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The Etiology of Beri-Beri.

By PATRICK MANSON, C.M.G., F.R.S., M.D., F.R.C.P., LL.D.,
President.

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Gentlemen,—The last two or three decades have been signalised by many important discoveries in the etiology of disease: of tropical diseases no less than of the more familiar diseases of temperate climates. In the group of tropical diseases we may confidently tick off as having had their exact causes finally determined malaria, Mediterranean fever, plague, leprosy, filariasis, ankylostomiasis, endemic haematuria, endemic hemoptysis, mycetoma, and some minor complaints. Quite recently, thanks to the insight of some of our American confrères, we are almost justified in adding yellow fever to the list, although it is true the actual germ of this disease has not been definitely isolated. The immense practical gains which have already sprung, or which will ultimately spring, from these discoveries are patent to everyone. Their scientific importance is in many instances of the first magnitude. These considerations, utilitarian and scientific, should stimulate to further effort towards attempting the solution of the many etiological puzzles which, more especially in tropical diseases, still remain unsolved.

Among other tropical diseases, the various affections whose leading symptom is intestinal flux, and which are included under the somewhat elastic names of dysentery, sprue, chronic diarrhœa, colitis, entero-colitis, etc., are, perhaps, the more important of the unsolved etiological problems. Although intestinal flux is one of the commonest symptoms in disease, especially in tropical disease, strange to say the cause of the pathological processes which lead to the symptoms are, if we except cholera, absolutely unknown; or, at all events, undetermined.

Perhaps only second in importance and in mystery to the intestinal fluxes, are those tropical affections which have in common as their leading pathological feature multiple peripheral neuritis. It is about the etiology of one of these, namely, beri-beri, that I propose to offer a few observations this evening.

Of the importance of beri-beri it is hardly necessary to speak. Everyone familiar with the literature dealing with the diseases of the East is aware of the almost leading place which, in certain localities and seasons, beri-beri assumes in their pathology. Instances in illustration of this can readily be adduced from Japan, the Philippines, China, Tonkin, the Netherlands Indies, Burma, the Coast of India, tropical Africa, the Brazils, West Indies, Sandwich Islands, and even Australia. Among British possessions nowhere is the disease more common than in the flourishing Straits Settlements, and in the neighbouring and intimately associated Federated Malay States. Here it is always in evidence. A large proportion of the beds in the State and other hospitals are occupied by the victims of beri-beri. Thus, in the State of Negri Sembilan, Dr. Braddon reports that in the year 1899, out of every 1,000 deaths of Chinese immigrants, 62 were attributed to beri-beri. Of every 1,000 deaths of the native Malays 140, and every 1,000 deaths among Tamils 150, were caused by this disease. So that about one-tenth part of the entire mortality of that State was attributable to beri-beri. During the nine years 1890-1899, in a mean population of 80,228, 6,001 cases of beri-beri were treated in the hospitals; of these 535, or 9.2 per cent., died.

In the year to which I refer, 1899, according to Dr. McClosky, in Pahang, in a population of 73,000 there were 146 deaths from beri-beri. On the assumption that the case-mortality in Pahang was similar to that of Negri Sembilan, this would represent a total of 1460 cases, or about 2 per cent. of the entire population. In Berak, also in 1899, according to Dr. Wright, in an estimated population of 294,297, there were treated in the hospitals 3,113 cases of beri-beri, with a mortality of 333. In the same year, 1,793 cases were treated in the hospitals of the Straits Settlements, with a death-rate a little over 32 per cent.; a death-rate, be it remarked, much greater than that occurring in the Malay States: a circumstance attributable in some measure probably to the fact that only graver cases were admitted.

It would be easy to bring together similar statistics

from other countries. The figures I give have been selected because they are recent, apply to British territories, and have been collected by responsible medical officers. They show quite conclusively that, in some parts at least of our Empire, beri-beri is a very important element in the State problems which the Government has to tackle. Directly or indirectly, it is a serious tax on these communities, and a distinct drag on their progress. Not only does it lead to great loss of life, but it is an enormous drain on the labour market and on the industrial resources; for beri-beri is a disease which, when not quickly fatal, usually runs a long course—probably of several months—during which the patient is, as a rule incapable of earning his living; and, in many instances, of even cooking his food, or in other ways attending to his personal requirements. It hampers every industry. It breaks out constantly on plantations, in mines, schools, gaols, and hospitals, and is a source of continual anxiety to the capitalist, the employer of labour, the Government official, and the medical men. To be able to place one's finger with precision on the cause, or on the medium or way in which it is conveyed, would probably be to enable us to stop this disease, and so confer an incalculable boon on the countries I have enumerated.

The etiology of beri-beri, therefore, is well worth the serious consideration of the sanitarian as well as of the epidemiologist. As the subject is to occupy the attention of the Commission which, as suggested in my Address last year, should be sent out to study the diseases of the South Pacific (a Commission which, I am pleased to be able to inform you, has already set out), I have thought that the present would be an appropriate opportunity to pass in review some of the facts which have been accumulated and theories which have been formulated in connection with the subject.

An additional consideration which has influenced me in selecting the etiology of beri-beri as the subject for my Address, and one which should urge us to fresh effort at solving the mystery of this disease, lies in the circumstance that there is a considerable body of evidence tending to show that beri-beri has spread into regions hitherto believed to be immune, and even into Europe and other temperate climes. As a matter of fact, beri-beri is constantly to be found in the shipping in the London Docks; and, doubtless, if carefully sought for, it could be found in all the large shipping ports, not only

in Britain, but on the Continent and North America. Moreover, beri-beri, or a disease closely resembling it, if not actually identical, has shown itself in more than one institution in this country—in the Richmond Asylum, for example. A similar affection has shown itself elsewhere in Europe—in France and Italy, for example—and also in the United States of America. It is quite possible, therefore, that in time an epidemic disease resembling beri-beri, if it be not true beri-beri, may attain a permanent lodgment in temperate climates, and thus add another burden to countries already sufficiently afflicted with their own indigenous diseases. In these days of rapid and increased communication, all kinds of diseases tend to become diffused.

The study of tropical disease, as compared to the study of the diseases of Europe, labours under this disadvantage: that whereas in the latter there is in most instances complete agreement amongst pathologists as to the pathological conditions indicated by certain names, in the case of tropical diseases, owing to the physical difficulties imposed by distance, and consequent rarity of opportunity for the comparison and identification of the diseases of places it may be thousands of miles apart, much confusion has crept into the nomenclature. In some places, a disease receives a name which in other places is applied to a totally different condition. Thus, as regards the disease I am discussing, the term "beri-beri" was applied in Assam and Ceylon to what turns out to be Anchylostomiasis, a condition widely different from the peripheral neuritis which the term "beri-beri" indicates in Brazil, Japan, Netherland Indies, and elsewhere. Furthermore, it is just possible that the term "beri-beri" includes more than one species of peripheral neuritis. It has even been suggested that what is known as "beri-beri" is, in many instances, if not in all, a metallic neuritis, produced by arsenic or other mineral.

In the tropics, as in temperate climates, there are undoubtedly several distinct kinds of the pathological condition passing under the name of multiple peripheral neuritis. For example, I have seen cases of this condition from the West Coast of Africa, which, although bearing a close resemblance to beri-beri, were probably of an entirely different nature. At all events, the cases I refer to did not exhibit the cardiac and dropsical symptoms usually present in true tropical beri-beri. I might remark in passing that there is a large and almost unworked field waiting for the neurologist in the Tropics; for example, the type of neuritis

I refer to, as well as that singular condition so common in Europeans in West Africa, and known as "West Coast Memory."

One well-marked type of peripheral neuritis has been very carefully described by Dr. Strachan. In many respects it, too, resembles beri-beri. Dr. Strachan describes a typical case thus: "A patient presents himself, complaining of numbness and cramp in his hands and feet, dimness of sight, and a tightness round the waist." This is always the remark first made by the applicant for treatment. If the case be somewhat more advanced, he may add to this statement that he fears he is "getting hard of hearing;" and he goes on to say that he suffers from severe burning in the palms of the hands and soles of the feet, and that very often this is worse at night than in the day, and that the pains and the burning heat prevent his resting. It is rarely that he gives more information than this. On examination, it will be seen that there is slight excoriation with fine branny desquamation of the edges of the eyelids, margins of the lips, and around the margins of the nostrils. The palpebral conjunctiva may be hyperæmic as well as the lips. The heat in the hands complained of by the patient will be found to be not merely subjective, but appreciable to the touch, and due to a hyperæmic condition of the palms. The acuteness of vision for form will be found to be more or less impaired, according to the stage to which the malady has progressed. Examination of the main nerves to the extremities will show that they are very tender on pressure, especially the ulnar nerve; and along the distribution of their terminal filaments they may be tracked by fine herpetic vesicles. On admitting such a case to hospital, and watching its further progress, it will be noted that at night the patient will be awake for hours, rubbing his feet and legs most probably, and moaning with pain. The loss of vision will proceed until he can with difficulty distinguish a large object immediately in front of him, and cannot recognise individuals. The muscles of his limbs will waste until the claw hand and foot are marked features; and this wasting of muscles and disappearance of fat will produce an emaciation which is very noteworthy in advanced cases. There will be found to be no alteration of the pupil to light and accommodation, no falling when the eyes are closed, and the sphincters will not be affected. Should the disease make further headway, the patient may become a mere helpless skeleton, unable even to feed himself, his breathing laboured from implication of trunk

muscles in the general muscular atrophy. Almost blind, and with perhaps an ulcer on the cornea, quite deaf, and with possibly small bullœ on the extremities. There may also occur, during the course of the malady, monoplegiæ, as facial palsy, or some of the external muscles of the eyeball, and, but rarely, of some group of muscles in an extremity. The temperature chart will show a sub-normal condition in the mornings, with an evening rise of from 1 to 2 degrees. A fatal termination is fortunately rare: when it occurs it is due to the dyspnœa and the riotous action of the heart, resulting from vitally important nerves, becoming involved in the now almost universal nerve changes. As a rule, however, under appropriate treatment, recovery gradually—with perhaps from time to time slight recurrences of the nerve inflammation—takes place. The patient becomes stronger, can help himself a little, assimilates food well, and puts on fat again. Then he is able to walk a little, first with help, and afterwards alone; his grasp, measured with the dynamometer, shows daily increase of muscular power, his sight clears up, and his deafness gradually passes away. Though, if this has been extreme, it is usually one of the last symptoms to disappear." This disease attacks hundreds of negroes in Jamaica, at all ages and of both sexes. It prevails most on the sea-coast and in low-lying regions. Dr. Strachan is inclined to attribute the affection to malaria; but he does not pledge himself to this opinion, and I think wisely: for, were this a malarial neuritis, a similar disease ought to be found in other malarial countries. In many respects Strachan's disease resembles arsenical neuritis, and is well worth further investigation in the light of the recent experiences in Birmingham and the North of England.

Another curious neurosis, also probably a peripheral neuritis, was noticed by Malcolmson and other writers on East Indian disease in the earlier part of the last century; I refer to what is known as "Burning Feet." This name adequately describes the leading symptom of the disease, for such undoubtedly it is. It was, and probably still is, very common in parts of India. It occurs in China to my knowledge.

It is evident, therefore, in investigating and discussing the etiology of beri-beri, if confusion is to be avoided, that a clear conception of what is meant by this term should be arrived at. What I conceive to be understood by the word "beri-beri" is a form of multiple peripheral neuritis which occurs endemically and epidemically,

and is specially characterised as compared to other forms of peripheral neuritis by proneness to œdema and to implication of the neuro-muscular system of the central organ of circulation; by complete absence of trophic skin lesions, of paresis of the muscles of the head and neck, of marked implication of the organs of sight, hearing, taste and smell, and of the mental faculties. In common with alcoholic and arsenical neuritis, there are troubles of locomotion, paresthesiæ of various descriptions, especially in the lower extremities, marked hyperesthesia of the muscles involved with, subsequent atrophy; and generally, after the initial stages, complete absence of patellar tendon reflex, the superficial reflexes and the action of the sphincters being in the vast majority preserved. The patient complains principally of weariness, palpitations, and breathlessness, weakness and numbness of the extremities, swelling of the legs. Although, at the commencement of the disease, and at the outset of such exacerbations as may occur during its progress, there may be slight elevations of temperature and gastro-intestinal disturbances, fever and diarrhœa are far from being prominent features in the progress of the complaint. The intensity and duration of the disease varies within wide limits. It may be of the most trifling description and only of a week or two's duration; or it may prove rapidly fatal; or it may persist in varying degrees of intensity for months. The leading feature may be paresis and muscular atrophy, or it may be extreme anasarca, or it may be serous effusion into pericardium or pleura, or it may be œdema of the lungs, or it may be rapidly fatal paralysis of the right heart or of the diaphragm and muscles of respiration. It occurs generally in limited epidemics in particular houses, institutions, plantations, mines, etc.; or it may be spread over a large area, but only attacking limited foci therein. It occurs at sea on board ship, where it is prone to be extremely fatal. The post-mortem lesions are those ordinarily found in multiple peripheral neuritis, inflammation, and degeneration of peripheral nerves, and, as Dr. Wright has recently shown, an ascending degeneration of the neuron, ultimately involving the corresponding intercranial cells. It may prove fatal very rapidly in a day or two from the declaration of the symptoms, or at any time during its progress. One attack confers no protection against a second. The case-mortality ranges from 5 to 50 per cent. In some epidemics only a small proportion of the affected community is attacked; in other epidemics almost every

one may be victimised. In some plantations over 75 per cent. of the coolies have been killed off by beri-beri in a single year.

What is the cause of this disease? Innumerable speculations have been advanced. So far, none of these has been proved to be correct. I shall pass over the theories of the earlier writers on the subject, and confine myself to what may be regarded as the not-disproven theories of more modern workers. These may be grouped under two headings: (1) the dietetic theory; and (2) the microbic theory.

The dietetic theory has been advocated by many writers, especially by Miura, who attributed beri-beri to the use of fish. A more plausible hypothesis has been advanced by Vinson, Le Roy de Mericourt, Rochard, Overback de Meyer, Mesé, and especially by Takaki, all of whom attribute the disease to a prolonged and uniform rice diet. Takaki, in particular, believing that the physiological deficiency of nitrogen in the almost exclusively rice diet, which at one time prevailed in the beri-beri-stricken Japanese Navy, was the cause of the disease, urged on the Japanese authorities the adoption of a more nitrogenous diet for their sailors; with the result that, whereas before the adoption of the more liberal dietary 32.45 per cent. of the force were annually attacked with beri-beri, after the adoption of the new dietary in 1884 the incidence of the disease rapidly fell to zero. In 1898 it stood in a force of 18,426 men at 0.08 per cent. only. So remarkable a result as this could not fail to call for the application of the principle involved to the army, to prisoners, and to similar public bodies; and, as stated in the *Sei-i-Kwai Medical Journal*, by Baron Saneyoshi, F.R.C.S. Eng., with equally happy results. Moreover, it has been observed that wherever throughout the Japanese Empire, from one circumstance or another, the diet of the people has been exclusively or mainly a rice one, beri-beri has appeared, to disappear again when this assumed dietetic error had been corrected.

This remarkable experience certainly tends to support Takaki's views; but if we consider the circumstances of certain epidemics elsewhere it becomes manifest that there is something more than—or rather, other than—nitrogen starvation at the root of beri-beri; that very probably nitrogen starvation has nothing to do with it whatever. Takaki's theory may have led to a successful practice; but success in practice does not necessarily prove the correct-

ness of the theory on which the practice is founded. If the nitrogen starvation theory be correct, how comes it that beri-beri not infrequently attacks the well-to-do? That it appears in hospitals and gaols, where the food is of good quality, physiological in the proportion of its elements, and sufficient in amount? For example, in the Tan tok seng Hospital, Singapore, the diet is a liberal one; nevertheless patients admitted for some trifling disease, such as an ulcer of the leg, after a time may contract and die from beri-beri. How comes it that the disease appears in gaols, schools, plantations, and mines, the dietaries of which have been specially devised with a view to avoiding deficiency in the nitrogenous elements? Many examples of this could be brought forward. 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 during the journey. On their arrival to Fiji they were divided into two bands; one, consisting of 50 coolies, was sent to work on a certain estate. The dietary was liberal, including meat or fresh fish to the amount of half a pound *per diem*, besides two pounds of rice, and a variety of condiments. Nevertheless within two months of the arrival of the coolies in the island beri-beri broke out, and in all 42 cases occurred. Eight of these 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 beri-beri broke out among them. The cases steadily increased in number, and by the end of six months 226 out of the 250 were affected. Sixty-nine died. The survivors, 181 in number, many still affected with beri-beri, were sent back to Japan. In Singapore Gaol, in 1898 and 1899, there were two kinds of diet in use: ordinary and penal. The ordinary diet was a sufficiently liberal one, including fresh meat and wheaten flour. The penal diet contained no meat. Nevertheless the greater number, absolute and proportionate, of cases of beri-beri occurred among these on ordinary diet—that is on the diet richest in nitrogen.

Macleod* relates an interesting epidemic on board ship, in which beri-beri attacked the captain and officers, and not the crew—an unusual occurrence. The dietary of these officers included such luxuries as haddies, clams,

* *Brit. Med. Jour.*, August 14th, 1897.

oysters, lobster and salmon. Here there could have been no nitrogen starvation. The disease elected to attack the better-fed members of the ship's company. There was no nitrogen starvation among the inmates of the Richmond Asylum before or during the epidemics of beri-beri there, so fully and carefully described by Dr. Conolly Norman. There was no nitrogen starvation in the Blind Asylum at Rio de Janiero, where not only the inmates, but the director and his family were attacked.

There are many additional instances on record, and which might be quoted, in which Europeans enjoying a liberal diet have fallen victims to beri-beri; and although it must be admitted that remarkable improvement has sometimes supervened on the introduction of a more liberal dietary in beri-beri smitten jails, and similar institutions, yet even in those same places, and while the inmates were still enjoying the improved dietary, which at one time seemed to be beneficial, the disease, after a year or more, reappeared. This has been the experience in the Singapore Gaol, where the disease reappeared in 1898, after having been absent for 14 years.

If the cause of beri-beri be deficient nitrogen in food, we ought always to find this condition preceding or accompanying its epidemic development, and where we get nitrogen starvation we ought always to get beri-beri. How far the first is from being the case, the instances I have quoted show; how far the second is from being the case, hundreds of unintentional experiments daily prove: for, surely, nitrogen starvation is common enough the world over; beri-beri has no such universal distribution.

F. C. Eijkman, of Batavia, has recently brought out a curious fact in relation to rice diet in beri-beri. The prisoners in Java are fed, amongst other things, on three qualities of rice—one, decorticated rice, in which the pericarp has been entirely removed, or at least in 75 per cent. and upwards of the grains, by milling. A second kind, in which the pericarp is retained entirely, or at least in 75 per cent. of the grains; and a third kind, consisting of a mixture of the first and second. Statistics applying to 280,000 prisoners show that beri-beri attacks 2.84 per cent., or 1 in 39 of the prisoners who are supplied with the first, or decorticated rice, whilst it attacks only 0.01 per cent., or 1 in 10,000 of the prisoners who consume non-decorticated rice; those fed on the mixture of these two qualities suffer in an intermediate degree, namely, 0.24 per cent., or 1 in 416. He further states that fowls fed exclu-

sively on decorticated rice are affected with a peculiar paretic disease resembling beri-beri; whereas fowls fed on non-decorticated rice are not so affected. The source and species of rice, Eijkman says, makes no difference in the result. Other observers in the Malay Islands have made somewhat similar observations on the influence of the quality of the rice. The Japanese substitute barley or wheat for rice as a preventive of beri-beri, and believe in their efficacy. A grave outbreak of beri-beri in the Pearling fleet, off the north coast of Australia, was arrested, it is said, by the timely substitution of wheaten flour for the damaged rice on which the crews were feeding. These are facts to be noted, but not necessarily interpreted as proofs that beri-beri is a rice-caused disease, much less a nitrogen starvation disease.

The Germ Theory of Beri-beri.—Another theory, and one much more plausible than the foregoing, is to the effect that beri-beri is a germ disease. Such a theory is quite compatible with the remarkable Japanese experiences to which I have already alluded, as well as with all the known facts. But as to whether the germ produces its morbid effects while proliferating in the human body, or as to whether it acts indirectly by producing outside the body a toxin which, on being ingested, inspired or otherwise absorbed, acts on the nerves, it is impossible as yet to say. There are arguments in favour of both hypotheses.

The fundamental nerve lesions in beri-beri resemble those produced by several well-known organic poisons, and are probably the results of the direct action of some such poison. If we adopt the first hypothesis, that is the infection hypothesis, we have the argument supplied by analogy for supposing that the lesions are the effect of a toxin elaborated by the germ while it is proliferating in the blood or tissues, that is to say, an intoxication produced by an infection. If, on the other hand, we adopt the second hypothesis, we must conclude that the specific germ resides in some external medium where it elaborates its toxin which is subsequently absorbed as such, the germ not entering the body, or, at all events, not necessarily so.

(*a*) The infection theory has had many advocates, including Scheube, Lacerda, Ogata, Masanori, Wallace Taylor, Cornelissen, Suguenoya, Pekelharing, and Winkler, Van Eecke, Rebourgeon, Musso, and Morelli, Glogner, Braddon, Hunter, Rost, and I do not know how many more. Many of these claim to have discovered a beri-beri bacterium.

Unfortunately, in some instances the observations are crude and open to objection on the ground of technique; more unfortunate than this, there is a suggestive want of uniformity as to the morphological and cultural characters of the various organisms separated, some describing a bacillus, others a micrococcus, one at least an endocorpuscular protozoon like that of malaria. There is also a suspicious unanimity as to the pathological effects produced by those very different organisms when injected into the lower animals. Some recent work by Hunter, in Glasgow, carried on under very favourable circumstances, led him to the conclusion that beri-beri is caused by a micrococcus which is visible in the blood, and which can be cultivated in various media, and on subsequent injection into rabbits give rise to something like a peripheral neuritis. His observations, like those of Van Eecke and Braddon, seem to confirm those of Pekelharing and Winkler. On the other hand, equally careful observations, made in equally favourable circumstances by more than one bacteriologist, working with material supplied by the Richmond Asylum epidemic, gave absolutely negative results; the same may be said of similar observations elsewhere. If beri-beri be an infection, I hold with Scheube—than whom there is no higher authority on this disease—that so far the germ has not been discovered, or, at all events, that no germ has been demonstrated to be the specific cause of the disease.

To my mind, the theory which conforms best to all the known facts in respect to the etiology and pathology of beri-beri is to the effect that this disease is purely an intoxication produced by a toxine elaborated by a germ whose nidus is located outside the human body; that in this respect beri-beri is on all-fours with alcoholism, the germ of which is the yeast plant, the nidus solutions of sugar, the toxine-alcohol, and, to complete the parallel, the pathological effects—a peripheral neuritis.

There is no evidence to show conclusively that beri-beri can pass directly from men to men like the ordinary infectious diseases; yet that it is produced by a living germ is certain. This is proved by the facts (*a*) that the cause can be transported from place to place, and therefore cannot be of a climatic or meteorological nature; and (*b*) that when so transported it can multiply and spread, and therefore cannot be of an inorganic nature. As already mentioned, it has recently been suggested that beri-beri is caused by arsenic. Now the clinical symptoms of beri-beri and arsenical poisoning are very different. I have

never seen skin lesion, other than accidental, in beri-beri. This in itself is almost conclusive. The diseases are not the same clinically. Professor Dixon Mann has recently shown that in arsenical neuritis arsenic can by chemical tests be detected in the hair. Some time ago he had the kindness to examine for me hair from two recent cases of beri-beri. In neither did he find a trace of the mineral. There is no evidence worth considering that tends to show that any other mineral is concerned in the production of the disease. Tin has been suggested; but there is no tin in Japan, or in the Kurile Islands, where beri-beri has occurred. A mineral cause would not be regulated in its incidence or effects by meteorological conditions, as beri-beri certainly is.

That the cause of beri-beri can be transported has been proved over and over again, as, for example, by the epidemic among Japanese in Fiji already alluded to; but it is more difficult to find facts to establish completely that when so transported it can multiply. If, however, we find an instance of some island hitherto free from the disease, among the natives of which beri-beri, on being introduced, has spread, we may regard it as presumptive proof that the cause of beri-beri is endowed with that special property of living things, the power to multiply. There is recorded at least one apparent example of such an occurrence. A number of Tonkinese and Annamese were brought to New Caledonia in March, 1891. Beri-beri broke out among them and caused many deaths. After a time the disease spread and in some instances proved fatal to certain natives, Kanakas, who had become associated with the Asiatics. These two things, portability and the power of multiplication, if established, certainly show that the fundamental cause of beri-beri is a living thing, a germ. The evidence that the multiplication of this hypothetical germ occurs outside the body, though not conclusive, is certainly stronger than any evidence hitherto advanced in favour of its multiplication inside the human body. Did the germ multiply inside the human body we might expect that the disease it produces would run a more or less definite course, as in other infections. But this is not so: for, if we remove the subject of beri-beri from the infected area or the conditions in which he sickened, after an interval of from a week to a fortnight the progress of the disease, if it had not proved fatal in the interval, will be arrested and slow convalescence supervene. Now, if beri-beri be caused by a germ living in the human tissues, it is not likely

that this germ would be killed off thus early; on the contrary, analogy would lead us to believe that the germ would continue to multiply till immunity had been produced; and this we know to be a long process in beri-beri, for those patients whose lives are spared and who continue to live in the endemic area generally exhibit active symptoms for months after the commencement of the disease.

In our experience of the disease at the Seamen's Hospital, Albert Docks, we have very strong evidence of this evanescent nature of the primary effects of the toxine of beri-beri. From October, 1890, to November, 1901, 135 cases of beri-beri have been admitted to this hospital. They all came direct from the ships in which they acquired the disease. 19 died; 4 on the first, 2 on the third, 4 on the fifth, 2 on the sixth, 1 on the eighth, and 3 on the fourteenth day after admission. This accounts for 17 of the 19 deaths. Of the two other fatal cases, one died from phthisis on the 104th day after admission, and the other, apparently from dilated heart, on the thirty-first day. With the exception of these two, neither of whom apparently succumbed to the immediate effects of disease, a fatal result never occurred later than a fortnight after the patient had been removed from the conditions in which he had contracted the disease. At the Seamen's Hospital we therefore have come to regard cases of beri-beri as safe when they have passed the fourteenth day. Would this be justifiable were the disease the result of an infection, immunity from which is only slowly acquired. Beri-berics when kept under beri-beri influences do not recover for months, during which the disease is liable to exacerbations in any of which death may occur. Beri-beri is so like alcoholism in these respects—keep the drunkard from liquor, in a few days he begins to recover; give him liquor, and he will not recover; take the beri-berie away from the circumstances under which he is being poisoned, in a few days he begins to mend; keep him under these circumstances, and he will continue sick and very likely die.

Pekelharing and Winkler, who advocate the personal infection theory, try to get over the generally-recognised beneficial influence of removal from the endemic area by assuming that in this area the disease is kept up by continual or repeated infections; and in their experiments they attempted to imitate what they assumed occurs in nature by introducing syringefuls of their cultures at short intervals into the experimental rabbits. Their followers have done the same. Small wonder they had fatal results,

and indications of peripheral neuritis; it is a wonder, rather, that any of their animals survived such treatment. Hirota publishes an interesting observation which lends strong support to the toxin theory. In some respects it resembles our experience at the Albert Dock Hospital. Infants suckled by beri-beri get the disease. He refers to fifty-two such cases. When the infants were weaned and fed on condensed or cows' milk improvement set in at once; five cases which were not so treated died. A child who acquires a germ disease from its mother's milk will not recover thus rapidly; but a child who has only become intoxicated from drinking an intoxicated mother's milk will.

But although we may conclude with a fair show of reason that beri-beri is a toxine-produced disease, we cannot say what the toxine is, what the germ producing it is, or where this germ resides. The whole epidemiology of the disease shows that the germ clings to people—witness its transportation to Fiji and New Caledonia by Asiatics, and to places, witness the persistency of the disease in certain buildings and ships. Instances of its tendency to cling to buildings are numerous, and there are some well-authenticated examples of a similar persistency in ships. A very telling example of the latter is recorded by Mr. Montgomery Smith, in the *British Medical Journal* of November 5th, 1898. In 1896 a ship, the *Lodestar* of London, arrived in Falmouth with a cargo of rice from Rangoon, after a long voyage, during which the entire crew was attacked with beri-beri, and three had died from the disease. The ship was sold to German owners, and re-named *Steinbek*. At Amsterdam she received a new crew, and took in fresh provisions. She then sailed for Java, where she loaded with sugar. She left Java on Jan. 27th, 1898, all being well on board. On April 29th, when off St. Helena, and after being three months at sea, beri-beri broke out, and when the ship arrived at Bermuda the entire crew, with the exception of one man and a boy, were down with the disease. One man died in Bermuda, the others, apparently, recovered. Two epidemics of beri-beri in the same ship, but in different crews and on different provisions, occurring at an interval of about two years, is surely no mere coincidence, but distinctly points to a persistent infection in the ship.

A Chinese revenue cruiser, well found in every respect, visited Corea. Many of the crew subsequently developed beri-beri. For several years thereafter, during the south-

west monsoon, cases of the disease kept cropping up in the crew. This example of ship infection came under my own cognisance, and I was familiar with the facts.

At the Albert Dock Hospital, as recorded by Dr. Rees (*British Medical Journal*, Sept., 1898), we came at one time to regard certain steamers trading to the port of London as infected ships. We called them beri-beri ships, as they almost invariably brought us cases of the disease on their return from their periodical voyages to the East.

Many similar facts could be adduced tending to show, although not absolutely to prove, that a ship can become infected with beri-beri. If a ship can become infected, why not the houses, and even the localities in which this disease, as is its habit, establishes itself? Granted that a place or ship can become infected, we have still to find the particular medium in which the germ operates, and the particular portal through which its toxine enters the human body. There is a marked tendency among the students of this subject to regard, not without reason, rice as the nidus of the germ; but, if rice be the medium, how is it that the disease sometimes occurs in individuals who have not consumed this cereal? The answer may be that other farinaceous substances are equally efficacious as culture media, if I may so speak. But if we concede this, how are we to explain the latency of the infection in buildings and ships which have had their stores frequently renewed in the intervals between the epidemics? The answer to this may be, that the germ clings to the walls, the wood, the utensils of the place; and that when cereals are brought in this germ drops into them and infects them. Thus infected, when consumed, whether on the premises or exported elsewhere, they may cause the disease. On the other hand, it may be that the germ distils its toxine from some other medium; it may be clothes, the soil, wood, or what not, and so poison through the atmosphere. This is speculation, but I think we have distinct evidence to show that beri-beri is, in a sense, a place disease.

In the foregoing reasonings—or, if you like, speculations—on the nature or cause of beri-beri, I have been powerfully influenced by the analogy of alcoholism. Analogy, I know, is not argument, but if it helps us to understand, or if it helps to suggest, it is not quite useless. Before, however, anything like assurance on the etiology of beri-beri can be attained, we want more facts; above all, carefully devised and executed experiments. It is to be hoped that the expedition to which I have alluded will, in the specially

favourable circumstances in which it will be placed, carry out a series of such experiments with the view to ascertain: first, the medium or media in or through which the disease is conveyed; and, secondly, having found this, by a process of exclusion to isolate the organism which undoubtedly is at the root of the disease. Should they succeed in this, it is more than probable that we will be in possession of that knowledge which alone can give precision and accuracy to efforts at cure and prevention.

There are several points that investigators in the etiology of beri-beri must be careful to attend to.

1. The diagnosis. They must avoid mistaking other forms of peripheral neuritis for that of beri-beri.

2. They must bear in mind the possibility that the disease may not have been contracted at the place in which it is declared.

3. That the toxine which produces an outbreak of beri-beri may have been imported as such, and not manufactured, so to speak, locally.

4. They must carefully differentiate between predisposing or favouring conditions, such as overcrowding, heat, and moisture, bad food, etc., and the actual direct cause.

Finally, they must recognise that the actual cause must correspond in its geographical distribution with the geographical distribution of the disease.