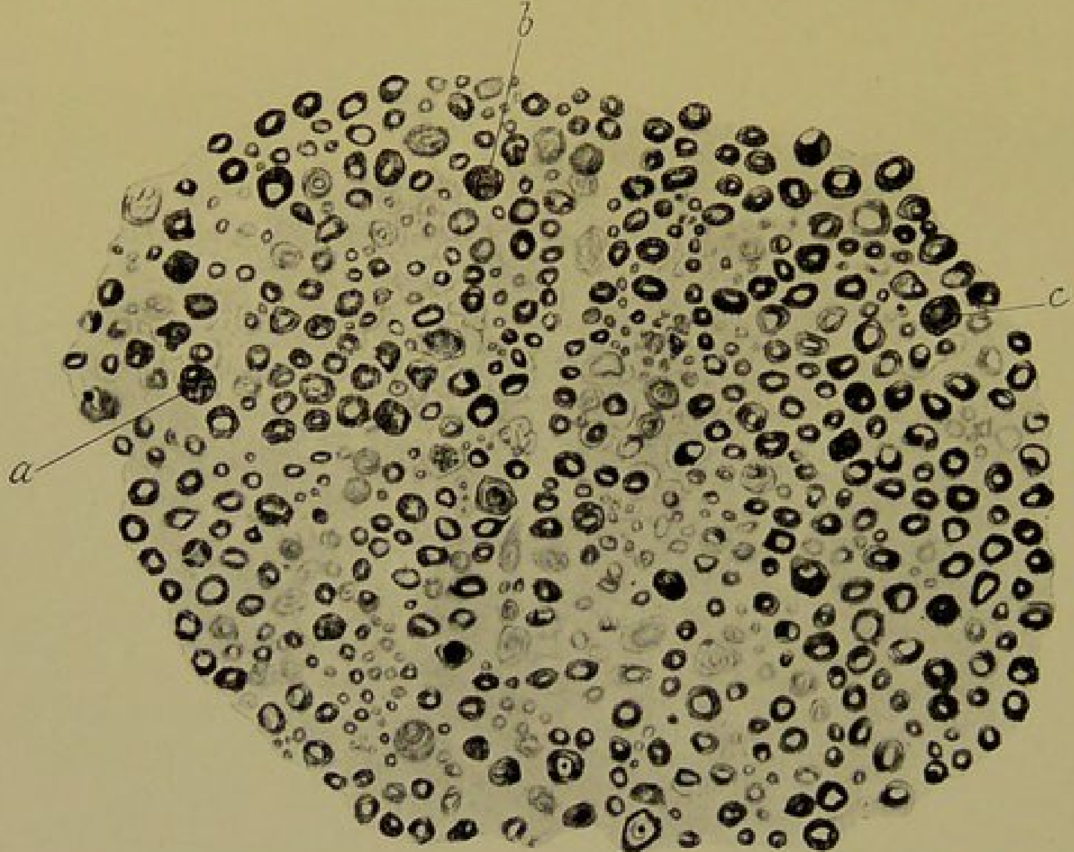

Figure 30. Drawing from a transverse section of a sciatic nerve showing marked degeneration (Marchi method), to illustrate the percentage of fibers showing varying degrees of degeneration in a given plane. A majority show blackening to some extent. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

If a comparison is now made between the pathology of polyneuritis gallinarum as described by these different investigators, and the pathology of beriberi as described by the different observers in Chapter II, the great similarity between the two conditions will be at once apparent. Indeed, the two conditions may be said to be identical except for the fact that the marked hypertrophy of the heart which is such a common finding in human beriberi, has never been found in polyneuritis gallinarum.

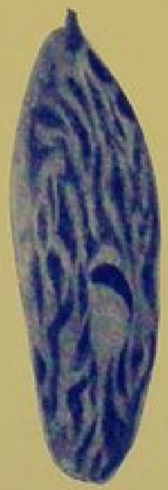

FIG. 1.

FIG. 2.

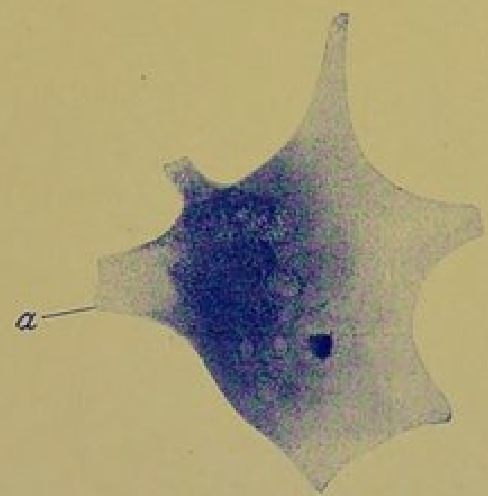

FIG. 3.

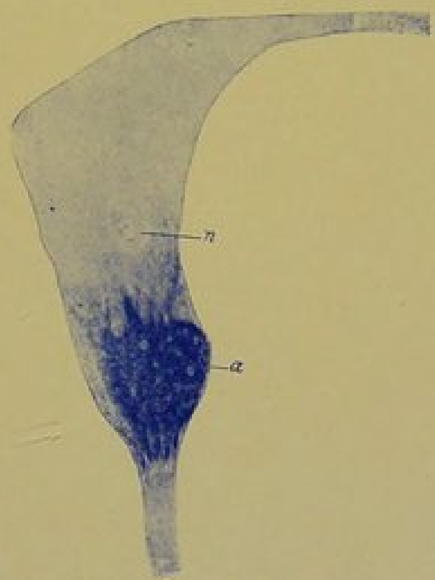

FIG. 4.

FIG. 1. Nerve cell from spinal cord of normal fowl. Nissl stain. Zeiss 4×4 mm.

FIG. 2. Same. Giemsa blood stain.

FIG. 3. Nerve cell from ventrolateral group of the lumbosacral cord of a fowl (No. 48, twenty-four days on polished rice) with marked paralysis of the legs and marked degeneration in the sciatic. The tigroid bodies are no longer apparent. The stainable material which appears granular has collected at one side of the cell around the implantation cone (*a*) of the axis cylinder. Giemsa blood stain. Zeiss $4 \times$ D.

FIG. 4. Nerve cell from same preparation as Fig. 3, same group. Note bulging of cell at *a* where the stainable material is collected in one mass. The nucleus, *n*, shows degenerative changes. Zeiss $4 \times 1/12$ oil immersion. Camera lucida, reduced ½.

[*From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.*]

Etiology. Eijkman performed many experiments to determine the cause of this disease. These experiments, which have been repeated and confirmed many times by other observers, may be summarized as follows:

Attempts to show that the disease was infectious all failed, and no specific organism could be found. The disease affected almost all fowls fed on cooked rice, but fowls fed on kitchen stuff escaped. Raw polished rice also produced the disease, but after a somewhat longer incubation period. Fowls fed on unhulled rice, or a rice that

Figure 31. Advanced degeneration in fiber from sciatic nerve, showing fragmentation of the axis cylinder (Haematoxylin and acid Fuchsin). [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

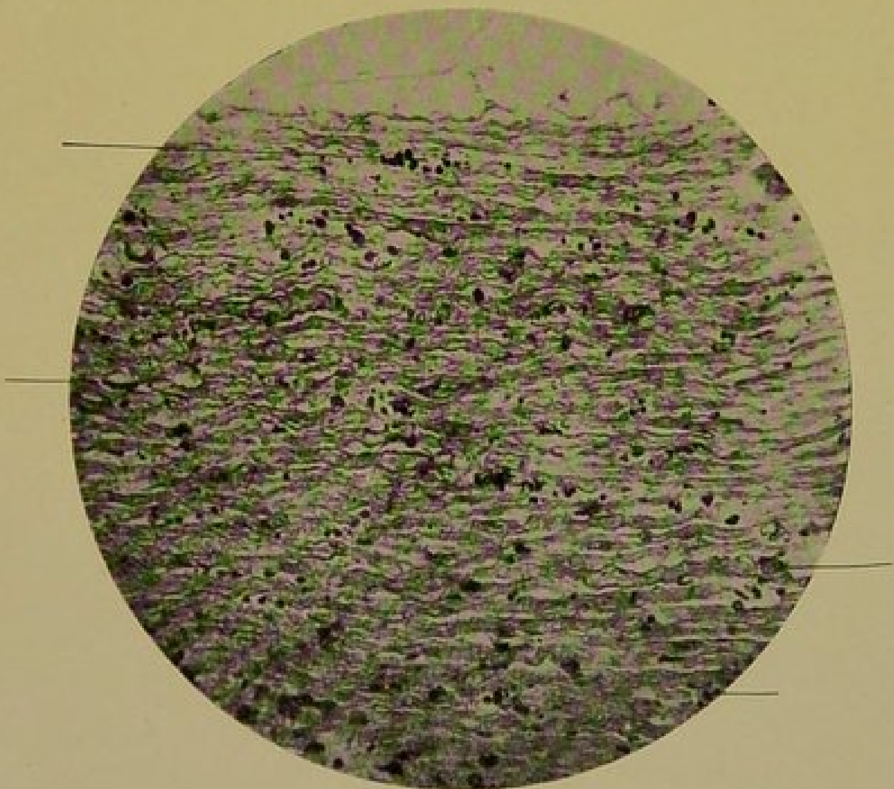

Figure 32. Longitudinal section of lateral column of thoracic cord of fowl with pronounced symptoms of polyneuritis, and marked degeneration in the sciatic nerve (Marchi method). Globules and droplets of degenerated myelin may be seen in the fibers. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

was hulled, but still retained the pericarpal layers were protected. From these facts Eijkman first thought that the disease was a toxic polyneuritis resulting from a nerve poison produced by the fermentation of the rice in the crop of the fowl, and that the pericarp protected the grain from the invasion of the microorganisms. This theory was shown to be incorrect because fowls fed on unhulled or unpolished rice which had been ground into a fine meal also protected the fowls just as well as when the entire grains were used as food. It should be said that Eijkman has now renounced the intoxication hypothesis

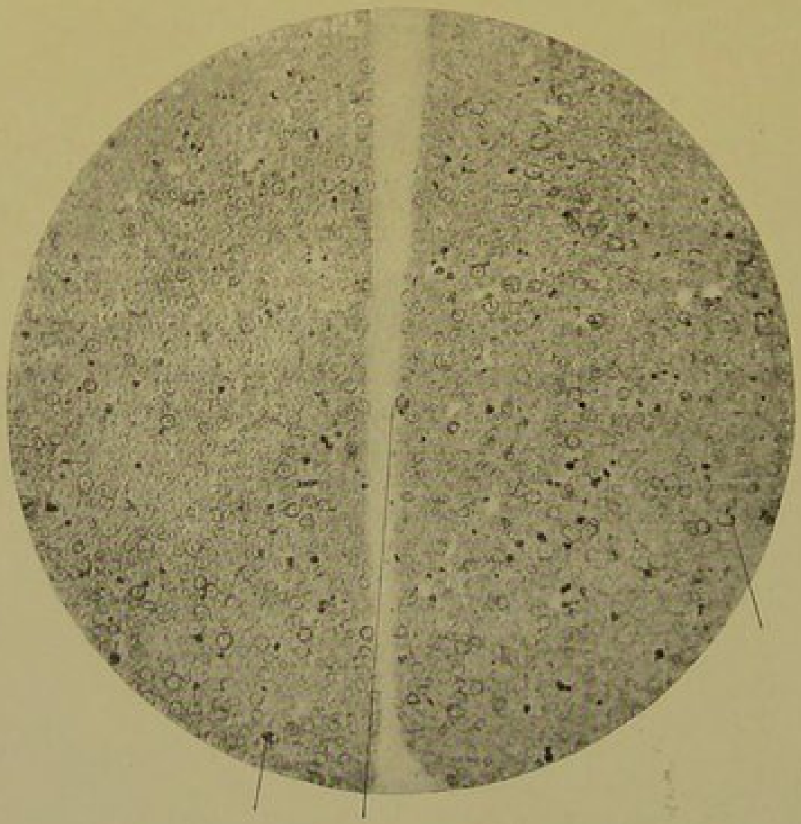

Figure 33. Transverse section of the posterior columns of cord of fowl, with pronounced symptoms of polyneuritis, showing globules of degenerated myelin in certain fibers (Marchi method,. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

and has supported the theory that the disease is caused by a deficiency in the food, for some years.

It was then shown that if rice polishings were added to the diet of polished rice, the fowls were protected, and moreover that fowls that had already developed the disease on a diet of polished rice could be cured by the administration of rice polishings. The amount of the rice polishings needed to protect the fowls was found to be about the quantity that had been removed from the polished rice eaten. Admixture of chalk or stones with the polished rice did not prevent the disease. It was then found that fowls fed on potato starch did not develop the disease. The rice previously used to produce the disease came from the tropics where beriberi was endemic, while the potato starch which protected came from Europe. This led Eijkman to suppose that there might be some organism present in the rice and starch from those regions, which was responsible for the disease. He therefore grew potatoes in Batavia, Java, and fed fowls on the starch obtained from them, but the fowls were still protected. Fowls fed on

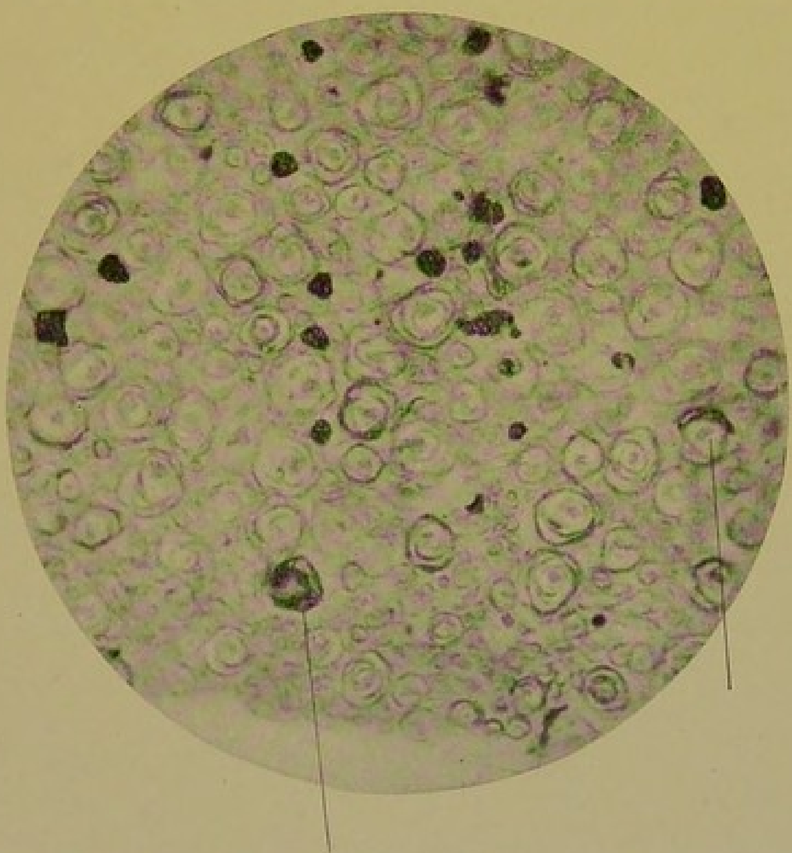

Figure 34. A higher power of same preparation as Figure 33. Golls column. Degenerated areas are clearly seen within the fibers. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

meat and milk sugar for a year were protected. Cane sugar and meat also protected. On the supposition that the various starches and grains used contained a poison, Eijkman performed further experiments. He concluded that such a poison was not formed in the crop of the fowl because he fed monkeys for a year on the contents of the crops of rice-eating fowls without producing any illness. He also fed fowls on extracts and distillate of the crop contents without producing the disease. Neither lactic acid nor alcohol produced neuritis in fowls.

Another great advance was made when Eijkman discovered that excessive heat destroyed the protective action of all forms of food. Thus he fed fowls on unhulled rice which had been heated to 120°C. for two hours, and they all died of polyneuritis. Sterilized barley, rye and millet produced the same effect, although these grains protected when fed raw, and moreover did not lose this protective action as the result of ordinary cooking. Eijkman further found that phytin could neither prevent nor cure the disease, but that on the other hand, the protective substance was present in a watery extract of polishings from

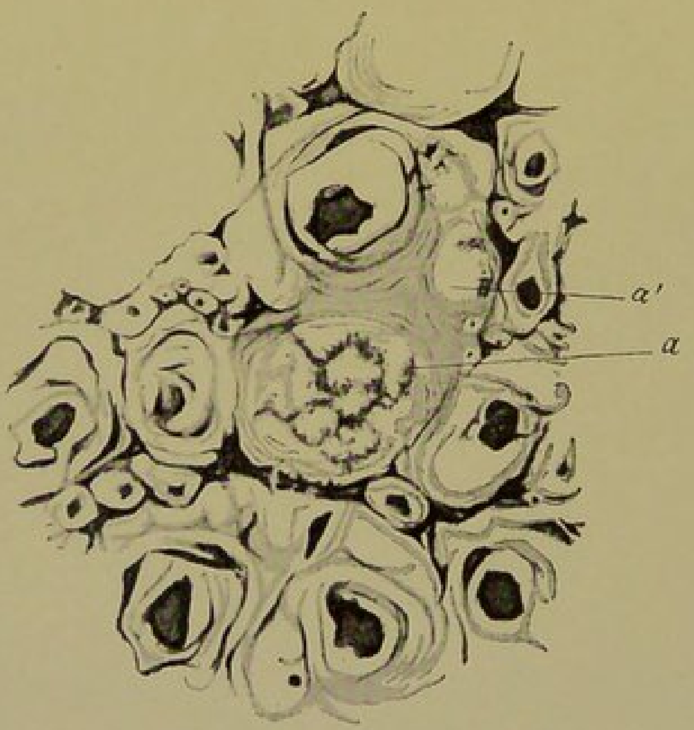

Figure 35. Cross section of fibers from column of Goll of the thoracic cord of fowl suffering from polyneuritis (Haematoxylin and acid Fuchsin). At a and a[1] two fibers are seen in which the axis cylinder has undergone fragmentation and granulation. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

which the phytin had been removed. This observation was subsequently confirmed by Fraser and Stanton and by Chamberlain and

Vedder, and was made the basis for devising a method for the extraction of the protective substance from the rice polishings. A substance rich in phosphorus was extracted from the polishings, but Eijkman was unable to protect fowls by the addition of this substance to the diet of polished rice. Eijkman concluded that an apparently physiological diet may produce disease and even death, and that although the polyneuritis of fowls might not be identical with beriberi in man, yet it was a similar condition, and that beriberi in man could therefore be prevented and cured by a diet similar to that which protected and cured fowls.

Grijns showed that sago, tapioca, and meat that had been heated in the autoclave at a temperature of 120° C. also produced polyneuritis quite as easily as a diet of polished rice. He also found in 1901 that katjang idjo had a protective and curative action on fowls fed on polished rice, but he believed that this polyneuritis was caused by an intoxication which was prevented by the administration of rice polish-

Figure 36. Fiber from ventral portion of mid-brain of fowl suffering with pronounced polyneuritis (Marchi method). Small globules of degenerated myelin are clearly seen. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

ings and katjang idjo. As a result of his experiments he also eliminated infection as the cause. He introduced the nerves from sick fowls into the peritoneal cavities of healthy birds, and injected healthy fowls with the blood of fowls suffering from polyneuritis gallinarum. All the fowls so treated remained well. Grijns and Haan tried complement binding experiments. The immune serum was taken from fowls that had been cured of the disease by feeding katjang idjo, and extracts of liver, spleen, kidney, spinal cord and blood of sick birds were used as antigen. In none of these experiments was there any complement binding, nor did the infectious theory of the disease receive any support from any of his experiments. This negative result has also been obtained by all other investigators, and at the present day there is no one, so far as I am aware, who believes that polyneuritis gallinarum is an infection.

However, in 1900, Sano came to the conclusion that polyneuritis of fowls was due to nothing but simple inanition. Sakaki performed many experiments and opposed this theory, but thought from the clinical course of the disease and the anatomic findings, that the disease was more like an intoxication by some poison contained in the rice and produced there by some fungus. That the disease is not due to simple inanition is conclusively shown by the experiment of Chamberlain, Bloombergh and Kilbourne, who fed fowls polished rice by hand to the amount of 118 grams daily. The fowls so fed developed polyneuritis in spite of the large amount of food so received. Again, if the disease were due to inanition, fowls fed on potato starch should be quite as subject to it as fowls fed on rice.

Maurer believed that polyneuritis of fowls was due to oxalic acid poisoning. This point has already been sufficiently discussed.

Sakaki and Kohlbrugge both thought that the disease was caused by a toxin produced in rice by the action of a fungus or bacterium. Kohlbrugge particularly as late as 1912 has maintained that the disease is produced by the acid fermentation in rice which is caused by a group of bacilli to which he gave the name of bacillus oryzae. He isolated these bacilli from rice and other grains, and fed fowls on rice plus agar cultures of these bacteria. These fowls died in four or five days, from polyneuritis, as he thought. He recovered the bacilli from the blood of the dead fowls. Kohlbrugge thinks the prevention of polyneuritis by means of the addition of rice polishings, katjang idjo, etc., is due to the acid contained in these substances, and that this acid inhibits the action of the bacteria. It is most improbable from what we know of the incubation period of polyneuritis gallinarum, that Kohlbrugge really produced this disease. He certainly offers no proof that the disease which he produced corresponded with polyneuritis gallinarum either in symptomatology or pathology, and apparently did not try to demonstrate degeneration in the nerves of his fowls.

Is polyneuritis gallinarum an infection, an intoxication or a deficiency disease? It is unnecessary to argue the point as to an infection, because no one now holds this view, but many still believe that it is an intoxication. The proof that polyneuritis gallinarum is not an intoxication may be briefly summarized as follows:

1. No toxin has ever been isolated from polished rice, nor any toxin been demonstrated in fowls suffering from polyneuritis.

2. Addition of rice polishings to polished rice prevents and cures the disease.

3. An unpolished rice that protects may be extracted by alcohol. The extracted rice no longer protects. But if this extracted rice is fed together with the extract, protection is again secured.

This would seem to prove that polyneuritis is not caused by a toxin, but by the lack of some substance which is present in unpolished rice and rice polishings. The case for the deficiency theory is made still stronger by the fact that the addition of many other food stuffs to a diet of polished rice will produce the same result. Thus, if fowls are fed on polished rice mixed with barley, or katjang idjo, or beans, or peas, or peanuts or potatoes, they do not develop the disease. These facts can only be explained on the basis of an intoxication, by supposing that all these food stuffs contain some principle which is capable of neutralizing this hypothetical toxin. This is quite improbable to say the least. But the deficiency theory does not rest on a probability, since as we shall see later, the actual chemical substance which is deficient has been isolated.

We may therefore regard it as proven that polyneuritis gallinarum is due to a deficiency, and we may now proceed to determine whether polyneuritis gallinarum and beriberi are the same disease. It will be well to consider first the views of different investigators on this subject. Most of them have been very cautious in expressing themselves. Thus Eijkman said: "Regarding the question of the relationship between polyneuritis gallinarum and beriberi, I have always expressed myself very reservedly. I have not claimed their identity in an etiological sense, but I also could not absolutely deny this, and am of the same opinion at the present time." (1911.)

Schaumann believes, not that both diseases are identical, but that there seems to exist many more reasons for assuming that they are intimately related to each other, than to presume the contrary, chiefly because the same cause need not necessarily have the same results in different organisms.

Shiga and Kusama say: "It would be too much to say that the polyneuritis of fowls and beriberi are identical without further proof." Fraser and Stanton also, while not denying the identity of the two diseases, have never expressed any conviction that they are the same, and have always expressed themselves very reservedly on this point.

On the other hand, Chamberlain and Vedder, and Tsuzuki have maintained that polyneuritis gallinarum and beriberi are essentially the same disease, and their case is very strong. The investigators who have held the contrary view have based this opinion on the fact that the symptomatology and pathology of polyneuritis gallinarum and beriberi differ at certain points; notably in the absence of cardiac hypertrophy in polyneuritis gallinarum.* But I believe it may be successfully maintained that an absolute identity in the symptomatology and pathology of the same disease is not to be expected in diverse species. The crucial point is the etiology. If the etiology is the same in both instances, we are dealing with the same disease, which produces different manifestations in very diverse species.

One or two examples will serve to clarify this point. Morphine produces narcosis in man, but it produces violent tetanus in the frog, yet when administered in sufficient dose, both die, and one dies of morphine poisoning just as truly as the other. It is impossible to produce in animals, anything at all comparable to typhoid fever as we know it in man. But animals inoculated with this bacillus die, and they die of typhoid infection just as truly as the man who dies of typhoid fever. We are therefore dealing with the same disease, but its manifestations are different in different species.

Now in the case of polyneuritis gallinarum and beriberi, the etiology is identical. We have seen that both diseases are caused by a deficiency in the food. That they are both caused by the deficiency of the same substance or substances is evidenced by the fact that they may both be prevented and cured by the administration of the same foods, i. e., either rice polishings, beans, katjang idjo, barley, etc. If the etiology is identical we are driven to believe that they must be the same disease even though they may present differences in symptomatology and pathology.

Moreover these differences are slight compared to the striking similarity which obtains between them; a similarity that will be at once apparent in reading the description of the two diseases.

Still further, the position taken by the observers who believe that there is no proof that the two diseases are the same is illogical. These observers, almost without exception, perform experiments on fowls, and apply the information so obtained to the prevention and cure of human beriberi. Thus Fraser and Stanton say: " Fowls fed on white polished rice known to have been associated with outbreaks of human beriberi, develop a form of polyneuritis clearly analogous to beriberi in its clinical manifestations and pathological effects. Other white polished rices produce a similar result. Fowls fed on unpolished rice remain healthy. These animals may therefore be employed to study the mode of operation by which a diet of white polished rice results in

* Tsuzuki claims that cardiac hypertrophy may be produced in fowls fed on polished rice by the addition of amounts of antiberiberin, which are insufficient to confer complete protection. This statement has not been confirmed as yet by other workers.

beriberi in man." It does not seem to me that this can follow unless the two diseases are the same. For if the two diseases are not the same, they may have a different etiology, and our deductions from these experiments may not be applicable to human beriberi.

If, however, we regard the two diseases as the same, the results that have been obtained from these fowl experiments to determine the exact nature of the substance that is deficient, must apply equally to beriberi in man. As we hold this latter belief very decidedly, we will now review very briefly the experiments that have been performed for this purpose.

Deficiency in Albumen. Matsuhita believed that the development of polyneuritis gallinarum was dependent upon the lack of albumen, chiefly because he found that fowls fed on polished rice plus eggs did not develop the disease. This supposition is easily shown to be incorrect. In the first place, a polished rice contains about seven per cent of albumen, and Shiga and Kusama, and Vedder have shown that the addition of egg albumen to the diet of polished rice does not prevent the disease. Eijkman showed that fowls fed on potato starch were protected, and Chamberlain and Vedder have shown that the substance present in an extract of rice polishings which prevents polyneuritis, is dialyzable. This positively excludes albumens from further consideration.

Deficiency in Fat. Since an exclusive diet of polished rice is very deficient in fat, it might be supposed that the disease is caused by this lack of fat. The experiments of Fraser and Stanton, Chamberlain and Vedder and others absolutely exclude this possibility, since they protected fowls fed on polished rice by means of a variety of extracts of rice polishings, none of which contained any fat, while the administration of large quantities of fat failed to protect.

Deficiency of Phosphorus. As late as 1912 Schaumann still adhered to the theory that polyneuritis gallinarum is caused by the deficiency of phosphorus in some unknown organic combination. The fact that many substances rich in organic phosphorus, such as phytin and lecithin from eggs all had failed to confer protection, should have thrown grave suspicion on this theory, but it was very generally accepted nevertheless. Fraser and Stanton then showed that an extract of rice polishings which was deprived of 85 per cent of its total phosphorus content, was still capable of preventing polyneuritis, while the administration of the 85 per cent of phosphorus compounds so removed failed to confer protection. Chamberlain and Vedder carried the demonstration a step further by showing that an extract of rice polishings which contained only 0.0016 per cent of phosphorus pentoxide was capable of protecting fowls when given in addition to the diet of polished rice. These authors concluded: "Multiple neuritis in fowls fed on polished rice probably is not due to lack of phosphorus compounds in the grain, as claimed by Schaumann, since out of each 1,000 parts of phosphorus contained in the rice polishings, at least 999 are not concerned in preventing neuritis." Since the polished rice which produces the disease contains from 0.2-0.3 per cent of phosphorus pentoxide, and the extract which protected only contained 0.0016 per cent of phosphorus pentoxide, it would seem reasonably certain that the protective action of this extract could not have been due to its contained phosphorus. This question has been finally settled by Funk who has succeeded in isolating an organic base from rice polishings which promptly cures fowls suffering from polyneuritis, and which contains absolutely no trace of phosphorus.

Deficiency in Inorganic Salts. The extracts of rice polishings, which have been found by various investigators to confer protection on fowls, have contained a small percentage of inorganic salts. Thus the extracts used by Chamberlain and Vedder contained 0.03 ash. But polished rice itself contains from 0.5-0.6 per cent of ash. It would seem highly improbable that the powerful action of this extract could be due to this additional small amount of inorganic material. This improbability is emphasized from the fact that Eijkman found that fowls were protected when fed on potato starch, which was, of course, practically devoid of inorganic salts. However, since inorganic salts are dialyzable, the protective action of the salts in these extracts had to be considered as a possibility. This possibility was dissipated by a long series of experiments performed by a number of investigators, in the course of which almost every conceivable inorganic salt that can occur in food has been fed to fowls and found to be totally devoid of protective power. In addition to salts used singly, mixtures of salts have also been used with negative results. Onion juice and lime juice both failed to confer protection, so that it appears highly improbable from these experiments that the disease is due to a deficiency of organic or vegetable salts. It may be added that the sugars have also been tried in a similar way, and found to have no influence on the disease. This question has received its final quietus from the discovery of the real organic substances which are responsible for the protective and curative action of rice polishings, and which are absolutely devoid of inorganic constituents.

It has been suggested several times that polyneuritis is caused by a too uniform or monotonous diet. This supposition is completely disproven by the fact that an exclusive diet of potato starch, than which nothing could be more nonotonous, protects fowls; while on the contrary it has been shown that fowls may be fed on a ration containing a liberal amount of proteids, fats, carbohydrates and inorganic salts, and still develop the disease, providing the ingredients of this ration are selected from such food stuffs as do not contain the neuritis-preventing principle. (Vedder.)

Deficiency in Nucleins. Schaumann in 1908 thought that the active principle containing phosphorus was probably mucleic acid. Grijns, in testing this hypothesis, isolated the nucleins in an impure state from katjang idjo. His dried preparation contained 1.43 per cent of phosphorus pentoxide, and another preparation in watery suspension contained 3.2 per cent phosphorus pentoxide. He was unable to protect fowls fed on polished rice by either of these two preparations. On the other hand, an infusion of katjang idjo with its nucleins removed had a favorable action on the course of the disease. Grijns concluded that the nucleins did not contain the therapeutic principle of katjang idjo, a conclusion with which de Haan agreed in 1910. Schaumann obtained similar results, for in a later publication, he stated that he had been unable to cure pigeons suffering from polyneuritis by the administration of nucleins obtained from yeast. Thus the experimental evidence would seem to show that polyneuritis gallinarum is not caused by a deficiency in nucleins. However, there is considerable evidence that the active principle or base which prevents and cures polyneuritis gallinarum is a constituent of nucleic acid. This subject will be further considered a little later.

The discovery of the substance in rice polishings that cures polyneuritis gallinarum. This most important contribution to our knowledge was made by Funk in December, 1911. He found that the active substance of an extract of rice polishings could be completely precipitated by phospho-tungstic acid, and also by silver nitrate in the presence of baryta. By combining these two methods, he was enabled to isolate a crystalline organic base having a melting point of 233°C. Chemical analysis showed that this base might be provisionally regarded as consisting of $C_{17}H_{20}N_2O_7$. The same base was subsequently obtained from yeast and other food stuffs, and the administration of about 0.02 gram of this substance to pigeons suffering from polyneuritis effected a rapid cure. Funk considered from the chemical reactions of this substance that it is a pyrimidine base analogous to uracil and thymine, and suggested the name vitamine for it, as being one of the nitrogenous substances, minute quantities of which are essential in the diet of birds, man, and some other animals.

Funk's observations were later confirmed by Vedder and Williams, who, following closely Funk's method, succeeded in obtaining this same crystalline base, which cured fowls suffering from polyneuritis, when administered in doses of 30 milligrams.

It seems extremely probable from the chemical reactions obtained with this base by these observers, that it is probably a constituent of nucleic acid. Thus, its precipitation by silver nitrate in the presence of barium hydroxide, but not in neutral solution, places this base definitely in the pyrimidine rather than in the purine group. The neutral reaction of the free base, and its precipitation by phosphotungstic acid are in perfect agreement with this theory. Furthermore, this base gives with bromine water, the same purple coloration that is given by cytosin and uracil. These pyrimidine bases are only found as constituents of nucleic acid, hence the probability that Funk's base occurs in the food as a constituent of nucleic acid.

But since nucleic acids are constituents of nucleins, and as the feeding of nucleins has failed to prevent polyneuritis gallinarum, the experimental evidence appears to contradict this view. However, nucleins and nucleic acids are commonly extracted from proteid substances by methods which depend upon the use of fixed alkalies. Vedder and Williams have found that Funk's base is rapidly destroyed by treatment with such alkalies. It seems probable, therefore, that this base exists in food stuffs as a constituent of nucleic acid as is indicated by its chemical reactions, but that it is not present in the nucleic acid or nucleins obtained from yeast, katjang idjo, etc., by methods involving the use of alkalies. This accounts for the failures which have resulted so constantly when nucleins or nucleic acid have been used as preventive or curative agents.

In March, 1912, Edie, Evans, Moore, Simpson and Webster also succeeded in isolating a similar organic base from yeast by precipitation with lead acetate followed by silver nitrate and baryta. The base obtained by these authors had a formula of $C_7H_{17}N_2O_5$ and also promptly cured pigeons suffering from polyneuritis. They called this substance *torulin*.

Several Japanese observers had also been working on this problem. Tsuzuki in 1912 wrote describing the preventive properties of a substance which he called antiberiberin, which he had isolated from rice polishings. This substance, however, was simply an alcoholic extract, from which the alcohol was evaporated off, the fat removed and the residue evaporated to dryness. This residue, or antiberiberin, therefore corresponded exactly to the extract previously used by Chamberlain and Vedder in the treatment of beriberi cases with such marked success. It was a complex substance chemically, and therefore its isolation did not advance our knowledge as to the actual composition of the neuritis-preventing compounds.

Suzuki, Shimamura and Odake, in July, 1912, also isolated a substance from rice polishings which they called Oryzanin. This so-called oryzanin was obtained from an alcoholic extract of rice polishings by precipitation with tannic acid. The precipitate was then broken up by baryta and the baryta removed by sulphuric acid. The residue was precipitated by picric acid, and the picrate of the base, which they named oryzanin, was thereby obtained. Small amounts of the oryzanin cured pigeons suffering from polyneuritis in a few days. They did not, however, succeed in obtaining any definite knowledge as to the chemical constitution of this base.

The question at once arises, are the bases isolated by these different observers the same; and, if so, why does their chemical composition vary? It is possible that Funk, Edie and his coworkers, and Suzuki, Shimamura and Odake all obtained the same base. The discrepancy as to chemical composition may have been due to the fact that the pure substance was obtained by all these observers in such minute amounts that it is not possible for the chemical analyses to be repeated and verified. But it is also quite possible that they obtained different bases, since the chemical methods used by these different observers were not the same, and since it has now been demonstrated that several different protective substances are present in rice polishings.

This latter information is obtained from the work of Vedder and Williams, who performed the following experiment: A quantity of extract of rice polishings was precipitated by phospho-tungstic acid. The precipitate was freed from phospho-tungstic acid, and the remaining solution was exactly neutralized and precipitated by silver nitrate. The precipitate (a) consisting of purine bases was filtered off and the filtrate was rendered alkaline with baryta and again precipitated with silver nitrate. This precipitate (b) containing Funk's base was filtered off and a filtrate (c) containing choline and other similar bases remained.

Three groups of fowls were fed on polished rice, and in addition each group received one of the substances (a), (b) and (c), and all three groups were protected from polyneuritis. This indicated conclusively that the protective substances in rice polishings could be separated into three groups by a chemical process. The experiment further showed that there was a real difference in the physiological action of these three groups, since only one of them, namely, group (b), containing Funk's base was capable of promptly curing fowls already suffering from polyneuritis. The other two groups of substances, although they protected fowls from developing the disease, were incapable of curing them promptly.

This experiment demonstrates that there are several substances contained in rice polishings which are all concerned in the prevention of polyneuritis gallinarum, but it is of course possible that these different chemical compounds may all contain Funk's base as a nucleus, and that their protective action may be dependent upon the presence of this base. This possibility can only be determined by further chemical work.

As will be seen in a later chapter, human cases of dry beriberi were treated by Vedder and Williams by the administration of Funk's base isolated from rice polishings, and the paralytic symptoms were greatly improved and possibly completely cured by this treatment. In other words, Funk's base appears to be a specific cure both for polyneuritis gallinarum and for dry or paralytic beriberi in man. This observation, if confirmed by other workers, affords final and convincing proof that dry beriberi in man and polyneuritis gallinarum are the same disease, and that they are both caused by the deficiency in the food of Funk's base.

The question as to how this base should be named naturally arises. The terms antiberiberin, oryzanin, and torulin have been used. None of these names are strictly satisfactory. The names oryzanin and torulin indicate a principle extracted from rice and from yeast; but it is highly probable that the base first isolated by Funk is found in rice polishings, yeast, katjang idjo and other foods that protect against beriberi. Funk has obtained the same base from both rice polishings and yeast. It is obviously unsatisfactory to give the same substance a different name for each food stuff in which it happens to be a constituent.

The structural formula of this base has not yet been worked out. It is believed to be preferable to wait until this work has been completed and to then give this base a proper chemical designation. In the meantime it can be referred to as a vitamine. This term, which was coined by Funk, is so expressive that it will probably be adopted by future workers. It indicates a nitrogenous substance which is essential in a diet on which health may be maintained. It may be used to include not only the substances that prevent the appearance of beriberi, but also the substances the lack of which are the cause of other deficiency diseases, such as scurvy.

CHAPTER XI

THE ETIOLOGY OF BERIBERI, CONTINUED

Beriberi in Animals

If polyneuritis gallinarum and beriberi in man are both the same disease, and are produced as a result of the same deficiency in the food, there is every reason for believing that animals more closely related to man ought also to suffer from beriberi if they are given a suitable diet. As a matter of fact we now know that this is the case, although this addition to our knowledge of beriberi is quite recent. The earlier attempts to produce beriberi in animals failed, partly because nothing was known concerning the incubation period of the disease and the experiments were not sufficiently prolonged. We now know that it is necessary to feed men for about three months on a diet of polished rice before symptoms of beriberi appear, and that the incubation period of beriberi in many animals is considerably longer than it is in fowls, and becomes increasingly longer the higher the animal in the zoological scale.

Beriberi-like diseases of animals have occurred spontaneously, or as the result of one-sided feeding, entirely apart from any attempt to produce experimental beriberi. Rupert said, in 1880: "It has been stated that other animals, such as hens, sheep, cattle, horses, dogs and pigs may suffer from beriberi, but I have not observed it myself."

Uchermann stated in 1902 that beriberi was observed in animals on board ships where the crews suffered from beriberi, and mentioned sheep, geese and fowls as being affected.

Nocht makes the following statement on this subject: Beriberi-like diseases also affect animals as the result of one-sided or bad feeding. It has been long known that dogs fed largely or exclusively with carbohydrates accumulate great masses of water in the tissues. The same thing has recently been observed by Von Gouin and Andouard in calves that were fed exclusively on molasses, beets or oil cakes without the addition of hay. In the sugar factories Sachsens says, further, that until they learned to prevent the disease it similarly affected oxen which were fed exclusively on beets. The animals showed fatigue, were short of breath and had swelling of the legs.

Unfortunately there are no accurate pathological findings in any of these cases, and we cannot therefore regard the diagnosis of beriberi as proven, although such instances retain considerable interest as possible cases of beriberi in animals.

Several investigators have succeeded in producing polyneuritis in animals as a result of an exclusive diet of polished rice, or by other diets that are capable of producing beriberi in man and polyneuritis in birds. Hose in 1905 fed three monkeys (Macacus nemestrinus) on bazaar rice, and two of these monkeys developed some of the characteristic nervous symptoms of beriberi.

Braddon in 1907 reported a case of paralysis in a rice-fed pig. This pig was fed experimentally on uncured rice at the Seremban hospital, and well cared for in every respect. It developed paraplegia in a month and died quite suddenly without fever or any other symptoms.

Schaumann succeeded in 1910 in producing such a condition in guinea pigs, rats, a dog, a goat and a monkey. For example, in experiment 14 two guinea pigs were fed on polished rice. Paralysis developed in both of these animals, occurring in the first in 17 days and in the second after 30 days. An investigation of the nerves of the first guinea pig showed the presence of degenerated fibers.

In experiments 42 and 43 seven rats were fed on horse meat which had been sterilized in an autoclave at 120° C. After about a month paralysis appeared in the hind legs, and the animals could no longer walk. Typical degeneration was not demonstrated in the nerves, though in one case the nerves showed a foamy appearance.*

Dogs fed on meat sterilized in the autoclave at 120° C. suffered severe paralysis which always appeared first in the hind legs. This paralysis first appeared after the experiment had lasted about a month and a half and became progressively worse. At first the gait was unsteady, but later the hind feet gave way under the animal. Finally these dogs became so completely paralyzed that they were unable to arise. (See figure 37.) Some of these dogs showed some symptoms of scurvy. The nerves of twô dogs were studied. One of these did not show typical degeneration although some of the fibers showed a foamy appearance. The sciatic nerve of the second dog contained a small number of fibers that showed typical degeneration.

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* Schaumann in a number of his experiments states that true degeneration was not demonstrated, but that the nerves presented a foamy appearance (Schaumstruktur). This foamy appearance in the myelin sheath is, however, an evidence that the myelin is breaking down, and is, therefore, probably the beginning of a true degenerative process.

In experiment 49 a goat was fed on polished rice and corn, beginning on June 19. By the end of August the weight of the animal had fallen off considerably. Soon afterwards paralysis of the hind legs set in gradually. By the middle of September slight paralysis of the forelegs was noticed. These paralyses increased in severity gradually but steadily until the middle of October the animal was entirely unable to arise. (See figures 38–40.) On December 14 the animal was killed and the cord and peripheral nerves studied. Considerable oedema was found in the left hind leg. No macroscopic changes were

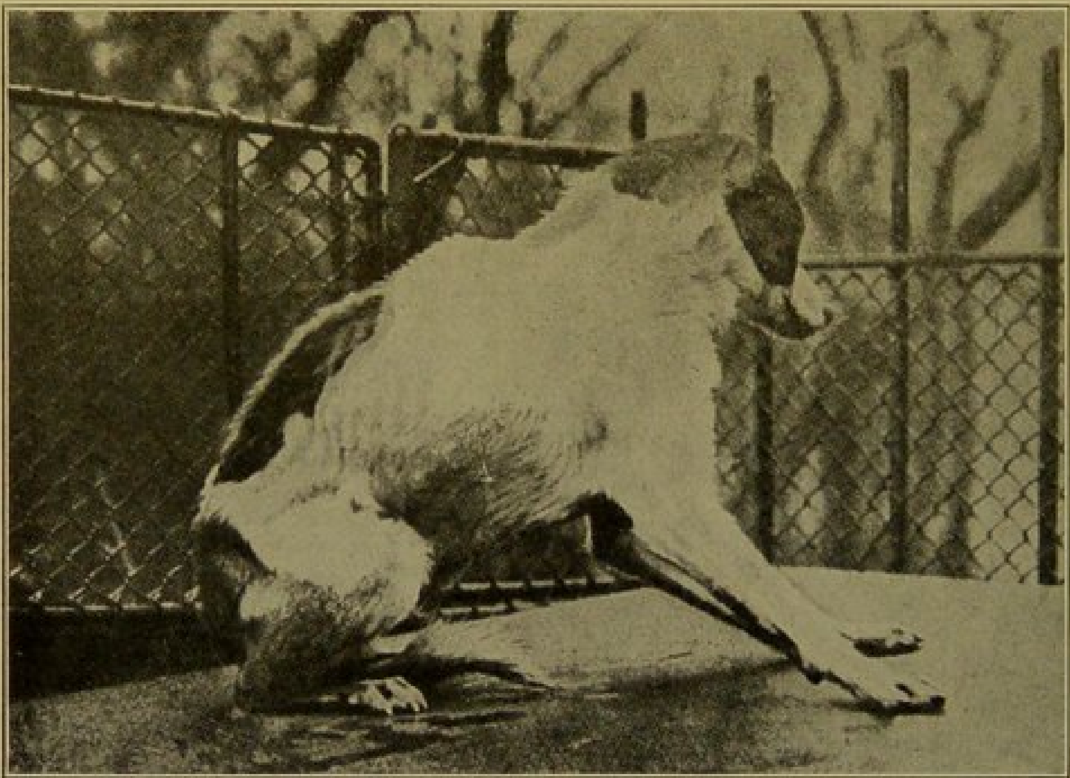

Figure 37. Dog with hind legs paralyzed as a result of feeding on sterilized meat. [From Schaumann.]

found in the cord. Microscopic changes were found, however, in the fibers in the thoracic region of the cord. Both sciatic nerves, the peroneal and femoral nerves showed marked degenerative changes. These changes were also demonstrated in both brachial plexuses.

In experiment 15 Schaumann fed a monkey with cooked polished rice. The animal died after 74 days' feeding, and before death paralysis of the hind extremities occurred. Investigation of the nerves showed a great deficiency of normal fibers, and although typical degeneration was not demonstrated, almost all the fibers were foamy. (See figure 41.)

Shiga and Kusama state that Kitashima has performed the same experiment with two Indian monkeys (Macacus nemestrinus) which both died with paralysis.

It may be questioned whether these cases of Schaumann's were true beriberi. The animals showed paralysis with evidences of peripheral neuritis, and oedema occurred in some cases, but the cardiac hypertrophy so characteristic of beriberi was never found. It is, however, evident that the condition in all of the animals was very similar to beriberi. The disease occurred in the guinea pigs and the

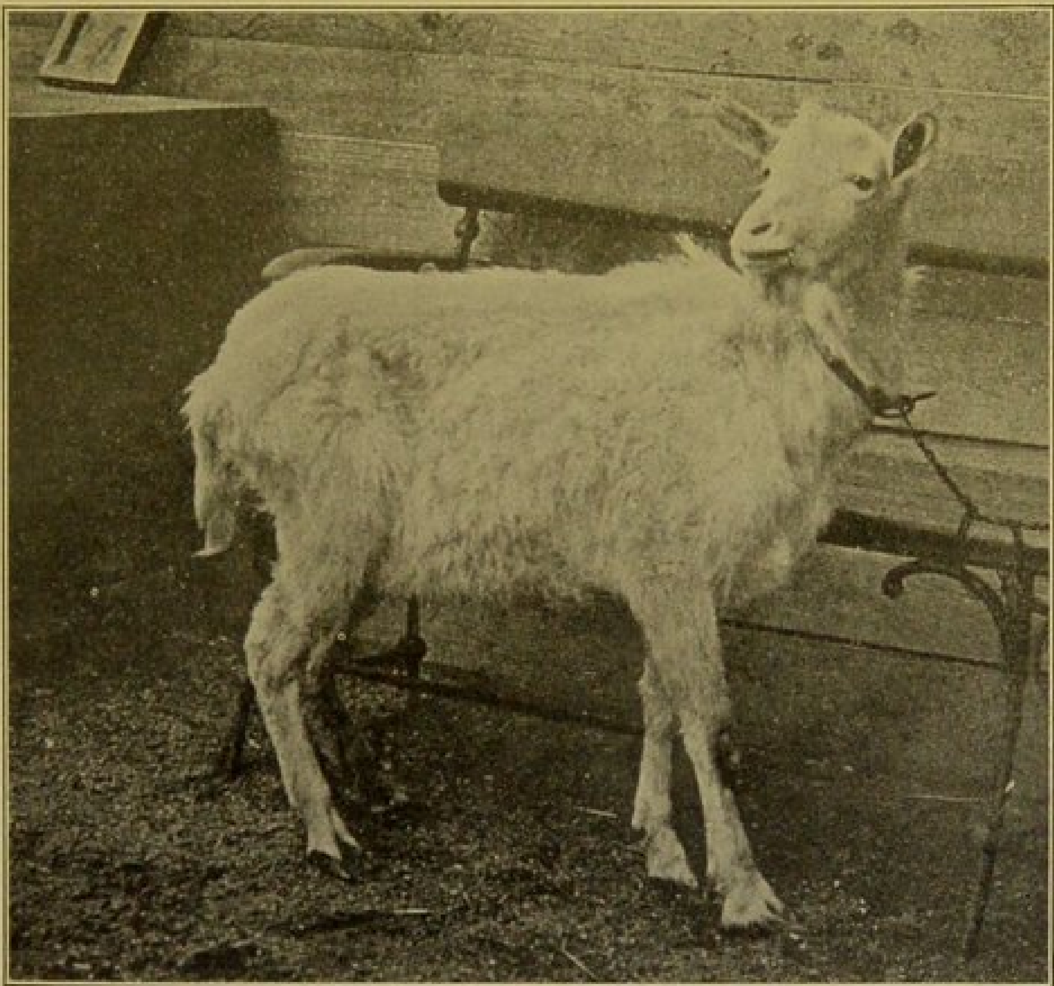

Figure 38. Goat at beginning of experiment. [From Schaumann.]

monkeys as a result of feeding on polished rice. In the goat it developed on a diet of polished rice with corn. It has been shown that corn will not prevent the development of polyneuritis in fowls, and Hulshoff Pol demonstrated that corn would neither prevent nor cure beriberi in man. It it therefore clear that this beriberi-like disease was produced in these animals as the result of a diet known to produce beriberi in man and polyneuritis in fowls. The rats and the dog were fed on sterilized meat. While raw meat undoubtedly contains the beriberi preventing substance, it has been amply shown that this substance is destroyed by sterilization, and that fowls fed on sterilized meat are not protected from polyneuritis. Therefore, although avoiding positive statements, it appears likely that the disease which Schaumann produced in these different varieties of animals was identical with polyneuritis of fowls and beriberi in man.

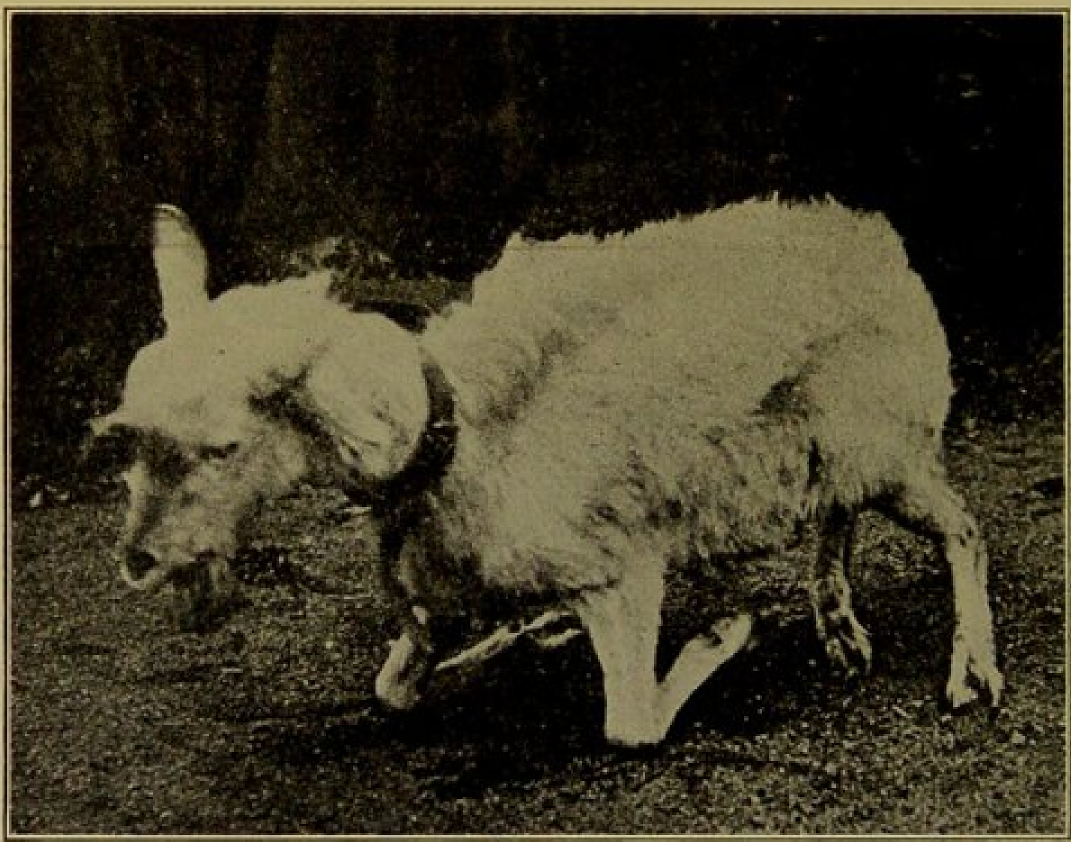

Figure 39. Same goat after three months feeding on highly milled rice and corn. [From Schaumann.]

Shiga and Kusama are among the observers who think that it is going a little too far to claim that polyneuritis of fowls and beriberi in man are identical. They claim that the main symptoms of beriberi are sensory and motor paralyses of the limbs dependent upon a peripheral neuritis, and dilatation and excentric hypertrophy of the heart. That both of these symptoms must be present before a diagnosis of beriberi can be made and that the change in the heart had not yet been proven in the so-called beriberi of animals. Therefore these observers undertook, in 1911, to determine whether true beriberi, identical with beriberi in man from a clinical and pathological point of view, could be produced in animals.

For this purpose they fed apes (Macacus cynomolgus) on cooked polished rice. At first they ate this freely, but after a few weeks their appetite was bad. One monkey died after five months' feeding, of general tuberculosis, without ever showing any paralysis. The other lost greatly in weight and after 37 days developed paralysis in both hind legs. The clinical picture of this monkey was very similar to that of fowls suffering from polyneuritis. At first the gait became

Figure 40. Same goat after four months feeding on highly milled rice and corn. [From Schaumann.]

uncertain, but the paralysis of the hind legs progressed gradually until it was complete and the body was dragged about by the arms. At the same time there was anaesthesia of the legs, and pain sense was much diminished. Knee reflex increased slightly at first and then vanished entirely. On auscultation the pulmonary and aortic sounds were accentuated. On slight exercise the heart action greatly increased and dyspnoea was considerable. Legs were slightly oedematous in the last days. Symptoms increased and heart action became gradually weaker and irregular. Pulse was weak, small and soft.

Body temperature fell and death followed in ten days of illness. This monkey then had ascending paralysis of legs, anaesthesia, loss of reflexes, oedema of legs and symptoms indicating that the heart was affected.

As a result of all their experiments two monkeys suffering from typical beriberi came to autopsy at which the following changes were noticed: Atrophy of skin and musculature. Slight oedema of both hind legs and feet. Pericardium contained a clear serous fluid, in one case six centimeters and in the other five centimeters. This is a

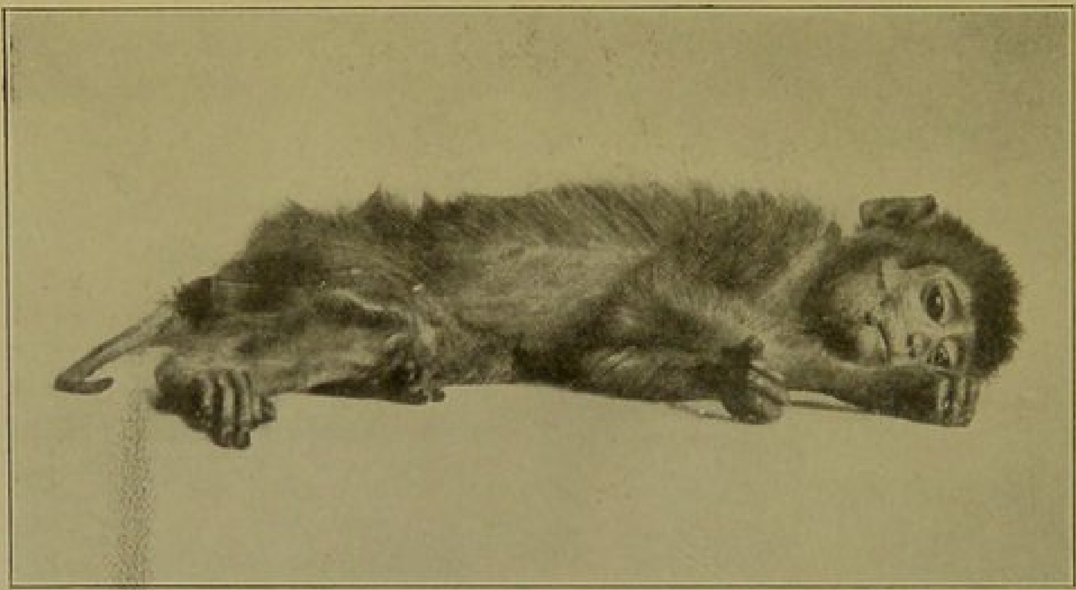

Figure 41. Monkey, paralyzed after 74 days feeding on highly milled rice. [After Schaumann.]

high degree of hydropericardium, since in normal monkeys only one or two drops of fluid are found. Heart in both cases was of good consistency and color, but was much enlarged. The base was very broad and the apex rounded, so that the entire heart takes a ball shape. In one case both ventricles and in the other case the left ventricle was greatly enlarged and contained a great mass of fluid blood and clot. Left and right ventricles were much dilated, and the wall and papillary muscles greatly thickened. Valves and large arteries normal. Lower lobes of both lungs were oedematous. Spleen, kidneys, adrenals, liver, pancreas and urogenital organs were normal with exception of atrophy and congestion. Mucous membrane of stomach and intestine slightly oedematous, but not abnormal. Brain and cord showed a non-inflammatory simple degeneration. A number of fibers of the sciatic, tibial, peroneal and phrenic nerves were degenerated. In the white matter of the cord there were also degenerated fibers in all the columns. Heart muscle is slightly hypertrophic and of normal appearance. Skeletal muscles on other hand greatly atrophied. Thus we see that in both monkeys were found anasarca, hydropericardium and oedema of the lungs, a striking change in the heart, namely hypertrophy with dilatation, a change of great significance with regard to beriberi, and in addition general venous congestion, degeneration of the nervous system, and fragmentation of heart and skeletal muscles.

In addition to the changes in the nervous system, dilatation and hypertrophy of the heart were found in these monkeys. Shiga and Kusama state: " It is a well-recognized fact that dilatation and excentric hypertrophy, especially of the right heart, is a very characteristic change in beriberi, by means of which this disease can easily be distinguished from the various infectious and intoxication polyneuritides. The disease in monkeys is therefore identical with beriberi in man."

Tsuzuki also showed that a diet of polished rice produced polyneuritis in dogs, cats, rabbits, guinea pigs, mice, rats and monkeys. These animals developed sensory and motor paralyses of the extremities with inability to walk, loss of patellar reflex and disturbances of metabolism, accompanied by wasting of the muscles. At autopsy degeneration of the nerves was demonstrated, and the monkeys and dogs also showed dilatation and hypertrophy of the right heart. On the other hand animals fed on polished rice mixed with rice polishings remained in good health. From these findings Tsuzuki has come to the conclusion that a disease is produced in experimental animals by rice feeding, which is identical with beriberi in man.

Finally Andrews, in 1912, succeeded in producing a disease in puppies indistinguishable from beriberi in man. While studying infantile beriberi in Manila, Andrews became convinced that this infantile beriberi was true beriberi, and, further, that it was caused by nursing mothers that were suffering from beriberi, because the mother's milk was lacking in some substance which is essential for the growth and development of the nerves of the child. He therefore persuaded mothers whose children had died of infantile beriberi to nurse young puppies from two to fourteen days old. In all sixteen puppies were used, but for various reasons only seven were nursed for a period of one month or longer. All of these puppies developed incoordination and weakness of the extremities, particularly of the hind legs. In several cases complete paralysis of the hind legs occurred. All showed oedema of the subcutaneous tissues. In all slight degeneration of the peripheral nerves was demonstrated by the Marchi method. And one of these puppies also showed great dilatation and hypertrophy of the right heart. (See figure 42.) The complete account of these experi-

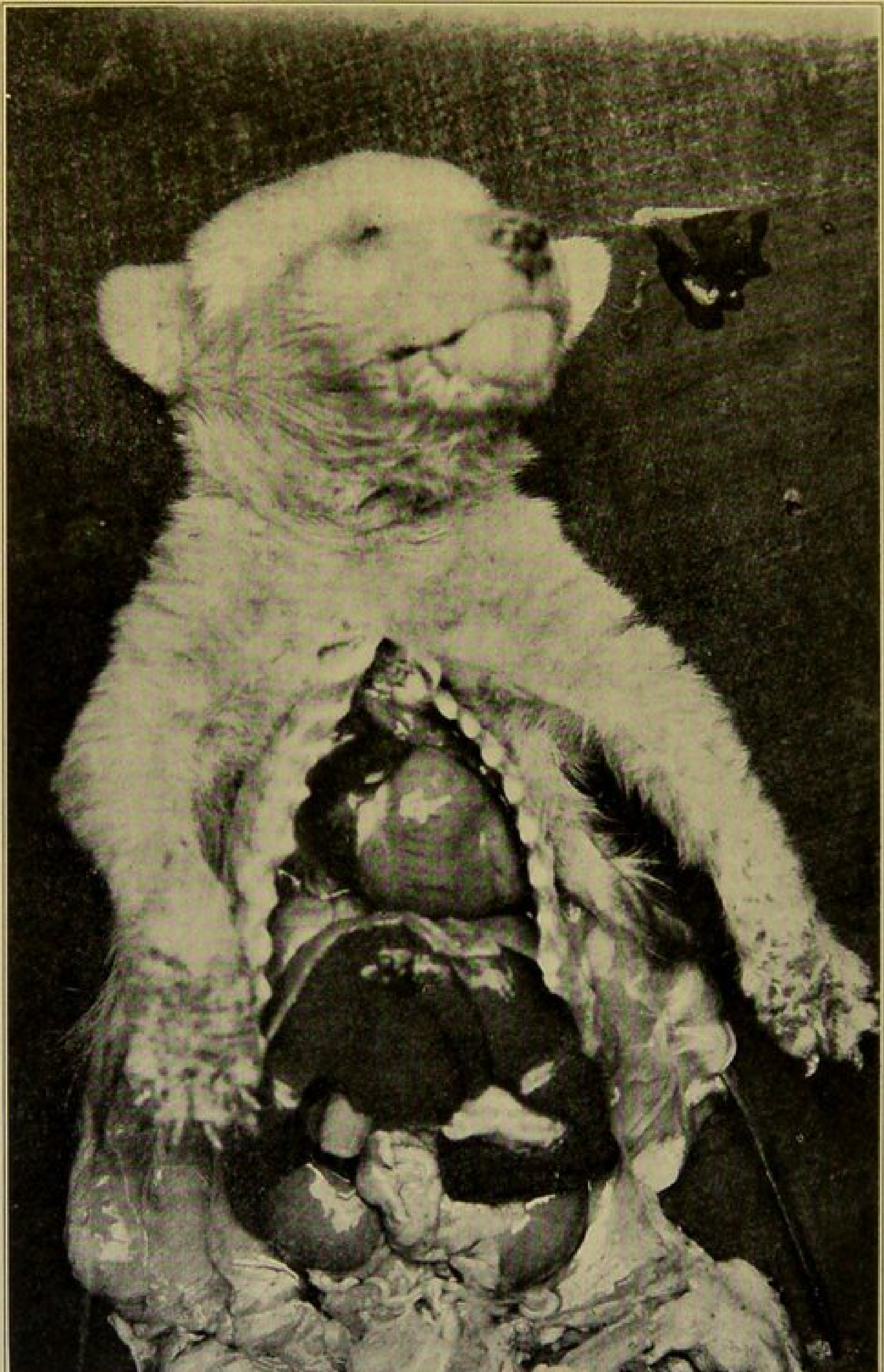

Figure 42. Puppy that developed beriberi after nursing a woman who had beriberi, and whose child had died of infantile beriberi. Note the greatly hypertrophied right heart. [From Andrews.]

ments may be found on page 406 of the appendix. One of these puppies therefore showed all the symptoms and anatomic changes found in beriberi, and we are driven to the conclusion that it suffered from true beriberi.

To recapitulate, therefore, we find that animals that have received a one-sided diet have been reported for many years to suffer from beriberi-like diseases. That Schaumann has succeeded in producing a disease very similar to beriberi in a number of species, including guinea pigs, rats, a dog, a goat and a monkey, that had been fed on diets known to produce beriberi. That Shiga and Kusama and Tsuzuki succeeded in producing true beriberi in monkeys by feeding polished rice, and that Andrews succeeded in producing true beriberi in puppies by feeding them milk from beriberic women whose children had died of infantile beriberi.

These results strongly confirm: (1) The belief that avian polyneuritis is the same disease as human beriberi, since this condition is not confined to birds and man, but may be produced by a polished rice diet in a number of other animals. And (2) the belief already expressed that beriberi is caused by a too exclusive diet of polished rice or by any other diet lacking in the vitamines which are necessary for normal metabolism, particularly of the nervous system.

CHAPTER XII

INFANTILE BERIBERI

Definition. Infantile beriberi is an acute or subacute disease affecting infants who are nursing mothers suffering from beriberi. It is characterized by cardiac hypertrophy and a peripheral neuritis, and results in a clinical picture of generalized oedema, dyspnoea, cardiac disturbance, gastro-intestinal derangements, oliguria and aphonia. It is a form of true beriberi, and like beriberi of adults is caused by the deficiency of some important substance in the food, i. e., in the milk from a mother who is suffering from a similar deficiency.

Historical. The discovery that nursing infants suffer from beriberi was made by Hirota, who first observed this disease in 1888. From 1888–1891 he reported thirty of these cases at a meeting of the General Association of the Medical Society of Tokyo. Miura says that in 1890 and 1891 other articles appeared in the Japanese medical journals describing kakke of sucklings, but without presenting sufficient proof that the disease was true beriberi. Hirota published his observations on infantile beriberi in 1898. Before the publication of his work it was generally supposed that beriberi did not affect nursing infants. Baelz said children never have this disease before the second dentition, and Scheube's youngest patient was eight years old.

When Hirota wrote the paper referred to above he had studied 52 cases of infantile beriberi, of which 42 cases recovered, five died and five were lost, and he presented a clear-cut description of this disease in infants. More recent observations have contributed little to the clinical picture that he drew. He also showed clearly that all of the symptoms of infantile beriberi are found in cases of beriberi in the adult, that the mother who nursed the child almost invariably suffered from beriberi, and also that the child usually recovered at once when removed from the breast and given artificial food, although ordinary medicinal treatment was useless. But he drew the conclusion from his observations that this infantile beriberi was an intoxication caused by the milk of the woman suffering from the same disease, since only in this way could he explain the wonderfully rapid improvement that occurred when another food was used in place of the mother's milk. This is the only argument he adduces in favor of the intoxication theory, and although it is quite apparent that this observation points quite as strongly to the theory of a nutritive deficiency in the mother's milk as it does toward an intoxication, Hirota's statement has been quoted many times by the advocates of the intoxication theory of beriberi.

In 1899, M. Miura published the results of four autopsies on infants that had died with the clinical diagnosis of infantile beriberi. Although Miura did not examine the nervous system in these cases, he says: "Through these four cases I was convinced that, as other authors claim, kakke can affect children that are still at the breast." Miura came to this conclusion because he found in each case hypertrophy of the right ventricle, without valvular disease and without any apparent cause for this enlargement of the heart, and he knew of no other disease except kakke which could produce this condition. An abbreviated account of these autopsies reported by Miura may be found on page 409 of the Appendix.

Hirota also wrote a second paper in 1900 reiterating his former statements, and adding the very interesting and important observation that severe beriberi may occur in infants nursed by mothers having themselves the lightest form of the disease, or in rare cases no symptoms at all at the time the child is affected. He quotes one case where the symptoms of beriberi in the mother appeared for the first time 29 days after the child became sick.

Hirota's papers shed a light upon the infantile mortality in the Philippines. For many years Filipino physicians had recognized a disease of young infants variously known under the names Taon, Taol and Suba. The nature of this disease had been under discussion for some time, but no satisfactory conclusion was reached until 1904, when Doctor Manual Guerrero read a paper on "The Etiology, Symptomatology, Clinical Forms, Diagnosis and Pathogenesis of Beriberi in Children." This paper was based upon 103 clinical cases of taon, and arrived at the conclusion that taon was similar to the disease described by Hirota as infantile beriberi. Guerrero performed no autopsies, and his paper was not published, but it produced a revolution in the minds of Filipino physicians with regard to taon, and a number of them began to issue death certificates for infantile beriberi.

In 1908, Albert reported a typical case of infantile beriberi with the autopsy findings, and stated that with the confirmation of this autopsy that infantile beriberi had acquired a definite place as a nosological entity in the Philippines. From this time on taon has been recognized as a clinical entity, and has been more properly called infantile beriberi.

In the latter part of 1909 the Bureau of Health attempted to confirm, by necropsy, the clinical diagnoses appearing upon the death certificates of infants in Manila. In examining the death certificates of infants of one year of age and under, it was found that in a large number of them death was attributed to "convulsions," "congenital debility," "beriberi," "acute bronchitis," "acute meningitis," or "enteritis." Autopsies were performed on these cases with startling results, which appeared in a paper by McLaughlin and Andrews in July, 1910. In this paper were presented the pathologic findings observed at necropsy of 219 infants under one year of age. Of this number 124, or 56.6 per cent, were found to have died of a condition which the authors called infantile beriberi. The authors had been unable to see the cases clinically, and the history obtained was meagre, so that this diagnosis was based solely upon the pathological findings. McLaughlin and Andrews came to the conclusion that infantile beriberi is one of the real factors in Filipino infant mortality, and is responsible for more deaths than appear in the statistics. It may even be the largest factor in the infant mortality of Manila, thus accounting in great measure for Manila's excess in infant mortality over that of other countries.

Three months later a very complete clinical account of the disease was published by Guerrero and Quintos. This paper was based on a study of 176 cases, and presented an excellent summary of our knowledge of the subject, and aided materially in spreading this information more widely. Guerrero and Quintos still adhered to an intoxication as the etiological factor.

Until January, 1912, there was very general agreement that infantile beriberi was caused by an intoxication transmitted by the mother's milk. On that date Chamberlain and Vedder presented a paper in which they clearly showed that cases of infantile beriberi could be cured by the administration of an extract of rice polishings, while permitting the infants to continue to nurse their mothers. This evidence that infantile beriberi can be cured by the same extract which cures fowls and cases of adult beriberi is not only additional evidence of the strongest kind that infantile beriberi, adult beriberi and polyneuritis gallinarum are all the same disease, but it definitely disposed of the theory that infantile beriberi is caused by an intoxication, since it is most irrational to believe that such an extract of rice polishings could cure a child in a few days, while it was still receiving the toxin which had originally produced the condition.

Finally Andrews,* in April, 1912, contributed a most important paper in which he for the first time correlated the clinical study of infant and mother suffering with beriberi, with the autopsy findings, with analyses of the mother's milk, and also succeeded in producing experimental beriberi in puppies that were allowed to suckle the mothers whose children had just died of beriberi. The discussion and conclusions drawn from this work by Andrews may be found on page 412 of the Appendix.

Prevalence. The only evidence I have been able to secure as to the prevalence of infantile beriberi in Japan is contained in Hirota's second paper, in which he gives the number of patients and nursing infants treated in the university clinic during the years 1897–1899. His table shows that during these three years 1,396 beriberics were treated, and that these patients had 396 nursing infants. Of these 396 infants 58 developed beriberi, being 4.2 per cent of the total number of patients, and 14.6 per cent of the total number of nursing infants. If this percentage is a fair index of what occurs in the community at large, the mortality from infantile beriberi in Japan must be very high, for the total number of cases of beriberi is large, and we must remember that practically all of the cases of infantile beriberi will die unless their diet is changed. This is no doubt impossible in the vast majority of cases because of poverty and the ignorance of the mothers as to the real cause of the disease.

Turning to Manila, we find that the death rate among infants is extremely high, *and that the mortality is greatest among the breast-fed babies.* In Europe and the United States the mortality is high among artificially fed children, but very low for the breast fed. This peculiar incidence of infantile mortality in Manila is clearly shown in the following table, taken from a paper by Albert:

INFANT MORTALITY IN BERLIN AND MANILA ACCORDING TO FEEDING.

	Total.	Breast fed.	Artificial fed.	Per cent of breast fed.	Per cent of arti ficial fed.	Undeter-mined feeding.
Infant death in Berlin during 1906..........	9,111	844	5,833	9.26	64.02	2,431
Infant death in Manila during 1909.........	3,871	2,328	778	65.30	20.09	565

* It should be understood that although the paper of Chamberlain and Vedder was published before that of Andrews, the work was performed contemporaneously, and a preliminary report was presented by Andrews at the same meeting of the Manila Medical Society at which Chamberlain and Vedder's paper was read. As a matter of fact, several of Chamberlain and Vedder's cases were obtained through the courtesy of Andrews, a fact which shows that there can be no question that they were both working with the same disease.

It is clear that there must be some reason for this great mortality among breast-fed infants in the Philippines, and that it must be due to some factor which is not operative in Europe and the United States. It is probable that the greatest part of the mortality among these breast-fed infants in the Philippines is due to beriberi. This is shown by the paper of McLaughlin and Andrews. These authors found that out of 219 necropsies on infants of one year of age or under 124 gave the pathologic findings of infantile beriberi. At first sight it is hard to believe that infantile beriberi can be so prevalent in Manila, and it may seen strange that under these circumstances the disease should have remained so long undiscovered. These statistics, however, are based on careful autopsies, and are far more reliable than the ordinary clinical diagnosis as borne on the death certificates, owing to the fact that in many instances the native doctor is not called to see the patient until the latter is moribund, or, in many cases, until after death, when the family want a death certificate signed. But even these clinical diagnoses, unreliable as they are, show a similar condition, since out of 176 cases that McLaughlin and Andrews investigated, the clinical diagnosis in 50 cases was beriberi, while at autopsy they found that 97 of the 176 cases were beriberi.

This remarkable incidence of infantile beriberi is readily explainable when we remember that large numbers of the native population in Manila live chiefly on polished rice with a little fish or meat. As for the disease not being recognized in earlier years, it is sufficient to state that these cases are practically never seen by an American physician, and that the disease has been well known for many years to native doctors under the name of Taon.

So far as I am aware infantile beriberi has not been reported from any other countries. But it is quite probable that it exists undiagnosed in many of the Oriental countries where beriberi is endemic among the adults.

Pathology. Hirota reports briefly an autopsy on one of his cases. He simply states that dilatation and hypertrophy of the right ventricle, general oedema and a recent broncho-pneumonia were found.

Miura in four autopsies found in each case hypertrophy and dilatation of the right ventricle, but he made no examination of the nervous system. (See page 409 of the Appendix.)

Albert in 1908 reported a typical case of infantile beriberi with the autopsy findings, which were briefly as follows: 1. Degeneration of the vagi and swelling of cells of right cervical ganglion. 2. Dilatation of right side of heart to a great degree. 3. Collection of fluid in the pericardium. 4. Subpleural haemorrhagic areas in both lungs. 5. Subcutaneous oedema in legs and chest wall.

Tanaka in 1910 reported a case of a child born of a woman who was suffering from a severe attack of beriberi. The child died a few hours after birth of failure of respiration attended by general cyanosis. The autopsy showed hypertrophy and dilatation of the right ventricle without any valvular or congenital defects or pulmonary disease, general venous congestion and degeneration of the peripheral nerves.

Guerrero and Quintos in two autopsies found hypertrophy and dilatation of the right ventricle, slight general oedema, and congestion of the liver, spleen and kidneys. They also report on the histological examination of pneumogastric nerves, finding congestion, and interstitial haemorrhage into the epineurium and perineurium, and fragmentation of the myelin in certain fibers throughout the entire nerve but particularly affecting the terminal branches. These observations are very important since they include lesions of the peripheral nerves that we believe are typical of beriberi. Unfortunately, however, these autopsies were performed in one case 32 hours after death and in the second case 22 hours after death. Post-mortem changes are very rapid in the tropics, and this long interval between death and the autopsy necessarily reflects some doubt upon the histological findings particularly in the nerves.

The observations of these several authors on the morbid anatomy of infantile beriberi agree very closely, but between them all they have only performed nine autopsies. This was the state of our knowledge of the pathology of infantile beriberi in 1910 when the paper by McLaughlin and Andrews was published. These authors performed 124 autopsies on cases of infantile beriberi and the following condensed description is taken from that article:

" The body is that of an apparently well-nourished infant, plump; skin is usually pale and anaemic. The face is full, with almost a swollen appearance. Flesh of thighs and legs is soft and flabby and, as a rule, pits on deep pressure. Occasionally the skin has a tough leathery feel, a leaden color and a slight goose-flesh appearance.

Subcutaneous fat is present, apparently in good amount, grayish-white in color and very moist; muscles are anaemic. Owing to the oedema the real amount of fat present is deceptive and hence the bodies may not be as well nourished as they appear.

Most often there is an increase of peritoneal fluid, which has a distinct yellowish color.

Heart. The pericardial sac is filled with a clear fluid, having a greenish tint. Probably the most striking and constant change is found in the right heart. Its musculature is coarse and firm and forms much the larger part of the organ, even in the contour of the apex. Its trabeculae and papillary muscles are prominent, while its cavity is enlarged. The wall of the right ventricle may measure from five millimeters to seven millimeters in thickness, whereas the left measures only three millimeters to five millimeters. The musculature of the left heart is soft and flabby and darker than that of the right. The blood vessels of the heart are congested and prominent and frequently a few haemorrhages show along the auriculo-ventricular junction. In many cases the foramen ovale is still patulous, but is competent.

Lungs. These organs are a light pinkish-gray anteriorly and a light purplish-gray posteriorly. They fill the pleural cavities and crepitate throughout. The anterior part of the lung is lighter and more fluffy than the posterior. Few or many petechial haemorrhages may show beneath the visceral pleura, especially along the junction of the lobes. Occasionally there is a slight increase of the pleural fluid.

A cut section shows a pinkish-gray surface, which may or may not exude some blood. Air can be expressed from all portions of the lung and usually also a slight amount of oedematous fluid. The posterior part of the lung is of a darker color and is heavier than the anterior and more fluid can be expressed from it than from the anterior part. The bronchi do not appear to be hyperaemic, but contain more or less frothy material and mucus. Sometimes this can be expressed from the smaller bronchi.

Spleen. This organ may be very hyperaemic and shows slight increase of splenic tissue, partially obliterating the normal markings.

Kidneys. The kidneys are of a reddish-gray color, foetal lobulations are prominent. A cut section is very moist and a considerable amount of blood oozes from it. Striations of the cortex are plainly seen. Except for congestion, the kidneys, in the greater number of cases, present a normal appearance. Occasionally a slight degree of albuminous degeneration or a few subcapsular haemorrhages occur. The adrenals show congestion.

Liver. The liver is dark reddish-brown in color and firm. Section shows congestion and rarely a slight "nutmeg" appearance is seen. The lobulations are usually clearly defined. Here, also, we may find some albuminous degeneration.

Stomach. The stomach nearly always contains some curdled milk and mucus. The mucosa is smooth and anaemic. No rice or other artificial food was found in the stomach of any of the cases; sometimes there is a trace of faecal material present.

Intestines. They are normal in appearance. The intestinal contents are semiliquid, apparently digested, and have a yellow color. The mesenteric glands may be slightly enlarged and soft.

Urinary Bladder. It may or may not contain urine.

Throat Organs. Except for some froth and mucus present in the larynx and trachea these organs are normal.

Thymus. The thymus is usually prominent and full. Some milky fluid can almost always be expressed from the cut surface.

Meninges and Brain. The meninges are congested and oedematous, and there is usually an increase of the cerebro-spinal fluid. The brain substance may be of normal consistency or soft and very moist."

Unfortunately in these autopsies it was impossible to secure satisfactory histological examination of the tissues owing to the length of time that always elapsed between the time of death and the post-mortem examination.

In his later paper Andrews describes 18 necropsies in eight of which the infants were seen during life. The macroscopic findings in these 18 cases agreed in all particulars with the description just given. With regard to these findings Andrews says: "The anatomic findings just described correspond very closely with those of moist beriberi in adults. Indeed, throughout the description, organ by organ, the findings are identical; or if any difference exists, it is of degree only.

"In these cases there are four points of special interest: First, the dilated and hypertrophied right heart; second, the congestion of the viscera; third, anasarca; fourth, the *absence of other findings* to account for death. I have relied on these points in making the diagnosis of infantile beriberi. In several cases I have seen a hypertrophied right heart in which I could account for the condition by a patent foramen ovale, which was not competent, or by an imperfect interventricular septum. All these cases have been excluded. Whenever death could be attributed to causes other than beriberi this has been done."

The necropsies in these later cases were secured soon after death and a microscopical investigation was accordingly made with the following result:

Heart. The muscle fibers of the right heart are hypertrophied and the muscle nuclei are apparently increased in number. In nearly all cases the cross striations are distinct without any appearance of degeneration. In a few cases there is a slight clouding of some of the fibers. The fibers of the left heart are of normal size, cross striations are distinct and no clouding of fibers is present. Congestion is present.

Lungs. The lungs present the picture of extensive hypostatic congestion and more or less oedema. The vessels are greatly congested, and the alveoli in the dependent portions of the lungs contain more or less granular debris. A few epithelial cells are scattered here and there in the alveoli and sometimes a few red cells. There is no evidence of fibrin by the hematoxylin and eosin stain and only a few leucocytes are to be seen. The bronchi present absolutely no evidence of inflammation. In the anterior portions of the lungs there is more or less evidence of emphysema as shown by the thinned and broken alveolar walls.

Spleen. The spleen shows intense congestion. In many places haemorrhages have taken place in the splenic tissue as shown by the almost solid mass of red cells present. There is no increase of splenic tissue.

Liver. Besides the congestion, the other changes are slight albuminous degeneration and fatty infiltration. The fatty deposit is scattered through the liver substance, but is probably more prominent around the portal-spaces. In some cases considerable haemorrhage is present beneath the capsule.

Adrenals. Other than congestion, they present nothing abnormal.

Thyroid. The sections of some cases show the presence of more colloid material than do the sections of others. Congestion is present.

Parathyroids. Aside from congestion they are apparently normal. The nuclei are deeply staining and are surrounded by a clear protoplasm. The cell membrane is clearly defined.

Thymus. In some cases there is possibly an increase of the cellular elements. Hassall's corpuscles appear normal. Congestion is present.

Kidneys. These organs are intensely congested. Albuminous degeneration of the convoluted tubules is shown in a number of the cases and a few show fatty degeneration in addition. The endothelial cells of the glomeruli seem to be increased in number, and in many cases there is a slight granular detritus in Bowman's capsule. *There is no infiltration of leucocytes.* There is apparently no difference between the sections of the kidneys in which oliguria was present and those in which it was absent. It is probable that the condition of the glomeruli and Bowman's capsule is due to the intense congestion present.

Nerves. Sections from various nerves (vagi, phrenic, intercostal and anterior tibial) were taken for staining. These were stained by Marchi's method and show degeneration of some of the fibers. The degeneration is not as extensive as is found in cases of adult beriberi, but is clearly defined.

The Heart. The weights of the heart in nine of Andrews' cases of infantile beriberi are as follows:

Case, number.	Age.	Weight in grams.
1435	....	22.0
1424	4 months	40.0
1488	1 month	27.7
1523	3 months and 12 days	33.7
1525	2 months	34.0
1536	1 month and 15 days	27.5
1561	1 month and 19 days	30.4
1595	2 months	54.0
1643	2 months	37.6
Average	....	34.1

The weights of the heart in eight infants who died of other conditions are as follows:

Case, number.	Age.	Diagnosis.	Weight in grams.
1603	5 months	Bronchopneumonia, marasmus	15
1605	7 days	Acute membranous enteritis	12
1623	7 months	Ulcerative colitis	25
1645	8 months	Gen. miliary tuberculosis	32
1654	9 months	Acute ulcerative colitis	17
1655	1 month	Acute colitis	25
1683	2 months	Lobular pneumonia	20
1689	9 days	....	14
Average	....	....	20

From these figures it appears that the average weight of the heart in cases of infantile beriberi is 34.1 grams, while the average Filipino infant's heart probably weighs about 20 grams. This difference is believed to be a fair indication of the amount of hypertrophy in infantile beriberi.

After comparing the observations of these different authors and checking them by personal investigation,* it seems probable that the essential morbid changes that occur in infantile beriberi may be summed up as follows: 1. A tendency to the accumulation in the tissues generally and in the body cavities of an excess of fluid, most commonly observed as (a) subcutaneous oedema. This may be general. More often it affects certain localities, as the feet, face, chest wall, etc. Even when no definite oedema is detected, after the tissues are cut it is apparent that they are more moist than normal. (b) A noticeable increase in the amount of pericardial, peritoneal or pleural fluid, which is usually of a distinct yellowish or greenish tinge. (c) Oedema of the meninges with increase in the amount of cerebro-spinal fluid. 2. Hypertrophy and dilatation of the right heart. This is usually the most pronounced change from the normal. The hypertrophy and dilatation which affects both right auricle and right ventrical is so pronounced that the heart of a three-months babe may be equal in size to that of a child of 10 years, and the right side of the heart may be four or five times the dimensions of the left side. The same is true of the thickness of the muscular wall, the right side being fully twice as thick as the left side. (See figure 43.) 3. Chronic passive congestion of liver, kidneys and spleen which may be so intense as to simulate active inflammation. 4. Punctate subpleural haemorrhages. 5. Degeneration of the nervous system. Degenerative changes have been demonstrated in the pneumogastrics, phrenic, intercostal and anterior tibial nerves and in the cervical ganglia. (See figure 44.)

It will be seen that these are exactly the same changes that are found post mortem in adults that have died of beriberi. If there were no other similarity between the two conditions we would, therefore, have very good reason for believing them to be the same disease. However, as will be seen, the symptomatology of infantile beriberi also presents a striking similarity to the symptoms observed in the adult.

Symptomatology. There are two typical varieties of infantile beriberi, an acute form and a chronic form. *Acute infantile beriberi.* This form, which is most commonly met with in Manila, is very abrupt in its onset. A typical case would be as follows: A young infant of from one to three months of age who has always apparently been healthy and well nourished is suddenly seized with paroxysms of pain.

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* Through the courtesy of Doctor Andrews the author was present at many of his autopsies on cases of infantile beriberi.

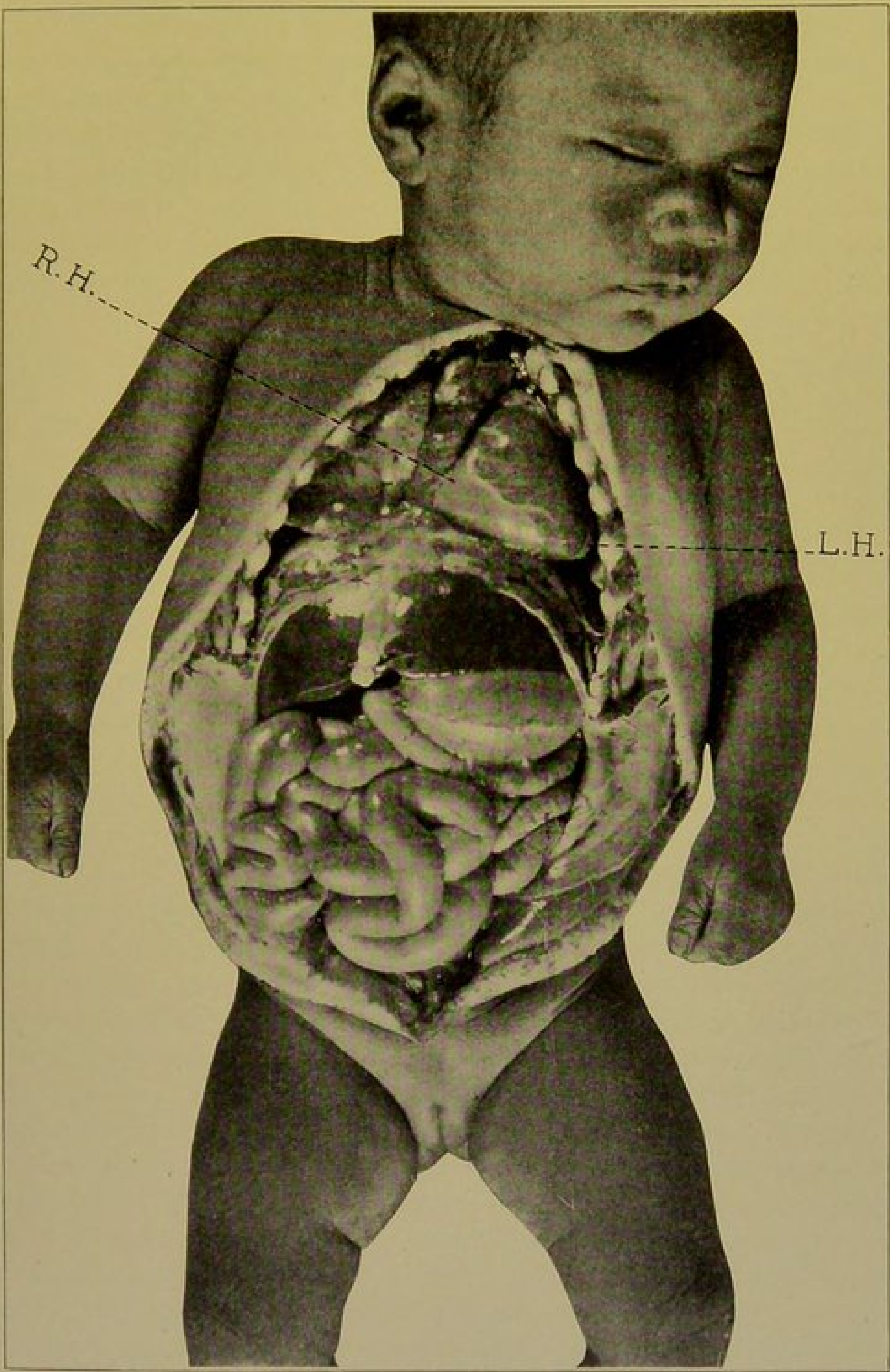


Figure 43. Child that died of infantile beriberi. The child is apparently well nourished. Note great hypertrophy of right heart. [From Andrews, and plate lent through the courtesy of the Philippine Journal of Science.]

During such a paroxysm the child straightens out his body and becomes quite rigid, the abdominal walls and epigastrium are tense and hard. He cries constantly, and gradually the face becomes cyanosed and the veins of the neck are engorged. The child acts as if in great pain. The pulse is very small and rapid, and the heart flutters. This attack passes off only to be repeated by others of a similar character at intervals of greater or less length and the child dies anywhere from a few minutes after the beginning of the seizure to 10 or 12 hours. In the rare cases in which an autopsy is obtained the picture outlined

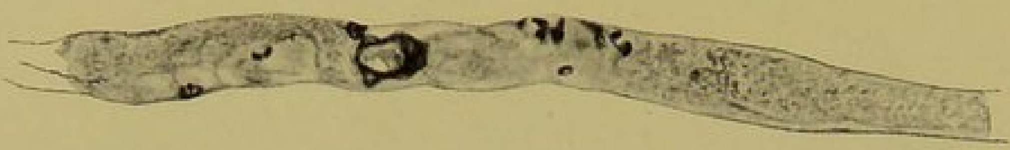


Figure 44. Degenerated nerve fiber from a case of infantile beriberi, Marchi stain. [From Andrews, and plate lent through the courtesy of the Philippine Journal of Science.]

above will be found. Such cases are frequently described in the death certificates as convulsions or meningitis, although there is no true convulsion, nor is there any fever. On questioning the mother, it will be found that the child was breast fed. Often the mother has had several children die in exactly the same way, and this history is of the greatest assistance in making the clinical diagnosis. It is by no means infrequent to find mothers who have had from three to six children who have all died of this dread disease. It is also by no means uncommon to find mothers who have had several children die in this way, and who have realized that the children died as a result of the breast feeding, and who have, therefore, fed one child on cow's milk or some artificial food, thereby saving its life. Such a history is almost diagnostic in itself and also clearly indicates that the disease is transmitted through the mother's milk.

Now, if the mother is questioned carefully, she will usually admit that she has or has had symptoms of beriberi, and an examination will almost surely demonstrate that she presents some mild symptoms of incipient beriberi, such as inability to walk far, hyperaesthesia in the calf muscles, diminished reflexes, delayed sensation or anaesthesia of certain areas on the foot and leg, etc. Nursing infants may be affected by this disease at any time after birth up to eight or ten months of age, but it is most common at about the third month. It has never been seen in infants who are artificially fed. It seems quite probable that the infants that die in this manner must have presented some symptoms of infantile beriberi previous to this acute cardiac attack. These symptoms are so slight, however, as to entirely elude the observation of the ignorant mothers who almost always state that the child was in good health prior to the fatal attack.

Chronic Infantile Beriberi. This form is more rarely seen, but the clinical picture which it presents is much more clearly defined and typical. The first symptoms are disturbances of the gastro-intestinal tract, manifested particularly in constipation and vomiting. Constipation appears to be an almost universal symptom, although Hirota has described cases having diarrhoea. This constipation is obstinate and does not yield to medicinal treatment. The vomiting is usually repeated several times during the day at irregular intervals which bear no relation to the time of nursing, and the ejecta appear to consist entirely of the milk with perhaps little mucus. The child now begins to be restless and fretful, especially at night, so that a good night's sleep is rarely obtained. These symptoms persist in spite of treatment and gradually the child becomes pale. This paleness increases until the skin is waxy or almost cadaveric except about the face which is apt to be cyanotic particularly about the lips and mouth. At the same time the child becomes very weak. All the muscles become soft and relaxed, although the limbs may not appear shrunken. The lips and eyelids may remain open during sleep.

Some time after the beginning of the symptoms detailed above, the circulatory system becomes affected. These symptoms may for convenience be discussed under the following subheads:

Cardiac Symptoms. On inspection the impulse of the heart is seen to be quite violent and rapid and the apex beat, which is usually quite visible, is displaced downward and outward appearing at about the sixth interspace well outside of the mammillary line. Epigastric palpitation is common. Palpation confirms these observations. Percussion shows the right heart to be greatly enlarged. On auscultation the heart sounds are found to be very rapid and greatly increased in volume particularly over the pulmonary valve where the second sound of the heart is heard as a dull thud instead of the usually snappy tone. There are usually no murmurs, however.

Vascular Symptoms. The pulse is rapid, soft and of low tension. It varies from 120 per minute to a pulse too rapid to count, but is usually regular. Hirota found a diastolic murmur in the femoral and brachial arteries in several of his cases.

The Blood. Takasu (1905) examined the blood of 38 children suffering with infantile beriberi and came to the following conclusions:

1. That the per cent of haemoglobin and the number of erythrocytes are both somewhat diminished in infantile beriberi. 2. In the acute severe cases, nucleated erythrocytes make their appearance in the blood stream. 3. In the chronic atrophic form of infantile beriberi the number of lymphocytes is increased.

Respiratory Symptoms. Severe dyspnoea accompanies the cardiac condition. This dyspnoea in certain cases does not appear to be constant, but recurs in paroxysms of variable duration. In other cases it is more constant.

Oliguria. This symptom is present to a greater or less extent in almost every case, and it is one that the mothers all notice. In the severe cases only a few drops of water may be passed in the twenty-four hours, and in every case the number of napkins used during the day is greatly diminished. It usually develops gradually and such urine as is passed is generally normal. Indican has been reported, but this reaction is often present in the urine of people who are constipated but do not suffer from any other disease. Since these children are almost always constipated we might expect to find indican in a certain percentage of cases.

Skin. The paleness of the skin with cyanosis around the mouth is quite distinctive. Sooner or later oedema makes its appearance in some parts of the body, in most cases the lower extremities being particularly affected.

Aphonia is a rather late symptom, and commonly appears suddenly. It usually alarms the mother, and justly so, for it is an indication that the disease is serious and well advanced. It must not be supposed from the use of the word aphonia that there is a complete loss of voice. The normal voice is lost, however, and all that remains is a plaintive whine or moan that is difficult to describe, but which is quite characteristic, and which when once heard will serve almost as a pathognomonic sign of the disease, since so far as I am aware a similar cry is heard in no other condition. And there is ample opportunity to hear it also for the child is usually very restless at this stage of the disease, rarely sleeps and whines or moans incessantly. This aphonia is probably caused by involvement of the pneumogastric nerve.

Nervous System. There are no symptoms referable to the nerves of the limbs, such as lack of sensation or paralyses. It should not be assumed from this statement, however, that such lesions in the nerves do not exist, but merely that it is a practical impossibility to make a satisfactory examination. The difficulty of such a procedure may be estimated by recollecting that the cases are usually infants of three months or less of age, and even the older cases who perhaps could understand a few words are accustomed to hearing only the native dialect. Even the sensation cannot be tested because the child is so restless and whines so much that the observer would be at a loss to determine whether he had elicited a response to stimulation or whether the movement or cry provoked at that moment was due to other causes.

This condition almost invariably ends in death if the mother continues to nurse the infant. This death may be very sudden and almost totally unexpected. In these cases death is usually due to cardiac failure and often resembles closely the sudden cardiac attack which constitutes the acute form of beriberi and which we have described under that heading. Since this acute seizure bears some slight resemblance to a convulsion, this may partially account for the large number of death certificates in Manila assigning convulsions as the cause of death. In other cases, one of the attacks of dyspnoea may become so severe that the child apparently dies of asphyxia. A slow form of death has also been reported, in which the child passes into a comatose state in which it lingers for some hours, and so dies very quietly.

Comparison with Beriberi in the Adult. At first sight it may appear that the condition that has just been described is quite different from beriberi as we are accustomed to see it in the adult. A little further consideration, however, will show that the acute form corresponds pretty accurately to the acute pernicious or cardiac form of adult beriberi after making due allowance for the fact that in the infantile form the child is unable to give us information as to its feelings. In the chronic form the symptoms correspond closely to beriberi in the adult with the exception of the motor and sensory disturbances which are so important a part of the clinical picture of beriberi, but which we must admit may easily be present in the infant without being demonstrable. The following table shows this striking similarity:

Infantile beriberi.	Adult beriberi.
1. Increased activity of heart.	1. Increased activity of heart.
2. Second sound increased over pulmonary valve.	2. Second sound increased over pulmonary valve.
3. Enlargement of heart down and to the right, almost always.	3. Enlargement of heart down and to the right, very common.
4. Dyspnoea.	4. Dyspnoea.
5. Aphonia very common.	5. Aphonia sometimes.
6. Vomiting almost constantly.	6. Vomiting often occurs.
7. Constipation usual.	7. Constipation common.
8. Cyanosis frequent.	8. Cyanosis frequent.
9. Oedema almost always.	9. Present in the "wet" form.
10. Oliguria common.	10. Urine often diminished.
11. Motor and sensory disturbances not demonstrated.	11. Motor and sensory disturbances usually found.

Etiology. Since infantile beriberi is encountered in infants who nurse mothers suffering from this disease, but is not found among artificially fed babies, and since merely removing them from the breast and feeding them with other milk is sufficient to cure them, it seems impossible to escape the conclusion that the disease is transmitted in the mother's milk. Accepting this as the fact, there are three further possibilities: (1) That an infection is so transmitted. (2) That a toxin is transmitted. (3) That a deficiency exists in the milk. Hirota first pointed out that it was extremely improbable that an infection was transmitted because the cases recover too promptly when fed artificially. The improvement takes place at once, almost miraculously, and in some cases in two or three days after the change in diet the infant may appear to have entirely recovered its health. Only the presence of aphonia or some other symptom due to degeneration of nerves remains. Now, if it were an infection transmitted in the milk the disease should run a definite course, like other infectious diseases, and it is incredible that it should be suddenly cured by a mere change of diet. Hirota concluded that the disease must therefore be due to a toxin transmitted in the mother's milk, a conclusion that can only be reached from these premises by ignoring the possibility that the mother's milk is deficient in respect to some element.

Guerrero and Quintos and practically all of the Filipino practitioners have also given their adherence to the intoxication theory. In coming to this conclusion they have been influenced chiefly by the authority of Hirota and by the experiments of Inagaki and Nakayama, Inagaki and Nemori, and Guerrero and Gavieres. These latter authors all performed experiments with frogs' hearts, and all agreed that the milk of a mother whose child suffered from infantile beriberi possessed the property of paralyzing the frog's heart. All of these authors concluded that the changes observed in the cardiac contractions must be due to the presence of a beriberic toxin in the milk.

The observed facts appear to be correct, since the experiments were carefully controlled by using normal milk, Ringer's solution, etc., in parallel experiments. But granting that the facts are correct, it does not logically follow that nothing but a toxin could produce this effect on the frog's heart. On the other hand, if such a toxin were present it should be possible to isolate this poison from the milk and prove its existence by unequivocal experiments. All attempts to isolate such a toxin from the milk of beriberic women have failed completely.

Direct proof that infantile beriberi is not a toxaemia was secured in 1912 by Chamberlain and Vedder.

These observers succeeded in obtaining typical cases of infantile beriberi, which were treated by the administration of a concentrated extract of rice polishings (see Appendix, page 405), in amounts equivalent to about 80 grams of polishings daily. *They received no other treatment and continued to nurse their mothers.* The mother's food was unchanged. Chamberlain and Vedder state: "The mothers have all had symptoms of incipient or marked beriberi. In the incipient cases the symptoms have been numbness and pain in the legs, severe pain when the muscles were squeezed, and in some instances localized anesthesia and loss of knee jerks. In the more advanced cases oedema and rather marked paraplegia were present. A number of these mothers have previously had infants die with symptoms similar to those presented by the children which were brought to us. In every case the diet of the mother has been chiefly highly milled rice, with a little fish and occasionally a bit of meat.

"The children have all been breast fed. With one exception all have been under three months of age. The disease usually has been ushered in with vomiting, which after a few days was followed by great restlessness, sleeplessness, continual whining and later by dyspnoea, increased cardiac action, and edema of the face and legs. Later still oliguria and aphonia developed in many of the patients. About one-half of the cases we treated have had aphonia, and some appeared to be at the point of death. On the other hand, several cases were milder. The above is not intended as a complete clinical history, but merely as an indication of the class of cases we have treated.

"The infants were all given twenty drops of the extract of rice polishings every two hours while awake, and the results have been truly marvelous. Improvement is immediate. The vomiting stops in 24 or 36 hours. The child, who has not passed any urine for several days, urinates five or six times freely. The edema disappears in the course of a few days. Usually on the first night after treatment is begun the infant falls into a deep sleep, although it may have been practically sleepless for several weeks. The dyspnoea and palpitation cease after two or three days. At the end of a week, or in less time, the patients are completely cured with the exception of the aphonia. The mother assures us that the baby is well, and that she would be completely satisfied if only it would recover its voice. The aphonia, however, does not disappear until after about two months of treatment, when the voice usually returns quite suddenly. This is probably due to the fact that the aphonia is caused by degeneration of the pneumogastric nerve, which only slowly regenerates.

"It can be said that this extract is a 'cure' in the true sense of the word, just as lime juice is a 'cure' for scurvy, and that it acts with as great promptitude as does fruit juice in infantile scorbutus." *

In these cases improvement was marked from the first day of treatment. These observations render it extremely improbable that a toxin is the cause of this condition. If the milk contained a toxin, since the children were permitted to nurse their mothers and thus to continue to receive this toxin, one must explain the results obtained on the supposition that the extract of rice polishings contained some substance capable of neutralizing this toxin. If this were the case, fresh cow's milk must also contain a substance capable of neutralizing this toxin, since cases of infantile beriberi can be cured by substituting cow's milk for part of the feedings and permitting the child to nurse the mother for the remaining feedings. Such a supposition is extremely improbable, and it should be emphasized that this same extract prevents and cures polyneuritis in fowls, and has been used in the treatment of adult cases of beriberi with marked success. That polyneuritis gallinarum and adult beriberi are not due to an intoxication, but to a deficiency, has already been established.

Having thus excluded the infection and intoxication theories, we are left to consider the theory that the disease is due to a deficiency in the diet. We must accept this theory tentatively, since it is the only one left to us. But an investigation of the facts only makes this theory seem more probable. The cases appear for the most part in families where polished rice is almost the exclusive diet. It has been shown that polished rice produces beriberi in men and polyneuritis gallinarum in fowls, because it is deficient in a substance necessary for nerve nutrition. The cases of infantile beriberi are all cured by proper feeding.

The disease is practically never seen among children of the white race.† This is undoubtedly because beriberi among the adults of the white race is also practically unknown. This is a strong argument against any infectious agency, as well as against an intoxication.

The great majority of these cases are seen among the poorest class of natives; in other words, the very ones who are of necessity compelled to live almost solely upon rice with a little occasional fish or

* Chamberlain and Vedder reported fifteen cases treated in this manner with no deaths. I have since continued this work and in all have treated about forty cases with uniform success.

† I have myself seen one case in an infant of a well-to-do Spanish family. The mother stated that she lived largely upon rice and bread because she did not like meat and many vegetables. She refused to eat beans. The child was cured by the administration of extract of rice polishings.

meat. Like beriberi in adults, it is reported to be found on rare occasions among well-to-do native families who are able to purchase a varied and proper diet. This fact has been urged against the rice hypothesis as the cause of both these forms of beriberi. But this is merely presumptive evidence. Such well-to-do families would certainly purchase the most highly polished grade of rice, since the whitest rice has always been the most highly esteemed, and it is quite conceivable that in a few instances, as a result of peculiarity of taste or for other causes, these individuals have subsisted almost wholly upon rice. There is absolutely no evidence to the contrary. The actual diets of these cases have never been reported, and in the absence of this evidence a few cases occurring in well-to-do families should not be allowed to counterbalance all the great mass of evidence showing that beriberi is caused by a deficiency in the diet usually due to the almost exclusive use of polished rice.

Infantile beriberi may be seen at any time of the year, but it occurs with the greatest frequency during the months of September, October and November. This is just the time when beriberi is most frequent among adults, so that the women who give birth to children at about this time are much more likely to suffer from beriberi than at other seasons of the year.

Finally we come to a most important point, namely, the age at which infantile beriberi appears. It sometimes appears soon after birth, and the great majority of cases appear before the end of the third month. Cases are practically unknown in infants of 12 months or more of age. Guerrero and Quintos tabulate 176 cases as follows:

1st month	39
2nd month	62
3rd month	49
4th month	12
5th month	6
6th month	2
7th month	3
8th month	2
9th month	1
Total	176

It is difficult to explain this peculiar incidence of beriberi in the first three months on an intoxication hypothesis, since children continue to nurse their mothers the greater part of the first year. But this peculiar incidence may be readily explained according to the deficiency hypothesis, as follows:

It is during the first few months of life that the infant subsists on milk alone. After the fifth or sixth month they may in many cases receive some other food which supplies the existing deficiency. Moreover, these infants are born of mothers that suffer themselves from beriberi. The mothers' systems are already suffering from the lack of the particular vitamines which prevent the disease, and they are therefore incapable of supplying the fetus with these substances in sufficient quantities. The child is therefore already suffering from this deficiency when it is born, and it is then fed on milk from the same mother which is also deficient in the necessary substance.

If this deficiency has been absolute, the child will have beriberi when it is born, as in the case reported by Tanaka. But if, as is more usual, the deficiency is only partial, and the child is born without symptoms of beriberi, but is then fed on milk from the beriberic mother, which is similarly deficient, beriberic symptoms will soon appear in the child, and almost always inside of three months. For we now know that men that are fed on a diet deficient in these vitamines, i. e., polished rice, develop beriberi after an incubation period of three months. From this it appears that even if the child was born normal, but was supplied with milk in which the vitamines were deficient, the disease would usually appear inside of three months.

But a few cases appear after a longer interval. This is due to the fact that these cases receive a partial supply of the essential vitamines in their mothers' milk; not sufficient to entirely protect them, but sufficient to prolong the incubtion period.

This theory also explains the well-known unusual prevalence of beriberi among pregnant and parturient women. Such women are attempting to supply the fetus or the nursing infant with the necessary vitamines of which they are already receiving barely enough to supply the necessities of their own metabolism. The new drain proves too much, and they develop beriberi themselves.

There is still one more point which can be explained in accordance with the deficiency theory, but hardly if beriberi were an intoxication. Hirota reported the case of a child suffering from beriberi although the mother was at the time apparently normal. The mother developed beriberi 29 days later. I have myself seen several similar cases, which, moreover, have occurred in mothers that so far as I am aware never developed symptoms of beriberi themselves. It seems strange that if beriberi were due to a toxaemia, and the mother was so thoroughly impregnated with this toxin that she was secreting it in her milk and thereby poisoning her child, she should not show symptoms of the disease herself. On the other hand, we may readily suppose that in these cases the mothers are receiving just a sufficient amount of the vitamines to prevent the development of beriberi in their own persons, but not enough to furnish a supply of these substances in their milk. The child would therefore suffer from the deficiency although the mother did not.

From all these considerations we come to the conclusion that infantile beriberi is due to a deficiency of some substance in the milk of the mother. Attempts have naturally been made to determine the exact nature of the substance that is deficient by means of analyses of the mother's milk. Most of the earlier analyses were unsatisfactory, but Andrews has reported 11 which cannot be questioned. The milk in each case was obtained from women whose infants had just died of beriberi, the diagnosis being confirmed by necropsy. A sufficient amount of milk was collected, under such precautions as ensured that the milk did not undergo bacterial changes, and the analyses were made by a competent chemist.

The following table, taken from Andrews' paper, shows the result of these analyses:

Case No.	Volume.	Specific gravity.	Water per cent.	Fat per cent.	Sugar per cent.	Proteid per cent.	Ash per cent.	Calcium oxide CaO parts per 1,000 of ash.	Phosphorus pentoxide P_2O_5 parts per 1,000 of ash.
*........	......	1.028	87.30	4.00	7.00	1.50	0.20	0.328	0.473
1........	......	1.032	88.26	2.82	7.70	0.92	0.30	1.603	0.946
1........	215	1.032	88.95	2.29	7.16	1.50	0.10	....	....
2........	......	1.032	89.75	1.76	7.53	0.85	0.11	....	....
3........	255	1.041	85.75	4.05	8.36	1.50	0.34	....	....
3........	195	1.029	88.27	3.52	5.22	2.70	0.29	....	....
4........	88	1.029	90.37	1.76	6.51	1.30	0.06	....	....
5........	120	1.036	89.43	1.06	7.71	1.70	0.10	1.072	0.323
6........	46	1.020	90.52	3.52	4.98	0.90	0.08	....	....
7........	130	1.033	89.03	2.11	7.61	1.15	0.10	0.742	0.471
3........	107	1.034	88.39	2.46	7.44	1.50	0.21	1.312	0.626
8........	149	1.033	90 14	1.06	7.64	0.90	0.26	1.502	0.663
9........	......	1.038	88.10	1.76	8.54	1.50	0.10	....	....
10........	51	1.029	88.27	3.52	6.66	1.40	0.15	....	....
11........	......	1.034	87.12	3.52	7.60	1.50	0.26	....	....

* The first line of figures in the table shows the percentage of the various constituents of milk of the average normal woman as given by Holt. The calcium oxide and phosphorus pentoxide, however, are taken from Hammerstein's Physiological Chemistry.

From these analyses it may be seen that, although the amount of fat is usually below normal, cases 3, 6, 10 and 11 contain plenty of fat. In view of this fact, and since case 3, in which the milk contained the most fat, was one of the most severe cases studied, we may conclude that infantile beriberi is not caused by a deficiency in fat. By the same reasoning we may conclude from these analyses that the disease is not caused by a deficiency in proteids, inorganic salts or phosphorus. Thus, in one case the amount of phosphorus pentoxide is almost double the quantity usually found in normal milk.

Since the deficiency clearly does not consist in any of these elements, and since the extract of rice polishings, which cures cases of infantile beriberi, is the same that cures cases of adult beriberi and cases of polyneuritis gallinarum, it appears that infantile beriberi is caused by the same deficiency of vitamines which produces adult beriberi and polyneuritis gallinarum.

We are now prepared to discuss the question as to whether infantile beriberi is the same disease as adult beriberi. This has been doubted by some authorities in Manila and elsewhere. As we have already said, the identity of the two diseases is to be established by a careful study of the pathology, symptomatology and causation of both.

It appears to me that so far as they have been investigated there is not the slightest difference in the pathological anatomy of these two conditions. The pathology of both diseases has been very fully described, and it is believed that by simply reading the one account, and then turning to the other and reading it, almost any one would be convinced that the two descriptions are of one and the same condition.

The same statement can be made with regard to the symptomatology of the two diseases. It is practically identical in both cases, except for the fact that paralysis and sensory disturbances in the limbs of the infants are not usually observed, and once more we emphasize the fact because these phenomena cannot be determined in young infants we should not assume that they are absent. The nerves in these limbs show the anatomic changes of degeneration. Infantile beriberi has now been observed and reported by a number of workers in Japan and the Philippines, notably by Andrews, who has correlated the symptomatology and pathology by studying the cases during life and subsequently performing the autopsies. Therefore the statements that have been made both with regard to the pathology and the symptomatology of infantile beriberi have been fully confirmed. Finally, it has been shown that the etiology of infantile beriberi and adult beriberi are the same, both being caused by the deficiency of certain vitamines in the food. It is, therefore, my belief that infantile beriberi is the same disease as adult beriberi.

Treatment. In accordance with the theory that the child was receiving a toxin in its mother's milk, Hirota and subsequent observers have treated this condition almost entirely by artificial feeding. From the first it has been recognized that medicines were useless. Under certain conditions this treatment would be perfectly satisfactory, but it is practically impossible to apply it to the infants suffering from beriberi in the Philippines. These cases occur among the very poor, who never dream of keeping ice, and there is no satisfactory supply of fresh milk in the Philippines. Canned milk is expensive. To feed an infant for a month on canned milk costs about 10 dollars. This is impossible for these people, and the physician who would recommend it under these circumstances is like the man who recommends a trip to Europe to a poor clerk. Such recommendations are productive only of despair. In addition to this, it would be unwise to recommend artificial feeding even in the few cases where perhaps this luxury was procurable, since the mortality among artificially nourished infants in the Philippines is also high. If it is difficult to train a mother to prepare an infant's milk properly in the United States, it is an impossibility among the natives in the Philippines. Realizing these facts, some of the practitioners in Manila, though still obsessed with the toxin theory, have begun to treat these cases by feeding the mothers rice bran and mongos. It is difficult to understand how this method of treatment can effect a cure, if the disease were an intoxication. Guerrero reports ten cases of infantile beriberi successfully treated in this manner. About fifty grams of rice bran and 160 grams of mongos (Phaseolus radiatus) are given daily to the mother in addition to her usual diet. At the beginning of treatment lactation is suspended for 10–45 days, with a view of giving time for the elimination of toxin. Rice bran may be given in the form recommended by Breaudat, mixed with simple syrup and essence of peppermint. Occasionally decoctions prepared from rice bran also have been used.

This method is open to the criticism that it necessitates feeding the child artificially during the time it is removed from the breast, and if this time is prolonged to 45 days, as was done in several cases reported, the mother's milk would be likely to disappear. It is also open to the further criticism that, since recovery is usually very prompt in these cases, practically always taking place in less than a month where they are artificially fed, there is no proof that it was not this artificial feeding of the child, rather than the feeding of rice bran and mongos to the mother, that produced the cure. Since the feeding of these substances to the mother could only do good in case the theory that a deficiency in the mother's food was the cause of the condition, it is unfortunate that Guerrero did not give this theory a fair chance by allowing the child to continue nursing while feeding the mother in this manner.

Again, rice bran is very unpalatable, and perhaps indigestible, and since it is very light, 50 grammes is a considerable bulk to eat daily. No method of administration wholly avoids these objections.

The following treatment of these cases is therefore recommended: The child should be given an extract of rice polishings, in such dosage that it will receive the equivalent of 100 grams of rice polishings daily. This treatment should be continued for several weeks, and the child should nurse its mother in the meantime. The mother should be prohibited from using polished rice, and should be instructed as to the nature of unpolished rice, and directed to some place where it may be purchased. She should also eat about a pound of mongos or other variety of beans each week. This is all the treatment that is necessary, and its rationale is as follows: The child receives the extract of rice polishings for the first week or two because this extract contains the substance that has hitherto been deficient in the infant's food in a very concentrated and digestible form. Since there is no infection and no toxin to be eliminated, it is unnecessary that the mother should cease to nurse the child, but in order to prevent a recurrence of the same disease when the rice extract is discontinued it is necessary that the mother should herself be properly fed. The undermilled or unpolished rice is much better for this purpose than the continued use of polished rice plus the administration of rice polishings. It accomplishes precisely the same end, namely, the ingestion of the pericarp and aleurone layer of the rice with their neuritis preventing vitamines, but in a perfectly natural manner, instead of necessitating the administration of a bowl of horse feed every day. (Rice polishings are used for fodder in the Philippines.) The addition of mongos or other beans to the diet is perhaps unnecessary, but is advisable, since in using both unpolished rice and mongos the patient is being doubly protected. In case, through ignorance or negligence, she returns to the polished rice, she will still be receiving a neuritis-preventing food.

Prophylaxis. The prophylaxis of infantile beriberi is exactly the same as that of adult beriberi, to the discussion of which the reader is referred. It is only necessary to say here that the disease may be absolutely prevented if those people who are in the habit of living upon an exclusive rice diet, or such a diet interspersed with fish and a little meat, can be induced to consume undermilled or unpolished rice in place of the accustomed polished or white rice.

CHAPTER XIII

SHIP BERIBERI

True Asiatic beriberi frequently occurs on ships. It has never been doubted that the beriberi occurring in the Japanese navy and in the Dutch East Indian navy was true beriberi. In addition to these classical cases, epidemics of true beriberi on certain ships have been reported by numerous observers. These epidemics have generally been observed on ships that have departed from countries where the disease was endemic, and whose crews have been composed in whole or in part of oriental rice eaters, and the disease has usually been confined to these orientals, while the ships officers and European members of the crew have almost invariably escaped. Such instances are so numerous in the literature and, as a general rule, add so little to our knowledge of the disease, that it is unnecessary to attempt to consider them here.* We have already seen that Asiatic beriberi is caused by a diet that is deficient in certain vitamines, this deficiency usually resulting from a too exclusive use of overmilled rice. If this be granted, it follows that beriberi will occur on shipboard, just as it does on land, whenever the circumstances of the voyage are such that the crew is compelled to subsist chiefly on overmilled rice for a number of months.

There is, however, a disease affecting European or American crews, particularly of sailing ships which may never have had any connection with the countries where beriberi is endemic. This disease is so strikingly similar to true Asiatic beriberi that it has generally been called ship beriberi. Yet practically all writers have thought that differences between ship beriberi and true Asiatic beriberi exist, and these differences have been so constant that the majority of those who have investigated this so-called ship beriberi have concluded that it is not identical with true beriberi. It is this so-called ship beriberi affecting sailors of the Caucasian race that we now propose to discuss.

In the first place, while true beriberi has been known for centuries, ship beriberi has only been distinctly recognized comparatively

* There is one instance, which is so instructive with regard to the etiology of the disease, that it is desirable to quote it. This is an epidemic on a ship which was reported by Spliedt, and an abstract of his account may be found on page 412 of the Appendix.

recently. It is true that old European authors in speaking of the hygiene of ships referred to white scurvy, marine asthma, scorbutic hydraemia, etc., and these conditions were very probably ship beriberi, but the fact was not recognized.

Shattuck reported an epidemic of what was probably ship beriberi on the Nelly Swift in 1881. Roosevelt reported an epidemy of beriberi on the Henry S. Sanford in 1887. In 1890 Putnam reported several cases among New England fishermen, and referred to other cases of what seemed to be the same disease antedating these by ten years. In the same year Birge recognized that beriberi might affect sailors of the Caucasian race. He described an epidemic that occurred among those fishing on the Newfoundland banks in October, 1890, when no less than 20 cases were landed from vessels which had returned from fishing on these banks. Eleven of these cases were from one vessel, which had a complete crew of 13. Of these two died within 28 hours, another died later of hydrothorax, and the rest recovered. These authors apparently considered the disease to be true beriberi, although they were undoubtedly dealing with the condition now called ship beriberi.

Bullmore investigated the disease in 20 ships and published his results in 1900. The Norwegian Commission studied ship beriberi as it occurred in 104 ships and reported in 1902. Nocht investigated 34 ships and published his conclusions in 1903. Exact information as to the disease, therefore, begins from the above dates.

In later years many authors have discussed ship beriberi, and a considerable treatment of the subject may be found in the books of Braddon, Jeanselme and Le Dantec.

Symptomatology. Nocht studied this disease in sailing ships returning to Hamburg. He investigated 34 ships that had been attacked by ship beriberi, and there had been 282 cases among the men who comprised the crews of these vessels. He is, therefore, well qualified to describe the disease, and his account is briefly as follows:

The symptoms of the disease and its course were practically the same in all the cases. Most of them were only seen by a physician during convalescence, but a few of the worst cases were seen in the last stages. The early symptoms were practically never seen, but the patients themselves described them vividly. The disease was never acute, and lasted several weeks in the shortest cases, and often lasted for months. It began with loss of appetite, nausea and obstinate constipation, and a feeling of general weakness. There was often an eruption of vesicles in the mouth. Soon swelling appeared about the ankles which progressed slowly but steadily upwards until it reached the abdomen or chest. With this was a feeling of formication and slight numbness (papiersohlengefühl) in the feet. Next shortness of breath and palpitation of the heart. They were unable to walk upon their swollen legs for weeks at a time, and finally became bedridden because of the advancing dropsy and increased shortness of breath. Death followed with the phenomena of heart failure. Towards the end there were often pains in the stomach and vomiting sometimes even of blood. Fever appeared only as a complication. In many cases the disease was associated with hemeralopia. So long as the ship remained at sea and had no fresh provisions the disease in no case showed an inclination toward recovery, but on the contrary the symptoms became worse from day to day and the longer the voyage lasted the more of the previously healthy crew were attacked. But when the ship put in port or received fresh provisions and vegetables from a passing steamer the picture changed. Fatalities occurred only in the first few days thereafter and among the most severe cases while the remainder invariably recovered in from 8 to 14 days, and so completely that no trace of the disease was left. It is always a matter of surprise to the seamen to see such a rapid recovery. Exceptions to the rule of complete recovery are very rare. *Such an exception was Seiffer's case in which a marked paresis of the legs with degeneration reactions in certain muscle groups and sensory defects remained for a long time. I have also observed some cases (one from the Netherland, one from the America and a few cases from the Kaiser) in which signs of a true neuritis still remained.* (Italics ours.)

Another description is the following given by Bullmore, who in his capacity as surgeon to the Falmouth Hospital studied the disease in 20 ships that were affected with the disease when they entered Falmouth:

During the first few days the patient complains of general malaise, loss of appetite, headache, etc. Little if any temperature. The malaise is generally followed by a strange loss of power in the lower limbs and complained of at first as stiffness. This loss of power slowly increases so that the men have to hobble about as best as they can with the aid of ropes, deckhouses, hatches, etc. About this time, too, in about 50 per cent of the cases, a numbness of the lower extremities is often felt and a tickling or pricking sensation is complained of. These symptoms are generally followed by oedema of the dorsum of the foot or ankle, which spreads slowly up the limbs to the trunk. I once saw a patient who was simply water-logged. He would pit anywhere below the neck, but his face and neck were quite natural. In a majority of cases the feet and legs are attacked first, but I have seen anasarca of the scrotum, abdomen and chest with no oedema whatever in the legs. *Many cases even have no oedema at all and are evidently the dry beriberi of some authorities.* (Italics ours.) When the oedema subsides, the state of the neurotic mischief becomes manifest; the legs are most sensitive to tactile impression and have a dull aching pain which the sailors bitterly complain of. The tongue is generally clean, pale, flabby and frequently tooth indented; the gums are pale, not spongy or swollen; the voice is natural; the breath is offensive; bowels as a rule freely open. Urine usually normal in amount and usually free from albumen. I have tested 20 samples and found albumen in two cases. Pulse is full, strong and slightly quickened, ranging from 90 to 120. Respiration is quickened. There is palpitation of the heart and epigastric pulsation is felt. The commonest forms of heart lesion in my experience have been dilatation of the left ventricle and mitral regurgitation. Pupils, smell and sphincters are unaffected. Deeper reflexes in well-marked cases are lost, but I have had distinct knee jerk and ankle clonus in mild cases.

Pathology. Autopsies have been only rarely obtained, since almost all the cases die at sea. One case is reported by Nocht, and the lesions were as follows: Severe anasarca of the lower extremities and small collections of fluid in the pleural and pericardial cavities (about 75 cubic centimeters). The abdominal cavity contained no fluid. The heart was generally hypertrophied and dilated and showed microscopically a granular clouding of the fibers but no fatty degeneration. Kidneys presented the picture of acute parenchymatous degeneration. No degeneration was found in the nerves, but Nocht does not say what nerves he examined. Aside from the fact that neuritis was not demonstrated, the above might well pass as an autopsy of Asiatic beriberi. In the absence of this neuritis a suspicion might arise that we are simply dealing with Bright's disease. However, the case was only one of a number of similar cases that developed on a ship and was observed in hospital in Hamburg before death. It is quite improbable that Bright's disease is epidemic on shipboard or that a fatal case of this disease would be mistaken for ship beriberi in a Hamburg hospital.

Mortality. This appears to depend upon the length of time the crew is compelled to live on an improper diet. If the voyage is prolonged and fresh food is not obtained from passing ships the disease not only affects more members of the crew but becomes increasingly severe in those affected and the mortality is then heavy. It is possible that if the improper diet were continued long enough, practically all would die. It will be seen from this that no exact percentage of death can be expected of a given epidemic. We have, however, the statistics from a large number of ships of different nationalities, and making voyages under various circumstances, and the average mortality of these ships may fairly be taken as the mortality of ship beriberi. The figures are as follows:

Norwegian Commission	104 ships	574 cases	85 deaths.
Bullmore	20 ships	91 cases	18 deaths.
Nocht	34 ships	282 cases	44 deaths.
Total		947 cases	147 deaths.

This shows that in a series of 947 cases the average mortality has been about 14.4 per cent.

Etiology. The disease is practically limited to sailing vessels, and for this reason has been called by Nocht *Segelschiff beriberi.* It also occurs more frequently in Norwegian ships than in ships from any other nationality, and because of this frequency the Norwegian government appointed a commission to study it. Of the 104 ships that this commission investigated, 79 were Norwegian. German ships are also quite frequently affected. The disease only appears on those vessels that make long voyages. It often occurs, for instance, on those vessels that make the trip from Europe around Cape Horn to North America. Such a voyage last for three or four months, during which the ship may not put in port. It was under precisely such circumstances that scurvy used to develop, and these ships usually carry lime juice for the prevention of this malady. Sailors frequently call these vessels "lime juicers" from this circumstance. Some of these ships stop at ports in Central America and then return home, but it is said that fresh provisions in these regions are scanty and expensive and the crew continues to live largely upon sea rations on the return trip. Ship beriberi has sometimes developed on ships that appeared to have been properly supplied with food. When the circumstances of such a trip are investigated it frequently transpires that the ship encountered stormy weather and was greatly delayed so that the provisions became exhausted and the men were obliged to live on a one-sided diet of hard tack and salt pork, etc. Sometimes provisions have spoiled, and flour, beans or salt meat have been thrown overboard. Sometimes indeed the men have been compelled to eat the spoiled provisions because there had been nothing else. Even at the best the food used on such long voyages is very monotonous. Rice is seldom used.

A concrete illustration of the above is the following account of an epidemic on the Tarapaca, reported by Le Dantec. This ship left La Pallice September 30, 1901, with a crew of 35 men, and reached Chile February 28, 1901. It remained 52 days in this country and sailed for Europe, taking 123 days on the return trip. The disease appeared while the ship was becalmed in the tropics by suddenly attacking three men, and all the crew were subsequently affected more or less severely. On arriving at Falmouth the captain was obliged to send ten men to the hospital, where the disease was characterized by generalized oedema, asthenia, breathlessness, etc. On the return voyage the potatoes and beans were thrown away and partially replaced by rice and peas. Salt bacon was used as a meat. (Jeanselme.)

The cause of this disease is undoubtedly to be found in the improper food supply. The disease is clearly not infectious, and, unlike Asiatic beriberi, this fact has been recognized by all writers. In the first place the disease does not manifest itself until the ship has been out of port for several months. Bullmore states that during all the years that beriberi cases have been landed at Falmouth no preventive measures have ever been taken to prevent its spread. The patients have been admitted to the sailors' home, and not a single fresh case has occurred from infection. It is not due to bad general hygiene, for with few exceptions the ships in which beriberi occurred were in good sanitary condition, although the ventilation might have been improved. This is not important, since on a sailing vessel the men spend a large part of the day on deck. Bilgewater, galleys, forecastle and water tanks were in a satisfactory state even when a majority of the crew were affected. It is not a place infection, because ships do not continue to have the disease. Bullmore quotes a Norwegian bark in Falmouth in 1896 when some of the crew had beriberi. This ship called again in December, 1899, and had been free from beriberi during this long interval, although no sanitary measures had been taken during that time beyond cleansing the water tanks. Up to this point there is very general agreement among authors.

There are two theories with regard to the food supply on which there can be a difference of opinion. The majority of writers have considered that the disease is an intoxication caused by spoiled food, while some have considered that it was due to some deficiency in the diet, and a few have claimed that it is due to both of these causes.

The conclusion of the Norwegian Commission was to the effect that beriberi is the Oriental name for multiple neuritis, and is the result of intoxication by spoiled animal or vegetable food. Beriberi in Asia is chiefly caused by spoiled rice, and is the vegetable form of the disease. The animal form corresponds to ship beriberi, and is caused by the use of spoiled preserved food. It is not caused by a specific microorganism, but since it occurs under certain conditions when bad food is used, it must be due to the working of certain widely distributed bacteria of putrefaction.

With regard to ship beriberi, the commission's conclusions are not borne out by their own facts. Ship beriberi has appeared many times when no decomposition of the food had occurred. Of the 104 ships that they investigated, they were only able to mention seven crews who received bad provisions, and in none of these cases was it evident that the cause of the disease was the damaged food. In some of these cases, indeed, the tainted aliment consisted of potatoes, which were thrown overboard, and the disease did not break out for from 4–6 weeks afterward. On the other hand, the report of the committee contains the evidence that six crews were attacked in spite of the fact that there was direct proof that the food was of good or even excellent quality.

Moreover, this committee, as well as Ekelof, who made a report of the sanitary conditions during the Swedish South Polar Expedition of 1901–1904, attributed ship beriberi particularly to spoiled animal food. This seems most improbable on theoretical grounds and experimental evidence. Meat, particularly canned meat which has decomposed, is of two sorts. It is either contaminated with the ordinary saprophytic bacteria, and is so offensive that it could not be used as food, or it is apparently good, but contains ptomaines, which are tasteless and odorless, and the meat may be eaten. But under these circumstances acute ptomaine poisoning results. If is safe to say that there is no known decomposition of meat which is unrecognizable by its odor and taste, and which will allow of meat being used for weeks or months with apparent safety, only to be followed by an acute intoxication like beriberi. No such form of putrefaction or decomposition has ever been demonstrated. Finally, it may be added that the medical inspector of the Medical Government Board of Norway, Doctor Geirsvold of Christiania, has examined a great number of boxes of tinned meat and fish from six beriberi ships. He examined them microscopically and made aerobic and anaerobic cultures of their contents, but none of the boxes showed any sign of being tainted. On the contrary, all boxes were sterile except one containing a small number of an aerobic bacillus, which had not been able to develop under the anaerobic conditions inside the tin. (Holst.)

Since it is therefore shown that the conclusion of the Norwegian Commission, that ship beriberi is caused by decomposed animal food, was not in accordance with the facts, and is theoretically improbable, while all are equally sure that some dietary defect is the cause, it seems reasonable to suppose that that defect is a deficiency. Nocht practically comes to this conclusion: While not admitting that the disease is true beriberi, he concludes that it is a disease of faulty nutrition closely related in its etiology to scurvy. It seems most probable that this is the case. It is admitted that a ration of salt pork and hard bread has frequently caused scurvy, and that the diet of these ships is extremely limited in variety and most monotonous even when it is plentiful and of good quality.

But why should Norwegian ships be so frequently affected? Holst has afforded a satisfactory explanation. He says: "The disease was rather rare on board Norwegian ships till 1894. After that year, it has, however, been frequent. This frequency coincides with some alterations of the food on board Norwegian ships on long voyages, introduced by a new scale of diet of the same year." "Norwegian crews eat bread as the staple of their daily food. Till 1894 our sailors used, on long voyages, biscuits baked of rye flour with bakers' yeast. If pigeons are fed on rye bread, no matter if it is baked with or without yeast, they do not get any neuritis." "After 1894, however, the sailors have been obliged to bake soft bread on board. For this purpose they either use wheat flour or wheat and rye flour in equal proportions. On long voyages, however, Norwegian sailors never use bakers' yeast, because they do not know how to keep it. If pigeons are fed on wheat bread they always die with Eijkman's neuritis, sooner if the bread is baked without, later if it is baked with yeast. As for the said mixture of wheat and rye flour, I have only made experiments with bread baked without yeast. This bread, too, produces neuritis in pigeons."

"Till 1894 the sailors ate almost daily, for dinner, salt meat and peas. After this year, however, the use of these nutriments has been reduced to once or twice a week. Since that time they have had tinned meat three or four times a week, tinned fish once a week, and dried fish once a week."

These changes undoubtedly explain the sudden increase in ship beriberi on Norwegian vessels after 1894. Canned foodstuffs are subjected to a temperature sufficient to sterilize them, usually 120° C. It has been clearly shown that the beriberi preventing vitamines are always destroyed by this temperature, and Grijns, Schaumann and others have succeeded in producing polyneuritis in animals fed on such sterilized foods.

Another article of diet largely used on sailing ships is dried potatoes. But dried potatoes are not simply dried. If this is done they acquire a disagreeable greyish color. It is said that they are therefore first boiled in water containing hydrochloric acid, or sometimes sulphate of lime, before being dried at 90° C. The beriberi preventing substance is freely soluble in an acid solution, and is probably removed from these potatoes. Furthermore, this substance is destroyed by heat. Potatoes so prepared are therefore probably deprived of any beriberi-preventing properties.

Holst has further shown that, although fresh meat does not produce neuritis in fowls, salt meat, when boiled for an hour at 100° C., does produce the disease.

From these facts it is evident that the diet on many sailing ships consists almost solely of articles that will produce polyneuritis in animals, and we might confidently expect beriberi to develop on such ships. The fact that this does not occur oftener is undoubtedly due to two circumstances: 1. That many of these ships carry a supply of peas and beans, which are known to prevent beriberi, and 2, to the fact that these ships seldom remain at sea longer than three months, which is the known incubation period of beriberi, while at each port a supply of fresh meats and vegetables is taken on, which prevents the disease from appearing. When for any reason the voyage is prolonged much over three months beriberi does appear.

We may therefore conclude that ship beriberi is caused by the consumption of a ration which is lacking in a definite chemical substance, as yet not identified, but which is necessary to maintain the human organism in health. Objections have naturally been urged against this explanation from time to time, which may be stated as follows:

1. Epidemics of ship beriberi have been reported in which it has been alleged that the diet has been satisfactory, or in which an ample amount of peas and beans were supplied.

2. That if ship beriberi were due to such a diet that it should often be seen on land in jails, asylums and similar institutions.

3. That ship beriberi is related to scurvy.

These objections may all be readily answered as follows:

1. In the instances in which it has been alleged that the diet was satisfactory, the fact that the staples used have consisted of wheat

flour and tinned or salt meat and vegetables has been overlooked. Until very recent years such a diet would have been considered satisfactory ,but we now know from experimental evidence that it will produce beriberi. The fact that beriberi has occurred although peas and beans formed part of the ration may have been due to several reasons.

(1) These articles may have become spoiled, and as a result have not been eaten. Force reported a case on the Nederland in which beans formed a part of the ration. He specifically states in his article, however, that there was complaint as to the quality of the beans.

(2) The beans and peas supplied may have been canned. Owing to the difficulty of properly cooking beans, and the cheapness of the canned beans now sold by many firms, these are coming into very general use. It is apparent that the sterilization to which they have been subjected unfits them for use as preventives of beriberi.

(3) A sufficient quantity may not have been eaten. It is well known that beans and peas are much relished as occasional dishes, but that the appetite revolts against their constant use. When all the articles of a diet are beriberi-producing with the single exception of beans, a very considerable quantity of these beans should be eaten in order to prevent the disease, and, in the presence of a sufficiency of tasty canned foods, many members of a crew would undoubtedly fail to eat several ounces of beans daily.

2. To those who object that if beriberi were due to such a diet the disease should often be seen on land, we may reply that the disease has probably occurred on land unrecognized for many years, and more lately has been fully recognized. Such instances were formerly very generally confused with scurvy, with which disease beriberi was probably often combined, and many of the older authors speak of white scurvy and scorbutic hydraemia.

Nocht quotes authors relating a considerable number of cases developing dropsy without hemorrhages or sore gums in the epidemic of scurvy during the siege of Paris in 1870. He has further stated that such cases often occur during epidemics of scurvy in Russia. Holst states that " many dropsical cases without sore gums and hemorrhages were also observed during the Crimean war, where scurvy was very prevalent (Grellois). Some of the Crimean cases were connected with anaesthesia of the feet and looked like beriberi, but as they were sometimes associated with a local gangrene of the feet or with distinct symptoms of scurvy, the opinion prevailed that they were due to the cold of the winter in addition to latent or manifest scurvy. Finally, I may add that during the first part of the nineteenth century not only scurvy, but also dropsy without sore gums and haemorrhages, was very common in European and American prisons. For instance, besides typhoid fever and consumption, this "prison dropsy," *Wassersucht der Gefangnisse,* is stated in 1847 to have been the most prevalent cause of death in 41 prisons in England, France and North America (Wald). In 1857 it caused one-half of the deaths in a prison in Breslau (Baer), and *if it were not that nothing is said about the occurrence of neuritis,** some reports from those days recall the descriptions of the Asiatic beriberi prisons of our own time." These examples are not only interesting as showing the close relationship existing between beriberi and scurvy, but as indicating that probably beriberi has existed many times unrecognized in European countries during famines or under other circumstances when people were compelled to subsist for long periods on a deficient and unbalanced food supply.

As is now well known, epidemics of undoubted beriberi have occurred in the Richmond asylum in Dublin (Norman), in various parts of the United States (Bondurant, Sams), and in Labrador and New Foundland (Little). In this latter instance beriberi resulted from the almost exclusive use of fine wheat flour, a fact which is strong confirmation of Holst's observation that ship beriberi appeared in Norwegian vessels after the use of a staple wheat bread became universal. The other epidemics just referred to have occurred in institutions whose inmates were supposed to be receiving a proper diet.

Another instance of this kind has lately been reported by Lovelace. During the construction of the Madeira-Mamore Railway in Brazil the employees suffered from beriberi. "In December, 1909, alarmed at the increase of beriberi among our employees of all classes, we caused rice to be eliminated from all company messes and removed from all commissaries. In lieu of rice we furnished macaroni. The staple foodstuffs of the laborers were made to consist of dry biscuit, meat (dried and tinned meat and codfish), beans and macaroni instead of dry biscuit, meat, beans and rice." "In 1910, on a rice free diet, there was relatively three times as much beriberi among our employees as there was in 1911, during which year all the messes and commissaries of the company served and sold rice freely. The rice has always been the same kind, white, polished rice." Although Lovelace himself does not say so, the inference is plain to the casual reader that beriberi may occur although the ration is absolutely satisfactory. If, however, we

* It should here be noticed that the mildness or absence of the neuritic symptoms is supposed to be the characteristic feature of ship beriberi as distinguished from oriental or true beriberi.

analyze this ration it is plain that every article in it is known to be a beriberi producer except the beans.

Dry biscuit and macaroni are made of wheat flour which has already been incriminated, and the meat was dried or tinned. The beans undoubtedly failed to protect, either because they were sterilized, or because they were eaten in insufficient quantity. It is evident that in this case beriberi continued after the change in the ration, because this change merely substituted for one beriberi producer (polished rice) another equally bad (wheat flour). If an unpolished rice had been substituted for the polished rice the beriberi would undoubtedly have disappeared. This case is of considerable interest both from these facts and because it is an instance of beriberi occurring on land on exactly the same kind of a ration that has usually been served on those vessels that have developed ship beriberi. But in this instance the neuritis has been pronounced and the disease has been considered identical with true beriberi.

The question naturally suggests itself, if wheat flour is always a beriberi producer, why do we not see more beriberi among the Americans and Europeans, who use wheat bread as a main staple of diet? Americans and Europeans commonly eat *three* staples. Bread, meat and potatoes, together with a considerable number of other articles of food. Fresh meat and fresh potatoes both contain the essential vitamines as has been shown by experiments on fowls. Two of the three staple articles of diet used by these races are therefore beriberi preventers.

3. Is ship beriberi a form of scurvy? Several observers have thought that the symptom complex called ship beriberi was only one manifestation of scurvy. Austregesilo believes that there are cases of scorbutic polyneuritis that cannot easily be distinguished from beriberi. The disease begins with pure scorbutic symptoms. If the disease were scurvy and beriberi mixed, the first symptoms should be mixed with those of beriberi. The complication of polyneuritis in scurvy is very rare. If it were a mixed infection with beriberi, polyneuritis should be common. The cure of the polyneuritis of scurvy is easily brought about by a change of diet, while the neuritis of beriberi is not so easily cured. Accordingly Austregesilo differentiates two forms of scurvy with polyneuritis.

1. Polyneuritis scorbutica acuta. This begins with acute symptoms of scurvy, such as purpura, gingivitis, dyspnoea, oedema, enlargement of the heart to the right, increase of the second pulmonary sound, anaesthesias of lower limbs, painful areas, etc.

2. Polyneuritis post scorbutica. Like the polyneuritides of other infectious diseases, such as diphtheria. It is evident that Austregesilo considered both scurvy and beriberi to be infectious diseases, a point of view that cannot now be maintained.

Most other authorities have held that beriberi and scurvy occurred coincidently, especially in cases of the so-called ship beriberi. Thus Van Leent said, in 1904: "There are many atypical cases of scurvy and beriberi among the fishermen on the high seas. That the disease is beriberi was first stated by Bonain, and was proven by Chastang. I am sure of the correctness of this diagnosis, since cases were shown to me by Dr. Wassell, the health officer of Thursday Island. These patients showed both the wet and dry forms of the disease, but also had symptoms of scurvy, such as bleeding from the gums and subcutaneous haemorrhages."

The investigations of Nocht, Bullmore, the Norwegian Commission and others show clearly that ship beriberi and scurvy are separate and distinct diseases. Epidemics of ship beriberi are reported from many vessels in which there was no trace of scorbutic symptoms, and scurvy has often affected the crews of ships without any admixture of beriberic symptoms. Scurvy is characterized by anaemia, a spongy condition of the gums, a tendency to haemorrhages under the skin, mucous membranes, etc., and fragility of the bones. Ship beriberi is characterized by a general tendency to anasarca, severe cardiac disturbances and a moderate amount of multiple neuritis. The conditions occur independently of each other and are clinically distinct. The confusion has arisen because in a number of cases the two conditions have coexisted. In these cases the symptoms of scurvy and beriberi are so intermingled that the physicians have been in doubt as to whether to call the disease beriberi or scurvy, apparently not realizing that both diseases were present. In some ships lime juice has formed part of the ration and has prevented the occurrence of scurvy, but has not prevented the occurrence of ship beriberi. Moreover, Holst and Fröhlich attempted to produce ship beriberi in guinea pigs by feeding a one-sided diet consisting of various sorts of grain, groats and bread. They did not succeed in this endeavor, but on the other hand they did apparently succeed in producing true scurvy in these animals by this diet. Thus they had sixty-four animals that died after eighteen days or more on this diet after developing symptoms of scurvy. These symptoms were pronounced haemorrhages in the muscles, especially of the hind legs, ribs and lower jaw, subcutaneous haemorrhages and petechiae in the skin, and also haemorrhages into the internal organs. Further, there was a pronounced fragility of the bones, with fractures between the epiphyses and the shafts, and looseness of the molar teeth, which could often be removed with the fingers. The histological changes were also those of scurvy. They conclude, "That a one-sided diet consisting of various sorts of grain, groats and bread produces in guinea pigs a disease that corresponds macroscopically as well as microscopically to human scurvy. On the other hand we have found that this disease does not occur after a one-sided diet consisting of fresh cabbage or fresh potatoes, whereas it is again produced by dried potatoes. That is, the disease originates in guinea pigs as well as in man as a result of a diet confined to some special nutriments. We have further observed that the disease is favorably influenced by different sorts of nutriments known from human experiments as antiscorbutics. We have also found that at least one of these nutriments, that is cabbage, loses a deal but not all of its preventive power when boiled for half an hour at 110° C."

These experiments seem to afford a complete demonstration that scurvy is caused by a one-sided diet, or by a dietary deficiency, and also that it is a different disease from beriberi since they were unable to produce beriberi by the diets used. But it is also apparent that beriberi and scurvy are closely allied diseases. Scurvy is produced by the lack of an essential vitamine. Beriberi is also caused by the lack of vitamines, which are different from that of scurvy. If the diet is such that the consumer suffers only from the lack of the scurvy vitamine, scurvy alone will result. If the beriberi vitamines alone are lacking, beriberi will result. If both are lacking, as is often the case, both beriberi and scurvy will result, and the symptoms of the two diseases will be combined. If the deficiency of the scurvy vitamine is absolute, and the deficiency in beriberi vitamines only partial, the symptoms of scurvy will appear first and with great severity, while the symptoms of beriberi will only appear after a longer incubation period, and *vice versa*. The remarkable variation in the symptoms appearing in different epidemics of ship beriberi may all be accounted for in this way. Further progress in the study of both beriberi and scurvy must depend upon a determination of the exact chemical constitution of these different vitamines. It is possible that they may be related in some way. For example, a common chemical nucleus may be contained in all of these vitamines.

Are Ship Beriberi and Asiatic Beriberi the Same or Different Diseases? Since most observers have considered them to be different and distinct affections, we will first see upon what reasons they have based this conclusion. These reasons are:

1. *That differences exist in the symptomatology of the two conditions.* According to Nocht's description the symptoms of the disease consist usually in weakness and a prominent dropsy of the lower limbs, often extending to other parts of the body. Associated with this are shortness of breath, palpitation of the heart, and frequently sudden death from paralysis of the heart. But the symptoms of peripheral neuritis are comparatively rare. Other observers have been similarly impressed. The Norwegian committee in examining fifty-seven affected ships only found neuritis in men from four ships. Now since it is generally considered that neuritis is the essential symptom of Asiastic beriberi and is practically always present, while dropsy, though often present, is by no means always found, this discrepancy in the symptomatology has been perhaps the main reason for considering these affections to be distinct diseases.

This point of view has been well expressed by Braddon, who says: "In both diseases dropsy is a common factor; in both signs of neuritis also occur. But while in true beriberi the former is rare and the latter predominates, in the ship disease the reverse conditions prevail. And this difference obtains not merely occasionally, but viewing the cases of either sort in the groups in which they occur as epidemics, it is a constant difference. Can two disorders distinguishable by a divergence so marked be classed as identical?"

If this difference were as constant as Braddon supposes, the argument would be very strong. This distinction, however, is more apparent than real. It may be admitted that peripheral neuritis is an essential part of the symptom complex called Asiatic beriberi, but it by no means follows that *advanced* neuritis is present in all cases. Indeed, almost all observers have recognized a *rudimentary* form of Asiatic beriberi in which practically the only symptoms are a little heaviness of the legs, a little oedema over the tibiae, slight numbness and anaesthesia of the skin, and possibly a slight hyperaesthesia of the muscles of the calf. These cases sometimes remain in this condition for long periods without becoming much worse, and certainly without any definite paralysis. (See Scheube, Die Krankheiten der Warmen Länder.) If cases of this kind should die from some intercurrent disease, it seems doubtful if any degeneration of the nerves would be found after an ordinary examination. In any place where beriberi is endemic many of the rudimentary or larval cases may be seen. Now is it not quite possible that Nocht only found advanced neuritis in a relatively small number of cases of ship beriberi, but that in reality a majority of them may have suffered from this early or rudimentary form of neuritis which escaped attention because it did not advance to the stage of definite paralysis? It seems to me that there is evidence in Nocht's account that this is the case. He mentions a feeling of formication and slight numbness of the feet (papiersohlengefühl) as common symptoms. These are the usual symptoms of the early neuritis of Asiatic beriberi. It seems fair to conclude that while we cannot definitely assert from Nocht's account that most of his patients suffered from such a rudimentary neuritis, yet neither can we exclude this possibility.

The same thing is true of the accounts of the disease given by the Norwegian Commission, which did not examine the individual cases with particular care. Indeed, Nocht criticises the findings of this commission on this point, for they did not find a single case of scurvy among all the vessels examined, while Nocht claims that he himself found undoubted scurvy in two of the ships which were included in the report of the Norwegian Commission, but which was overlooked by them. They would very likely have overlooked such a rudimentary neuritis as that referred to in these cases.

Now, when we come to consider Bullmore's description of the disease we find even more evidence that neuritis existed in the cases he is describing. He says: "*The malaise is generally followed by a strange loss of power in the lower limbs and complained of at first as stiffness. This loss of power slowly increases so that the men have to hobble about as best they can with the aid of ropes, deckhouses, hatches, etc.*" "*Deeper reflexes in well-marked cases are lost, but I have had distinct knee jerk and ankle clonus in mild cases.*" Surely there must have been fairly marked paralysis present when patients had to have the assistance of ropes and deckhouses to hobble about. Again Bullmore says: "*Many cases have no oedema at all, and are evidently the dry beriberi of some authorities. When the oedema subsides the state of the neurotic mischief becomes manifest.*" There is nothing in this description which is inconsistent with the supposition that the disease described is Asiatic beriberi. Bullmore's reasons for supposing that the two conditions differed were not based on the symptomatology, but on the etiology of the disease. He was convinced that ship beriberi is not infectious, whereas he believed that Asiatic beriberi is infectious.

Birge states that the symptoms in all the cases he observed were similar. These symptoms were general oedema, breathlessness, *numbness of the limbs, shuffling gait and inability to bend the knees; knee jerk was lost in two cases and diminished in all the sufferers.*

While it is true, therefore, that the typical dry atrophic beriberi which is common in countries where beriberi is endemic, has not been observed in some epidemics of ship beriberi, Bullmore and Van Leent have clearly seen such cases.

On the other hand epidemics of true beriberi frequently occur in which there is little or no nerve degeneration. For instance, Ellis, describing the beriberi in Singapore asylum, says: "The large majority of the cases have been in the first instance of the so-called moist variety of beriberi, viz., that in which there is no tenderness in the calves or forearms, no hyperaesthesia or anaesthesia so far as one can make out, no muscular atrophy, in fact no obvious neuritis, but in which there is considerable general or localized oedema, with great weakness and loss of knee jerks, the superficial reflexes being usually unaffected. The oedema frequently clears up in the course of a few weeks under treatment, but unfortunately relapses nearly invariably occur. Sooner or later serious symptoms supervene, these being lung oedema, hydrops pericardii, cardiac failure, functional murmurs, reduplicated heart sounds, epigastric tightness with praecordial and substernal pains, dyspnoea and vomiting, this latter symptom being generally of grave import."

It has also been asserted that the acute, pernicious cardiac form does not appear. Even in the most severe cases the disease remains chronic until death. This assertion is not strictly correct. It is admitted that serious cardiac disturbance resulting in death is common. Exact statistics are difficult to obtain, but of the thirty-four ships that Nocht investigated so far as his statistics go, they show that of 486 men who comprised the crews of those vessels, 282 developed ship beriberi and 44 died. In the vessels investigated by the Norwegian Commission there were 547 cases of ship beriberi with 85 deaths. Practically all of these men died as a result of cardiac paralysis. But Nocht appears to think that in true Asiatic beriberi the acute pernicious cases sicken and die in 24 to 48 hours, while in ship beriberi even these fatal cases have remained sick for weeks before death.

It is probably true, however, that in these fulminating cases of Asiatic beriberi symptoms were present for some time without exciting attention because of their triviality. While no one will deny that cases may have occurred that die suddenly of acute pernicious beriberi in 24 to 48 hours without having previously shown symptoms of the disease, such cases must be very rare. Scheube says: "According to my experience, these very acute cases do not occur in Japan.

* * * In the cases observed by me a week or two or a month elapsed between the commencement of the attack and its fatal termination." This distinction between true beriberi and ship beriberi is therefore not to be regarded as important.

Now if the conception of beriberi which the author advances is accepted, all difficulty in considering ship beriberi and true beriberi as one and the same is overcome, so far as their symptomatology is concerned. This conception, it will be remembered, is that the symptom complex of beriberi consists of three distinct elements, namely: 1. The symptoms caused by degenerative changes in the nervous system and by a more or less severe peripheral neuritis. 2. Cardiac and circulatory disturbances. 3. A general tendency toward anasarca. And, further, that these three sets of symptoms may be found blended together in any proportion. That is, either the cardiac disturbances or the oedema or the neuritis may predominate or may be so mild as to be almost negligible. No reasonable explanation for the existence of oedema in wet beriberi and its absence in dry beriberi has heretofore been afforded, yet no one at the present day doubts that they are both true beriberi. The only possible conclusion is that the oedema is independent of the neuritis. Why should we have difficulty in believing that under certain circumstances we may have cases where the chief symptom is oedema, and the neuritis is exceedinly mild or possibly even absent.

2. *That differences exist between the convalescent periods in true beriberi and ship beriberi.* It has been alleged that true beriberi is always followed by a very long convalescence, but patients suffering from ship beriberi recover very quickly if they receive fresh food, particularly meat and vegetables. This statement is based upon the misconception that there must always be advanced neuritis in true beriberi. It is quite true that cases in which the neuritis is advanced and the nerves are profoundly degenerated require months to recuperate, but mild cases, and the rudimentary cases of true beriberi to which we have just referred, recover quite promptly when given a proper diet.

3. *The extraordinary liability of ship's officers to ship beriberi.* This has been noticed by several observers. Sometimes ship beriberi affects the captain or other ship officers first, and they have very frequently perished from this malady. On the other hand it has been noticed that in those ships where the officers are Europeans while the crew is composed of Asiatics, this Asiatic crew frequently suffer severely from true Asiatic beriberi, while the European officers almost invariably escape. This seems at first sight to constitute a difference

between these diseases, but this apparent discrepancy is susceptible if a very simple and satisfactory explanation. Ships carrying an Asiatic crew invariably provide a different ration for the European officers from that furnished the Asiatics. The latter are almost always furnished overmilled rice as the staple of their ration, and of course if they subsist too exclusively upon this rice they develop beriberi. The Europeans, on the contrary, usually have an entirely separate and much more varied ration, and therefore escape the disease. Conditions are quite different in the case of those ships affected with ship beriberi. These are practically always sailing vessels, and officers and crew all belong to the Caucasian race, and *two separate sets of rations are not provided.* Moreover, in these sailing and fishing vessels with small Caucasian crews the distinctions of rank are much less marked than is the case in a steamer which carries a larger and more heterogeneous crew. In the case of the sailing vessel, officers and crew frequently eat at the same table, and the officers always eat food from the same general stock of provisions as that furnished the crew. It is therefore clear that if the food is of such a quality that beriberi will develop on a ship of this type the ship's officers will be equally as liable to contract it as any of the crew.

4. *Ship beriberi a food disease, while Asiatic beriberi is not.* Nocht, Bullmore and others have been convinced that the ship beriberi affecting Europeans was a disease caused by an improper or insufficient dietary. They have been equally convinced that true Asiatic beriberi was an infectious disease, and as a result have concluded that the two conditions could not be identical. We have disposed of this objection in the preceding chapters in which we have shown that Asiatic beriberi is not an intoxication or an infection, but is clearly caused by the deficiency of some important element of the food.

We, therefore, incline to the opinion that there is no valid distinction between ship beriberi and Asiatic beriberi, provided it is admitted that wet beriberi and dry beriberi are two different forms of the same disease. A further discussion of this point will be found in the concluding chapter.

Treatment and Prevention. The treatment of ship beriberi is very simple. It is a matter of general experience that practically all cases except those already moribund recover when placed on a proper diet of fresh meat and vegetables, and recovery is generally so speedy as to appear almost miraculous. Such a diet is therefore sufficient for most cases. If we are correct in our conclusion that ship beriberi and Asiatic beriberi are the same disease, it is possible that some of these moribund cases might be saved if they were given large doses of an extract of rice polishings prepared as described in the Appendix, page 405.

Again assuming this conclusion to be correct, the disease can be prevented on sailing ships if they can be taught to carry a proper ration. Fresh vegetables, including potatoes, and meat, should be used as long as possible on beginning the voyage. Some ships have carried a stock of dried peas and beans. These latter supplies are as readily carried as flour, hard tack, etc., are known preventives of beriberi, and if not too continuously used are relished by all classes of men. It seems probable that beriberi has not developed on ships that actually used a sufficient amount of these vegetables. Owners should therefore be instructed to provide sufficient of these vegetables so that bean and pea soup can each be served at least once a week during the voyage. They should also be informed of the merits of undermilled rice, which will also keep on long voyages and will prevent beriberi. A sufficient supply of this rice could be carried to provide rice pudding for the men twice a week. Since it has now been conclusively shown that fine wheat flour is quite as apt to produce beriberi as polished rice, and since this flour in some form constitutes a main staple on such ships, an attempt should be made to substitute either rye bread or bread made from whole wheat flour for the use of this highly milled or fine wheat flour. It is believed that a few such simple changes in the ration of these ships would result in the eradication of ship beriberi.

CHAPTER XIV

EPIDEMIC DROPSY

History. In 1877 a disease whose principal feature was dropsy occurred in Calcutta. It disappeared during the hot weather and reappeared in the cold season until 1881, when it seemed to disappear. A similar disease was observed in Mauritius in 1878, lasted about a year and also disappeared. Nothing further was heard from this disease until 1901, when it reappeared in Calcutta. When this disease first appeared in Calcutta it was supposed to be beriberi, and Fayrer described the epidemic in Mauritius as beriberi. On closer study later observers thought it was a separate disease and called it epidemic dropsy. These observers thought that although dropsy occurs in both affections, they were quite different in other respects. This so-called epidemic dropsy has been quite constantly present in various parts of India since 1901, and has been accepted as a clinical entity by most of the classical authors, including Manson, Scheube, Braddon, Castellani, etc. However, in 1908 Dr. Pearse, the health officer of Calcutta, claimed that epidemic dropsy and beriberi are the same disease. Since that time there has been considerable difference of opinion on the subject.

Symptomatology. In order to obtain an account of the disease which will present the strongest possible case for its existence as a clinical entity, I shall quote the description of Macleod from Allbutt and Rolleston's Tropical Diseases. Macleod has been one of the strongest exponents of the theory that epidemic dropsy is distinct from beriberi, and his description of the symptomatology is as follows:

" Pyrexia, gastro-intestinal disturbances, burning and pricking of skin, and deep-seated pains in body and limbs were the most common initial symptoms. In a considerable proportion of cases, however, anasarca was the first indication of disturbed health, and the symptoms just mentioned accompanied or succeeded the dropsical swelling. The dropsy was an invariable and essential feature of the complaint, and was always either initial or early. The lower limbs were affected in the first instance, the trunk and upper extremities subsequently in severe cases, the face rarely. The effusion was in most cases confined to the skin and subcutaneous areolar tissue; oedema of the deeper cellular tissues took place in severe cases; the serous cavities of the chest — pleurae and pericardium — were sometimes filled with serum, the peritoneum and arachnoid cavity very seldom. The anasarca of the lower limbs often persisted after every other morbid condition had disappeared. The pyrexia was of mild type; seldom preceded by rigors or resolved by sweats; remittent, with morning temperatures of 99° or 100° F., and evening temperatures of 100° or 101° F. In some few cases, when the lungs became congested or inflamed, higher readings were noted. Vomiting and diarrhoea were frequent premonitory events, and diarrhoea and dysentery sometimes appeared during the course of the attack, and were apt to be troublesome and exhausting. Itching, burning, and other unpleasant sensations often preceded and accompanied the development of the anasarca, and in a considerable proportion of cases the surface became erythematous or affected with an urticarial, scarlatinal, or morbillous rash. Vesicles and petechial and purpuric spots were also observed. These rashes appeared in the earlier stages of the attack; eczema, desquamation, excoriation, and ulcers were occasionally observed later. The deep-seated pains probably depended on the pyrexia, and occurred within the first fortnight. The condition of the urine varied as regards colour, quantity, specific gravity and frequency of discharge. No tube-casts or albumin were found. In severe cases respiration and circulation were much disturbed. The cough, dyspnoea, and orthopnoea observed in some cases were evidently due to oedema or congestion of the lungs, and effusion into the cavities of the chest — conditions which occasionally caused sudden death. Anaemia was a prominent and constant feature of the disease, which in Mauritius received the name of 'acute anaemic dropsy.' The red corpuscles were diminished in number, the leucocytes increased, and an unusual amount of granular and molecular material was observed in the blood. The disease in severe cases produced considerable prostration and emaciation. No enlargement of the spleen was noticed, but in some cases, in which cardiac and pulmonary complications existed, the liver was found to be tender and its area of dullness extended. Neither anaesthesia nor paralysis was observed, though these symptoms were carefully looked for both in India and Mauritius. The duration and severity of the disease varied considerably. From three weeks to three months may be stated as the limits of duration. Debility, anaemia and persisting oedema of the legs were the only sequels observed. The case mortality varied between 2 and 8 per cent. Some Calcutta returns gave higher figures, but they probably included an excess of fatal cases. Death was caused mainly by pulmonary and cardiac complication, and in some cases was sudden and unexpected. Post-mortem examination revealed effusions and congestions. The subcutaneous effusion was in some cases hard and sanious. Punctate extravasations in the skin and serous surfaces were observed; congestions of stomach and intestines, of the liver and mesenteric glands, and cloudy swelling of the renal epithelium, were also noted. No bacteriological investigations were made either in India or Mauritius in the outbreak of 1877–78. The descriptions of the phenomena of the disease more recently recorded by Doctors Rogers and Cobb agree very closely with the foregoing."

Etiology. Although little is known on this subject, yet what little evidence is obtainable points to its intimate relationship with rice. Thus Rutherford says: "In all except the two fatal cases, disappearance of the dropsy and recovery soon followed admission to the hospital and administration of a diet of which milk, fish and chupatties were the main ingredients, as contrasted with the ordinary prison diet consisting chiefly of rice, pulses and vegetables."

An account of the occurrence of epidemic dropsy in Comilla jail, by Anderson, gives just the kind of a history that we have learned to associate with beriberi. From June 15 to August 30, 1907, there were thirty-two cases. The first case was admitted June 15th, with general anasarca, puffiness of eyelids, oedema of the lungs and dilated heart. Temperature and reflexes were normal. The diet consisted chiefly of polished rice. From the 16th to the 26th of July there was an epidemic of dysentery, as the result of which all food was most carefully boiled. On the subsidence of the dysentery the cases of dropsy came into the hospital in large numbers. In consequence of this the diet was changed August 18th, the Rangoon (polished) rice was stopped and country rice (unpolished) was issued. Potatoes were obtained from the bazaar for issue, and meat was also issued four times a week. The last case of epidemic dropsy occurred on August 30th.

Campbell reported an outbreak of epidemic dropsy in the lunatic asylum in Dacca. The diet had been chiefly rice, with meat twice a week. The treatment, on which recovery was prompt, consisted of absolute rest and a good and nourishing diet. Campbell says: "Rice is a possible cause, and in my opinion probably *the* cause."

Braddon, who insists that epidemic dropsy is not the same disease as beriberi, gives one instance where the former was caused by a rice diet. Thus, with regard to the epidemic dropsy at Ascension in

1895–98, Braddon states that "The disease clearly seems to have been associated with inferior diet, rice being most probably at fault, and to have ceased when more generous rations were provided."

Finally, Greig is of the opinion that epidemic dropsy is a disease due to defective nutrition, an opinion from which Pearse dissents. Thus, in the annual report of the Health Officer of Calcutta for the year 1910, Pearse says: "Captain Greig is evidently of the opinion that epidemic dropsy is a disease distinct from the beriberi of Chinamen in Calcutta, and that it closely resembles so-called ship beriberi. He thinks it is not infectious and could find no germ in the blood or excreta. He seems to have adopted the extraordinary theory that it is due to defective nutrition arising from the use of a diet deficient in certain constituents, and that this deficiency was due to the process of milling of the rice and wheat used chiefly by Bengalis. I cannot subscribe to these opinions. The theory explains nothing. It does not explain the sudden outbreak at the Alipore Reformatory and its extension over the city, the subsequent subsidence and the sudden recrudescence of a still more severe character in the following year (1909), with a much reduced incidence during 1910. The rice and wheat used by Bengalis has been prepared in the same manner for many generations. Why should a disease brought about by such means attack chiefly groups of persons living in one house in one street, or in one institution, who are living under identical conditions with their neighbors in adjoining houses and streets? Why should an outbreak occur and then subside to reappear after an interval? The population using this milled rice and wheat is enormous, and if it were a matter of deficient nutrition arising from the particular form of preparation of rice and wheat we should have had the whole population more or less affected, and affected more or less continuously for years. Is it likely that those affected have taken such a limited diet that the deficiency in rice and wheat has not been compensated for? Is not milk largely consumed, and would that not balance the deficiency of phosphorus complained about in the milled rice? It was noticed that the disease largely attacked the well-to-do during the recent outbreaks, but will anyone say that their diet was so entirely composed of milled rice and wheat that they suffered from this disease in consequence?

"Take the symptoms of the disease itself. Is there any disease known to medical science due to a deficiency of diet which will produce fever followed by paralysis. A deficiency of diet even in any particular constituent produces a gradually developing disease, not a sudden outbreak, and produces more or less symptoms in every individual partaking of the deficient diet."

We cannot agree with this criticism of Captain Greig's opinion as to the etiology of epidemic dropsy. Pearse is himself the strongest exponent of the theory that epidemic dropsy is really beriberi. We do not think there can now be any doubt that beriberi is caused by a dietary deficiency. If the diseases are the same, as Pearse claims, epidemic dropsy must necessarily have a similar causation. The arguments which Pearse urges against this hypothesis may be summed up as follows:

1. This theory does not explain sudden outbreaks in institutions.

2. It does not explain the epidemic character of the disease.

3. The food used by the victims is the same that has been used by these races for centuries, while the disease has only recently appeared.

4. If the disease were due to a deficiency the whole population should be affected.

5. The disease has frequently been observed in well-to-do families who presumably ate an adequate diet.

It is unnecessary to answer these objections here, since they are part of the arguments that have been continuously urged against the acceptance of the theory that beriberi is caused by a dietary deficiency, and they have all been disposed of in the preceding chapters on the etiology of beriberi.

Are Epidemic Dropsy and Beriberi the Same Disease? *The case for the affirmative.* Pearse, as the result of his experience as health officer of Calcutta, has had an ample opportunity to study epidemic dropsy. As a result of his observations of the outbreak of 1907 he formed the opinion that beriberi and epidemic dropsy were the same disease, and published his conclusions in the Journal of Tropical Medicine, March 2, 1908. Pearse says: "The recent outbreaks of beriberi and epidemic dropsy in Calcutta and Howrah afford strong grounds for believing that we have only one disease to deal with, and not two, as has been hitherto supposed. The so-called epidemic dropsy which was first described in 1877, on the strength of a few cases, has reappeared in this city during the past six months. A much larger number of cases have been observed, and during the same period there has also occurred an unmistakable outbreak of beriberi in the Alipore Reformatory. In the absence of any positive or even negative bacteriological evidence, we must for the present fall back upon a comparison of the courses and symptoms recorded for these cases. Let us consider the symptoms of these cases of so-called epidemic dropsy. The most essential symptom is said to be dropsy, oedema of the lower limbs first occurring, the trunk and upper extremities being subsequently affected in severe cases. Pyrexia, more or less, generally less, occurs early, and there are burning and pricking of the skin and deep-seated pains in the limbs. The oedema may be slight, and limited to the feet, but in some cases is extensive, and serous effusions occur in the pleura and pericardium; vomiting and diarrhoea are recorded as frequent premonitory symptoms. A kind of erythematous rash affects parts of the lower limbs. Dry cough, dyspnoea, and anaemia occur in severe cases. There is more or less prostration, which is very marked in certain cases. In the earlier outbreaks no anaesthesia or paralysis was observed, and some authors have stated that the knee jerks were invariably present, and that though deep-seated pain in the muscles was complained of, no tenderness of the calves could be elicited. The duration of the disease varies considerably, and debility, anaemia and oedema are the symptoms usually prolonged. Death is due to pulmonary and cardiac complications, and in some cases is sudden and unexpected. Later accounts refer to dilatation of the heart, haemic murmurs and palpitation, and the pulse is described as soft."

"Now, in the recent outbreak, we have had in Calcutta cases showing all degrees of severity of the above-mentioned symptoms. Several deaths have occurred. Deep-seated pain, with distinct tenderness of the calf muscles, has been frequently reported. In some cases wasting of the calf muscles has been noticed, and the knee jerks have been distinctly impaired or absent. There has not been any definite paralysis, but unsteadiness of gait has been observed in several cases. Cardiac troubles, shown by shortness of breath, palpitation, reduplication of sounds, rapidity of pulse, irregularity of beat, murmurs and faintness have been frequent."

"The differentiation of this disease from beriberi has hitherto been based almost entirely on the more marked nervous phenomena characterising the outbreaks of beriberi, and upon the absence of typical beriberi cases in outbreaks of epidemic dropsy. The occurrence of paralysis, of marked anaesthesia over certain areas, and of loss of deep reflexes is particularly relied upon. There are some who go so far as to make the existence or absence of the knee jerks a test for the two diseases — absence negativing epidemic dropsy. At the same time there are a considerable proportion of cases in a beriberi outbreak which, taken alone, would be absolutely indistinguishable from so-called epidemic dropsy. Amongst the Alipore Reformatory series of fifty cases of beriberi there were two deaths, and many of the patients had tingling and weakness in the lower extremities; but the knee jerks were normal in eighteen cases and exaggerated in five others, only in a few cases was anaesthesia detected, and there were but eight cases showing any definite paretic condition.

"In view of these nerve symptoms it can hardly be argued that the reformatory outbreak was not beriberi, but one of epidemic dropsy, and yet there were in this localized outbreak nearly 75 per cent of the cases showing very mild symptoms, and those symptoms were identical in character and also in degree with those shown in the other cases which cropped up in various houses scattered over the city.

"Beriberi is described as essentially a form of peripheral neuritis, but the majority of the symptoms found in epidemic dropsy are common to the two diseases.

"There is absolutely nothing known connected with the causation of either disease which helps us to distinguish them. They are both essentially household diseases — cases occurring in batches only where people are closely associated together. There is little fever in either disease, and when it is present it does not pursue any regular course.

"On the other hand, the combination of symptoms in the two complaints is very similar. The greater or less oedema, especially over the shins, the hyperaesthesia of and deep-seated pain in the legs, the cardiac symptoms and the mode of death are common to both. The dropsy is shown in the same manner, even to effusion in the pleural and pericardial sacs; the digestive functions go on practically undisturbed, and the urine is free from albumen. Even the nervous phenomena, if of less degree, are identical in character, viz., those of a peripheral neuritis. McLeod says that epidemics of dropsy have been repeatedly observed on land and at sea, but that it is difficult to decide whether they were instances of 'wet' beriberi or of epidemic dropsy. The nervous phenomena do not always declare themselves in an outbreak of beriberi, as oedema without albuminuria may occur and remain almost the only symptoms. The conditions found *post mortem* are in no way characteristic, but are similar in the two diseases."

"The combination of oedema with symptoms pointing to peripheral neuritis with 'rheumatic'-like pains, and with disordered heart action, is only known to these two diseases. All the symptoms in the two diseases are similar in character, if not always in degree, and cases occur in outbreaks of each disease which are indistinguishable the one from the other. Finally, death is brought about in a similar manner — sometimes suddenly and sometimes slowly — by nervous disturbance of the heart's action."

Megaw also described a number of cases of alleged epidemic dropsy in detail, and concluded that they were really cases of beriberi.

Are Epidemic Dropsy and Beriberi the Same Disease? *The case for the negative.* Braddon says: "Since the disease was differentiated by Lovell, MacLeod, Davidson, and O'Brien, it has been recognized as an entirely distinct disorder from beriberi by such authorities as Scheube, Manson, and Cantlie; and those who will read the very clear and concordant accounts of it by these observers will find it difficult to understand why it should ever be confused with beriberi. To the two affections there is, indeed, but the single symptom of dropsy common. Some digestive disturbance, some general malaise, some fever, even slight disorders of skin sensation, there may be in either; but these signs are neither constant in both, nor in any way specific. But the differences are constant and very marked. An acute, abrupt fever always ushers in epidemic dropsy, which is never present in beriberi. On the other hand, the prominent and often acutely painful disorders of sensation and movement, the tenderness and cramps of the muscles, the final wasting and paralysis, always present in some degree in every beriberic, never occur in epidemic oedema. This is a gulf of difference, and it might be thought impossible that the two diseases should be confounded."

If this statement were correct it may be admitted that such a difference would serve to distinguish epidemic dropsy from beriberi. However, a study of the cases reported as epidemic dropsy shows that the disease is by no means always ushered in by fever, and that disorders of sensation, and movement, and even paralysis do occur in a certain proportion of the cases.

Anderson, who described thirty-two cases, said: "In only one case there was a paralysis implicating the lower extremities, and this occurred on the subsidence of the dropsical symptoms. This patient gradually improved and in two months' time was able to walk about."

Delany states that disturbances of cutaneous sensation and disturbances of motion occur in both diseases. Delany investigated epidemic dropsy in a number of jails in eastern Bengal. He had had considerable experience with beriberi, and stated that he saw no case of beriberi, nor one that he could be sure had ever suffered from beriberi. *He saw, however, some forty-six cases said to be suffering from beriberi, which should have been called epidemic dropsy.* He states that the diseases resemble one another as follows:

"(a) Both occur mostly in epidemics.

"(b) The knee jerks are altered in each.

"(c) Dropsy of various degrees occur in both.

"(d) There is considerable cardiac disturbance in each; dilatation and heart murmurs being present or palpitation and dyspnoea only.

"(e) In each disease the pericardium, pleura and peritoneum may contain fluid.

"(f) In each there is frequently oedema of the lungs.

"(g) Cutaneous sensation is disturbed in both diseases.

"(h) Hyperaesthesia occurs in both (see later difference).

"(i) In each disease motion is frequently disturbed or interfered with.

"(j) And in each disease death occurs with distressing dyspnoea and orthopnoea."

"But the diseases differ as follows:

"(a) Knee jerks in beriberi are at first and for a brief period (rarely over 48 hours) increased and painful, and then lost in probably more than 95 per cent of cases. In epidemic dropsy knee jerks are diminished or lost in no more than 30 per cent of cases.

"(b) Anaesthesia is a marked feature of beriberi, and will be found in practically every case either in small patches or over extensive areas. In epidemic dropsy cutaneous sensation is lessened over the dropsical areas and not in patches otherwise than over dropsical areas; but in this disease, though cutaneous sensation is diminished, it is not lost, and probably is only so diminished from mechanical interference with nerve termini by the effused fluid.

"(c) In beriberi true paralyses occur, with toe drop, wrist drop, paraplegia or paralysis of all four limbs. In epidemic dropsy various forms of paresis are simulated by mechanical obstruction around the joints, caused by the effused fluids; the very weight of a swollen limb may cause a difficulty in using it. An ataxic gait is simulated owing to the swollen legs, and this may be more apparent when the external genital organs are swollen.

"But in beriberi a characteristic symptom is the presence of varying degrees of paralysis in cases that have no dropsy whatever (dry beriberi), and this occurs, according to Hunter and Koch of Hongkong, in quite 50 per cent of the cases, these cases having, besides the characteristic, patchy anaesthesia.

"(d) The hyperaesthesia differs in the two diseases, being present in the dropsical skin and subcutaneous tissue when gently pinched in epidemic dropsy; but in beriberi the muscles are painful on moderate deep pressure in oedematous and non-oedematous parts alike.

"(e) Some few cases of epidemic dropsy are found to undergo a general emaciation, and so simulate the atrophic stage of beriberi in which the muscles atrophy to such a degree that the patients look like living skeletons. But these cases of emaciation are able to move their limbs about in bed, though they are feeble. In any large outbreak of beriberi these cases of atrophy with extensive and severe paralyses are present in quite large numbers, and are often bedridden for many months.

"(f) A marked feature of beriberi is the sudden deaths that occur in addition to the distressing deaths with dyspnoea and orthophoea, such as also occur in epidemic dropsy. These sudden deaths occur not alone in cases with paralysis and dropsy, but in persons apparently well, or who have but the mildest symptoms.

"(g) There is some leucocytosis and anaemia (diminution of haemaglobin) in epidemic dropsy, but in beriberi anaemia is not present.

"(h) Of minor importance are the presence of rashes (subcuticular mottling and staining along the course of superficial veins), with dry skin and slight desquamation and initial fever in epidemic dropsy.

"(i) Lastly, the symptoms of beriberi are essentially those of peripheral neuritis, and the central nervous system is unaffected in every case (Hunter and Koch, Manson, Braddon, Wright)."

This is not a very serious list of differences upon which to base such an important distinction. It is apparent that with the exception of fever, rashes and anaemia, the distinctions consist more of differences in degree of symptoms rather than of the existence of symptoms that are distinct in the two diseases. Moreover, Delany's own cases that he reports in the same article do not bear out these statements as to differences. Thus, he found that in 158 cases which he insisted were epidemic dropsy that knee jerks were diminished or lost in 104 or 66 per cent of the cases, and four of these 158 cases suffered from paraplegia. Delany also attributes to Wright and others the statement that in beriberi the central nervous system is never affected, while Wright has described extensive changes in the cord in beriberi. (See chapter on Pathology.)

Moreover, Delany's differential points do not agree with the facts in cases of epidemic dropsy reported by other observers. Of the 32 cases of epidemic dropsy reported by Anderson, 19 cases showed absence or diminution of the patellar reflex. Monro reported impairment of knee jerk in 45 out of 71 cases of epidemic dropsy.

This is quite characteristic of all the papers on the subject. The distinction between epidemic dropsy and beriberi appears to rest on no better foundation than the facts: 1. That in the former dropsy is the main symptom, and the nervous changes, while present, are much less severe than in beriberi. 2. That fever, rashes and anaemia are present in epidemic dropsy, but not in beriberi.

1. The fact that, as a rule, oedema is the preponderating symptom in epidemic dropsy, and neuritis is the main clinical distinction in beriberi, does not afford sufficient ground for establishing epidemic dropsy as a separate disease. The exceptions to this rule are numerous. Many cases reported as epidemic dropsy have had marked peripheral neuritis, and many cases of beriberi have slight or almost no neuritis. We have already discussed this point very fully in the preceding chapter on ship beriberi. If this were the only point of difference between epidemic dropsy and beriberi, the conclusion would be justified that, like ship beriberi, it is merely a form of true beriberi. Greig considers that epidemic dropsy closely resembles the so-called ship beriberi.

2. If fever, rashes and anaemia were constant in epidemic dropsy, and constantly absent in beriberi, this would be a sufficient reason for considering epidemic dropsy to be a distinct disease. But this is not the fact. It can be easily shown by a few quotations that these symptoms are often absent in epidemic dropsy. Anderson, in describing his cases of epidemic dropsy, says: "Pyrexia, when present, was of a mild type and remittent in character, rarely reaching over 100° F. Blood examinations showed a moderate reduction in erythrocytes, but anaemia was not a prominent feature of these cases." Rutherford says of his cases: "It would seem that the above were cases of epidemic dropsy. The fact that fever and skin eruptions were not observed can hardly invalidate the diagnosis." With regard to the eruption or rashes of epidemic dropsy, Pearse states: "This is a very variable sign and only occurs in a few cases."

On the other hand, pyrexia, anaemia and skin eruptions have been frequently observed in beriberi. Scheube says: "Fever is not a constant symptom in beriberi. Many cases run their course from beginning to end without fever; in other cases a rise of temperature lasting from one to several days is observed, partly at the beginning of the illness, partly during its course." "Anaemia is a frequent but not a constant concomitant; it is rarely absent, however, in serious cases." "Exceptionally, exanthems, such as petechiae, erythema multiforme, herpes labialis, etc., are observed in beriberi."

Monro reported a case of ship beriberi associated with an erythematous eruption, and after stating that several of the cases in the Richmond asylum epidemic were ushered in by an erythematous eruption, says: " When one bears in mind the variety of diseases which may be associated with an eruption of the exudative erythema type, it is not surprising that a cutaneous eruption more or less akin to that type should be observed in an occasional case of beriberi."

This is undoubtedly the correct explanation of the fever and rashes which occasionally occur in both epidemic dropsy and beriberi, but which are not a necessary or characteristic part of either disease. The anaemia which sometimes occurs in both diseases is simply the anaemia that will occur in any debilitated or poorly nourished person.

We may therefore conclude that the fever, anaemia and skin eruptions observed in epidemic dropsy do not constitute any difference between that disease and beriberi.

Now when we remember that this so-called epidemic dropsy was first described as beriberi both in Calcutta and Mauritius, and that it was only later elevated to the rank of a separate disease on the basis of these distinctions, it seems obvious that the original opinion that the disease was beriberi was the correct one.

The above discussion is based solely on the symptomatology of the two diseases. We have already seen that while our knowledge of the etiology of epidemic dropsy is incomplete, yet so far as it goes it points to a dietary deficiency as the cause of that disease.

The author has never seen epidemic dropsy, and is therefore unable to express any opinion based on personal observation. But from a study of the literature it would seem that Pearse and Megaw are amply justified in their contention that epidemic dropsy is merely one form of true beriberi.

CHAPTER XV

THEORETICAL CONSIDERATIONS

The evidence presented in Chapters IX and X demonstrates that beriberi is caused by a diet deficient in certain substances. We now wish to discuss the manner in which this deficiency produces the pathological changes and symptoms characteristic of beriberi, the relationship or interdependence of these changes, and the relationship existing between dry beriberi, wet beriberi, ship beriberi and epidemic dropsy.

Both before and since Scheube and Baelz published their observations there has been a great difference of opinion as to what constitutes the essential lesion of beriberi. Some have considered beriberi to be a disease of the blood, and others have regarded it as a disease of the cord (Bentley), or as a disease of the arteries (Yamagiwa). But since Scheube and Baelz demonstrated the existence of a peripheral neuritis in beriberi, and believed that the central nervous system was unaffected, the disease has been very generally considered as a peripheral neuritis. All the complex manifestations of beriberi have been attributed to this basic factor, the variations being supposed to depend upon which nerves were affected, although there have been many dissenters from this view.

We may therefore ask the question: Is beriberi, so far as it relates to the nervous system, a true peripheral neuritis, or is the entire nervous system affected? The evidence upon which we answer this question may be summed up as follows:

(1) The changes found in the cells of the cord and the fibers of the cord by such observers as Wright, Dürck, Tsunoda, Rodenwalt and others, seem to be too advanced and appear too contemporaneously with the changes in the peripheral nerves to be altogether secondary in nature.

(2) Degeneration in the cells and fibers of the medulla has also been described by some of these observers.

(3) Demonstrable degenerative changes have also been found by Vedder and Clark in the cord and medulla of fowls suffering from polyneuritis gallinarum, which is probably the same disease as beriberi in man.

(4) The sympathetic system may be widely involved (Ellis).

(5) Neuritis appears in fowls before paralysis occurs. Vedder and Clark found that degenerative changes were to be observed in the sciatic nerves of fowls that had been fed on a polished rice diet for 35 days or more, even though symptoms of neuritis did not manifest themselves. Figure 45 shows the degenerative change in the sciatic nerve of such a fowl, which appeared to be normal at the time it was killed. It was manifestly desirable to determine at what period these degenerative changes could first be detected. Accordingly, fowls were fed on polished rice and killed at varying intervals of time, ranging from seven to 23 days. None of these fowls showed symptoms of peripheral neuritis, and most of them could not be distinguished in

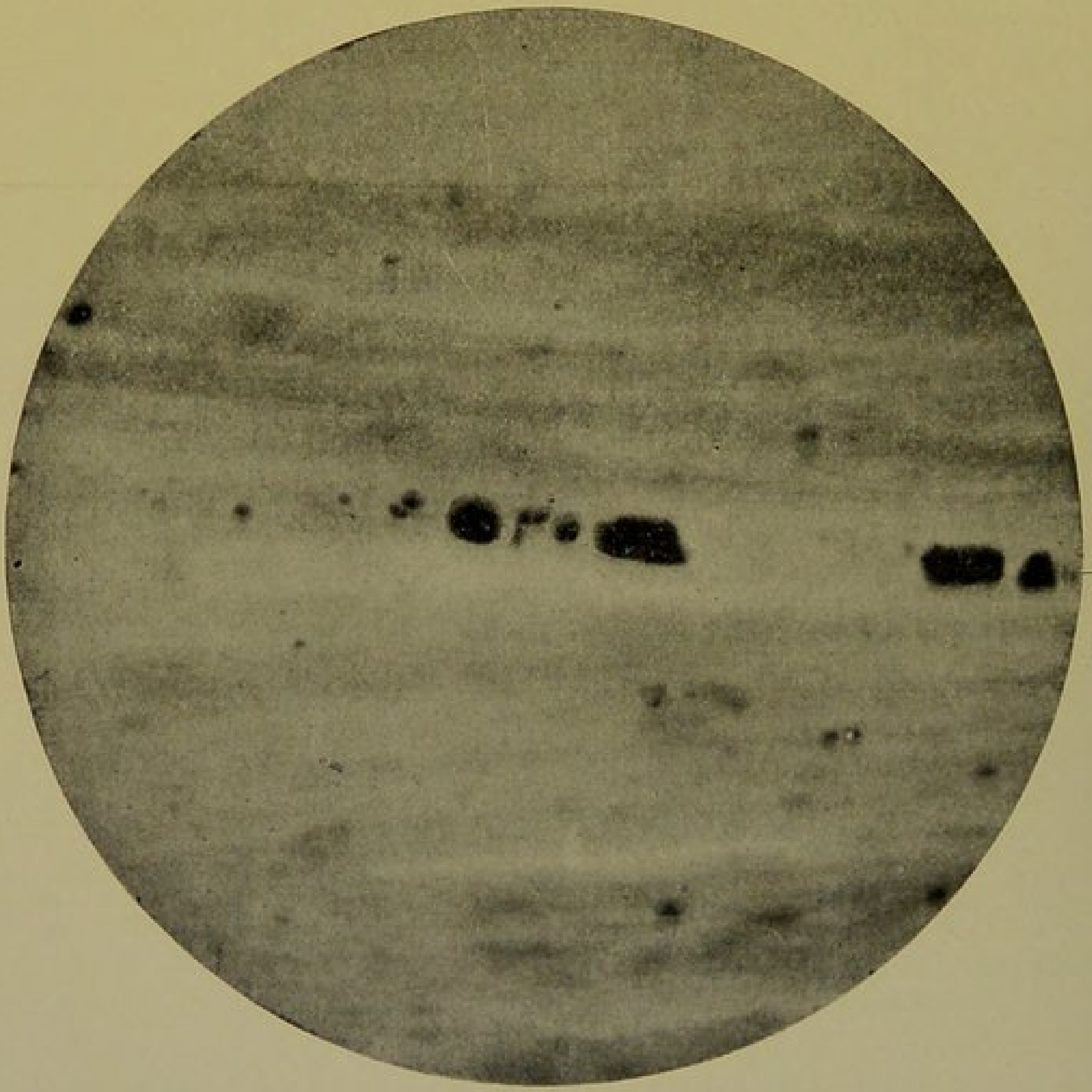


Figure 45. Teased preparation (Marchi method) of the sciatic nerve of a fowl that was fed for 35 days on polished rice without showing any symptoms of polyneuritis. Some fibers show marked degeneration. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

any respect from normal fowls. The nerves of these fowls were studied, particularly by staining for mitochondria, and fresh normal fowls were used for controls. In normal nerve fibers stained by the mitochondria methods the medullary sheath is seen to contain innumerable bacilli-like rods arranged in a radial direction around the axis cylinder. When seen from above the fiber appears to contain both rods and granules, but when a fiber is split down the middle only the rods are to be observed. The granular appearance, when viewed from above, is due to an end view of the radially arranged rods. All four normal fowls showed this appearance, as illustrated in figure 46. All

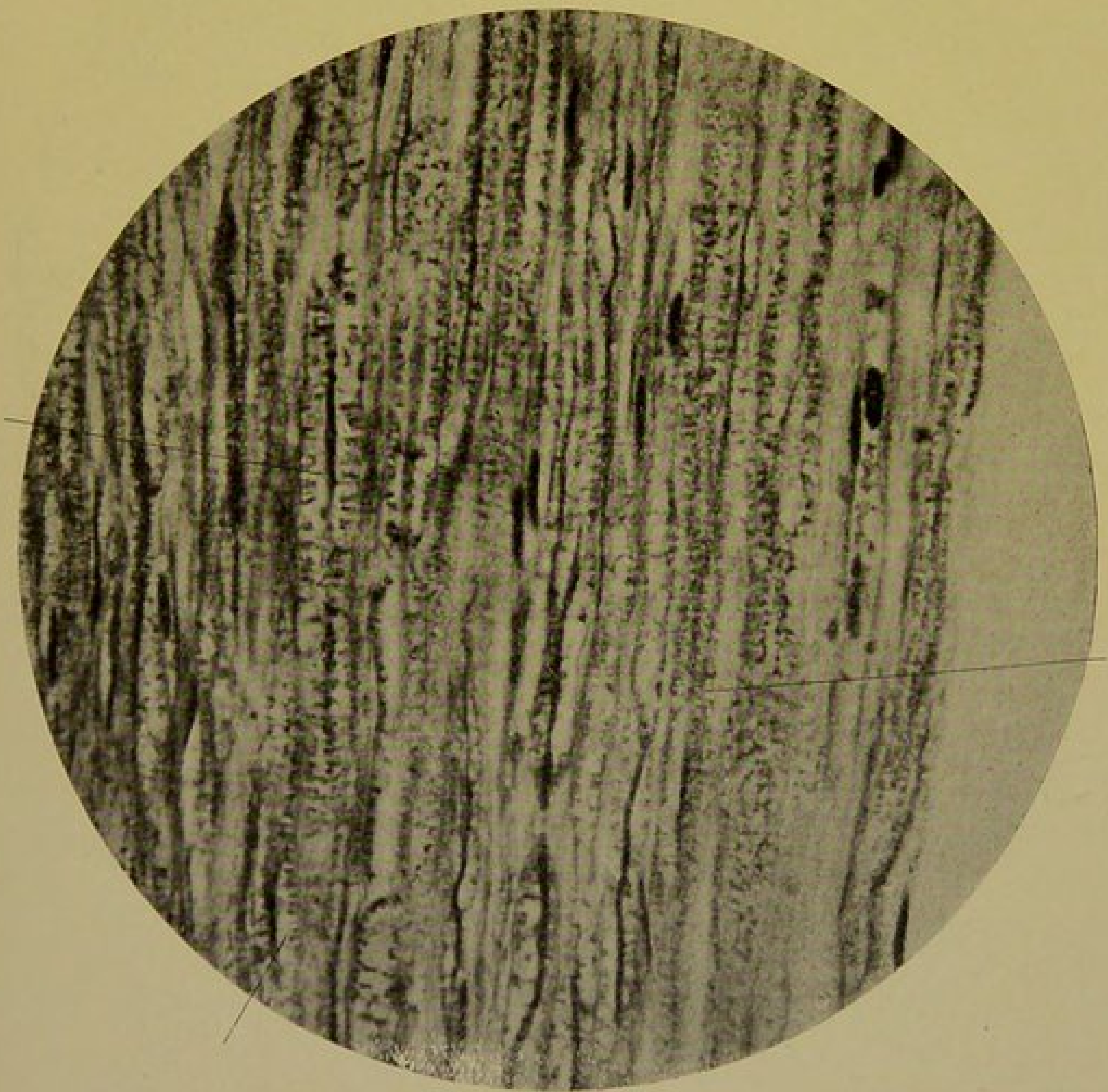


Figure 46. Longitudinal section of sciatic nerve of a normal fowl stained by the mitochondria (iron-haematoxylin) method. The stainable substance is seen in the form of little rods arranged radially around the axis cylinder. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

the fowls fed on polished rice, however, showed pronounced changes. Even after only seven days' feeding on polished rice the nerves showed marked changes, and the normal mitochondria had disappeared from practically every fiber of the sciatic nerve. The stainable material, instead of being present in rods, was seen as smaller or larger irregularly branched and anastomosing globules. Figures (47, 48, 49) show the changes observed in the nerves from fowls fed for 7, 15 and 22 days on polished rice, and stained by the mitochondria method. A comparison with the normal nerve stained in the same manner will

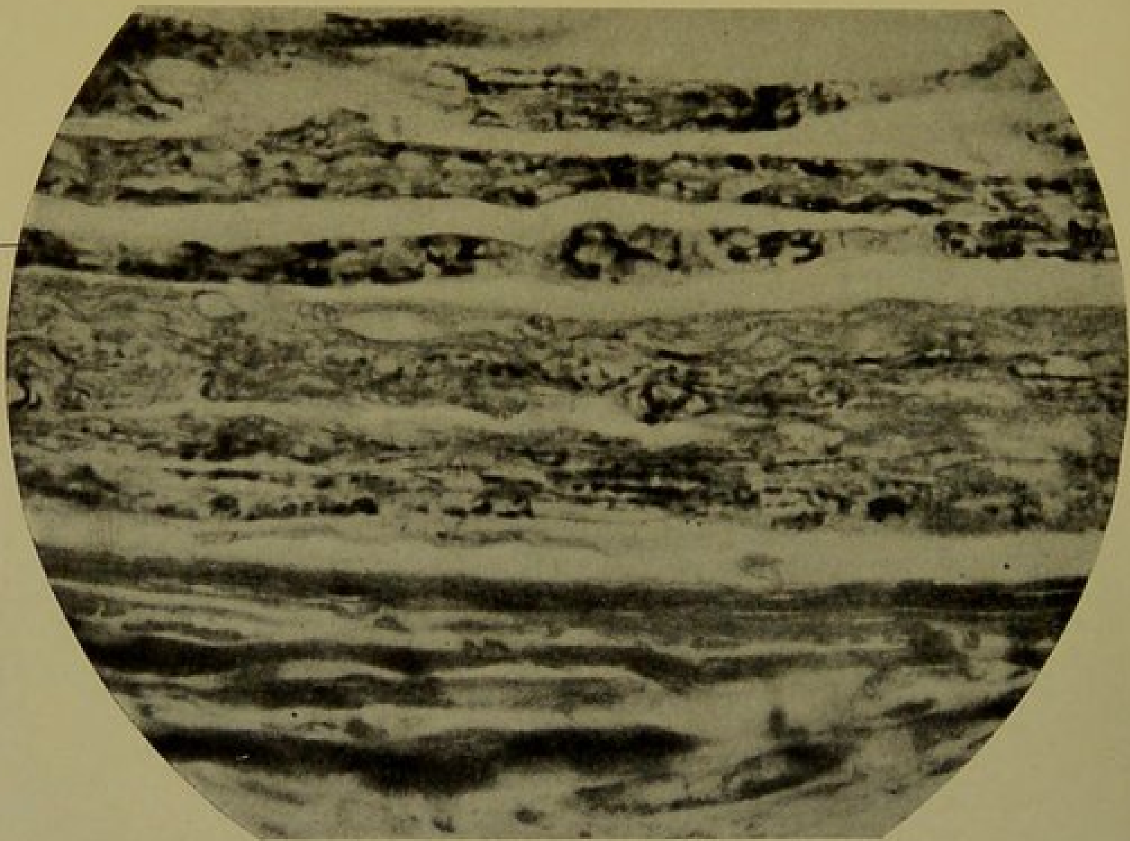


Figure 47. Longitudinal section of the sciatic nerve of a fowl fed for seven days on overmilled rice, to illustrate the changes in the medullary sheath. The stainable material is seen as irregular and branched masses. Mitochondria (iron-haematoxylin) method. Compare with figure 46. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

serve to convince anyone that a most pronounced change occurs in the structure of the nerve fibers of fowls that have been fed on polished rice for so short a period as seven days. This change is progressive, the longer the fowl is kept on polished rice, and leads to the condition ordinarily termed degeneration, as may be seen by figure 50, which shows a nerve stained by the same method from a fowl in which paralysis had occurred. It is therefore quite certain that the degenerative changes commence in the nerves of fowls long before any symptoms of the disease can be observed.

While it seems quite possible that the tingling, slight anaesthesias and other nervous symptoms that are observed in cases of human beriberi that have not yet developed definite paralyses may be due to such early changes in the nerves, yet changes occur in the nerves in human beriberi before any symptoms can be observed. Rumpf and Luce have shown that the neuritic changes may, under certain circumstances, be far advanced even in mild beriberi cases, and occur long before the appearance of the first clinical manifestations of the disease.

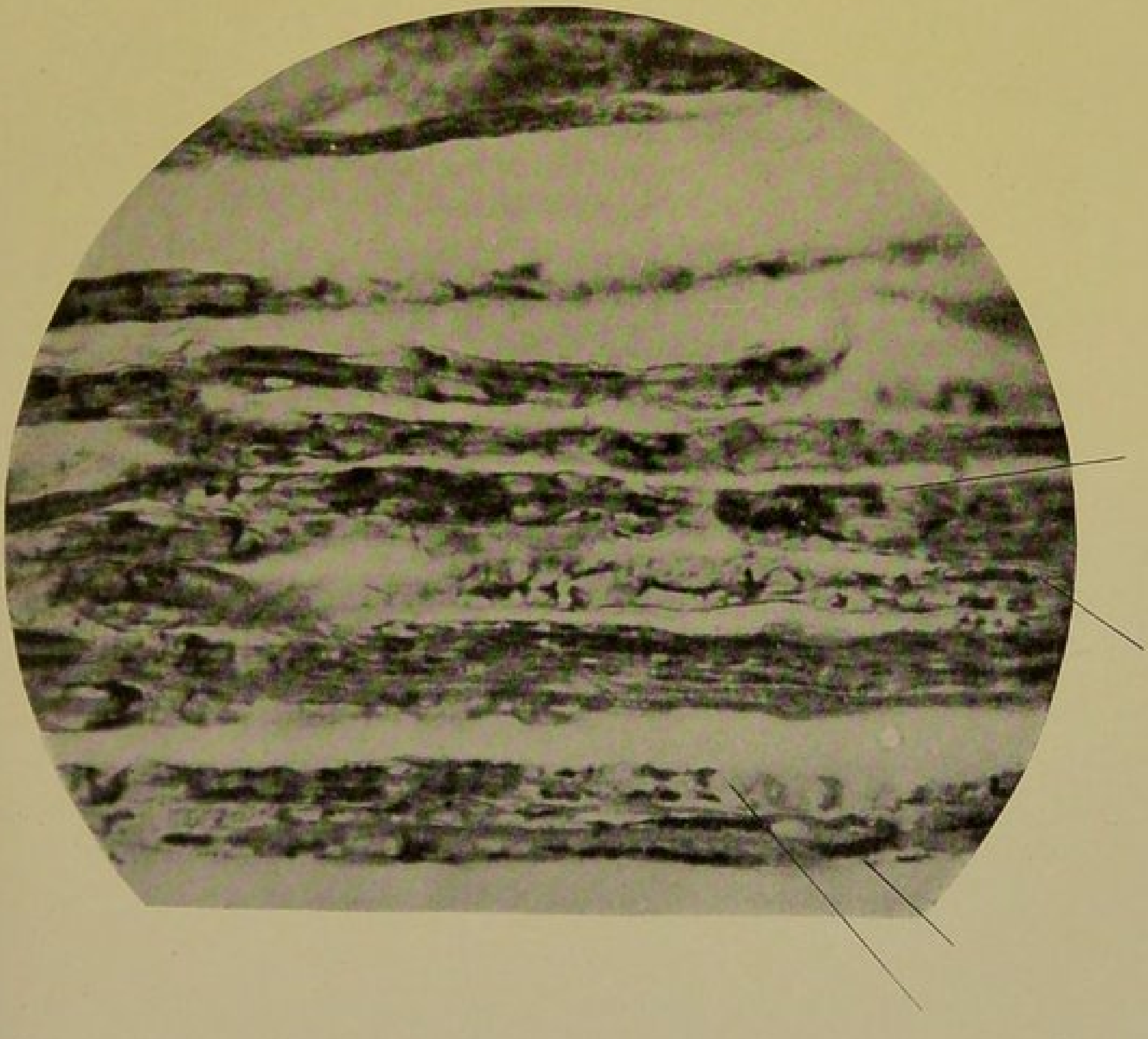


Figure 48. Longitudinal section of sciatic nerve from a fowl fed for eleven days on overmilled rice. Same mitochondria method. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

(6) In fowls the neuritis remains after the paralysis is cured. We have repeatedly cured fowls that were paralyzed as a result of an exclusive diet of polished rice by the administration of a hydrolyzed extract of rice polishings. In a number of such cases, after the paralysis was entirely cured and the birds were able to walk as well as ever, they have been killed and the nerves examined. In all such cases the nerves have shown pronounced evidences of degeneration of exactly the same type as is seen in birds that have died of polyneuritis gallinarum. It is therefore evident that in fowls, at least, the paralysis is not caused by the neuritis.

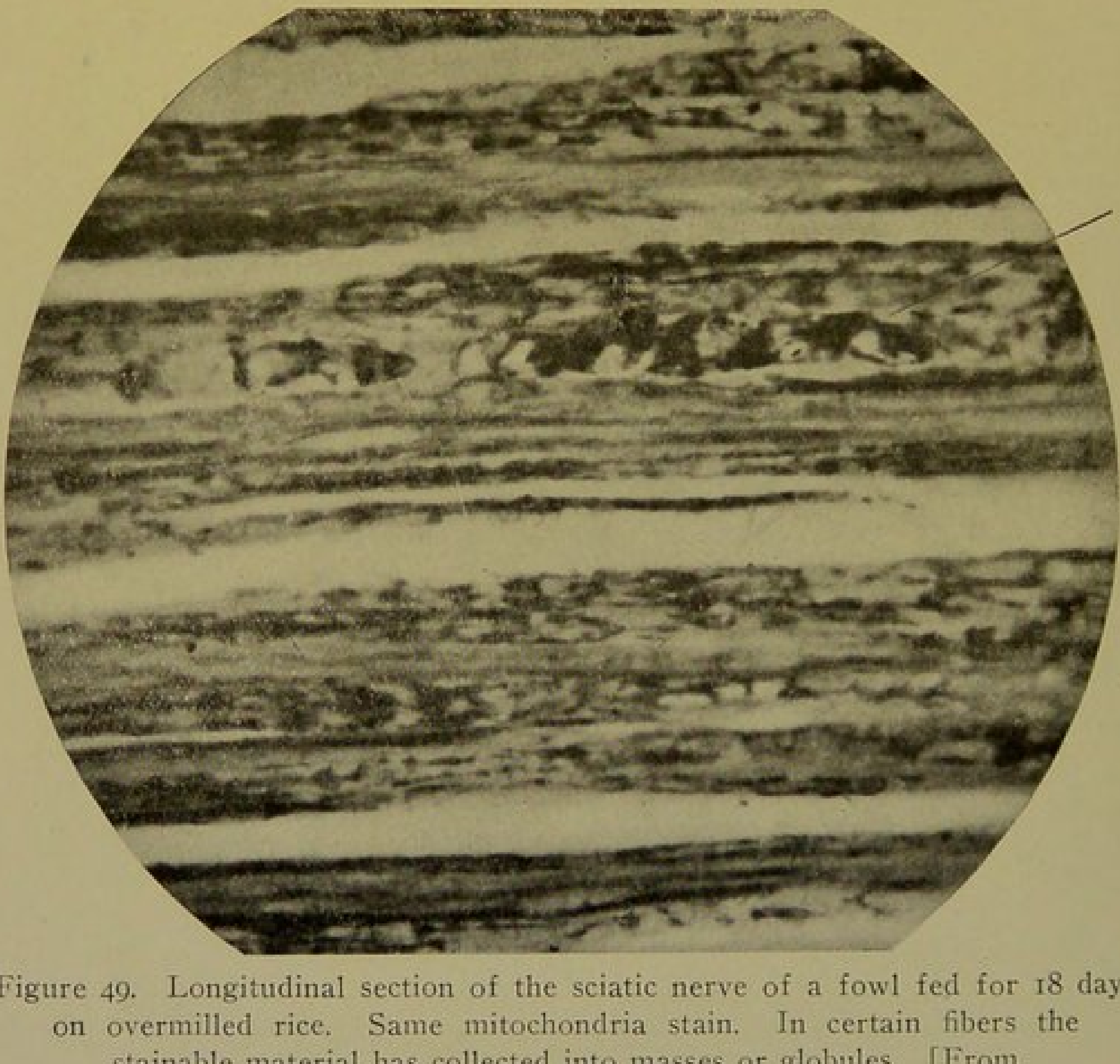


Figure 49. Longitudinal section of the sciatic nerve of a fowl fed for 18 days on overmilled rice. Same mitochondria stain. In certain fibers the stainable material has collected into masses or globules. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

It is extremely probable that the same thing is true in human beriberi. We have succeeded in giving marked relief to a case of dry or paralytic beriberi by the administration of Funk's base or vitamine. This case, who was bedridden and unable to walk, improved wonderfully, and began to hobble about immediately after this treatment.

He was unable to walk normally for some time longer, which was probably due to the fact that his muscles were greatly atrophied. (Figure 51.) But the fact that he was able to commence walking, and that the pain and tenderness from which he had previously suffered acutely at once disappeared, indicated that the paralysis was cured. We were, of course, unable to examine this man's nerves. But we know that degenerated nerves require weeks or months to return to

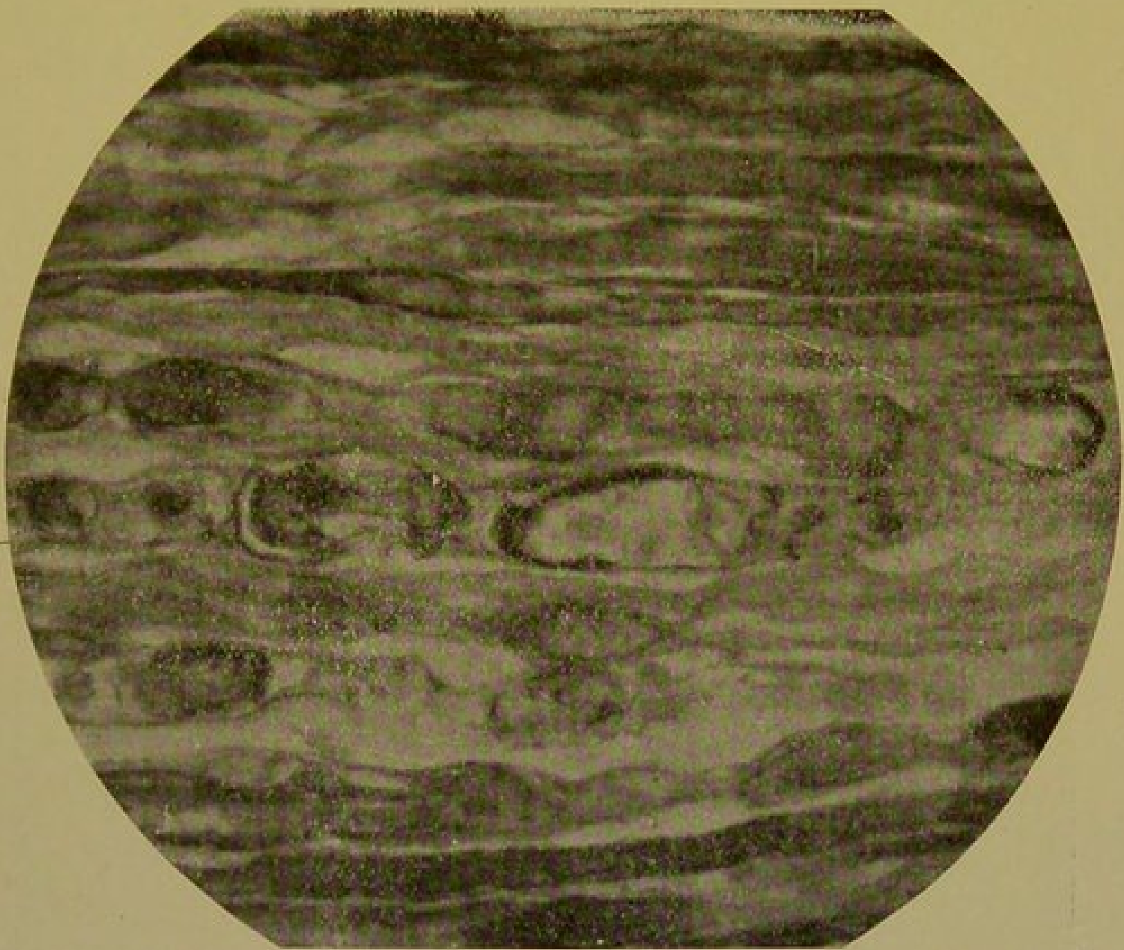


Figure 50. Longitudinal section of the sciatic nerve of a fowl showing pronounced symptoms of polyneuritis. Globules are more discrete than in figure 49, and stainable material is chiefly in the periphery of the globules. Same mitochondria stain. [From Vedder and Clark, and plate lent through the courtesy of the Philippine Journal of Science.]

normal. It seems clear, therefore, that the paralysis in this case could not have been caused by the neuritis, or otherwise such prompt recovery could hardly occur.

We conclude, therefore, that peripheral neuritis *per se* cannot be the essential lesion in beriberi, because degeneration of the nerves occurs before symptoms arise, because advanced degeneration may be present accompanied by no symptoms at all, and because degeneration of the nerves remains long after recovery has occurred.

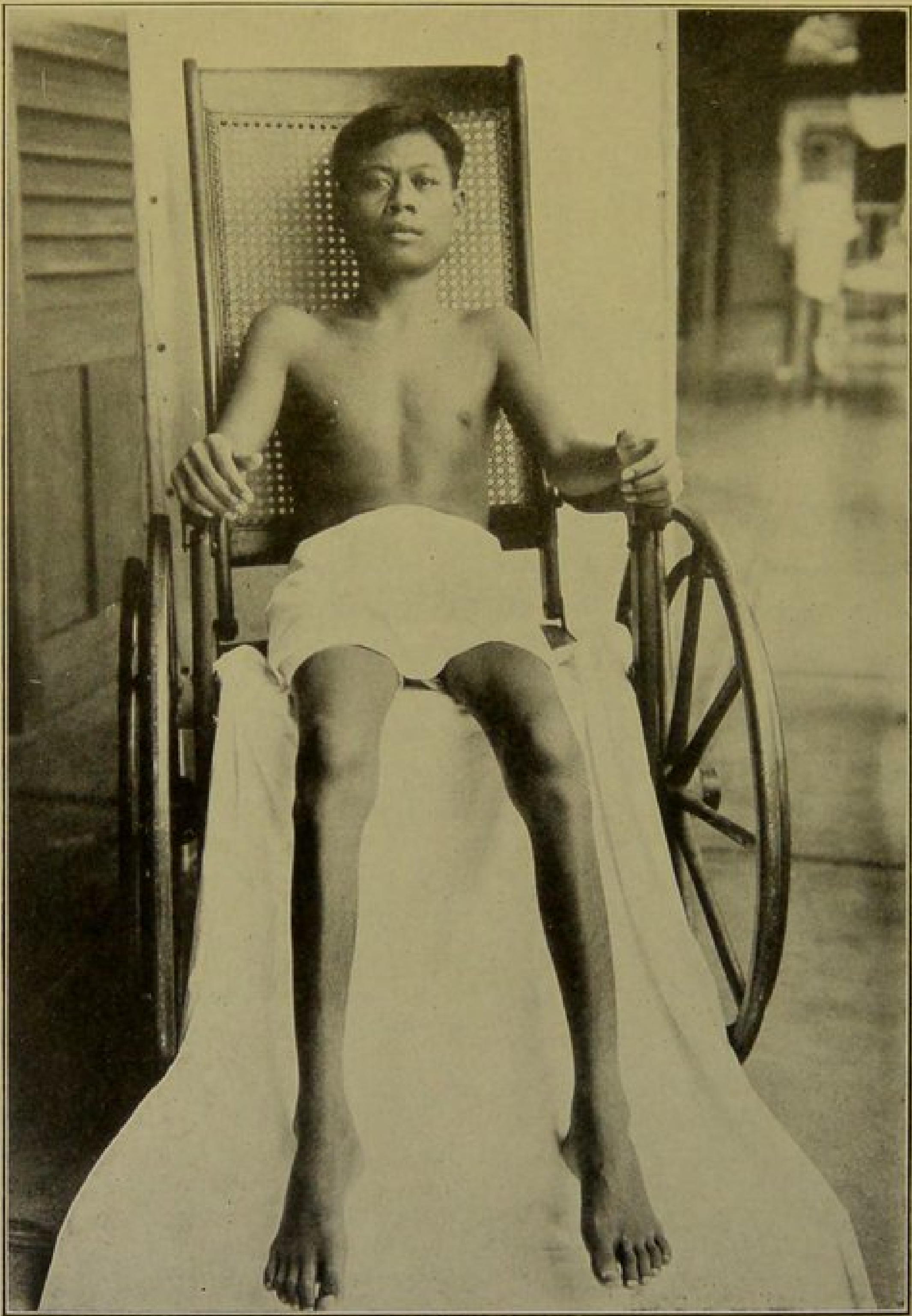


Figure 51. A case of "dry" beriberi, with advanced degeneration of nerves and muscles, and who was treated by the administration of Funks base. He showed marked improvement after receiving an amount of this substance obtained from twenty kilos of rice polishings.

(7) Funk has shown that in fowls suffering from polyneuritis gallinarum there is a great change in the chemical constitution of the brain. This would indicate that there may be great change in the brain in beriberi even although it has not yet been demonstrated by histologic methods.

(8) Finally, beriberi has now been definitely shown to be a disease caused by the deprivation of certain substances in a deficient dietary. It follows that the degeneration in the peripheral nerves is caused as a result of faulty metabolism, and there is every reason to suppose that as the chemical constitution of the various parts of the nervous system varies very slightly, that the entire nervous system is in all probability more or less affected by the degenerative process. This degeneration may affect all parts simultaneously, but produce the most serious lesions in those portions of the nervous system which require the larger amounts of this substance for their normal metabolism.

It is believed that, so far as dry or paralytic beriberi is concerned, the cause of the symptoms is to be found in a degenerative process affecting the entire nervous system, but particularly the cells of the cord and brain. By consulting the chapter on pathology it will be seen that degenerative changes have been found in the cells of the cord in human beriberi by a number of investigators. A pronounced change in the cells of the cord has also been demonstrated in polyneuritis gallinarum by Vedder and Clark. (See plate V.) In the fowls, at least, these changes had not advanced sufficiently far to be called true degeneration, but consisted chiefly of a dissolution of the tigroid bodies and the collection of the broken down tigroid substance in one corner of the cell. Quite similar changes have been demonstrated in the nerve cells of pigeons that had been exhausted by long flights. Funk has shown that chemical changes also take place in the brains of fowls suffering from polyneuritis gallinarum. Since the symptoms of paralysis are evidently not caused by the peripheral neuritis, it seems quite probable that they are the direct result of these changes in the cells of the cord and brain. Funk's vitamine, which prevents the development of the disease, and which is present in varying amounts in different foodstuffs, is a building stone which is essential for the normal metabolism of nervous tissue. A certain amount of this vitamine is constantly necessary in order to maintain the nervous system in a healthy condition. If the supply of vitamine is cut down by feeding on polished rice, or any other dietary which contains an insufficient amount of this substance, the normal metabolism of the nervous system at once suffers. If the faulty diet be continued, the degeneration of the nervous system progresses steadily until a point is reached at which the symptoms of beriberi appear. The result of such a diet on the structure of the peripheral nerves in fowls has already been pointed out. It is probable that, so far as the nerve cells are concerned, the deprivation of this vitamine or metabolic building stone results in changes that at first simulate the alterations produced by excessive fatigue, but that later changes assume the character of a true degeneration. We therefore have a rational explanation for the sudden cures which have been reported by a number of investigators who have worked with polyneuritis, and which we now report in human beriberi. If the nerve cells are not completely degenerated they are capable of quickly recovering and resuming their functions when a sufficient supply of the vitamine so necessary to their metabolism is furnished. The patient then quickly recovers in spite of the fact that many fibers of his nerves are degenerated. Vedder and Clark found that only a relatively small percentage of the nerve fibers were completely degenerated, i. e., axis cylinder destroyed, although the medullary sheath of practically every fiber might show more or less degeneration. It seems probable that the animal is able to do without this small percentage (approximately 10 to 15 per cent) of completely degenerated fibers, so long as the remaining majority of the fibers are capable of transmitting impulses.

We are therefore inclined to regard dry or paralytic beriberi as caused by a defective metabolism resulting in more or less degeneration of the entire nervous system, and that the paralytic symptoms are particularly caused by the degenerative changes in the cells of the cord and possibly the brain.

What is the cause of the changes in the heart? Hypertrophy of the heart is usually present, and degeneration of the heart muscle is also common. The degenerative changes in the heart might be the result of degeneration of the vagus, or of the nerves of the sympathetic system, but the work of Vedder and Clark (Appendix, page 401 affords very little basis for this theory, and it is very difficult to account for the hypertrophy in this way. Several writers have recognized this difficulty and have attempted to account for the cardiac hypertrophy in various ways. Thus, Miura tried to explain it as caused by the increased resistance due to the compression of the pulmonary arterioles by a paralyzed diaphragm. This theory never received any credence. If the diaphragm were *paralyzed* it is hard to understand how it could exert any compression on the lungs, and, moreover, paralysis of the diaphragm is a late symptom in only a few cases, and quickly followed by death.

Glogner thought that there was a vaso-motor paralysis with dilatation of the vessels, particularly in the lungs, thus throwing an additional burden on the heart. Thus he says: "From the above cases it is certain that the most severe changes may take place in the striated muscle and elastic tissue of the great vessels, especially the pulmonary artery, without any considerable disease of the peripheral nerves, and that therefore the essential element in beriberi can have nothing to do with the peripheral nerves, in spite of the fact that this view has been held for the past 20 years." But so far as the hypertrophy of the heart is concerned this theory is in contradiction to known mechanical laws, since dilatation of the vessels decreases the resistance and lowers the blood pressure, thus reducing the amount of work to be performed by the heart.

Yamagiwa, on the contrary, thought that the arterioles were contracted, and that the hypertrophy was directly caused by the increased resistance thus produced. However, there has been no confirmation of his observation, and this theory has also failed of general acceptance.

Recent experiments have thrown some light on this subject. Chamberlain and Vedder found that the administration of an alcoholic extract of rice polishings to infants suffering from infantile beriberi resulted in an immediate alleviation of the serious cardiac disturbance which is one of the main symptoms of that disease. Vedder and Williams found that this same extract, when administered to an adult case of pernicious cardiac beriberi, afforded quite as prompt relief from the distressing cardiac symptoms. Since, as will be seen later, the extract in this form is quite incapable of promptly relieving the nervous or paralytic symptoms of beriberics, it follows that there is some substance in this extract which exerts a direct and immediate action on the heart. The action of this extract may be explained as follows: The heart muscle contains some substance which is essential to its normal metabolism and action. This substance is supplied in a proper diet; but an improper diet, such as overmilled rice, is deficient in this substance. As a result of this deficiency changes occur in the heart muscle, which eventually result in degeneration, and sooner or later the cardiac symptoms of beriberi appear. The extract of rice polishings contains this substance in a readily assimilable form, and consequently its administration results in prompt relief.

The hypertrophy of the heart may also be explained in accordance with this theory, as follows: As the first result of the deficiency in this vitamine which is essential to the normal metabolism of the heart, and possibly before degeneration has occurred, the individual fibers of the heart become weaker, so that the heart cannot perform the same amount of work as formerly. An attempt is therefore made to compensate for this insufficiency by increasing the number of fibers. In other words, the heart hypertrophies. This result would naturally be expected from what we know of the tendency for the heart to hypertrophy when for any reason it is unable to perform the work which is demanded of it. This theory is a more rational explanation of the degeneration and hypertrophy of the heart occurring in beriberi than has yet been afforded.

We may now inquire what relation does this substance bear to Funk's base or vitamine? No positive answer can be returned to this question at present. Cooper has found that when pigeons are fed on polished rice they may be protected from polyneuritis by feeding them five grams of ox heart muscle daily, while the daily addition of as much as 20 grams of beef to the rice diet was necessary to prevent polyneuritis for the same period. Therefore he concludes that heart muscle is considerably superior to voluntary muscle in anti-neuritic power. This experiment indicates that the substance which is necessary for the metabolism of the heart may be the same as Funk's vitamine, which is necessary for the metabolism of the nervous system, since the feeding of normal heart muscle prevents the development of polyneuritis.

As we have already pointed out, there is considerable evidence that Funk's vitamine may occur in food as a constituent of nucleic acid, and it is interesting in this connection to note that heart muscle is said to be much richer in nucleo-proteid than skeletal muscle (Hammarsten).

On the other hand, there is evidence that this cardiac vitamine is not identical with Funk's vitamine. The alcoholic extract which relieves the cardiac symptoms so promptly is equally efficacious in dispelling the dropsy in cases of wet beriberi, but is quite ineffective in curing the paralytic symptoms of dry beriberi, while the administration of Funk's base promptly cures this paralysis. These results, and the fact that cardiac changes are more frequently associated with the wet form of beriberi than the dry form, indicate that this cardiac vitamine may possibly be identical with the vitamine of wet beriberi. But, however, this point may be decided by future research, it appears fairly evident that the cardiac condition in beriberi is not the result of the nervous changes which may have occurred, but is caused by the deficiency of some substance in the food.

If we have arrived at a rational explanation of the disease process in dry beriberi, we have now to decide what is the relationship between dry beriberi and wet beriberi.

In the preceding chapters of this book we have treated beriberi as one disease. In the past, and while the causation of beriberi was unknown, the disease has been separated from other diseases on the basis of its symptomatology. The association of dry and wet beriberi has been so general that it has seemed proper to recognize that beriberi is one disease which may be either wet, dry, or mixed. This classification has had the sanction of the clinicians of the past fifty years, and the introduction of a new classification at this time would only result in confusion unless accompanied by unassailable evidence. In the absence of such absolute proof it has been thought wiser to treat beriberi as one disease, in accordance with the opinion of modern authorities. At the same time, the author has had a growing belief that dry beriberi and wet beriberi are separate and distinct diseases which, however, are usually associated.

In the first place we must remember that very eminent clinicians, whose powers of observation were quite as keen as those of modern observers, for many years considered the two diseases as absolutely distinct and independent. That it has come to be generally accepted that they are both forms of the same disease, chiefly because it has been found that the symptoms of dry beriberi and of wet beriberi may be commingled in all degrees. This, however, might easily be the case if wet beriberi and dry beriberi were two separate diseases which frequently coexist in the same patient. We have already seen that such association of diseases occurs in the case of ship beriberi and scurvy, and there can be no doubt that scurvy is a different disease from beriberi. Obviously the assumption that dry beriberi and wet beriberi are the same disease rests upon a very insecure basis. It has been the generally accepted belief that the symptoms of dry beriberi are caused by the peripheral neuritis that exists, but no one has been able to afford any rational explanation for the occurrence of the dropsy on this basis. It appears and disappears quite independently of the nervous lesions.

The evidence which has caused the writer to incline to the belief that the older authors were correct, has been obtained through the treatment of cases of beriberi with the extract of rice polishings already described. Thus it has been found:

1. That adult human cases of wet beriberi may be promptly cured by the administration of this extract. I have used this treatment myself in several cases of undoubted beriberi of the wet form, in which general dropsy was most pronounced. This dropsy has disappeared within two or three days in a most remarkable manner after the administration of the extract from about five kilos of rice polishings.

2. A similar result has been recorded by Chamberlain and Vedder in cases of infantile beriberi, which are chiefly of the wet type of beriberi. Cures were very prompt, and the oedema disappeared in the course of a very few days.

3. This same extract has been administered to typical cases of dry beriberi, over a period of several weeks, and giving the extract from a kilo of polishings daily without producing any noticeable improvement.

4. Similar results were also obtained by Hulshoff Pol after the administration of a decoction of katjang idjo. This observer found that the cardiac disturbances were relieved and the oedema in cases of wet beriberi promptly dissipated by this treatment, but that the symptoms of paralysis remained unaffected.

5. In my experience fowls always suffer from the dry form of beriberi. Other observers have reported instances in which oedema was present, but I have never seen a fowl suffering from polyneuritis gallinarum in which there was any true oedema. If a fowl suffering from the paralysis of polyneuritis is given even enormous doses of this extract, equivalent to several kilos of polishings, the paralysis is not thereby immediately cured.

6. If this same extract of rice polishings is treated chemically (hydrolyzed with five per cent sulphuric acid) it becomes violently poisonous, whereas it was formerly not at all toxic, and at the same time it acquires other new properties, and if administered to fowls suffering from polyneuritic paralysis, in doses sufficiently small to avoid poisoning, these fowls are promptly cured, so that in one or two days they are able to walk about as though they had never been paralyzed.

7. After eliminating the toxic substances by precipitation with various reagents, the remainder of this extract (Funk's base) may be given to human cases of dry beriberi, and produces marked results, which can almost be called a prompt cure of the paralysis.

In brief, the untreated extract contains substances which produce an immediate cure of cases of wet beriberi and of pernicious cardiac beriberi, while the substances which will cure dry beriberi can only be obtained after various chemical manipulations. It seems quite probable from these facts that there is a distinct chemical difference between the substance which cures wet beriberi and the substance which cures dry beriberi. In other words, there are two separate vitamines contained in an extract of rice polishings. One cures wet beriberi and one cures dry beriberi. But if this is the case, wet beriberi is caused by the deficiency of one substance, and dry beriberi is caused by the deficiency of another though possibly a related substance. Wet beriberi and dry beriberi are therefore distinct diseases, just as scurvy and beriberi are distinct. All three are caused by the deficiency of vitamines that are essential to life, *but the vitamines in each case are chemically different*. If these observations are confirmed, we have as good reason for considering wet beriberi and dry beriberi to be distinct diseases as can be desired.

The reason why wet beriberi and dry beriberi are so generally associated is apparent. Both of the vitamines which respectively prevent these two diseases are present in the outside layers of grains like rice and wheat. When the grain is highly milled both vitamines are removed, and if the individual subsists too exclusively on these grains he will suffer from two deficiencies, or will develop both wet and dry beriberi, that is, the combination of the two diseases, which has been called "mixed" beriberi. The disease may appear first as the dry type or as the wet type, depending upon which vitamine is most completely removed and upon the relative susceptibility of the patient. On the other hand, the wet beriberi may suddenly disappear, leaving the patient shrunken and affected with dry beriberi. This possibly results from the fact that the patient has eaten some food containing the vitamine which protects against the wet form.

Another possible explanation of wet beriberi is the influence of salts on oedema. There is clinical evidence showing that a salt free diet reduces the oedema of nephritis, while a diet rich in salts increases this oedema. The same may be true of beriberi. Certainly in ship beriberi salt is in excess both in food and in the environment. Efforts have been made to produce oedema in fowls developing polyneuritis as a result of an exclusive overmilled rice diet, by administering large doses of salts, and have been unsuccessful. This negative result in fowls does not entirely exclude the possibility that the excessive consumption of salt may produce oedema in men suffering from beriberi.

But it seems quite impossible that the sudden cures which have occurred in cases of wet beriberi as the result of administration of the extract of rice polishings can have been caused by any change in the patient's salt metabolism. These patients have all continued to eat the same diet which they were receiving prior to treatment, and which was responsible for the development of the beriberi.

It is true that the exact method in which this vitamine of wet beriberi affects the metabolism is yet unknown, and remains a subject for further investigation. Fischer has stated that the cause of oedema is to be sought in the tissues, and that it is a result of the production of acids in the tissues. These acids increase the affinity of the tissue colloids for water, whereby they are enabled to absorb an increased amount of water from any available source. If, as Fischer claims, this is the ultimate cause of all oedemas, it may be that the deficiency of this vitamine so affects metabolism that the tissues become acid. Such questions remain as subjects for future investigation. But that such a vitamine actually exists, and does in some way affect metabolism so that its absence results in dropsy, may be regarded as the most probable explanation of the facts already stated.

If this observation be confirmed, the long discussion as to the nosology of ship beriberi and epidemic dropsy may also be regarded as settled. These so-called diseases are, then, evidently epidemics chiefly of wet beriberi, but having also an admixture of some of the symptoms of dry beriberi, and occur under such dietary circumstances that the usual relationship between the vitamines of wet beriberi and dry beriberi is disturbed. In other words, the particular ration eaten contains enough or nearly enough of the dry beriberi vitamine, and a great deficiency in the vitamine of wet beriberi. The resulting disease is therefore chiefly of the wet type. Infantile beriberi also belongs chiefly to the wet type.

In conclusion we may say that an entirely new conception has been given to medicine by the work of Holst, Funk, and the later investigators of beriberi, the conception of the vitamine. The discovery of these substances is bound to produce a revolution in existing theories of metabolism, for such substances have been undreamed of by physiologists. In the past the value of a food has been estimated by its content in fats, carbohydrates, proteids and inorganic salts, and by its caloric equivalent. More recently it has been found that individual proteids consist of numerous amino-acids, and that each proteid differs in the quality and number of these amino-acid building stones. That proteids which are deficient in certain of these amino-acids will not alone suffice to maintain an equilibrium of nitrogen metabolism. The later experiments of Osborne and Mendel have shown the necessity for certain inorganic salts, if bodily metabolism is to be properly maintained. It is now apparent that the vitamines must also be taken into consideration in future experiments on metabolism. It has been repeatedly shown that animals may receive a sufficiency and even an excess of fats, carbohydrates, proteids and inorganic salts, but if the diet is deficient in these vitamines they will lose weight, will not maintain nitrogen or phosphorus metabolism, and in the end will develop beriberi or scurvy. By the addition of these vitamines the animals may be kept in good health for long periods, and will increase in weight. It is hard to overestimate the importance of these substances or the influence which their discovery will exert on the future study of metabolism and disease.

It is, further, quite possible that the various forms of scurvy and beriberi are not the only deficiency diseases. Pellagra, rickets and other diseases may later come to be included in the same category. This possibility may be suggested as one which has not been sufficiently considered or tested in any way, but it is undesirable to speculate further on this subject at present.

CHAPTER XVI

PRACTICAL CONSIDERATIONS

The practical considerations resulting from the foregoing discussion are of the greatest importance, since they involve not only the treatment of the disease, but its prevention.

Treatment. There are no drugs that afford any specific benefit in the treatment of beriberi, and their use is purely symptomatic, but they are of use on occasions. Constipation is frequently troublesome and must be overcome. For this purpose the saline cathartics are probably superior, particularly in cases of "wet beriberi," where they encourage the abstraction of fluid from the tissues. In cases with marked cardiac debility the use of digitalis is recommended. Cramps and the pain caused by excessive muscular hyperaesthesia may be treated by the bromides. Strychnine may be useful in the treatment of the paralysis or as a general tonic, but it is apparent that it can only be used as an adjuvant.*

Patients not suffering from cardiac involvement should be encouraged to stay about and out of doors, since a moderate amount of exercise will keep such muscles as are not involved, or only partially involved, in better condition. A patient whose heart is evidently affected should, on the contrary, be kept in bed. In these cases massage and electrical stimulation of the muscles are useful measures.

Since, however, the disease is caused by a deficient dietary, the real treatment should be directed toward correcting this deficiency. Adult cases, whether acute or chronic, wet or dry, should be given a liberal and varied diet, including meat and a number of vegetables, particularly beans and peas. All canned foods should be excluded, since the neuritis-preventing principle is destroyed by sterilization, and for the same reason care should be taken that none of the food is cooked to excess. Meats should be served rare, and the vegetables should not be cooked any longer than is absolutely essential to render them palatable and digestible.

Practically all of the cases of beriberi occur in natives who are rice eaters, and who demand rice as a staple part of their diet no

* Cooper has recently found that although strychnine does not cure polyneuritis of pigeons, yet its administration prolongs the life of the birds affected by this disease.

matter how varied it may otherwise be. Care should be taken that the rice furnished them should be undermilled and should contain the greater part of the pericarp. This undermilled rice should be furnished in all cases, because it is known that the beriberi-preventing vitamines are present in it while we cannot be certain that they would be present in sufficient amounts in even a varied and liberal diet. They are either totally lacking, or present in too small quantities to effect a cure in many proteid, fatty, and carbohydrate articles of food, as has been shown by the experiments on fowls detailed in a previous chapter. Moreover, some natives will continue to make rice the chief part of their diet, even when they are provided with a liberal ration. Undermilled rice will in itself suffice to effect a cure, but it should be combined with the liberal diet outlined above, both because improvement in the disease will thus be effected more rapidly and in the interest of better general nutrition. This diet will be sufficient treatment for a majority of chronic or mild cases, but it must be continued for several months, since the nerves regenerate very slowly. As a result, while improvement will generally be noted from the first, complete recovery does not occur until from two to six months have elapsed. Such a dietary is by no means sufficient for acute cases, or those cases suffering from cardiac involvement or very large effusions.

When a cardiac crisis appears, as evidenced by precordial pain, palpitation, breathlessness and cyanosis, prompt action is necessary, as this condition is responsible for most of the fatalities that occur in beriberi. In the past nitroglycerine and amyl nitrite have been used, and when these failed, bleeding from a vein of the arm or neck has been frequently tried. Anderson first tried venesection on two acute cases with a good result. Later Baelz recommended this procedure, and it has since been well spoken of by many authorities, including Scheube and Manson. The abstraction of blood may relieve the overdistention of the right heart, and thus tide over this very critical moment. It is needless to say, however, that this treatment is merely palliative and does not permanently relieve the cardiac distress which is liable to recur at any time and thus end the patient's life.

The writer has found that a far better method of treatment consists in the administration of the extract of rice polishings already described. Cases that appeared to be at the point of death from cardiac failure have been promptly and permanently relieved in this way. The following case may be quoted as an example: Cirilo Taguinez, who had suffered from beriberi for some time, was admitted to the Philippine General Hospital, September 6, suffering from an acute cardiac crisis. Through the courtesy of Doctor Sison, I was invited to see this case and treat it. When first seen, on the morning of September 9, the man was sitting up in bed and gasping for breath. Pulse 150, respiration 45, and his heart was violently palpitating. He presented the typical history and appearance of a case of chronic beriberi suffering from an acute cardiac exacerbation. The muscles of the entire body were wasted and extremely painful to touch, and in addition he had been unable to take any nourishment for several days because of persistent vomiting. The resident physician stated that he had not expected the man to live through the preceding night.

The patient was at once (11:00 a. m., September 9) given the extract obtained from a kilo of rice polishings. This was retained, and his symptoms at once began to improve, and by the evening of the same day his pulse had dropped to 80, his respiration to 30, and the vomiting had ceased. On the following morning another acute exacerbation occurred, and he was again given the extract from a kilo of polishings. Again the symptoms improved, and thereafter he was given the extract from a kilo of polishings daily for about two weeks. The cardiac attacks never returned, the hyperaesthesia of the muscles was greatly relieved, the vomiting ceased and his appetite returned. The whole appearance of the man was changed, although he still suffered from paralysis and was unable to walk. The marvelous improvement in this case and the time of first administration of the extract are shown in the hospital chart (figure 52).

Similar results have been obtained in other cases, and it has also been found that cases of wet beriberi may be just as promptly cured in this manner. Large effusions disappear in the course of a few days after the use of the extract is commenced. Its use is therefore recommended in cases of wet beriberi, or in cases suffering from acute cardiac embarrassment. This extract will not, however, effect such a cure in cases of dry or paralytic beriberi.

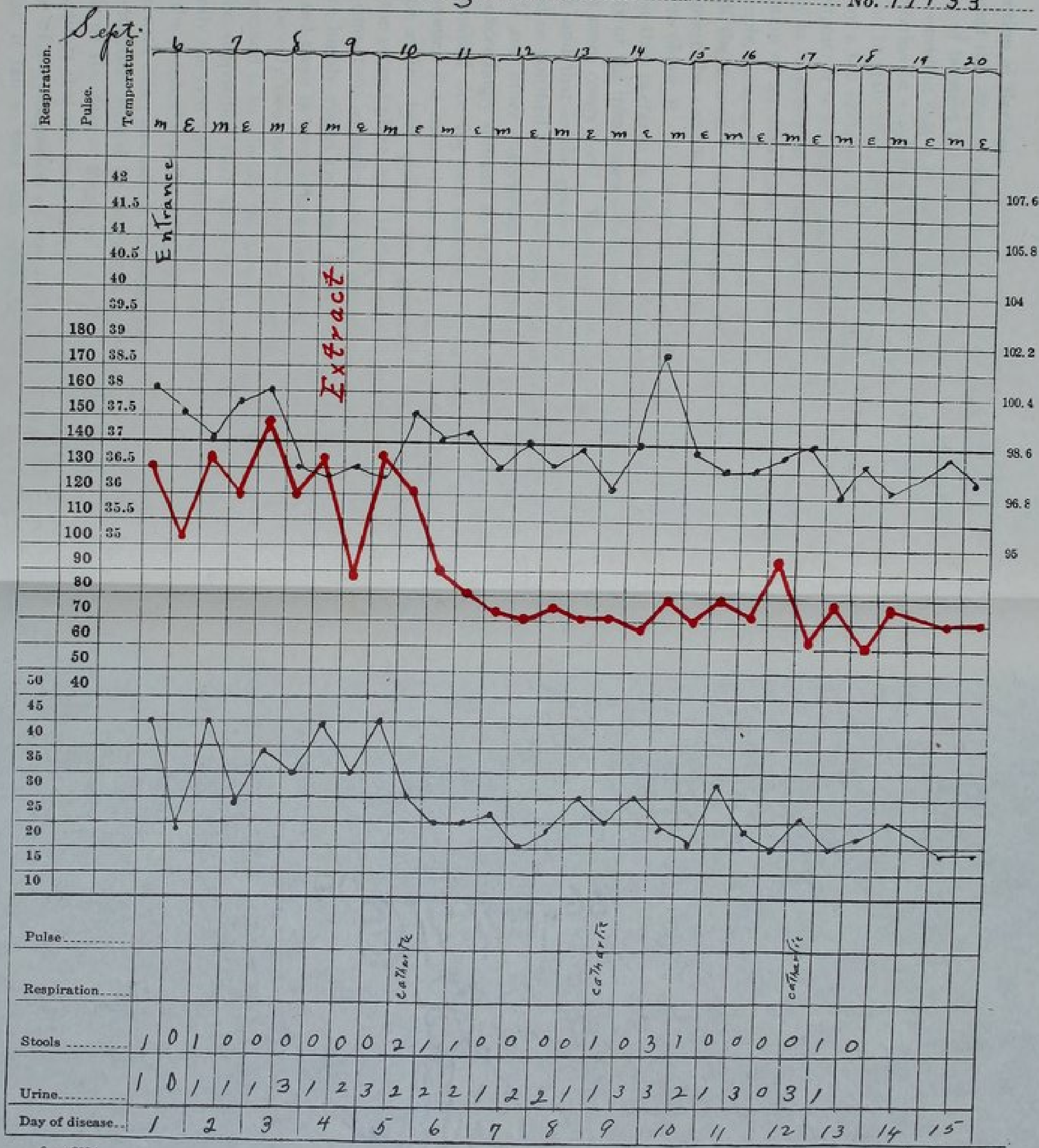
One case of dry beriberi has been treated by the author by means of a quantity of Funk's vitamine isolated from this extract by the method described by Funk. The results were very promising, and a great improvement in the paralytic symptoms followed. Unfortunately, the excessive labor and cost of isolating this vitamine render this treatment impracticable for general use at present. It is to be hoped, however, that this vitamine may at some time in the future be synthesized and placed on the market. This is a chemical problem deserving immediate attention. Its solution will enable dry beriberi to be cured in several days instead of several months.

PHILIPPINE GENERAL HOSPITAL.

Floor 5

TEMPERATURE RECORD.

No. Bed 29 Name Cirilo Taguinez No. 17133



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L. M. Smith.

The Prevention of Beriberi. It is far more important and satisfactory to prevent this disease than to treat it. The great prevalence and distribution of beriberi has already been discussed in a preceding chapter, and it is evident that it is one of the greatest curses that afflict the native population in tropical and sub-tropical countries. We are now in a position to state that beriberi in these native races is almost always caused by a too exclusive diet of highly milled rice, and from a scientific standpoint it is a simple matter to prevent the disease. All that is necessary is to prescribe a sufficiently varied diet and to insist on the consumption of an undermilled rice. Unfortunately the problem is not so simple, because this is a recommendation which is utterly at variance with the economic and sociologic habits of entire races. It is useless to prescribe a varied diet to natives who are so poor that they are unable to obtain it. There are a few natives who live chiefly upon rice because they prefer it to other food, but in all oriental countries the majority of the inhabitants subsist upon rice because they are unable to obtain more costly food. Therefore only one measure will prevent beriberi, and that is the general substitution of undermilled for highly milled or polished rice. This may be readily accomplished in jails, hospitals and other government institutions by an executive order, but it is exceedingly difficult to induce the people as a whole to use the undermilled rice for two reasons. In the first place they have been accustomed for many years to consider the highly milled and polished rice as the best quality, and generally purchase it by preference. In the second place, even if they wish to purchase undermilled rice they cannot do so under present conditions because all the rice mills produce highly milled rice, and all the rice that is imported is highly milled and there is very little undermilled rice on the market. There appear to be only two methods of attacking this sanitary problem. The first method is to educate the people to demand the undermilled rice, on the supposition that when the demand for this article increases sufficiently the rice mills will change their methods of milling and will furnish the people the undermilled rice.

In accordance with this plan, which has been highly recommended, a campaign of education should be waged by the health officials to inform the people of the danger they run in using the highly milled rice. To me it appears that any such educational campaign is doomed to failure because of the magnitude of the undertaking, and because those who propose it fail to take into consideration the inertia and disinclination of oriental peoples to change their habits. Some conception of the magnitude of the undertaking may be obtained if we imagine a similar condition in the United States or Europe. Let us suppose, for instance, that some serious disease such as cancer were caused by eating white bread and that it could be entirely prevented by eating whole wheat bread. How long would it take us by a campaign of education to change the habits of the entire people and induce them all to eat whole wheat bread? Europeans and Americans are intelligent and are not constitutionally opposed to a change of custom, yet it must be admitted that it would require years to effect such a change, probably at least a decade. All intelligent people know that typhoid is a disease contracted directly from an antecedent case of the same disease, and yet whole cities still continue to use diluted sewage for their drinking supply, from streams which everyone knows are grossly contaminated. To effect such a radical change in the staple food of an oriental people by education alone would require a long time, if indeed it could be accomplished at all. And in the meantime they would still suffer from beriberi, a disease that is clearly preventable. Such a situation is intolerable.

On the other hand is the possibility of enforcing the use of an undermilled rice by placing a tax on highly milled rice which would make the price of this latter prohibitive for the poor people. This method has been suggested and urged by Dr. Victor G. Heiser, Director of Health for the Philippine Islands, and after considerable discussion with physicians, lawyers, legislators and others a bill was introduced in the Philippine Assembly, in 1911, imposing a tax of five centavos (two and one-half cents United States currency) per kilo on all polished rice sold, whether foreign or domestic. The Legislature, however, adjourned before the matter could be fully considered. A similar bill (see Appendix, page 414) was re-introduced in 1912 and 1913, but owing to the fact that the Islands were already suffering from a serious shortage of rice, it has been deemed inadvisable to pass the bill.

The Far Eastern Association of Tropical Medicine met in Hongkong in January, 1912, and considered this proposition very fully. But while this association accepted the fact that beriberi is caused by a too exclusive diet of polished rice, it refused to unequivocally recommend such a tax on this rice, because it believed that such action would exceed its authority and because it doubted the expediency of such a tax. The association, however, passed a set of resolutions on the subject which may be found in the Appendix, page 413. No decisive action has therefore been taken on this proposition in any part of the world, and meantime the prevalence of beriberi is increasing rather than diminishing, because the use of highly milled rice is becoming more extensive year by year. We may expect that this extension of the disease will continue, because as European civilization progresses in the tropics fewer natives will pound their own rice, and more of them will take their rice to the mills or will be employed in some industrial occupation. These latter, being paid in money, will purchase their rice in the open market and will obtain the highly milled rice. It will be just as impossible to prevent this state of affairs without taking some decisive action as it would be to stop the progress of that civilization itself.

Those modern nations who have colonies in the tropics justly take pride in the advances they have made in sanitation, yet here is one disease, clearly preventable, which is even more prevalent than was formerly the case, simply because these governments have not yet been aroused to action.

Let us consider the arguments for and against the solution of the difficulty by means of a tax such as has been proposed. The argument for a tax may be briefly summed up as follows: Something must be done to meet an intolerable sanitary condition. Only two remedies have been proposed, namely, the gradual education of the people and a tax on highly milled rice. All who have some insight into oriental habits and ways of thinking will agree that while education might conceivably have some effect upon the oriental people who are eaters of rice at some time in the distant future it will fail to produce any radical change in their habits of life for at least a generation; a fact which removes education from consideration as a solution of the problem at the present time.

The objections to such a tax are: 1. That it would be difficult to enforce. 2. That it would derange commerce. 3. That it would cause native discontent.

1. A tax on highly milled rice would be difficult to enforce. In many countries the enforcement of such a tax would be simplicity itself. In the Philippine Islands, for instance, the tax could be collected at each rice mill, by officers of the Internal Revenue Department, and would be no more difficult of collection than is the internal revenue tax on spirits. It could also be collected on all imported rice by the customs officials, just as are other duties. The machinery is already in existence and all that is needed is the law. But this is not the case with all countries. Many of them, for instance the British Colonies that enjoy free trade, have no customs officials, and therefore the machinery for the collection of such a tax on imported rice would

have to be created. This, however, would not be a serious objection. One inspector for each of the principal ports of entry could collect this tax, and this office could easily be created by the same law that imposed the tax. Moreover, it is far from certain that it would be necessary or desirable to impose an import tax. So far as I am aware, practically all nations have an internal revenue tax on spirits. Now, if Indo-China, which is one of the chief exporters of rice, should pass a law taxing highly milled rice, and should collect this tax by its officers of internal revenue, it would have the effect of increasing the cost of all the highly milled rice exported through Saigon, by the amount of the tax. This highly milled rice would be increased in price when imported into a British colony under free trade laws, even though no additional tax was imposed by that colony. *The essential point is, therefore, that each government should impose a tax on the highly milled rice actually produced by its own mills. The tax on imported highly milled rice could then be ignored. The machinery for the imposition of this tax already exists in practically every civilized community* and its collection would be comparatively easy.

2. A tax on highly milled rice would derange commerce. This is the most serious objection, since we are dealing with a staple article which is the very existence of many countries. Let us take for discussion Indo-China and the Philippines, which are typical exporters and importers. The officials from a country like Indo-China, which exports large quantities of highly milled rice from Saigon, naturally fear that if they should impose a tax upon this rice they would lose this trade, which would be gained by some country which imposed either no tax or a smaller tax.

The situation in the Philippines is different. Here not sufficient rice is raised to support the population, and large quantities of it are imported, all of it highly milled. Now suppose a tax were to be levied in the Philippines alone on this rice, at the port of entry. There is at present a shortage of rice throughout all the Orient, including the Philippines, and none of the exporting countries are producing undermilled rice. Now it cannot be expected that a tax on overmilled rice in the Philippines alone would compel the exporters of other countries to change their methods of milling so long as they can find plenty of other markets that are only too anxious to accept the overmilled rice produced at present. Therefore, either the people in the Philippines would be unable to buy this imported rice at the increased price, in which case it would be sent to some other country, and the Philippines would face a famine. Or in case the people were able to pay the increased price they would then have the same old unsanitary rice at the higher price.

Now let us suppose that the tax were levied upon the highly milled rice produced in the Philippines, but no import tax were levied on this class of rice. This would simply result in increased importations of foreign overmilled rice. For it may be taken for granted that the people would continue to consume the highly milled rice to which they are accustomed so long as it could be imported at the same price as formerly. The Philippine rice mills would then be in a bad way, for they would be unable to sell their overmilled and taxed rice in competition with the overmilled imported, but untaxed, rice, and they would also be unable to sell their undermilled rice until the amount of imported rice was insufficient to supply the demand.

This reasoning with regard to the Philippines would only be correct during a general shortage of the rice crop throughout the Orient. In years when the crop is abundant in exporting countries, and there is therefore competition among these countries in selling their rice, if there were a tax on highly milled rice imported into the Philippines the exporting countries would find it to their benefit to take the trouble to produce the desired undermilled rice for the Philippine trade.

It seems probable therefore that an importing country like the Philippines would be able to enforce such a law as that proposed without deranging commerce except during years when the rice crop is short. An exporting country, however, would suffer loss of trade if it imposed a tax, unless other exporting countries had taken similar action. Situations such as these make it apparent that there might be a considerable economic danger to a nation which alone and unsupported passed such a law, and probably no single nation will take this risk. What, then, remains? Plainly the only solution consists in an international action by which all rice-producing countries will impose this tax on highly milled rice at the same time. This is difficult, but not impossible, and a method for obtaining this result will be suggested later. In the meantime, however, let us suppose that such a tax has been imposed in all rice-producing countries. What would be the result in countries like Indo-China and the Philippines? If Indo-China still attempted to export highly milled rice it would be necessarily increased in cost by just the amount of the tax. But since this would also be the case with other rice exporting countries, Saigon rice would suffer no disadvantage, and would compete for trade on exactly the same terms as before the tax was imposed.

In the Philippines there would also be the same tax on overmilled rice. But if the people turned to imported overmilled rice they would find it had been taxed in the country where it was produced and was therefore no cheaper. This would result in the desired end. The poor people of all countries, who are the ones that chiefly suffer from beriberi, would find the price of the overmilled rice beyond their reach and would be unable to buy it. The mills would be compelled to furnish the kind of rice that the mass of the people could buy, and trade would not be disturbed but would go on as before, except that all the rice of trade would be undermilled instead of overmilled.*

But it must be emphasized that such a tax to be successful must be such as to make overmilled rice prohibitive in price to the poorer people. In other words, the tax will not be actually collected and it is not intended that it should be. It will raise no revenue. If it were collected and revenue were thereby raised it would simply indicate that the people were purchasing the same overmilled rice at a higher price than before. This would not improve sanitary conditions, but would constitute a heavy tax upon the main staple of food.

The effect of such a law on the millers of rice should also be considered. Many in this business would at first oppose such a law because they would fear the disturbance of their business. However, the law would not in any way affect the volume of their trade. A certain quantity of rice is grown and it must be milled, that is husked, cleaned, picked over and separated into grades. It would simply mean that the milling process would not be carried so far. No changes in machinery would therefore be required, and no change in method *except that the milling process would not be carried so far.* It seems, therefore, that such a law would not affect the millers adversely. It is difficult to see how trade would be disturbed provided this tax were imposed by all countries using or producing rice at the same time.

There is one more point that must be considered, namely, the adoption of a standard by which it can be determined whether a rice should be classed as overmilled or undermilled. For most purposes this can be determined readily on simple inspection by anyone who is familiar with the two varieties of rice, or by staining the rice with iodine, according to the method described in Chapter V. But when it becomes a question of imposing a tax on a given rice it is apparent that a fixed

* A very small quantity of highly milled rice may still be produced for Europeans or those natives who prefer this variety and are able to pay the price. Those people who can afford this luxury will also be able to afford a varied diet, and would not have beriberi in any case. Provision should be made in the law to exempt from tax the overmilled rice produced for consumption in Europe and North America, since there is practically no beriberi in those countries.

standard is essential in order to avoid disputes and to remove the temptation to favor certain dealers for either personal or monetary considerations.

Such a standard fortunately exists in the chemical determination of the amount of phosphorus pentoxide contained in a given rice. It has been shown by a large number of investigations performed by different students of the problem that practically all of the phosphorus in rice is contained in the outer layers of the grain that are removed in milling. An undermilled rice is therefore rich in phosphorus, while an overmilled rice is correspondingly poor in that element. It is now very generally agreed that a rice which contains 0.4 per cent phosphorus pentoxide contains sufficient of the pericarpal layers to prevent beriberi even when used as a staple article of diet. The estimation of phosphorus is a chemical operation of comparative simplicity and of great accuracy, and it has been so generally used with satisfaction that the Far Eastern Association of Tropical Medicine recommended this standard for universal adoption. It is believed that when international action is taken this standard should be adopted as the best and most readily applicable method of determining accurately the safety or danger of using a given rice as a staple article of diet.

3. Such a tax would provoke native discontent. We have seen that the operation of this tax will not increase the price of rice to the poor, but cause the markets to be supplied with undermilled rice instead of highly milled rice. The undermilled rice would be no more expensive than is the present highly milled rice. Indeed, it is to be hoped that it would be cheaper for reasons that will appear later. Any discontent that would be produced by the operation of this law would therefore be due solely to the fact that the native would be compelled to subsist on undermilled rice instead of upon highly milled rice, thus effecting a mild revolution in his dietary habits.

That a certain amount of discontent might be produced in this way may be admitted, but it would be trivial in extent and only temporary in duration. That this would be the case is indicated by the experience in the Philippines in those institutions where this change has already been affected. When undermilled rice was first supplied to the Philippine Scouts (native soldiers) instead of the highly milled rice to which they were accustomed, complaints were numerous. Investigations of these complaints clearly showed that the rice supplied under the new contract was of a poorer quality than that formerly used, and contained a large quantity of dirt, chaff, unhulled and broken grains. This difficulty was corrected, an absolutely first-class quality of undermilled rice was supplied and the complaints ceased. The undermilled rice has now been used by these Scouts from August, 1910, until the present time and appears to give excellent satisfaction, for complaints are at present unknown.

On May 4, 1909, the Governor General of the Philippines issued an executive order forbidding the use of highly milled rice in any public institution. As a result of this order undermilled rice was furnished all government hospitals, jails, lighthouses, etc. Complaints also followed this innovation. Doctor Heiser, the Director of Health, says: "It was apparent that much of the unpolished rice that was issued in the beginning was not very clean and contained many husks. This gave rise to much complaint among those who were required to use it. It was frequently alleged that the husks tickled the throats and often caused gastritis. On investigation no reliable evidence as to the gastritis could be obtained. Commissary officers, prison wardens and others who were directly charged with carrying out the orders to use unpolished rice, were constantly besieged with complaints, and it was but natural that they should take the course of least resistance and recommend that its use be discontinued. To add to the difficulties of those who were insisting on the use of unpolished rice, the rumor spread that unpolished rice, when stored in bulk, soon spoiled, thus causing great financial loss. Investigation of this matter showed that there was no reason to believe that unpolished rice, when stored under the same conditions as polished rice, spoiled more quickly."

Efforts were then made to obtain an undermilled rice clean and free from husks. Such a rice has since been continuously furnished to governmental institutions, and all complaints by those consuming it have ceased, although at various times officials still claim that it is difficult to obtain such a rice. In short, it appears quite evident that such complaint as there has been has arisen, not because the use of undermilled rice was ordered, but because it was of a poor quality.

The lesson learned from this experience is that when the change to undermilled rice is made, great care should be taken to see that the mills produce a good quality of rice. The method is new to them, and without some supervision they are almost sure to turn out a rice that is dirty and contains many unhusked grains. When this difficulty is overcome it is believed there will be little objection to the undermilled rice on the part of the natives. The native in tropical countries is obstinate in clinging to his customs, but is generally docile and makes no disturbance when innovations are forced upon him unless his religious prejudices are disturbed.

Moreover, there are several good reasons why any objection to undermilled rice will be but temporary on the part of the native. In the first place it is not such a radical change in their habits after all, at least for many of them, who have lived on hand-pounded rice in the past at some period of their lives. A hand-pounded rice is essentially an undermilled rice. In the second place an undermilled rice is a *better* rice. It has a rich flavor that is lacking in highly milled rice, and has a *higher food value*. I have personally prescribed undermilled rice for a number of beriberi patients and have taken pains to secure it for them, and their unanimous testimony is that they like it better than the highly milled rice because it tastes better and because they do not have to eat so much of it. It satisfies their hunger better. Many of them have said that they would always buy that kind *if they could only find it on the market.*

Statements as to taste are individual preferences and can only be accepted with a reservation, but the increased food value of undermilled rice is susceptible of demonstration. Rice polishings, or the bran removed from an overmilled rice by the present method of milling, contains a very high percentage of albumens and fats. It is impossible to give figures with mathematical accuracy, because these figures vary more or less for the polishings from different grades of rice. However, in general rice polishings on analysis average 5 per cent of total nitrogen, of which about 4 per cent is of proteid origin. This indicates that about 25 per cent of the total bulk of these polishings consists of various proteids. Moreover, the remaining one per cent of non-proteid nitrogen represents largely amid substances like asparagin and arginin, which possibly have some dietary importance. Rice polishings also contain from 8 to 10 per cent of fats, approximately one per cent of sugar, which is chiefly in the form of sucrose, a very high percentage of mineral salts, including the chlorides and phosphates of sodium, potassium, calcium, magnesium, with traces of iron, manganese and other similar elements. Now, since overmilled rice is very rich in carbohydrates but very poor in proteids, fats and inorganic salts, it follows that an undermilled rice which contains a much higher proportion of proteids, fats and salts approximates more closely a physiologically balanced diet. These food principles are, moreover, readily dissolved from the polishings and are quite capable of digestion and assimilation. It may be noted that at present these polishings enjoy a ready sale as fodder for animals. From these considerations it is believed to be certain that no serious disturbance on the part of the natives in any country would result from the introduction of undermilled rice, and that the mild opposition which might occur could be changed to approval by education.

We have now to consider the possible benefits of such a law aside from the fact that it would result in the eradication of beriberi. First, it is believed it would result in cheaper rice for the poorer classes. An undermilled rice should sell at a cheaper price because less time and labor are expended upon it. Time and labor are not very expensive articles in the tropics, but they have some value, and the undermilled rice should be cheaper by just the value of the time and labor saved. This would result without any loss to the rice millers, who would still have the same margin for profit as before. Indeed it is conceivable that their profits might be increased, for under these circumstances they might be able to mill more rice per day and make an increased profit while still selling the product at a lower price. This is economic speculation about details which would have to be worked out, but the fact is undoubted that there would be a saving in time and labor for some one. But even if the actual price of rice remained the same there would still be a relative saving for the consumer, since because of the increased food value of the undermilled rice, less of it would have to be consumed. This has frequently been found to be the case in actual practice.

Secondly, the use of undermilled rice would probably cause a great sanitary improvement aside from the prevention of beriberi. It is a well-known fact that large numbers of the poorer part of the population are continually undernourished, and for this reason easily fall victims to infections that they could throw off if their resistence were increased by proper food. The prevalence and extent of tuberculosis in the Philippines and other oriental countries is appalling. Fresh air and nourishing food are the best remedies for this disease. There is as much fresh air in these countries as elsewhere, and if more nourishing food were supplied the incidence of this disease would fall. The same thing is true to a lesser extent of all the infectious diseases. Sanitarians have discovered that when a pure water supply is substituted for a contaminated water in a given community that the death rate drops not only for intestinal diseases, *but for other diseases as well.* This observation has been called Hazen's theorem. Its cause is still in doubt, but it may be surmised that when the population is freed from the intestinal diseases that were water borne, their resistance to infection is increased with the result that the death rate from other infections drops. Sedgwick has found that conspicuous among the diseases so prevented are pneumonia, pulmonary tuberculosis, bronchitis and infant mortality. If this holds true for the water supply, how much more important might be the effect of improving the present deficient food supply? There are many countries where thousands suffer from beriberi and thousands more are on the verge of that disease, and the majority of the population are habitually underfed. Is it too much to hope that with the eradication of beriberi and the added resistence gained by an improved food supply the mortality in these countries will be tremendously reduced? On the contrary it may be confidently expected. And having seen the possibility of this great improvement, we should be encouraged to attack the problem, even though there may be difficulties to overcome.

The main difficulty to be met is that already indicated, namely, the necessity for securing international action in order to avoid commercial derangements and to ensure the widest possible action of so beneficial an endeavor. It appears to me that there is an easy and practicable method for securing this international action. It consists in the appointment of an international commission to discuss this subject and recommend to the participating governments such a law as will bring about the desired end. This is not a new or untried experiment. There have been two great international conferences held to recommend methods of reducing the consumption of opium, and its deliberations have proved to be of the greatest value, and have resulted in the passage of laws by most of the countries who sent delegates; laws which promise to greatly simplify that vexed sanitary, moral and economic question. The eradication of beriberi is a sanitary and economic problem. No moral issue is involved, and the subject is much simpler, since there is no question of a habit-forming drug and of devotees who must learn to exist without it. There is every reason to believe that an international conference on beriberi could be held and that its deliberations would be just as fruitful as those of the two opium conferences.

But some one must take the first step. It is therefore respectfully recommended that the President of the United States should invite all of those nations who are interested in the problem to participate in such a convention by appointing a delegate or delegates who shall form a commission to meet at some point to be agreed upon. And that this commission should discuss the advisability and practicability of generally extending the use of undermilled or unpolished rice by means of a tax to be levied by all nations on highly milled or polished rice, or by any other better method that the commission may devise.

Conclusion. The inspiration of this book has been the desire to present a convincing exposition of the etiology of beriberi, with a solution of the sanitary problem which we face because of the prevalence of the disease. It appears to the author that the first part of the program has been achieved with some degree of success. It would be too much to hope that his solution of the problem will be fully accepted, but it is not too much to hope that it will stimulate an interest in the subject in the minds of those authorities who have it in their power to take action on this important matter.

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APPENDIX.

IAC. BONTII. DE MEDICINA INDORUM. LIB IV. PART 3. METH. MEDENDI INDICA.

LUGDUM BATAV. APUD FRANCISCUM HACKIUM 1642.

CAPUT I. DE PARALYSEOS QUADAM SPECIE, QUAM INDIGINAE BERIBERII VOCANT.

Affectus quidam admodum molestus, hic homines infestat, qui ab incolis Berberi (quod ovem sonat) vocatur. Credo quia quos malum istud invasit nictando genibus, ac elevando crura, tanquam oves ingrediantur. Estque species paralyseos, seu potius Tremoris: Nam Motum, sensumque manum, ac pedum, immo vero aliquando totius corporis depravat, ac tremere facit. Causa hujus morbi praecipua est, crassus, ac lentus humor pituitosus, qui nocturnis teporibus, praefertim pluvio coelo, (pluviae aute his assiduae cadunt ab initio Novemb. usq. ad Maij initiu,) nervos corripit, dum nimirum homines diurnis caloribus defatigati, noctu omne tegmen ac lodices a se reiiciunt, unde facillime, jam in cerebro praecipue genitus, nervos iste humor phlegmaticus invadit. Nam noctes, in his locis, comparatione caloris diurni, frigidae appelari possunt. In hoc casu artus prolongantur, non contrahuntur, insinuante se inter juncturas phlegmate, ita ut nervi ac ligamenta inde laxentur. Quamvis autem hoc malum plerumque per gradus, as pedetentim homines invadat, tamen aliquando valde subitum est, dum nimirum homines aestu defatigati, potum es Palma Indica copiose ac confestim ingerunt; non secus ac, in patria, diebus canicularibus aliquando vidimus fieri, cum quis cursu, aut aliquo alio vehementi motu calefactus, potum cerevisiae, aut lactis pressi, nimis avide haurit, ita ut inde saepe summum vitae discrimen, immo ipsam mortem iucurrat. Porro signa hujus mali aspectu obvia sunt Adest enim spontanea universi corporis lassitudo; motus ac sensus, praecipue manuum ac pedum depravatur, ac hebescit; ac in iis sentitur plerumque titillatio talis quaedam, qualis in patria frigida, ac hyemali tempestate manuum, ac pedum digitos corripit, nisi, quod hic tantus dolor non adsit. Tum etiam vox aliquando ita impeditur, ut aeger vix articulate loqui possit: quod mihi ipsi accidit, dum hoc morbo laboranti vocis sonnus, per integru mensem tam exilis esset, ut me vel proxime assidentes vix intelligerent. Adsunt, praeter haec, aliquando multo plura signa, ac Symptomata, quae tamen omnia tenacem, ac frigidum humorem sapiunt: sed praecipua enarrasse sufficiat. Accingamur ad curationem itaque, quae plerumque hic in longum trahitur; dum nempe humor iste lentus, ac frigidus aegra discutitur: per se tamen (ut plurimum,) lethalis non est: nisi musculos pectoris, ac thoracis invaserit, & hoc modo, spiritus, ac vocis viam intercludat. Sed hoc imprimis curandum est, ne (si ullo modo fieri possit) te lecto affigas decumbendo: Sed vel ambulando vel equitando, vel simili aliquo motu validiore omni conatu te exerceas: currere quidem impossibile est. Frictiones quoque fortes, ac dolorificae hic summe necessariae sunt, quas commode hic servi Bengalenses ac mulieres Malayccae adhibent. Nam nostra gens tali exercitio non assuevit, ut nec balneis, quae hic frequentia sunt. Fomenta, ac Insessiones hic conficiunt ex herba nobili Lagondi dicta, quae folio quidem Perficariam refert, estque odoris suavis, ac aromatici. Certe nobis non tantum usum Chamomeli, ac Meliloti praebet, sed discutiendi, ac resolvendi viribus iis, meo quidem judicio, praestat: Pedes, ac manus praeter es inungendi sunt oleis Caryophyllorum, ac macis: sed mixtis ol. rosaceo: nam sola adhibita nimis caustica sunt, & cutem facillime eroderent. Habemus praeter haec nobilem Naphtae speciem, allatam ex Sumatra, Javae regno e regione in conspectu sita. Quam Minjac Tannah Indi vocant, quod oleum terrae significat, quod non secus, ac nobis cognita Naphtha, quod oleum petrae vocamus, e terra erumpat; vel ex rupibus, in subjecta flumina praecipitetur. Hoc oleum a Barbaris in tanto pretio habetur, ut rex Achinensis qui potentissimus istius insulae est Tyrannus, sub capitali poena istud evehi inde prohibeat: ita ut incolae, nocte intempesta, si quae nostra aut Anglorum navis eorum littoribus adpellat, ad nos istud furtim deferant. Hoc oleum, partibus affectis illitum, miraculi instar aegros consolatur. Odore est porro gravi: sed tamen non fastidioso.

Sed cum hic morbus fit chronicus, ac longi temporis, nihil aeque prodest, quam decocta ex radicibus Chinae, Sarsae parillae, ac Liguo Guajaco: quae blando, ac amico nostro corpori calore, frigidos istos, ac crassos humores per sudores, ac urinas egregie discutitiunt, ac evacuant. Interpositis tamen subinde commodis per alvum evacuationibus, inter quas principem locum obtinet

Extractum, quod hic conficimus. Ex aloe, & gutta gambodja dicta vulgo (corrupte apud nos gutta gamba) cujus descriptionem inferius videbitis.

Sanguinem hic mittere nefas: non enim plethora, sed cacothymia in vitio est: & quis sanguinem fontem caloris, ac thesaurum vitae non esse intelligit?

Hujus affectus relinquiae porro commode discutiuntur Theraca, Mithridatio &c. sudorem, ac urinam moventibus ac nervos roborantibus medicamentis. Reliquas hujus mali molestias opportuna exercitatio, ac valida Naturae vis sanabunt.

Beriberi at Alipur.

In 1908 Daley reported 50 cases in the reformatory school at Alipur. The first case occurred on September 5th. Burma rice (polished) had been issued since April, 1907. After the epidemic broke out the boys were divided into two batches, one receiving Burma rice and the other ordinary country (unpolished) rice. This experiment began on October 12th after which date there were only ten more admissions to hospital from beriberi, *all from the Burma rice batch.* It is noteworthy that none of those fed on country rice including some Eurasian lads and the hospital attendants took the disease.

Diet of Native Egyptians According to Doctor Lahn.

I. In Cairo and Alexandria the natives may be considered as falling into three classes, i. e. poor, medium and well-to-do, as follows:

1. *The Poor Class,* which form the majority of the population, eat beans, either boiled or dressed with oil and meat soup, pounded beans cooked with parsley and onions, lentils, peas, rice, uncooked vegetables such as leeks, onions, cucumbers, melons and watermelons. They also make considerable use of sour milk and old stored cheese.

2. *The Middle Class,* which is smaller in number than the former, eat a certain quantity of pulse, rice, meat and vegetables cooked with butter, and some fruit. A sect of the Copts, about 5,000 in number, eat on account of religious rites special food during three months of the year (March, April and August) consisting of vegetables and pulse, cooked with olive oil, linseed oil or sesame

oil. During the three months they eat neither meat nor fowls, but at other times their food differs very little from that of the Mohammedans.

3. *The Well-to-do Class,* which is the minority, eat all kinds of food: pulse, rice, vegetables, fruits, pastry and sweetmeats. They eat bread made of pure wheat.

The natives in the provinces may also be divided into three classes as follows:

II. Lower Egypt.

1. *The Poorer Class* eat maize mixed with fenugreek (1:10). They use pure wheat 35 days only during the year. Their food is limited to salt, onions, cheese and old cheese liquid. They also eat pulse and vegetables as mentioned in (1) above. They rarely use butter, and eat meat on feast days only.

2. *The Middle Class* make their bread of half wheat and half millet. Their food consists of pulse, vegetables and fowls, all cooked with butter, and a certain quantity of milk.

3. *The Higher Class* is the same as the wealthy people of Cairo and Alexandria, see (3) above.

III. Upper Egypt.

The inhabitants are the same as Lower Egypt, and the same notes apply, with the exception that they make their bread with Upper Egypt millet instead of Lower Egypt maize, mixed with fenugreek or barley.

The inhabitants of the ports, such as Damietta, Rosetta and Suez, live according to the three above-mentioned categories, but in addition eat rice cooked with fish and sea fruits.

In nearly all cases the rice eaten is imported from India and Burma, and therefore probably milled. The rice grown in the country is of such high quality that most of it is exported on account of the greater price realized.

Maurer replied to Eijkman's criticisms as follows:

"The mode of action of oxalic acid is extraordinarily manifold. It injures the mucous membrane, the blood, the central nervous system, the heart, and disturbs metabolism. Oxygen absorption and carbon dioxide excretion are decreased. On this ground Kobert classifies oxalic acid with phosphorus, hydrocyanic acid and carbon monoxide in a group as very specific metabolic poisons. The result of animal experiments are also extraordinarily different, and not only dependent upon the quantity of the poison, but also *the kind and quantity of the food used.* (Italics ours.) The poisonous action is increased by paucity of calcium in the food and through addition of acids, and is decreased by calcium rich food and increase of food. Hens fed with oxalic acid usually show the deleterious effect of the poison on the mucous membrane, and particularly by disturbances of metabolism, and many animals die in a comatose state, *but the action on the nervous system is only seldom seen, and only in a few cases have I succeeded in producing undoubted paralyses and their accompanying phenomena.* (Italics ours.) I was compelled in 1903 and 1905 to interrupt my animal experiments in Sumatra, and I am not therefore able to state accurately how paralysis may be brought about, but I believe it may be done by forced feeding in order to produce filling of the intestine and constipation, and the addition of larger doses of the poison. Now, because this paralysis appeared in a very short time (17 days) on a food which never causes polyneuritis (rice with hulls) and because the animal only recovered from its paralysis in several months, I believe I am right in believing that the oxalic acid is the cause of the paralysis. As I also found in the intestinal tract of hens bacteria and also yeasts and fungi which in sugar-containing food produce quantities of oxalic acid, I drew the conclusion that the polyneuritis of fowls of Eijkman is in the last analysis an oxalic acid poisoning, which develops when we feed fowls on sugar-producing food (starch) which lacks the natural antidote to oxalic acid (lime). Such a food is hulled rice. Polyneuritis is cured by feeding unhulled rice, lime-containing food, or better, raw meat, which deprives the lower organisms of the substance for the production of oxalic acid. When after these findings I investigated regularly the urine of beriberi cases, I could always find oxalic acid in abundance in fresh cases. I also found in their feces oxalic acid producers, and believe from this that beriberi is also a chronic oxalic poisoning in which the poison is produced in certain circumstances in the intestine. *But I am far from claiming that the material so far furnished by me is sufficient to show conclusively that oxalic acid is in fact the looked-for poison in these disease processes.*" (Italics ours.)

Ashmead's views on the etiology of beriberi are shown in the two following letters which were published in the Journal of Tropical Medicine, 1901, page 281:

"Will you permit me to observe, regarding your notice of beriberi on the schooner *Alert,* that I have analyzed the situation of several beriberi ships, in respect to the cause, and I have always found some source where the poison of carbonic acid gas came from plentifully. I maintain, even against the Dutch East Indian doctors (beriberi specialists of Java), that in all these outbreaks on ships it is some emanation of carbonic poisons which lies at the bottom of the trouble. The food has nothing to do with it. Beriberi means 'Goat's gait' or 'Sheep's run,' and it has reference to the symptoms of paresis of the nerves of the legs, always symmetrical; the dropping of the toes, or pes equinus; and the laboured lifting of the leg and thrusting it forward, due, in my opinion, to carbonic poisoning of red blood corpuscles and peripheral nerves. The quick recovery of all crews as soon as they are removed from the ships to a purer atmosphere is the same effect which the Japanese obtained by removing their sick from the low situated wards of Tokio to higher ground. They thus obtain for them an increased supply of oxygen. Carbonic acid gas being heavier than air, sinks to the lowest levels, where, in Japan and the East, are always found the worst type of the disease.

"In my special inquiry into diet as a cause, the captains of ships have told me that the food throughout the voyage, of those who escaped and those attacked, was identical. I found, too, that worm-eaten rice of ships could not have produced beriberi, otherwise all the negroes of the Savannah delta, upon whom the damaged rice is usually bestowed, would be permanent prey to beriberi.

"Beriberi is not contagious, so that there is no need of disinfection. If the deficiency of haemoglobin of the blood (there is never a deficiency of red blood corpuscles in beriberi) was due to a micro-organism, as some beriberi specialists claim, why is not the spleen enlarged? And why are children and women in Japan so seldom affected? Nearly always men, and very robust ones, are affected with beriberi.

"Dr. Takaki's Japanese theory that rice produces beriberi does not hold water. All that rice may have to do with it is that it represents insufficiency of alimentation. You might as well incriminate the oatmeal when, as it so often happens, beriberi breaks out in a Scotch crew."

"The disease, beriberi, reported as having attacked three of the crew on a Nova Scotian schooner which arrived to-day from Lagos, West Coast of Africa, by way of St. Martins, is the same disease that attacked the crew on the *Robert S. Patterson,* from Navassa Island, in 1894. I investigated that case with the Japanese physician, Dr. Tschupija.

"The ship had left Navassa fourteen days before her arrival at Perth Amboy, N. J. While loading phosphate earth as cargo, seventy-four negroes begged Captain Barton to bring them home. Some of them had been there for a year. Sickness developed on the trip and three died and were buried at sea. A fourth died off Sandy Hook. An analysis of the phosphate earth of Navassa showed 3.98 per cent of carbonic acid out of 100 component parts of bone phosphate of lime. The earth's composition was fifty-five grains silician matter, forty-five grains soluble matter, three-quarters per cent carbonate lime, and it was really a deposit of coral or sea shells, or coprolite insects of sea decay.

"On visiting the *Robert S. Patterson* at Perth Amboy I found one man lying dead and ten others in various stages of beriberi (kakke) as I had known it in Japan.

"These seventy-five men, who had worked in the phosphate quarries, had been shipped in a space less than five feet high, thirty feet wide and fifty feet long. This space had no portholes. Even a considerable part of this space was filled with phosphate earth or cargo. In a space of 7,500 cubic feet, seventy-five men lived thirteen days with the least possible ventilation, with four lanterns consuming part of the oxygen necessary for life, with all the foulness engendered by breathing, etc. These men were very poorly clad, and coming from many hardships suffered in a tropical clime, were so apathetic that nothing could induce them to go on deck for fresh air. It was evident in that case, and it is probably true also of the Nova Scotia schooner *Alert*, that carbonic poison was the cause of illness. Beriberi is not the sleeping sickness of Africa."

BRADDON classifies rices according to the mode in which they are prepared as follows:

I. Red Rice. Retaining all or almost all of the pericarp and aleurone layers, and is therefore better protected from the action of Saprophytes and subsequent decomposition.

II. Cleaned or White Rice, which may be:

1. Fresh rice:

(1) Used as newly prepared from padi, *it presents the character of the seed unaltered.** (Italics ours.)

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* If it is this class of rice to which Braddon refers when he says, "Fresh rice is never toxic," we agree with him. But the wholesome quality of this rice depends not upon its

(2) Selected. Washed, picked over and freed from adventitious bodies and diseased grains.
(3) Unscoured. Retaining much of the gluten layer.

2. Uncured rice:
(1) Stale. After cleaning, kept for a long time.
(2) Unselected and unwashed.
(3) Scoured, the gluten layer almost or wholly lost, and therefore more liable to decay.

3. Cured rice:
(1) Fresh cleaned or stale.
(2) Sterilized by boiling, therefore protected from spread of any specific organism originally present on or in the seeds.
(3) Unscoured and retaining the whole of the aleurone layer.

This is an extremely faulty classification and conveys an erroneous idea as to the different varieties of rice. The reader would gather from this classification that fresh unscoured and cured rice are white rices. This is seldom the case. A white rice is usually one from which the colored pericarp has been removed by milling or scouring.

Again it would lead the reader to believe that there are three varieties of cured rice, i. e., Fresh, Sterilized and Unscoured, whereas all cured rice is sterilized or parboiled, since this is the process of curing; it may be scoured or unscoured, although as a matter of fact it is practically always unscoured because of the impossibility of making it white, and it may be either fresh or stale. Since Braddon's whole argument depends upon the varieties of rice, this matter of classification is important, and the reader is asked to bear in mind the classification which we have made in the previous chapter on the preparation of rice.

Abstract and criticism of the work upon which Pekelharing and Winkler based their conclusion that beriberi is an infectious disease.

Pekelharing and Winkler examined sections of heart, kidney, spleen, liver, spinal cord, muscles and nerves from sixteen dead bodies. No microorganisms were found. Examination of cerebro-spinal fluid was also negative.

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freshness and lack of toxicity as Braddon believes, but on the fact which he ignores, that the seed is practically unaltered and retains the nutritive principles contained in the outer layers of the grain. It is obvious that a highly milled rice may also be fresh. Fresh, highly milled rice produces beriberi quite as readily as the same rice when it has become stale.

Blood of beriberi patients was then examined microscopically by taking a drop from the finger after sterilizing the skin, and cocci and bacilli were found in many cases. They say: "At Atjeh not only were they met with in those suffering from beriberi, but when the blood of healthy persons who had passed some time at Atjeh was examined the presence of bacteria was recognized. We could conclude from this that at Atjeh, where beriberi is very general, pathogenic bacteria pass through the circulation of all or almost all of those living there."

Cultivation of these Bacteria. They employed finger blood collected in a similar manner for inoculation, and state that "Although bacteria were always found in the blood employed for inoculation, the tubes for the most part remained sterile. In fifteen cases, however, we obtained some growths of bacteria; from twelve patients growths of micrococci were developed in tubes and from three some growths of rod-like bodies. The rods differed from each other in every instance." Micrococci were therefore obtained from twelve cases. They were evidently not all the same organism for some of them were white, some yellow. As they say themselves: "Some further researches will be necessary to decide whether the different forms of micrococci that we obtained in our cultures from beriberics are of different species, or whether they are not some varieties of the same species." They also admit the possibility of accidental pollution during manipulation.

Inoculation Experiments. They injected twenty-five cubic centimeters defibrinated blood, taken a few minutes before from a beriberi patient in a state of dyspnoea, into the abdominal cavity of a monkey. A considerable number of bacteria could be detected in this blood by the microscope. They also removed a piece of popliteal nerve from a beriberi patient that had just died and introduced it under the skin of the thigh of a monkey. Neither of these monkeys developed beriberi.

Inoculation of bacteria isolated. They say: "We provided ourselves at first, for purposes of injection, with micrococci of the white growth variety. These were obtained nine times." One of these growths was lost. "The eight remaining growths did not, however, completely resemble each other. While six possessed the faculty of liquefying gelatine, the other two did not."

These six micrococci were then cultivated in broth or on agar, and the broth culture or a suspension of the bacteria from the agar cultures were injected into rabbits and dogs both subcutaneously and intraperitoneally. A few of the results of these inoculations are as follows:

"1. Rabbit. Four injections under the skin in nine days. The eighth day the animal is unable to stand; the next morning the animal is found paralyzed in both its hind legs, it died soon after with violent dyspnoea. Upon opening the thorax half an hour later the heart was still contracted. An abscess was found under the skin at the spot where the injections had been made. Recent and extensive degeneration was evident in the different nerves which lead to the muscles of the hind legs; no degeneration was found in the phrenic nerves."

"2. Rabbit. Twenty-three subcutaneous injections were made in twenty-five days, and then the animal was slaughtered. At the autopsy several abscesses were found under the skin, some ascites and on the left side of the chest a purulent pleurisy. No degeneration of the nerves was found."

"8. Dog. Seventeen subcutaneous injections in thirty-six days. In the course of the experiment, as a consequence of the injections, there appeared five abscesses, each of which was opened as soon as it appeared. During the last few days of life the dog did not jump as well as usual. The animal was killed on the thirty-sixth day, when in several branches of the nerves in the hind legs nerve degeneration was found."

"9. Dog. Fourteen subcutaneous injections in twenty-three days. When the animal was killed no nerve degeneration was found."

These are fair samples of the inoculation experiments which were performed. It is quite certain that they contain not the slightest evidence that beriberi was produced in these animals by inoculation with these six cultures of cocci.

On the basis of this evidence the authors conclude as follows: "What we have said seems to authorize us to admit that beriberi is caused by a micrococcus which exists in the places where the disease prevails, and which can penetrate into the human body. It is very probable that this microorganism enters by the organs of respiration with the air inhaled, and that from them it penetrates into the circulation." Again they say: "It is true that to us it scarcely seems possible that the micrococcus producing nerve degenerations which we cultivated six times from the blood of beriberi patients, and which was also obtained from the blood of a rabbit injected by a bacterial culture and suffering from nerve degeneration — it seems scarcely possible to us, we say, that this micrococcus can be rejected as the cause of beriberi."

To one reading this evidence critically at this later day it seems scarcely possible that these organisms should have been considered the cause of beriberi on such fragmentary and inconclusive evidence which may be criticized as follows:

1. The microscopic examination of the blood from the finger of beriberics. It is quite possible that the organisms found were contaminations from the skin since it is now well recognized that it is impossible to sterilize the skin by scrubbing and the use of bichloride. The same organisms were found in many healthy individuals.

2. Cultivation of these bacteria from finger blood. It would seem obvious from what we know at the present day that the majority of these attempts at cultivation failed because there was no organism in the blood, and that the fifteen cases where growth occurred were simply contaminations from the skin and air. This is the more probable since in these fifteen cultures they obtained three varieties of bacilli and four or five varieties of cocci. Even in dealing with the white microccus isolated from six cases that they regard as the cause of beriberi there is not the slightest evidence warranting the conclusion that they were all the same organism.

3. The inoculation into animals never produced beriberi, although nerve degeneration was frequently found. There are, however, a number of organisms that produce nerve degeneration.

The weakness of the argument of these observers may be further demonstrated by a final quotation in which they say: "In researches on the pathogenic peculiarities of bacteria it is a general rule that a single injection of a small quantity of microorganisms ought to produce some visible symptoms of the disease, if the bacteria are really to be considered as the cause of the disease. *The study of beriberi has, however, taught us that this rule cannot be applied here.* (Italics ours.) Beriberi is an essentially chronic disease. The nerves are destroyed fiber after fiber, and when degeneration attacks any nerves which lead to the less important organs, it may have made great progress before the patient himself suspects that he is ill. It could not be admitted that these slow and progressive degenerations were caused by an organism which, when once it had penetrated into the body, developed itself there, slowly but surely, as in the case of tuberculosis. What is opposed to it is that not only were we unsuccessful in finding in the nerves the bacteria met with in the blood, but especially and in a decisive manner, there is what experience has shown us concerning the genesis of the disease. This experience taught us that it was not until after a residence of some weeks at least in a place where beriberi was raging that an individual, in previously good health, could be attacked by the disease.

"It was not right, therefore, to seek the cause in a period of incubation of long duration, because then it would matter little whether the infected person remained in the infected place or not. If an individual susceptible of taking a disease such as measles, scarlatina, typhus or smallpox has once been exposed to contagion, or if the virus of tuberculosis or of syphilis has penetrated into the body, it matters little, as regards the symptoms of the disease declaring themselves, whether he renews contacts with the source of the disease or keeps distant from it. *It is otherwise with beriberi.* (Italics ours.)

"Those only are attacked who have lived continuously for a considerable time in the places where the disease is rife. To go into a place where the disease is not raging is not only the best means of cure, but is also a means of preventing the disease developing further, even after the first symptoms begin to show themselves. That is the reason why, when some animals have been inoculated with blood from beriberi patients, the results have always been negative; it was not therefore allowable to conclude from such results that organisms causing beriberi were not present in the blood."

It seems obvious that the truths observed in this last quotation are quite incompatible with acceptance of an infection as the cause of beriberi.

The conclusions drawn by Fraser and Stanton from their experiment are as follows:

Twenty cases of beriberi occurred among 220 people on white rice. No case occurred among 273 people on parboiled rice and under similar conditions to those which obtained in the white rice parties at the time beriberi was prevalent among them.

Since all cases presenting doubtful signs of the disease were excluded, we are of the opinion that there were many other cases which in the ordinary routine of clinical practise would have been regarded as beriberi. Such cases only occurred among people who consumed white rice.

No case of beriberi occurred in any coolie who had been on white rice for a less period than eighty-seven days.

Systematic examinations were made of the blood and urine of patients suffering from beriberi. Various methods of staining were employed, but in no instance were any organisms found except those well known as the causative agents of other diseases.

During the course of the inquiry, patients in various stages of beriberi were at times in contact with parties of men on parboiled rice.

The results of observations made on such occasions furnished evidence that the disease is not a directly communicable one.

Removal of patients suffering from beriberi from one place to another did not influence the progress of the disease, and removal of entire parties from the place where the disease had occurred did not influence the progress of the outbreaks so long as they continued on white rice.

In three instances in which definite outbreaks of beriberi occurred among parties on white rice, substituting of parboiled rice was followed by a cessation of the outbreaks.

No evidence was obtained to show that any article of food other than rice was a possible source of a causative agent of the disease.

Ankylostomes and other nematode worms were not found in a larger proportion of patients suffering from beriberi than in the general population under observation.

The general results lend support to the view that the disease beriberi as it occurs in this peninsula, has, if not its origin in, at least an intimate relationship with the consumption of white rice, and justify further research along these lines.

Investigation of the Cases of Beriberi Occurring in the Philippine Scouts During 1911 and 1912.

There were only five cases of beriberi in the Philippine Scouts during the years 1911 and 1912. In order to investigate the origin of these cases the following letter was sent by the Chief Surgeon of the Philippines:

Headquarters Philippines Division,
Office of the Chief Surgeon,
Manila, P. I., *July* 26, 1912.

The Surgeon,
Camp Stotsenburg, Pampanga:

Sir:—

Referring to the case of Private J. E. L., 26th Company, Philippine Scouts, reported as being on sick report from June 15th, 1912, with beriberi, a report is desired, embodying as much of the following data as is obtainable:

1. The symptoms in detail on which the diagnosis was based. Could neuritis, due to alcohol or other intoxication, be excluded? If anchylostomiasis was present, what was the severity of the infection as indicated by the number of worms found and by the degree of the anaemia?

2. A detailed account of the food eaten by the patient for three months previous to the development of the disease:

(a) Did he eat the regular Scout ration?

(b) Did he fail to eat any of the regular components of the ration, either because he did not like them, or because, for any reason, they were not furnished?

(c) Did he eat the undermilled rice furnished the Scouts?

(d) If married and he ate with his family, can any evidence be secured showing that he exchanged his ration, in whole or in part, for more rice, and, if so, was *polished* rice purchased?

Very respectfully,

(Sgd.) WM. H. ARTHUR,
Colonel, Medical Corps, U. S. Army.
Chief Surgeon.

1ST INDORSEMENT.

OFFICE OF THE SURGEON,
CAMP STOTSENBURG, PAMPAGA, P. I., *July* 30, 1912.

Respectfully returned to the Chief Surgeon, Philippines Division, Manila, P. I., submitting the following report in the case of Private J. E. L., 26th Company, Philippine Scouts, as directed:

1. The symptoms on which diagnosis was based:

Anasarca developing within forty-eight hours; fever, muscular tenderness, areas of hyperaesthesia of lower extremities; pleural effusion, difficult breathing, precardial distress, absence of knee jerk, both sides, ataxic gait.

Anchylostomiasis was negative.

Neuritis of alcoholic origin or due to other intoxication was excluded.

2. During quarantine duty for rinderpest, on which patient's company has been serving since February, 1911, rations have been commuted, the small detachments purchasing their subsistence where they were.

(b) Was on furlough from February 15, 1912, to April 15, 1912, visiting his brother at Aguilar, Pangasinan, P. I., where polished rice was used.

(c) He has been eating polished rice almost entirely during three months before admission.

(d) He is married, and when in garrison eats and lives with his family, commuting his ration entirely and buying polished rice.

(Sgd.) T. C. LYSTER,
Major, Medical Corps, U. S. Army.

In reply to the same letter of investigation with regard to the case reported January, 1912, the following information was obtained:

1. In the case of Private M. D., 45th Company, Philippine Scouts, patient was admitted to hospital with a diagnosis of chronic articular rheumatism. He suffered from slight swelling of the knees, later extending to the ankles, which were slightly painful. He did duty for quite a while in this condition before arriving at this station. After admission to the hospital patient complained of soreness and stiffness in knees and ankles. Later he had a marked shuffling gait and was seemingly unable to lift feet from the floor; severe pain on pressure. Patient ran an intermittent temperature while in hospital, ranging from normal to 105° F. at times. Diagnosis was changed to beriberi, dropsical.

2. Patient was not addicted to use of intoxicants. Anchylostomiasis was not present.

3. Patient ate regular Scout ration.

4. Patient ate the undermilled rice furnished Scouts.

5. Patient was not married and had no opportunity to exchange any part of ration for more rice or other articles of food.

It is quite clear from the facts furnished by Major Lyster that the first case had not been eating the improved ration at the time he developed beriberi. In the second case there is grave doubt as to the diagnosis of beriberi. The high fever and the limitation of symptoms to the joints point rather to acute articular rheumatism or some other disease of the joints.

Investigation of the other cases gave similar results. Either there was doubt as to the diagnosis, or there was a clear history indicating that the patient had not eaten the improved ration.

The conclusions from the following papers represent the work of the United States Army Board for the Study of Tropical Diseases, on polyneuritis gallinarum:

1. Chamberlain, Bloombergh and Kilbourne. The influence of rice diet on the production of multiple neuritis of fowls, etc.

(1) Fowls develop multiple neuritis when fed exclusively on polished rice, whether Filipino No. 1 or Saigon choice rice is used.

(2) Forcibly feeding polished rice to such fowls as have no appetite for it will not prevent the occurrence of neuritis.

(4) The administration of certain inorganic salts of phosphorus and of potassium, either alone or combined, to fowls subsisting on polished rice neither prevented multiple neuritis nor deferred its onset.

(5) Fowls fed unhusked rice, *palay*, do not acquire multiple neuritis.

(6) Fowls fed undermilled (unpolished) rice do not acquire the disease.

(7) Whether the undermilled rice has a red or a yellowish-white pericarp is immaterial.

(8) Fowls fed on undermilled rice combined with large amounts of sodium chloride do not develop multiple neuritis.

(11) Fowls kept entirely without food and those which are given all they will eat of polished rice lose weight with almost equal rapidity in the great majority of cases.

(12) A loss of at least 21 per cent of the body weight almost invariably occurs before any signs of multiple neuritis become apparent.

(14) Spasticity is a late symptom in some fowls which develop neuritis and are then saved from death by the institution of mixed feeding.

(15) In neuritis-producing rice and in beriberi-producing dietaries both the phosphorus and the potassium are markedly reduced in amount, the latter in greater degree than the former.

(16) As an *index* of the beriberi-producing power of a given rice, reduction in the potassium content is probably quite as reliable as reduction in the phosphorus content.

2. Chamberlain and Vedder. A contribution to the etiology of beriberi.

(1) Polyneuritis gallinarum is not prevented by adding to a diet of polished rice any of the following substances: Potassium phosphate, potassium citrate, potassium carbonate, potassium chloride, magnesium phosphate, phytin, phosphoric acid, or phosphoric acid combined with potassium chloride.

(2) The neuritis-preventing substance in rice polishings is soluble in cold water and in cold alcohol.

(3) Polyneuritis gallinarum may be prevented by means of an extract of rice polishings containing only those substances soluble in cold water and cold alcohol. This extract, so far as at present known, has the following composition:

	Per cent.
Total solids	1.34
Ash	0.03
Phosphorus pentoxide	0.00165
Nitrogen	0.0406
Sucrose	0.88

(4) Multiple neuritis in fowls fed on polished rice probably is not due to lack of phosphorus compounds in the grain, as claimed by Schaumann, since out of each 1,000 parts of phosphorus contained in the rice polishings at least 999 are not concerned in preventing neuritis.

(5) The neuritis-preventing substance contained in rice polishings is capable of dialysis through a parchment membrane. This excludes all colloids from consideration.

3. Chamberlain and Vedder. A second contribution to the etiology of beriberi:

(1) Of 1.34 per cent total solids contained in this extract, 0.03 per cent was ash. This we believe to be negligible, since it consists entirely of inorganic constituents, chiefly of lime, magnesia and potassium carbonate. We have tried salts of calcium, magnesum and potassium and found them wanting. Nitrogenous matter comprises 0.04 per cent of the total solids. Of this only 0.02 per cent was present in the diffusate, which has been shown to contain the neuritis-preventing principle, and the remaining 0.02 per cent can be eliminated because it remained in the dialysate which failed to prevent neuritis. The 0.88 per cent sucrose is of no importance. Combining these unimportant substances and subtracting them from the 1.34 per cent of total solids, we find that there is only 0.4 per cent remaining. The neuritis-preventing principle must, therefore, be sought for in the 0.4 per cent of solid matter, and must be a substance that is dialyzable, that is, soluble in water, in 95 per cent alcohol and in 0.3 per cent hydrochloric acid, which is easily decomposed by heat and which possesses a strong affinity for bone black. The same substance or a similar substance is also contained in a decoction of ordinary white beans. Bodies corresponding to this description are found among the decomposition products of the proteids.

4. Chamberlain, Vedder and Williams. A third contribution to the etiology of beriberi:

(1) These experiments all substantiate the theory that polyneuritis gallinarum and beriberi are caused by the deficiency of some as yet unknown substance in the food. We have shown previously that this substance is not phosphorus.

(2) Kohlbrugge's theory that beriberi is caused by an acid intoxication, which is due to the fermentation of rice by various saprophytic bacteria contained in the kernel, must be regarded as untenable.

(3) To the list of substances which we have shown in previous papers to be of no importance in preventing neuritis of fowls there

may now be added the following: Nitrogenous compounds such as arginin, histidin, asparagin and various amino-acids; lipoids of the lecithin group and cholin; extract of onions.

(4) The neuritis-preventing principle is insoluble in ether.

(5) The neuritis-preventing principle is absorbed by animal charcoal, and the filtrate through the charcoal will not prevent neuritis. After absorption the active principle cannot be removed from the charcoal by maceration with water, absolute alcohol or ether.

(6) The administration of large quantities of sodium chloride failed to produce oedema in fowls suffering from polyneuritis.

(7) Five cubic centimeters of our extract daily, (equivalent to five grams of rice polishings) is sufficient to protect fowls subsisting upon polished rice. Two and one-half cubic centimeters (equivalent to 2.5 grams of polishings) is insufficient to confer complete protection against polyneuritis.

5. Vedder. A fourth contribution to the etiology of beriberi:

(1) The administration of large amounts of alcohol has failed to produce neuritis in fowls.

(2) Fowls develop polyneuritis when fed on a diet containing a sufficiency of all the common alimentary principles, providing no one of the ingredients of this diet contains the neuritis-preventing substance.

(3) The neuritis-preventing substance is not volatile, but is destroyed by heat.

(4) The neuritis-preventing substance is not an inorganic salt.

(5) The neuritis-preventing substance is probably not an alkaloid.

(6) Since it has been shown that this substance is neither a fat, proteid, inorganic salt or alkaloid, it seems probable that it is an organic base as claimed by Funk, but we have been unable as yet to confirm his work.

6. Vedder and Clark. A fifth contribution to the etiology of beriberi:

(1) There appear to be three types of polyneuritis gallinarum:

(a) A form in which the symptoms of neuritis and those of general prostration are combined. This is the usual form. When these birds are given an extract of rice polishings they improve at once in general condition, but the symptoms of neuritis only disappear after several months of treatment.

(b) A form in which there is pronounced neuritis, but the fowls remain in good general health. These fowls will also recover from the neuritis after several months' treatment with the extract of rice polishings.

(c) A form described above as fulminating cases, in which the symptoms of neuritis are absent, but in which greater general prostration occurs. These fowls recover speedily when given an extract of rice polishings.

(2) In polyneuritis gallinarum developing after a prolonged diet of polished rice the heart may show no microscopic change. In other cases the heart may show slight oedema, a slight increase in pigment or an appearance of beginning mucoid or parenchymatous degeneration.

(3) While in marked cases of neuritis every fiber of the vagus may and usually does show degenerative changes, as indicated by the Marchi method, no fiber has been observed in which the change was far advanced. We have not been able to correlate the extent of degeneration in the vagus with the changes in the heart, nor with the severity of the symptoms before death.

(4) No marked changes suggestive of degeneration have been observed in the cervical sympathetic ganglia nor in the post or preganglionic fibers.

(5) In every one of the 56 fowls which had been fed 35 days or more on polished rice, changes indicative of degeneration (Marchi method) were seen in the fibers of the sciatic nerve, regardless of whether symptoms of neuritis had or had not manifested themselves before death.

(6) Advanced degeneration in the pripheral nerve fibers manifests itself by a change in both myelin sheath and in the axis cylinder. The myelin sheath breaks up into globules and droplets, which stain black in the Marchi solution — indicative of fatty degeneration. The axis cylinder breaks up into segments or disintegrates in all those fibers showing advanced degeneration in the medullary sheath.

(7) The degree of degeneration in the sciatic nerve corresponds closely with the extent of the paralysis of the legs. Advanced degeneration was observed in only 10 to 15 per cent of the fibers of the sciatic nerve of fowls showing pronounced symptoms of leg paralysis. In the remaining fibers the change was not advanced.

(8) We could detect no difference in the degeneration in the sciatic and its peripheral branches either as regards extent or time of onset.

(9) Degeneration was observed in both dorsal and ventral nerve roots, being most pronounced in the latter.

(10) Degenerative changes in both axis cylinder and medullary sheath were seen in fibers of all columns of the thoracic spinal cord.

(11) Changes were observed (Nissl method) in certain large cells of both ventral and dorsal horns of the grey substance of the lumbo-

sacral cord. In the cells of both horns the tigroid bodies were not visible, and the stainable material was collected at one side of the cell around the base of one of the processes. Cells were occasionally seen whose nuclei stained very poorly.

(12) Mitochondria were observed in the nerve cells of the lumbo-sacral cord even though there was a pronounced alteration of the tigroid bodies. The mitochondria here were of similar appearance and almost or quite as numerous as in corresponding cells of the normal cord.

(13) In the medullary sheath of fibers of the sciatic nerve of normal fowls numerous small, bacilli-like rods, arranged radially around the axis cylinder, were made apparent by the various mito-chondria methods. These structures are probably mitochondria.

(14) Fowls show alteration in the medullary sheath of the sciatic fibers after only seven days on a polished rice diet. In the sciatic fibers of fowls fed seven days on polished rice alone the rods are scarcely to be observed. Instead, the stainable material shows remark-able alterations and occurs in the form of irregular, branched and anastomosing masses.

(15) In fowls fed for a longer period these masses show, in a cer-tain per cent of the fibers, progressive changes which manifest them-selves in the form of more definite skeins and segmentations and larger masses and globules of stainable material. In fibers showing marked degeneration by the Marchi method these masses occur as larger or smaller vesicular, oval globules and correspond to the black globules shown by the Marchi preparations.

(16) When fowls are fed on polished rice, and in addition given some protective substance such as is contained in extract of rice polish-ings, or in various foods, but in insufficient quantity to confer com-plete protection, the disease appears in its characteristic form and with all the evidence of nerve degeneration, but after a prolonged incubation period, 45 to 90 days or even after one year of such feeding (Eijkman).

(17) When fowls are fed on polished rice, and in addition receive daily 10 grams of white wheat bread or five cubic centimeters of canned milk, they receive little or no protection from polyneuritis galli-narum.

(18) When fowls are fed on polished rice, and in addition receive daily 10 grams of meat, cooked or uncooked, 10 grams of potatoes, cooked or uncooked, or five cubic centimeters of fresh cow's milk, they receive partial protection, as indicated by the prolongation of the incu-bation period.

(19) When fowls are fed on polished rice, and in addition receive daily 10 grams of dried peas or 10 grams of peanuts, they receive complete protection for at least 60 days.

(20) In addition to the changes demonstrated above, Funk has shown that chemical changes take place in the brains of fowls suffering from polyneuritis gallinarum. It therefore appears that the disease is not simply a peripheral neuritis, as has been generally supposed. On the contrary, the entire nervous system is affected.

(21) The symptoms of the disease are not chiefly referable to degeneration of the peripheral nerves, since the degeneration occurs before symptoms arise, and because advanced degeneration may be present, accompanied by no symptoms at all, and because degeneration of the nerves remains after recovery has occurred.

7. Vedder and Williams. Concerning the beriberi-preventing substances or vitamines contained in rice polishings:

(1) Undermilled rice may be stored for one year in a damp place without losing its protective powers against polyneuritis gallinarum. It is improbable, therefore, that a rice which originally affords protection against beriberi will lose this property by storage even in damp places.

(2) The neuritis-preventing substances or vitamines contained in rice polishings are only slightly soluble in cold 95 per cent alcohol, since three successive extractions, using a total of six liters of alcohol to each kilo of polishings, fails to remove all of the neuritis-preventing substances from rice polishings.

(3) Strong alkaline reagents such as sodium hydroxide, ammonia and barium hydroxide, destroy the neuritis-preventing vitamine, and the use of these reagents must be avoided in endeavoring to isolate this substance.

(4) Basic lead acetate does not precipitate the neuritis-preventing vitamine, and a considerable portion of this substance may be recovered from the filtrate.

(5) The therapeutic properties of an alcoholic extract of rice polishings are greatly altered by hydrolysis (treatment with five per cent hydrochloric or sulphuric acid). The unhydrolyzed extract is not poisonous, and is only slowly curative. The hydrolyzed extract is exceedingly poisonous in large doses and promptly curative in small doses.

(6) We have confirmed Funk's observations by isolating a crystalline base from an extract of rice polishings by Funk's method. This

base in doses of 30 milligrams promptly cured fowls suffering from polyneuritis gallinarum.

(7) Funk's base or vitamine is present in rice polishings in considerable amounts, and only a very small portion of it can be obtained by Funk's method.

(8) Two groups of substances (purine bases, choline like bases) may be isolated from rice polishings in addition to Funk's base, and are capable of partly or wholly protecting fowls fed on polished rice against polyneuritis gallinarum, but are incapable of curing fowls that have already developed the disease. The chemical nature of these two groups of bases requires further investigation.

(9) We have confirmed the observation of Suzuki, Shimamura and Odake, that Funk's base may be precipitated from unhydrolyzed extract by tannic acid, but did not succeed in obtaining large amounts of this substance by this method.

(10) It is probable that this base or vitamine exists in food as a pyrimidine base combined as a constituent of nucleic acid, but that it is not present in the nucleins or nucleic acids that have been isolated by processes involving the use of alkalies, or heat.

(11) The administration of unhydrolyzed extract of rice polishings to cases of adult wet beriberi, or to cases suffering from acute cardiac insufficiency, results in the prompt dissipation of oedema, and relief of the cardiac symptoms.

(12) The administration of unhydrolyzed extract of rice polishings to cases of dry beriberi is followed by little or no improvement in the paralytic symptoms.

(13) The administration of Funk's base to cases of dry beriberi is followed by an immediate improvement in the paralytic symptoms. This should remove the last doubt that dry beriberi is caused by the deficiency of this substance in the diet. It also finally proves that dry beriberi of man and polyneuritis gallinarum are essentially the same disease.

(14) We have succeeded in curing a case of infantile beriberi (of the wet type) by administering that portion of the extract of rice polishings represented by the filtrate from the phosphotungstic precipitate. Since this filtrate does not contain Funk's base, this is evidence that wet beriberi is cured by some other substance.

(15) Conclusions 11, 12, 13 and 14 are striking confirmatory evidence for the hypothesis previously stated by Vedder and Clark, that wet beriberi and dry beriberi are two distinct conditions, each being caused by the deficiency of a separate vitamine.

THE METHOD OF PREPARING EXTRACT OF RICE POLISHINGS.

Rice polishings or tiqui-tiqui may be obtained from any rice mill, but should preferably be from a recent milling. The finest grade of polishings should be carefully selected, since some of this product is very coarse and consists mostly of hulls. The tiqui-tiqui is first sifted to remove hulls and weevils. Gauze of about seven meshes to the centimeter is used for this purpose. This fine powder is weighed and mixed with 90 per cent alcohol in the proportion of three liters of alcohol to each kilo of polishings. It is then allowed to macerate for 24 hours. A glass jar or white enameled receptable serves for this purpose, and the mixture should be repeatedly stirred or shaken, since the tiqui-tiqui sinks rapidly to the bottom, forming a densely packed mass which the alcohol penetrates with difficulty. During the extraction the alcohol becomes of a deep green color, due to the fat that has been dissolved out. At the end of 24 hours the alcohol is siphoned off and filtered until absolutely clear. Since a very considerable quantity remains in the tiqui-tiqui, this should be squeezed in a press, or washed with fresh alcohol, and the residuum filtered and added to the alcoholic filtrate already obtained. The extraction should then be repeated several times, again using three liters of alcohol to each kilo of polishings. This is necessary because the neuritis-preventing substances are only slightly soluble in cold 90 per cent alcohol, and experience has shown that if the polishings are not repeatedly extracted the full therapeutic action of the polishings is not obtained. The combined alcoholic filtrate is then placed in a water bath provided with a thermometer, and an electric fan is so arranged as to throw a strong current of air on the surface of the alcohol. As a result of the heat and the movement of air the alcohol rapidly evaporates. It is essential that the temperature of the extract should not be permitted to rise above 80° C., since extended observation has shown that greater heat is liable to decompose the active neuritis-preventing principle. Whenever the temperature of the extract approached 80° C. the fire should be extinguished until the temperature drops. This process is continued until all the alcohol is evaporated. The residue is poured into a separating funnel and allowed to stand for about an hour, when it will be observed that the liquid has separated into two layers. The upper and larger portion is of a deep green color and consists of the fat. The lower and smaller layer is brown in color, of syrupy consistency, and contains a number of substances that have been extracted by the alcohol. This lower layer is carefully drawn off, leaving the fat behind. It varies in amount, but about 25 cubic centimeters usually will be obtained from each kilo of polishings. The brown syrupy fluid so obtained from one kilo of polishings is diluted to 60 cubic centimenters with distilled water, whereupon a heavy precipitate is formed. This precipitate consists of substances that were soluble in alcohol, but are insoluble in water. After allowing the mixture to stand for a while the precipitate settles and the clear fluid is filtered off. This filtrate constitutes the extract as we have used it. Each 60 cubic centimeters contains the substances that have been extracted by this method from one kilo of polishings.

THE EXPERIMENTAL PRODUCTION OF BERIBERI IN PUPPIES THAT WERE NURSED BY WOMEN WHOSE CHILDREN HAD DIED OF INFANTILE BERIBERI. TAKEN FROM THE PAPER, "INFANTILE BERIBERI," BY ANDREWS, IN PHILIPPINE JOURNAL OF SCIENCE, 1912, VII, 81.

Experiment No. 1.

The two puppies were three days old, and the woman began to nurse them August 12, just one week after the death of her child of typical infantile beriberi. The woman had numbness and areas of anaesthesia in her legs. It was with some difficulty that she could walk, and any exertion produced palpitation of the heart. She suffered from shortness of breath. Her knee jerks were absent. During the first four days the puppies lost in weight; they then gained continuously until two days before death, when a slight drop occurred. They nursed for six weeks and died within 24 hours of each other, September 22 and 23.

Although the puppies gained in weight, they never became fat, and were in fact rather lean looking. Nothing of importance occurred until the fourth week, when it was noticed that they had some difficulty in walking or standing. The ankles of the front feet turned under them; they swayed from side to side, and apparently could not control the muscles so as to go just where they desired. As time passed all these phenomena were augmented and other symptoms appeared. The hind legs became more seriously affected than the fore-legs. The puppies sat on their haunches and moved their legs as little as possible. On getting up they fell to one side or the other and stumbled on their noses; apparently they had lost control of most of the muscles of locomotion. This condition continued to grow worse until death. During the fifth week it was noticed that they were becoming anaemic. Also during the last two weeks the front feet became oedematous.

Necropsy was performed about ten hours after death. The bodies of the puppies were emaciated and the subcutaneous tissues were anaemic and oedematous throughout. The peritoneal cavity contained a slight increase in fluid. The heart was neither hypertrophied nor dilated. All the internal organs were anaemic and oedematous. The intestines contained a large number of ascaris and hookworms. The faeces were dark colored and in a few places in the mucosa of the intestines haemorrhages had taken place.

Experiment No. 2.

Two puppies, four days old, were given to Case III to nurse on September 26. The one-month-old child had died one week previously of typical infantile beriberi. The woman showed marked symptoms of beriberi; numbness, anaesthesia and formication of legs; shortness of breath, distinct heart murmur and loss of knee jerks and other reflexes.

For the first three days the puppies lost weight. They then continued to gain until the end. One died October 19, after nursing 23 days, and the other October 22, after nursing 26 days.

Both these puppies became plumper and apparently fatter than the first two. Nothing of importance was noticed in either of them until the 14th of October, when both began to show symptoms of weakness in the legs. This grew worse until it seemed that the hind legs were practically paralyzed. The puppies would rise up on their front feet and then fall over. Their feet and legs became oedematous. The first one, which died on the 19th, developed no further symptoms; but the second, living three days longer, developed *marked dyspnoea,* and the legs became greatly oedematous. It made no attempt to move its hind legs, but dragged them along. Toward the last it could not raise itself on its front feet.

Necropsy. Puppy which died October 19. The body tissues are oedematous, and the muscles are pale. The heart is apparently normal. The lungs are congested and oedematous. The spleen and liver are dark colored, firm and congested. The kidneys are pale. The intestines contain a few hookworms. All tissues are very moist.

Necropsy. Puppy which died October 22. The subcutaneous tissues showed marked oedema. The muscles are pale. Increase of fluid in the peritoneal and pericardial sacs. *The right heart is dilated and hypertrophied.* The lungs are congested and oedematous. The spleen and liver are dark colored and congested. The kidneys are pale. Intestines contain a few worms.

Experiment No. 3.

In this instance the woman, Case VIII, objected to nursing a puppy whose eyes were closed. To overcome this difficulty I had to give a puppy that was 14 days old, and this fact may have had an influence on the effect produced in the puppy. The woman did not exhibit marked symptoms; slight shortness of breath and numbness of legs were most noticeable. She was given two puppies, but one was soon taken away because she had not sufficient milk for both. She began nursing the puppies October 30, about one week after the death of her child from typical infantile beriberi, and continued nursing one of them till December 29, when it died. During the first three weeks the puppy gradually lost in weight. It also vomited occasionally after nursing, and had a number of convulsions. These attacks lasted from five to seven minutes, the woman said. They would begin with whining and frothing at the mouth, and then the muscles would become rigid. I never saw the puppy in one of these attacks. They were said to occur at night as well as in the daytime. Altogether it had six convulsions that the woman noticed.

At the end of third week it was somewhat emaciated, but began to gain in weight, and continued to gain until the last week of life. During the third week of nursing it was noticed that its front feet were becoming oedematous. This condition became worse, and later the hind feet began to swell. The puppy became very weak and staggered about while walking, but it never lost complete control of its muscles, and was always able to move about. It died December 29, after it had been nursed by the woman for two months.

Necropsy. Body of an emaciated puppy. Subcutaneous tissues are oedematous and anaemic. Twenty cubic centimeters of fluid in the peritoneal cavity. The heart is pale, otherwise apparently normal. Lungs are slightly congested and oedematous. No increase of fluid in pericardial or pleural sacs. Spleen dark colored, normal markings. Kidneys pale, moist. Liver dark red, apparently normal. Stomach normal. Intestines show the presence of hookworms and several minute areas in which small haemorrhages have apparently taken place.

Experiment No. 4.

The puppies were seven days old when the woman, Case X, began to nurse them on November 15, 1911, five days after the death of her infant from typical infantile beriberi. The woman had loss of knee jerks. She easily became tired on exertion, and her legs were weak. There was no numbness or areas of anaesthesia in the legs.

Puppy which died December 14, 1911. This puppy lost in weight for the first five days, then gradually increased until death.

At the end of the first two weeks it was noticed that its feet were beginning to swell and were becoming oedematous. From this time on it exhibited symptoms of weakness. Its front ankles turned under it when it attempted to stand. In walking it staggered from side to side and fell over easily. As time passed these symptoms became more marked. There was never paralysis.

Necropsy. Apparently a fairly well-nourished puppy. Feet oedematous. Subcutaneous tissues very oedematous and anaemic. Slight increase of fluid in the peritoneal cavity. Heart firm, normal. Increase of fluid in the pericardial sac. Lungs congested and oedematous. Spleen normal. Kidneys apparently normal. Liver dark red, normal. Stomach normal. Intestines show a very few hookworms.

Puppy which died December 31, 1911. The puppy lost weight the first two weeks, but was sick and nursed but little several days of this time. During the third week it gained in weight and its feet began to swell. As the fourth week came on the oedema of the feet increased in amount and the legs became weak, the ankles of its front feet turning under it when it stood up. It staggered first to one side and then to the other, stumbled on its face, and in other ways exhibited a weakness or loss of control of its muscles. It lost its footing easily. This condition continued through the fifth and sixth weeks until the puppy died, December 31, having nursed six weeks.

Necropsy. Body of an apparently well-nourished puppy. Feet and ankles oedematous. Subcutaneous tissues oedematous and anaemic. Increase of fluid in the peritoneal cavity. Pericardial sac shows slight increase of fluid. Heart apparently normal. The lungs are congested and oedematous. Spleen normal. Kidneys apparently normal. Liver dark red, normal. Stomach normal. Intestines contain a few hookworms.

In all these necropsies the vagi, sciatic and intercostal nerves were preserved and stained for degeneration. In all those examined a few fibers were found in which degeneration was present.

MIURA, M., PATHOLOGISH. ANATOMISHER BEFUND AN DEN LEICHEN VON SAUGLINGEN MIT DER SOGEN. KAKKE-DYSPEPSIE. VIRCH. ARCH., 1899, CLV. 316.

As early as 1890 and 1891 there were articles in the Japanese medical journals that described kakke of sucklings, but the anatomic proof of the existence of this disease was only obtained later.

In August, 1896, Hirota made the diagnosis of kakke in an eight-months-old girl who later died in the hospital. The autopsy was performed by Yamagiwa, and the following report was obtained from him:

Body weight seven kilos; well nourished. Only a slight quantity of serous fluid in the peritoneal cavity. Each pleural cavity contained a slight quantity of serous fluid, and the thymus appeared enlarged. Five cubic centimeters of clear yellow serous fluid in the pericardium. The right auricle was filled with fluid blood and clots, and the right ventricle greatly distended. The musculature was pale red and cloudy. Pulmonary valves intact. The left ventricle contained only a small quantity of fluid blood and clots; the musculature was pale red and soft, and the aortic and mitral valves were soft. Weight of heart 50 grams.

On the under surface of the left lung were numerous sub-pleural haemorrhages. The lung was dark red in color and the bronchi filled with foamy fluid. The right lung was the same. Mucosa of the larynx was injected. Spleen, kidneys and liver, nothing abnormal found.

Diagnosis. Dilatation and hypertrophy of the right ventricle, atelectasis of the lungs.

Miura says: Since I knew of no other disease besides kakke which could produce so considerable a hypertrophy of the right ventricle I came to the conclusion from the pathologic finding that this could only be a case of kakke. Up to this time I had not been able to recognize kakke of sucklings because the symptoms of these infants did not appear to coincide with those of beriberic adults.

In the same year Miura obtained three more autopsies, which were as follows:

Case II. Boy of three months. Body weight 5.5 kilos. Well nourished. Lips and extremities considerably cyanosed. Widespread and intense lividity of the dependent portions. The size of the thymus corresponded to the age of the child. In both pleural cavities about a spoonful of slightly reddish fluid, but no signs of pleurisy. Forty cubic centimeters of serous fluid in the pericardium, which was clear and bright yellow.

The heart. The right ventricle was greatly dilated and hypertrophied and was ball-shaped and distended with blood. The ventricle was six centimeters long and seven centimeters in circumference around the base. The mitral and pulmonary valves were normal. The right auricle and its veins were filled with fluid blood. The left ventricle was smaller than the right, its length being four centimeters and circumference 5.5 centimeters. Aortic valves were normal. The wall of the pulmonary artery was quite as thick as that of the aorta. The musculature of the right ventricle was over six millimeters thick, and contained small areas of fatty degeneration in the trabeculae and papillary muscles. The weight of the entire heart was 50 grams.

The left lung. The posterior and under part of the upper lobe is atelectatic, as was the lower portion of the lower lobe.

The right lung. A considerable amount of diffuse punctiform subpleural haemorrhages.

The mucous membrane of the bronchi was reddened, and the contents were sero-mucus. Spleen soft and hyperaemic. Kidneys. The cortical substance was cloudy, and on the cut surface there were numerous hyperaemic glomeruli. The mucous membrane of the intestines was congested, but intact. Liver congested and presented the appearance of a nutmeg liver. The subcutaneous tissue of the whole body, particularly of the scrotum and legs, was exceedingly oedematous, the thickest part of this tissue measuring over 1.5 centimeters in diameter.

Diagnosis kakke. Dilatation and hypertrophy of the right ventricle, catarrhal pneumonia, anasarca.

Case III. Boy nine months old. Weight seven kilos. Badly nourished. Two spoonfuls of serous fluid in the peritoneal cavity. About a teaspoonful of clear yellow serous fluid in the pericardium. The right auricle and ventricle were filled with masses of blood. The length of the right ventricle was seven centimeters, while that of the left ventricle was only 5.5 centimeters. Thickness of the right ventricles was six millimeters and that of the left eight millimeters. The musculature was pale, cloudy, but apparently healthy. All valves normal. The weight of the heart was 60 grams. Thymus was of the usual size. Patches of broncho-pneumonia in both lungs. Spleen normal. Slight cloudiness of the cortical portion of the kidneys. Intestines. Peyers patches and follicles were considerably swollen. The stomach wall showed circumscribed congested areas. Liver was firm, but infiltrated with fat. Oedema on the backs of the hands and feet and calves of the legs was pronounced. In these parts the tissue so infiltrated measured two centimeters in diameter.

Diagnosis kakke. Hypertrophy and dilatation of the right ventricle, catarrhal pneumonia, anasarca.

Case IV. Boy three months old. Body weight six kilos. Poorly nourished. Extensive cadaveric lividity of the back, and cyanosis of the finger tips. The pericardium contained only a slight quantity of fluid. Right auricle was distended with clots. Both ventricles appear to be about the same size. Musculature pale, but not cloudy. All valves normal. Entire weight of heart 35 grams. Lungs. The lower portion of both lungs contained areas of catarrhal pneumonia. Spleen normal. Kidneys normal. Other organs normal.

Diagnosis. Bronchitis, catarrhal pneumonia, hypertrophy of the right ventricle.

Through these four cases I was convinced that, as other authors claim, kakke can affect children that are still at the breast.

Infantile Beriberi, by Vernon L. Andrews, Philippine Journal of Science, 1912, vii, 88.

Conclusions.

1. The high infant mortality in Manila is due to infantile beriberi.
2. This high death rate of infants is due primarily to the quality of the mother's milk.
3. The mother's milk lacks something which is essential for the growth and development of the nerves of the child.
4. The disease is not due to an infection or toxaemia of either the mother or the child.
5. Another link has been added in the chain of evidence showing that beriberi is a nutritional disturbance.
6. As a prophylactic measure, the dealers handling rice should be required to keep on hand the undermilled variety, and a campaign of education should be carried on for the purpose of enlightening the poorer classes, especially the pregnant women.

Spliedt, Eine Beriberi Epidemie an Bord, Arch. f. Schiffs u. Tropenhyg, 1899, iii, 207.

Abstract.

A new ship on its first voyage proceeded from Hamburg to Hongkong, and there took on a crew of Chinese stokers. These men were examined by a physician before being signed, and were well at that time, nor had they ever suffered from beriberi. On October 15 the ship sailed for Hamburg, and while there two cases of beriberi appeared on December 26, one of which died of the disease. On December 27 the ship sailed for Boston, and on account of storms the trip lasted 54 days. One case of beriberi occurred on each of the following dates: January 8, January 19, January 29, February 16, February 22, February 25, March 9, April 1. Of a crew of 23 men 10 developed beriberi and four died. The clinical history of these cases is briefly given, and an account of the autopsy findings in one of the fatal cases, and there is no doubt that the disease was beriberi. The diet of these men consisted of fish and rice, with a few vegetables at first, but later consisted of fish and rice exclusively. This epidemic throws a light on a number of vexed questions. In the first place it disposes of the theory that beriberi is a place disease. The ship was new, built in Germany, and on its first trip. It manifestly could not harbor a beriberi germ or produce a beriberic atmosphere. Infection is improbable. The ship sailed from Hongkong October 15 immediately after taking on a healthy crew, and the disease did not appear until December 26, or 72 days later, after the ship had reached Hamburg. If the disease were infectious it is necessary to assume that the men were infected when they came on board, and that the infection remained latent for 72 days. This is improbable, and all the evidence lends support to the theory that the beriberi was caused by the dietary deficiency. The minimum incubation period of 72 days also agrees closely with the 79 days obtained by Fraser and Stanton in their experiment.

Resolution Adopted by the Far Eastern Association of Tropical Medicine at Its Manila Meeting in 1910.

"*Resolved*, That in the opinion of this Association sufficient evidence has now been produced in support of the view that beriberi is associated with the continuous consumption of white (polished) rice as the staple article of diet, and the Association accordingly desires to bring this matter to the notice of the various governments concerned."

Resolutions Adopted by the Far Eastern Association of Tropical Medicine at Its Hongkong Meeting in 1912.

"*Resolved*, That the results of the work submitted to this meeting of the Far Eastern Association of Tropical Medicine have been to confirm the accuracy of the resolution adopted at the meeting in 1910, and it is resolved to adopt as a standard that a harmless rice shall contain not less than 0.4 per cent of phosphorus pentoxide. It is further *Resolved*, (1) That efforts of an educational nature for the suppression of beriberi should be generally adopted; (2) that in view of the varying economic conditions obtaining in the different countries concerned uniformity of legislation appears impracticable, but any action taken should be based on the work done, and the above standard of phosphorus content is recommended for adoption; (3) it is suggested that legislation which is directed either to the taxation of polished rice or of the dealers in polished rice will be most effective."

AN ACT*

IMPOSING AN INTERNAL REVENUE TAX ON POLISHED RICE MANUFACTURED IN OR IMPORTED INTO THE PHILIPPINE ISLANDS.

By authority of the United States, be it enacted by the Philippine Legislature, that:

SECTION 1. Polished rice, for the purposes of this Act, shall embrace every kind and class of rice from which the pericarp and subcortical, or other layers, have been removed, and which shows upon analysis less than four-tenths of one per cent of phosphorus pentoxide (P_2O_5).

SEC. 2. There shall be levied, collected, and paid, on all polished rice, polished within the Philippine Islands, at the time of its removal from the building or establishment where the operation of polishing is performed, an Internal Revenue tax at the rate of five centavos on each kilogram; *Provided,* that the tax imposed in this section shall not be collected on rice polished in the Philippine Islands and withdrawn from the building or establishment wherein it was polished for export to any point outside of the Philippine Islands, if such rice is actually so exported, and proof of such exportation submitted to the Collector of Internal Revenue in such form and within such time as he may by regulation prescribe.

SEC. 3. There shall be levied, collected, and paid, upon all polished rice imported into the Philippine Islands from the United States or foreign countries, in addition to the import duties imposed (if any), an Internal Revenue tax at the rate of five centavos per kilogram. This tax shall be paid to the Collector of Internal Revenue, or his duly authorized representative, by the owner or importer of such rice, while same is in the custody of the proper Customs Officer; and such rice shall not pass out of the custody of said Customs Officer until the tax shall have been so paid.

SEC. 4. All the provisions of Act Numbered Eleven hundred and eighty-nine, entitled "The Internal Revenue Law of 1904," as amended, regarding the time and manner of collection, and manner of accounting for the specific tax imposed by the provisions of said Act on distilled spirits, fermented liquors, and tobacco products, and all the provisions of said Act, and the regulations issued thereunder, applicable to manufacturers of such articles, shall apply to importers and manufacturers of polished rice.

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* This bill has been introduced in the Philippine Legislature for several years, but has not yet been passed.

SEC. 5. The Collector of Internal Revenue shall issue such rules and regulations as may be necessary to carry into effect the provisions of this Act, and are not in conflict therewith, and such regulations, when approved by the Secretary of Finance and Justice, shall have the force and effect of law.

SEC. 6. Any person violating any of the provisions of this Act, or of any lawful regulation issued thereunder, shall be punished by a fine of not less than one hundred pesos, nor more than ten thousand pesos, or by imprisonment for a period of not less than one month, nor more than five years, or by both such fine and imprisonment, in the discretion of the Court.

SEC. 7. The Collector of Internal Revenue, with the approval of the Secretary of Finance and Justice, may compromise any civil or other case arising under the provisions of this section, instead of commencing or prosecuting suit thereon, and with the consent of the Secretary of Finance and Justice, he may compromise such case, if action has been begun thereon.

RESOLUTIONS

SECTION OF TROPICAL MEDICINE AND HYGIENE

17TH INTERNATIONAL MEDICAL CONGRESS, LONDON, 1913.

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1. The Section is of the opinion that beriberi among natives who live principally on rice is brought about by the continuous and too exclusive use of rice submitted to a too complete milling, which removes the cortical and subcortical layers of the grain.

2. The Section urges all authorities charged with the health of native communities to restrain by every means in their power the use of this rice in the dietary of coolies.

3. In view of the proved non-infectiousness of beriberi, the Section suggests that all port and sanitary authorities should abolish foreign quarantine and other restrictive measures against this disease.

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