ment. Finally she was given tuberculin over a period of five months in doses ranging from 0.0005 gm. to 0.6 gm. At first the cough and expectoration increased, but soon the condition began to improve and for more than a month before the patient was discharged the symptoms were entirely absent and the physical signs showed much improvement. After discharge she worked for a time in a bleachery without breaking down; at present she is a waitress in a summer hotel and reports that her health is excellent, eight years after the use of tuberculin.

In considering again the results of treatment in this series of cases, one cannot but be impressed with the after-condition of the arrested cases as compared with that of the improved cases—health being reported good in 81 per cent. of the former and in only 29 per cent. of the latter. The oft-repeated moral is again brought forcibly to mind by these figures, that in order to give patients the best chance for recovery and for subsequent usefulness in life, they should be treated at an early stage while yet the disease may be arrested. We have learned that patients are practically never cured during residence at a sanatorium; they are merely started in the right direction. It is fairest to them, therefore, to begin treatment at a stage when they may be given the best chance to regain health.

In reviewing the work accomplished in the last twenty years, we feel that our attitude has been one of conservatism in regard to the results obtained. When one reflects on the condition of affairs in the treatment of tuberculosis twenty or twenty-five years ago, and recalls the sense of hopelessness that was felt whenever a patient presented himself with symptoms of pulmonary disease, especially among the less favored classes, we feel that we are justified in looking with great satisfaction—even enthusiasm—on the work of twenty years at the sanatorium.

It is often impossible to impress on others by figures alone facts which through long years of experience stand as positive proofs to us of what we wished to obtain. It was never believed or even hoped that sanatorium treatment alone would eradicate tuberculosis; but it did not take long to convince us that it was a great step in the right direction and that infinitely more could be done than heretofore to bring people back to health, even under what had been considered in former years most unfavorable conditions.

In stating our results, it must be remembered, too, that in using the term "arrested" we have applied it to the results obtained in many cases in which at the beginning of treatment the physical signs and symptoms of disease were well marked, and in spite of which condition a successful result was often obtained for a number of years. The surprising part has often been that such patients have remained so long without relapse on resuming the ordinary conditions of life.

To those who have been closely connected with the work, the fact that has been of far greater influence than the mere collection of figures, although these themselves have given us the greatest satisfaction and more than we had dared hope for in former years, are the faces and general aspect of patients who on reunion days at the sanatorium appear to give their tribute of gratitude for help which they have received in former years. The evidence that these persons give, not only of the good done to themselves, but of their influence on others in teaching methods which tend to prevent disease, is the most gratifying part of all our work.

We have no sympathy with the attitude, which happily is now lessened, that because sanatorium treatment has not proved to be a panacea it has therefore failed in

its purpose. On the contrary, with greater confidence than ever before, we feel it to be one of the great and important factors to be resorted to in conjunction with every other known method of combating the disease which still holds the highest place in the mortality list of the civilized world.

THE ETIOLOGY OF BERIBERI

CARL LOVELACE, M.D.

PORTO VELHO, BRAZIL

IN *THE JOURNAL*, some time ago, there appeared an editorial comment¹ on the sanitary work incident to the construction of the Madeira-Mamoré Railway, in the states of Amazonas and Matto Grosso, Brazil. I take it, therefore, that a brief description of this work would be deemed of interest to physicians. For this reason, and in order to give a side-light on my subsequent remarks, I venture to prefix my observations on peripheral neuritis in Brazil, with the following:

THE MADEIRA-MAMORÉ RAILWAY

The Madeira-Mamoré Railway is 227 miles long. It extends from the head of navigation on the Madeira River southward and upward to the navigable waters of the Mamoré River—from Porto Velho de Santo Antonio to Guajara-Mirim. Except for the improvements made by the company, both of these formidable names locate mere spots in the Brazilian jungle. The first train over the whole line was run on April 30, 1912.

Porto Velho is situated in south latitude 8° 45'; is 300 feet above sea-level; has a rainfall of 90 inches per year, and a temperature range from 56 F. in the cool June nights to 102 F. in the hot September days. It is on the right bank of the Madeira River, which at this point has an annual rise and fall of 45 feet. The annual volume of water discharged by this river is about the same as that of the Mississippi. Boats drawing 8 feet of water ply on it all the year, and ocean-going vessels of 7,000 tons come to Porto Velho every year during the period of high water, from December to May.

Three previous attempts to build this railroad were unsuccessful, because of the terrible rates of sickness and death among those concerned. Mr. Neville B. Craig² has written a most entertaining volume describing one of these melancholy failures.

WORK OF AMERICAN PHYSICIANS

The sanitary branch of this work has from the beginning, in 1907, been under the direction of American physicians employed by the contractors. In 1910, Dr. Oswaldo Cruz, Brazil's foremost sanitarian, visited Porto Velho, sojourned here three weeks, approved the work then being done, and urged the compulsory administration of daily prophylactic doses of quinin to all employees not protected by screened houses. In a non-military organization this has been found impossible to carry out perfectly, but even its partial enforcement has been of untold benefit. Without the powerful influence and personality of Dr. Cruz the liberty-loving Brazilians would have rebelled against this regulation.

In 1911 the number of employees was about 5,000, comprising, approximately, 250 North Americans, 2,000 Brazilians, 1,000 Spaniards, 750 Greeks and 1,000 others, representing practically every country in the world. The

1. Sanitary Work in Brazil: Good Health a Commercial Asset, *THE JOURNAL A. M. A.*, Sept. 24, 1910, p. 1120.

2. Craig, Neville B.: *Recollections of an Ill-Fated Expedition.*

number of physicians at this time was nineteen, of whom eighteen were Americans. In all, forty physicians have been employed, of whom thirty-six were American, two Brazilian, one Spanish and one English.

The sanitary measures adopted have consisted in the provision of screened houses for all employees of the higher grades; in antimosquito campaigns in and about the permanent camps, that is, camps destined to become towns; in the compulsory, prophylactic administration of quinin to employees; in the regulation of food and water-supply; in the usual measures against the so-called quarantinable diseases; in attention to disposal of garbage and sewage, and, finally, in the prompt hospitalization of all except slight cases of illness.

The nearest city and base of supplies is Manaus, where, for many years, yellow fever has been rampant. On seventeen occasions cases of yellow fever have been brought to Porto Velho by the river boats, and last year a number of employees contracted the disease at the old town of Santo Antonio, 3 miles from Porto Velho. We have been able to prevent the disease from getting a foothold anywhere on our line of work, only three cases having occurred in which the infection did not originate outside of our zone.

Malaria, yellow fever, blackwater fever, bacillary dysentery and beriberi are the chief tropical diseases with which we have to contend. We have had one rather sharp outbreak of typhoid fever, and lobar pneumonia has killed more than 200 of our employees. The hospital consists of six detached wards with a normal capacity of 250 beds, an operating-room, a clinical laboratory, a post-mortem room and the necessary out-buildings. We do autopsies on the bodies of all persons dying in the hospital. The material is only too plentiful. In addition to our employees, we receive a number of patients from among the *seringueiros* for hundreds of miles around. From Jan. 1, 1908, to Jan. 1, 1912, there were admitted to the hospital of this company 30,430 patients.

DESCRIPTION OF A FORM OF PERIPHERAL NEURITIS

Among the 30,430 admissions to the hospital of the Madeira-Mamoré Railway between Jan. 1, 1908, and Jan. 1, 1912, the diagnosis of beriberi or of "polyneuritis" or of "multiple neuritis" was made 963 times. The affection is known locally as *polyneuritis*, and following the teaching of the celebrated Brazilian physician, da Silva Lima, a goodly portion—in North Brazil, a majority—of the profession affix the word *palustre*. They regard the affection as a multiple peripheral neuritis incident to malarial infection. Oswaldo Cruz himself shared this opinion until his visit to this hospital in the summer of 1910.

Symptoms.—Few diseases present such a variety of clinical aspects. The onset may be sudden, the course swift and tragic. We have a number of charts of intelligent patients, with clear histories, in whom the duration of the disease from its very first symptom up to death by cardiac dilatation occupied less than one week. On the other hand, the onset may be so gradual and the symptoms so poorly defined that the disease is well advanced before the patient seeks relief. Some recover in a few days; others are bedridden for months. Some are waterlogged from the beginning; in others there is little or no edema. In some the affection throughout seems to be entirely cardiac; in others the heart appears to be absolutely unaffected even though the paralysis be extreme. The deep reflexes may be lost as a first manifestation of the disease; quite frequently they are markedly exag-

gerated not only in the beginning of the disease, but also throughout its course and immediately before its fatal end. They may be exaggerated to-day, and absent a week from to-day.

Sometimes the pain, particularly in the legs, is excruciating; more often the legs feel dead with vague, slight pains, or the "pin-and-needle" sensation. A patient may enter the hospital to-day with no symptoms save the subjective ones of pains in his legs, and in forty-eight hours have become so edematous as to be almost unrecognizable. The pain may be chiefly substernal, or in the thighs, or in the forearms. It may be entirely absent.

Death may come with dyspnea, cyanosis and a feeble, fluttering pulse, while the patient seems yet robust; or it may come as a terminal dysentery or pneumonia after he has been exhausted by many weeks of suffering.

Clinical Classification.—What one may take as the type of our patients presents himself for treatment complaining that his legs are swollen and that his calves are sore and painful. One finds on examination a rapid heart frequently with the pauses equal, and sometimes with a reduplication of the second sound over the pulmonary area; edema of the legs of maximum intensity over the pretibial area; knee-jerks usually exaggerated, but frequently lost, and areas of tenderness on the legs, giving rise to the "stiff" gait, with or without areas of anesthesia and of paresthesia. Fully three-fourths of our cases present these symptoms and these alone. The tachycardia may be slight and may not be noted unless one makes the patient walk about. The arrhythmia may be absent. Edema is present at some time in perhaps 90 per cent. of all cases. Pain in the legs, especially the calves, and in the thighs, particularly along their internal and posterior aspects, is also a fairly constant feature.

Patients of this group—and it comprises 75 per cent. of the total—usually recover on being put to bed and given an easily digestible diet, with treatment of any associated malady as malaria or uncinariasis. A few, however, grow progressively worse in spite of any and all treatment.

The severe cases fall into two groups: (1) those in which symptoms, apparently cardiovascular, dominate the situation, and (2) those in which paralysis of various groups of muscles, with pain and tenderness along the nerve trunks, is the characteristic feature. To the former of these two groups belong the acute pernicious cases characterized usually by anasarca and a rapidly developing dyspnea, cyanosis and death.

Any case may at any time develop these pernicious symptoms. Even in these fatal cases the edema may be slight. Sometimes the patient dies suddenly of heart failure after he has so far recovered, apparently, as to have been allowed to sit up.

A striking and cheering feature of a proportion of this group is the rapid recovery, which begins on the institution of rest in bed and good nursing.

Our severe cases of the paralytic or atrophic type fall clinically, also, into two classes: (a) a smaller group with a rapid onset of paraplegia, and (b) a larger group characterized by the slow development of paralysis, by some sensory disturbances and by extreme chronicity. These are the cases which accumulate in our wards and overcrowd them, unless they are invalided away.

A man may walk into the hospital with a mild tertian infection, which yields promptly to quinin. He has experienced nothing beyond the usual phenomena of a malarial attack, save, perhaps, an unwonted feeling of

weakness in his legs. He is surprised to find that, after the subsidence of the fever, his legs become weaker instead of stronger, until in a few days or weeks he is unable to stand. His heart may apparently be unaffected. He has no pain. The blood and urine are negative. Usually, but not always, there is edema of the legs. The knee-jerks are lost; or, without any coexisting malaria, these phenomena may develop within a very few days. The frequent association of malaria with this form of the disease has done much to hang the whole beriberi symptom-complex on the malaria peg in the minds of those whose work has been confined to regions where both affections are rife.

The second group of the severe cases with slight cardiac involvement corresponds exactly to the picture conjured up by the words "multiple peripheral neuritis." If these patients are able to walk the diagnosis may be made at long range. If they are bedridden the most cursory examination will suffice. All the dear old textbook descriptions here come into their own: the "step-page" gait, the lost tendon reflexes, foot-drop, wrist-drop, atrophied muscles, areas of anesthesia, areas of hyperesthesia, areas of paresthesia—all the well-beloved phrases troop gallantly to service and describe with precision the unfortunate patient.

Mortality.—Of 797 patients admitted to the Candelaria Hospital during the years 1910 and 1911, 120 died—a mortality of 15.6 per cent. The mortality varies in a most extraordinary manner. Sometimes it will be not more than 2 or 3 per cent. for months, and then a time will come when half the patients die.

Pathology.—No one feature of the gross pathology as seen at our autopsies is characteristic. Atrophy of the skeletal muscles is sometimes present. In the acute cases it is absent. Dilatation of the right ventricle is almost invariably present. The left ventricle may be dilated. In old cases there is hypertrophy of the right ventricle. Pericardial effusion is fairly constant. The other serous cavities usually contain more or less fluid, and at times the whole cadaver is water logged. The kidneys may be congested, but there is no nephritis. The cardiac cases that have dragged on for some time may show chronic passive congestion of the liver.

Our attempts to estimate duodenal congestion have been unsatisfactory. The paraplegic cases seldom come to autopsy unless a terminal affection—notably bacillary dysentery—sets in. Signs of chronic malarial infection are, in this region, frequently present as a matter of course. No attempts to demonstrate degeneration of the peripheral nerves have been made.

EVIDENCE THAT THIS AFFECTION IS BERIBERI

In writing the foregoing I have sought to describe what I see here. I believe that I have presented a clinical entity which must be classified as beriberi. At any rate it constitutes my first proposition, namely, that this affection is beriberi. To the above one might add abundant historical evidence—if libraries occurred in the Brazilian forest. Leopold³ referred to north Brazil as "the fatherland of the disease" [beriberi]. Bon-durant,⁴ of Mobile, mentions Brazil first in his list of countries where beriberi prevails. Manson⁵ speaks of the "epidemic wave" of the disease which passed over Brazil in the early sixties. Castellani and Chalmers⁶ refer to Brazil as a place where beriberi is said to occur. Herzog⁶ mentions the occurrence of beriberi on the

Atlantic coast of South America and particularly in Brazil. Osler⁷ has seen cases of beriberi from Brazil. Magalhães⁸ wrote an exhaustive monograph on the cardiac phenomena of cases studied in Rio Janeiro.

RICE NOT A FACTOR

My second proposition is that this affection as it occurs in Brazil is not etiologically related to a diet of polished rice. To posit this negation requires some temerity on the part of a mere clinician, after reading the papers of Fraser and Stanton,⁹ and many references to the work of Chamberlain and Vedder,¹⁰ Heiser and others in the Philippines. I do it because I have seen some patients with beriberi whose diet was varied and abundant—who had not eaten a grain of rice for many months before the onset of the disease; a large number of patients with beriberi, who, enjoying a liberal, protein-abounding diet, had eaten it only occasionally throughout their lives, and a great number of sufferers from the disease, in whose diet it could not be considered the staple article. Of the latter class I have seen a goodly number who for months before the onset of the disease had had rice excluded from their diet.

Unlike the Oriental, the South American, by nativity or adoption, is a meat-eater. He eats the European breakfast, but he eats two full meals every day and partakes liberally of meat at both. Beans, which are supposed to have a therapeutic value in the treatment of beriberi in the East, are staple articles of diet throughout North Brazil. They abound on the tables of the poorer classes. *Feijoadá*, a compound of bacon, red beans and dried beef, lightly touched with garlic and bathed in its own gravy, is the dish universal among the poor, and not despised by the wealthy. The bean with meat is the staple article of food of the Brazilian peasant. Rice and *farinha* (cassava) and bananas are side dishes. It must be admitted that the Brazilian laborer eats some rice practically every day, and that the incidence of beriberi is perhaps highest in his class; but the same line of reasoning would incriminate polished rice as a causal factor in lobar pneumonia, malaria, mecinariasis and gonorrhea. Among our Brazilian employees lobar pneumonia is twenty times more frequent, relatively, than it is among our American employees.

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 the 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. Conditions along the line of work were such that a large majority of the laborers were deprived of rice. The men who boarded at the company's messes ate no rice at all. The beriberi rate climbed steadily throughout the year 1910, and dropped abruptly at the end of the year exactly as it had done in 1909. In 1910 on a comparatively 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 all the commissaries of the company served and sold rice freely. The rice has always been the same kind—white, polished rice.

7. Osler: *Practice of Medicine*.

8. Magalhães: *O Coração no Beriberi*.

9. Fraser and Stanton; *Jour. Trop. Med. and Hyg.*, Nov. 5, 1911, et seq.

10. Chamberlain and Vedder: *Philippine Jour. Sc.*, November, 1911.

3. *Sajous' Cyclopedia of Medicine*, I.

4. Manson: *Tropical Diseases*.

5. Castellani and Chalmers: *Manual of Tropical Medicine*.

6. Herzog: *Osler's Modern Medicine*, III.

One of our American physicians, who did not eat a grain of rice while in Brazil and who purposely refrained from eating it because of its supposed association with beriberi, contracted the disease after about ten months' service here and was invalided home. Three other members of our staff, who lived at headquarters and who ate rice only occasionally, certainly not more than once a week, were invalided home with the diagnosis in both cases of beriberi. One of these men ate at the table of the chief engineer, the other two lived at this hospital. At neither table did rice appear except occasionally. Two other physicians stationed in the camps contracted the disease and were invalided home. Because one of these physicians had malarial parasites in his blood, when he got home, his affection was there diagnosed as "malarial neuritis." In all, six physicians have contracted the disease here—six healthy, young adults who lived on a full protein-rich diet.

The incidence of the disease among physicians has been greater than among any other class except the Brazilian laborers. Does not this fact alone speak volumes?

In 1910, out of a total of 690 admissions to the first-class ward of this hospital, there were twenty-four cases of beriberi. Many of these patients came here and were invalided back to the United States during the time that rice was prohibited. They did not eat a grain of rice. They were clerks, mechanics, camp foremen, time-keepers, etc. Their diet here would not have suffered, in comparison, as to quality, quantity and variety, with the diet of persons similarly employed anywhere in the United States. Fresh meat, onions, potatoes and an abundant supply of the best American tinned meats, fruits and vegetables were supplied in lavish profusion, in addition to the bacon and beans which have belted the globe with steel rails. Among the men from whom these cases were drawn (and no account is taken of a number of contract-expired men, who left of their own accord when the disease first manifested itself) the food-supply was above criticism from any standpoint.

TIME INCIDENCE

If beriberi were due to polished rice, *per se*, one would expect its occurrence to be fairly uniform throughout the year, and from year to year, in a population that eats the same kind of rice in apparently the same quantities all the time. Such is not the case. Of 565 patients admitted to the Candelaria Hospital in 1910, 114 were admitted during the first six months, and 451 during the last six months of the year. In 1910, 565 were admitted; in 1911, with a force of employees 25 per cent. greater and the Brazilian contingent relatively much greater, 232 cases were admitted. Practically, we, as well as the laity, recognize the period from July to December as being the beriberi season. This was the case in 1908, 1909, 1910, and from present indications, it will be the case in 1912. The year 1911 was an exception, the admissions for beriberi being fairly evenly distributed over the twelve months.

PLACE INCIDENCE

The constant shifting of laborers from camp to camp makes it well-nigh impossible to present figures of value as to relative admission rates for beriberi from the various camps. That certain camps yield a much higher percentage of beriberi patients than others is, however, firmly impressed on the minds of all who have, in any capacity, managed the labor on this work. In the fall of 1910 more than three-fourths of all the West Indian

Negroes in one of our camps (Camp 16) contracted the disease. The same camp furnished us beriberi patients of all nationalities, and, of all grades of employment so long as it was active. In the same year, of four West Indian Negroes living in a palm shack set back from the right of way in the woods, near Camp 22, two died of beriberi, a third was invalided to Manaos and the fourth with the "rudimentary" type of the disease was lost sight of. No other cases of beriberi occurred in any of the other 200 or so laborers strung along the right of way for a distance of several kilometers. The only thing in any way peculiar about this hut was that it was set back in the woods instead of being out in the open, as were the others. In Porto Velho, in 1910, in a period of four months, of three men in succession employed as job printers in a certain house, two died of the disease and a third was invalided to Manaos. In a period of five months in 1909-1910, three men employed as night watchmen in this hospital died of beriberi, and a fourth was invalided home with the same diagnosis. A considerable number of our orderlies were attacked, one of our cooks, two of our nurses and, as stated, two of our hospital physicians.

The rate has been very high among the crews of the company tugs that ply between Porto Velho and the mouth of the Madeira River. In 1910, on two occasions, one of these tugs was put out of commission because of the death or disability from beriberi of her officers, especially her pilots and engineers. The officers living "first-class" have had the disease at least as often, relatively, as the men. The captain of one of the company's larger passenger carrying steamers was invalided home last year with beriberi. The universal complaint of the first-class passengers on this steamer is that they get meat served in too many ways, with too much grease. Fresh beef, dried beef, fish, potatoes, onions, bread made from American flour, beans and rice, with tinned milk, butter and fruits form the bill-of-fare on all these boats.

I have seen cases of beriberi in robust people who have never had malaria or hookworms. I have seen it in nearly all races and nationalities. It has occurred here among all grades of employees. It is, I think, more frequent among those whose resistance has been lowered by other diseases or by the abuse of alcohol. Children usually escape and women are not attacked as often as men. As most of our employees are young men, I cannot speak positively of the age incidence.

CONCLUSIONS

1. A fatal form of peripheral neuritis occurs among residents of the Madeira Valley and among the employees of the Madeira-Mamoré Railway. This neuritis must be classified as beriberi, or as a member of an as yet hypothetical beriberi group.

2. This disease bears no intimate relation to the consumption of rice, polished or unpolished, as a staple article of diet.

3. This disease is not due to the absence of protein in the diet of those whom it attacks.

I desire to make acknowledgment to Dr. E. J. Whitaker, whose assistance in the preparation of this paper has been most valuable.

Candelaria Hospital.

Sleeping Out.—There are two classes of people who should sleep in the fresh air in all seasons—those who have tuberculosis and those who do not want to get it.—E. Cummings in *Jour. Outdoor Life*.