

Experimental Beriberi and Beriberi in Man, with special reference to its forms, as observed in Amazonas

by

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(With Plates 34-36).

The etiology of beriberi is still a matter of controversy amongst us. The greatest divergence of opinion reigns with regard to many of its clinical phenomena. This being the case, any contribution, however modest, to the solution of this important problem of nosology is of the greatest interest. Consequently I thought that my cooperation in the analysis of the problem might be of some use, especially as the results given here are those of clinical observation and experimental work.

The disease is frequent in tropical regions, and takes a prominent place in the archives of our medical history, not only because it wrought havoc amongst our soldiers in the Paraguay campaign, but as it still causes a great mortality on board our men-of-war and amongst the heroic pioneers in the uncultivated lands and fields in the north of Brazil. Therefore, I feel constrained to spare no trouble or painstaking in the study of this scourge.

It was unquestionably only after the epidemic in Bahia, in 1864, that the attention of medical men in the New World was called to beriberi. The foremost place of honour

undoubtedly belongs to SILVA LIMA, one of the very first to study the disease from the clinical point of view. The name of SILVA LIMA must be mentioned with pride and esteem, as that of a pioneer in studying beriberi or even of its rediscoverer, 200 years after it had been mentioned as a Brazilian disease by WILLEM PISON in his work "De Medicina Braziliensi" published in Holland in 1864.

From the time of SILVA LIMA up to the present date, many of our compatriots have contributed to the study of the clinical symptoms of this disease, and TORRES HO-MEM brings the value of Brazilian studies into relief, while making a special reference to the work of the great Bahian doctor.

I cannot pass over this interesting chapter of pathology, nor forget that it is my duty to take part in the debates which followed the experimental work of EIJK-MAN. Such studies have thrown so much light upon the subject, and called forth so many magnificent experiments and observations in the Orient, that we might almost conclude that all problems were solved, as well from the clinical as from the experimen-

tal point of view. But there being still some reluctance amongst our most considered medical authorities to accept the conclusions drawn from these experiments in the East, I think the subject is actually of the highest interest, as well from the scientific as from the practical point of view.

I have divided this work into three parts: 1. Beriberi in man and its symptomatology. 2. Experimental Beriberi and its relation to Beriberi in man. 3. Ætiology of Beriberi.

Beriberi in man and its symptoms.

All Brazilian authors define Beriberi by the discrimination of its symptoms and its etiological cause. SILVA LIMA describes the former as follows: "constitutional disease, endemic or epidemic, characterised by insensibility of the extremities, general weakness and inability to move, with pains and heaviness in the muscles, often accompanied by rigid oedema, anasarca, swelling of the face, anemia, epigastric oppression, dyspnoea (generally gradual), partial paralysis, sometimes accompanied by constriction round the trunk, weakness and hoarseness; spasmodic movements of the limbs; in fatal cases the end survenes from asphyxia and extenuation; in the favorable ones, after abundant diuresis, a slow and gradual restoration to normal conditions sets in and the nervous and circulatory systems are regularised."

AZEVEDO SODRÉ defines it as "an infectious, probably contagious illness, becoming endemic or epidemic in tropical and sub-tropical regions, the characteristics of which are: a more or less accentuated motor paralysis beginning with the lower extremities, accompanied by partial oedema and disturbances of the senses, and sometimes general dropsy; by visceral alterations to which special attention is called; by perturbations of the heart and exacerbations of the lungs: by chronic progress, sometimes interrupted by acute exacerbations which may give rise to aggravation of the symptoms already existing and to new ones; death

may be caused by asphyxia or cardiac syncope".

MIGUEL COUTO also describes the symptoms without making a synthesis of them.

From the ideas which we shall expose presently and from the result of modern study of beriberi, we may say that it is a disease produced by insufficient alimentation, characterised by a generalised neuritis, attacking the sensory and motor nerves and also those dependant on the great sympathetic, thus provoking multiple visceral perturbations, those of the heart being pathognomic.

Prodromatic periods: According to what I observed in the province of the Amazonas, anorexy, is perhaps the initial phenomenon of beriberi; before the disturbances of sensibility and motility set in, the patients complain of want of appetite.

TORRES HOMEM, SILVA LIMA and SODRÉ think that in many cases the forerunners of the disease are melancholy, disinclination to work, fatigue arising from the slightest exercise, bad dreams, nightmare, sleeplessness, anorexy and palpitations. SODRÉ, PEKELHARING and WINKLER however affirm that if the muscles were examined by electricity before these symptoms set in, the characteristic marks of the disease would already be found; for them, galloping beriberi lasts longer than is generally supposed, the prodromatic symptoms passing unperceived.

In the state of Amazonas I saw cases of galloping beriberi, almost without prodromatic symptoms. It is as if the disease broke out suddenly, affecting the peripheral nerves as well as those of sensibility. I observed some superacute cases where the first and slighter perturbations (as for instance anorexy, general weakness, feeling of discomfort) lasted only three or four days, before the disease burst out with all its more serious symptoms.

PLEHN observed cases in Cameroon that developed fully in from twelve to forty-

eight hours. SILVA LIMA cites one that only lasted five days.

Nevertheless, we may affirm that the disease has generally a well characterised, distinct, initial and prodromatic state. This is ushered in by anorexy, as is also the case in experimental beriberi. Birds, before manifesting the typical signs of the disease, show almost complete anorexy. I noticed the same in the animals I experimented upon. ARLINDO de ASSIS also verified this fact and had to feed his artificially, to prevent them from dying of starvation, as he writes in his thesis which was suggested by Prof. CLEMENTINO FRAGA.

In the Malay peninsula, FRASER and STANTON also observed lack of appetite as an initial symptom of the disease in the labourers who furnished them with matter for their classic experiments.

Besides anorexy some of the primary symptoms are:— fatigue after the least effort, palpitations and heaviness, a slight torpor of sensibility and weakness in the inferior extremities. These symptoms are described by all the authors on the subject. SAMPAIO VIANNA found a lack of appetite in 34% of the cases under his observation. I also noticed the appearance of vomiting in the beginning of the disease. This is a very bad sign. A sensation of fulness in the stomach often accompanies the want of appetite. The patients refuse to eat, because they feel as if their stomachs were full. In the north the patients have an expression of their own for this feeling of "stuffiness". I consider this symptom as almost constant. SAMPAIO VIANNA observed "fulness" in 27% of his cases.

The consequence of the alteration of the nerves of the stomach is gastric embarrassment, and with this often comes fever.

Fever: According to my observations beriberi is an apyretic disease. Fever, when present, is a complication. SODRÉ is one of the modern authors who speak of a fever-temperature during the the course of the illness. He states that SARAIVA of Bahia

called attention to the existence of fever in beriberi, when he circumstantially described the febrile forms observed in the plains of Paraguay. I believe that there was some confusion amongst the cases of beriberi and malaria, which probably attacked the same patients in the Paraguayan war and believe that this also applies to the malarial polyneuritis cases in the Amazonas province described by many doctors, and which I have never had the chance to see. I cannot deny the existence of the malarial polyneuritis of the North, but I have never met with it. I think that either they are cases of beriberi, so called because the disease attacks a patient in a state of convalescence from malaria, or perhaps malaria and beriberi attack the same patient simultaneously, slight fever being present.

SODRÉ in his magnificent work published in the "Twentieth Century Practice: 1898, Vol. XIV, insists on the value and possibility of beriberic fever, and says that he has observed fever in beriberi to be very irregular and inconstant in its appearance, course and type. According to him, some patients never have fever; in others it exists only when the acute exacerbations of the symptoms follow the first stages of the illness.

"The fever may or may not be preceded by shivering; may last only one, or more days, the temperature rising to 39, 5 The febrile state may be continuous, remittent or intermittent. In some cases the fever precedes numbness and other positive signs of the disease, in other cases it follows them. MANSOON also mentions fever in beriberi". In an epidemic in Hong-Kong, which he observed, 7 of the beriberi patients had fever after the symptom of numbness, it being more or less accentuated, sometimes very strong and preceded by shivering. SILVA LIMA says, "*Beriberi is an apyretic disease; fever is rarely met with in the course of it and is not a symptom of the illness, but simply a complication, and it seems to me due to the typhoid element.*" TORRES HOMEM writes: "*except in the acute form described by Dr.*

SARAIVA, which I mentioned, I do not think any medical man ever noticed a rise in temperature." ALMEIDA COUTO says that he does not consider beriberi a malarial disease, as it was at that time supposed to be, amongst other reasons as it is an apyretic disease. EDWARD B. VEDDER (Beriberi, 1913) says that fever in cases of beriberi is not a characteristic of the disease, and may possibly be caused by a chill, a slight attack of gastro-enteritis or other like complication. MIRANDA AZEVEDO in 1874, basing himself on his own observations and on the opinions of RIBEIRO da CUNHA and COSTA ALVARENGA, declares that beriberi is an essentially apyretic disease.

It has now been demonstrated that the majority of brazilian observers deny the existence of a special febrile phase in beriberi. This I had the opportunity of confirming even in hyper-acute cases, in contradiction to the observations of SARAIVA in the Paraguayan war and also those of Prof. SODRÉ.

Weakness of the legs. These symptoms of the prodromatic period are followed, sooner or later, by more typical indications of the disease. Weakness of the legs, which at first only shows itself when going upstairs, is followed by the sensation of weight. When walking the patient feels as if he were traversing a river with a strong current. Then after some days, his legs feel altogether too weak to bear the weight of his body.

Numbness. Numbness or torpor of cutaneous sensibility is a relatively precocious symptom. It begins at the legs, extending symmetrically to the feet, and then to the thighs. Thence it reaches to the soles. The patient feels as if he were treading on an india-rubber floor, or on layers of cotton. The numbness now goes upwards and affects the skin of the abdomen. PEKELHARING says that it always spares the groin and the neighbouring parts. SODRÉ speaks of anesthesia round the mouth.

Sometimes, instead of numbness, the patients feel formication or prickliness, so that some complain of a sensation of walking

on needles. This perturbation may also affect the mucous membranes. COSTA ALVARENGA describes a very curious and quite unique phenomenon. The patient, when he passed his tongue over the roof of his mouth, felt as if it were covered with threads or hairs.

The painful sensibility gradually disappears. In the beginning transmission of painful feeling is slow; it diminishes gradually until there is complete anaesthesia. SODRÉ also noticed that heat was less perceived. WERNICH describes as a constant phenomenon the existence of an anaesthetic area round the ankles; in this region, slight impressions were not felt. PEKELHARING and WINKLER describe, amongst the earlier symptoms, an increase in the tactile zones, specially in the lower extremities. SODRÉ, who had the opportunity of verifying and confirming these assertions, claims that this is one of the first symptoms of beriberi. The latter, as well as PEKELHARING and WINKLER, say that in the initial stage of the disease, its presence is revealed by the electrical examination of the muscles and of the nerves. "Faraday's" current shows a diminution of the irritability of the muscles, either direct or indirect, and at the same time a remarkable diminution of the indirect irritability by galvanic currents, as also a somewhat lengthy contraction when anode and cathode are shut.

Locomotory perturbations. In nearly all the forms of beriberi the symptoms follow one after the other and gradually increase. To the initial phenomena, all of which affect the sensibility, succeed others influencing motility.

We not only observed this phenomenon constantly, but also found it described in all the classics.

The feeling of tiredness is followed by more or less accentuated phenomena of paresis.

The course of the disease then assumes its characteristic appearance. The patient finds great difficulty in getting up when lying or sitting down, and only succeeds by reiterated efforts. When beginning to walk, he

stretches his feet wide apart, to have a firmer support; at the same time, he feels bound to keep his attention fixed on the ground, which seems to him, judging from the sensation in the soles of his feet, to be elastic and flexible. He can only keep his equilibrium by the aid of his sight, as the muscles of his legs do not seem to him to obey his will. (SILVA LIMA, MIGUEL COUTO, AZEVEDO SODRÉ).

Later on, the gait becomes even more irregular. The patient lifts his heels very high, implanting the outside border of the foot on the ground. The paralysis of the extensors of the toes causes the point of the foot to sink to the ground, and in order to prevent this, the leg must be lifted very high. FRANCISCO DE CASTRO calls this way of walking "high stepping". Birds suffering from beriberi, also show this characteristic "high stepping". After this simple difficulty in walking, comes an almost complete paralysis beginning in the extensory muscles of the lower extremities, the anterior tibial, the extensory hallucis and the commum extensors of the toes and finally the flexors of the foot. etc. etc.

In the beginning paresis is incomplete but it becomes more and more intense and gradually invades a greater number of muscular groups; after the muscles of the leg, it attacks those of the thigh, then of the fore-arm, the arm, the hand, the abdomen and the thorax. In the upper extremities the extensory muscles are also the first attacked. PEKELHARING observed that the biceps and the great pectoral are the last involved. SODRÉ says that he never saw the sternocleido-mastoidian attacked. SILVA LIMA records a case where the paralysis was total and the patient moved only his head.

Complete motor paralysis is very rare. I never saw it. Often, the movements are quite incoordinate. SILVA LIMA says that in his observation VIII «the patient moved his arms and legs, but his movements were limited, incoordinate and jerky. For instance, if he wanted to lift his finger to his mouth or his forehead, he never got it to the right place,

nor could he calculate the muscular force necessary for these movements. Abrupt movements of the fingers and hands, due to sudden contraction of the flexors were added to these symptoms on the ninth day.»

Paralysis may also attain other muscles, for example those of the pharynx, as observed by SILVA LIMA and SODRÉ, and also the muscles of the larynx. In experimental beriberi, I observed paralysis of the pharynx and of the oesophagus. Birds in this and at last stage of the disease swallow with the utmost difficulty.

Perturbations of the voice were observed by SILVA LIMA as comparatively frequent phenomena. In his observation VII he noticed a difference in the tone of the voice and has described cases of aphonia. SODRÉ says that paralysis of the larynx may cause sudden death. TORRES HOMEM and MIGUEL COUTO call attention to paralysis of the bladder. In these latter cases miction is slow and requires great efforts on the part of the patients. SILVA LIMA never noticed paralysis of the bladder.

Myalgia. It is constant phenomenon in beriberi be it spontaneous or provoked. SILVA LIMA, as we have already seen, observed that the pain is seated in the paralysed muscles. In the confirmed cases of the disease the patients cannot bear pressure on the muscles of the legs and of the fore-arm. "It is this hyper-sensitiveness which renders walking difficult, when the paralysis of the muscles is not very great". SILVA LIMA also noticed neuralgic pains varying, as to seat, intensity and duration.

It was the neuralgic pains which certainly led to the theory of rheumatism in beriberi, in vogue at the time of JULIO DE MOURA. Pain on pressing of the gastrocnemius is a first-class and well-known diagnostic sign; the same also refers to the muscles of the thigh and the forearm.

Muscular atrophy. In beriberi the muscles are always attacked. Muscular atrophy is recognised by the naked eye when it takes the dry form. This is the rarest form in the north and I seldom met with it. I remember

however one patient who was all skin and bones.

SODRÉ and other Brazilian medical men mention the existence of muscular hypertrophy. Evidently this is an error of interpretation. The muscular hypertrophy could only be apparent, the dominant feature in the pathological course of the disease is atrophy. The illusory hypertrophy is a consequence of oedema which does not attain the muscular fibre, but the interstitial connective tissue. In the first stages there may be a certain degree of hypertrophy of the heart, because it is the perypheric resistance (resulting from the vaso-motor alterations) which causes the modifications of the rhythm and the reduplicating of the sounds. In the motor-muscular system, the atrophic process is however the predominant lesion and as its consequence follows the functional disablement of the respective muscle.

In the oedematous form, the oedema masks everything and the muscle in spite of having its fibres attacked seems hypertrophied, increasing in size because of the diffuse oedema. Hence the mistaken idea of the existence of hypertrophy in beriberi.

Abolition of tendon-reflexes. In the beginning of the disease the tendon-reflexes may appear exaggerated, but the general rule is the abolition of reflexes. The sign of WESTPHAL nearly always exists; the rotular reflex is the first to weaken when the disease sets in, and with the progress of the symptoms it disappears altogether.

Oedema. The perturbations of vaso-motor innervation may be simultaneous with those of the nerves of motility and sensibility, or they may precede or follow them.

As a rule oedema appears at the same time as numbness and anaesthesia. Sometimes it is evident only after weakness of legs and difficulty in walking have set in. In the galloping form of beriberi, in which the disease takes immediate possession of the whole of the sympathetic system, oedema, dyspnoea and asystolia predominate.

Oedema nearly always begins on the *crista tibiae*; it is hard and elastic. SODRÉ

says that one of the initial symptoms of beriberi is a slight tumefaction of the crest and anterior face. In some regions, oedema, is characteristic of beriberi. In the north of Brazil it is the most general. Dry or atrophic beriberi, as we have already remarked, is rare. Such is the importance of oedema in the symptomatology of beriberi that SILVA LIMA divides the illness into three clinical forms: paralytic, oedematic and mixed. Here we may say that we do not approve of this division. In the paralytic form there is always oedema: in the oedematous form there is always paralysis. Indeed, modern tendency is not inclined to accept these classifications as separations of well-defined types.

VEDDER observes that some patients attacked by rudimentary forms of beriberi, surprise medical men by suddenly, showing cardiac affections, and dying almost suddenly. Cardiac insufficiency may occur in all stages of this illness. VEDDER observed in the East, that the disease sometimes remains in the rudimentary stages during months or even years. It is interesting to register that AZEVEDO SODRÉ in 1898, before VEDDER, says: "the symptoms of beriberi may last weeks and months, being sometimes more, sometimes less accentuated; when they are better, the patients feel very well and take up their former occupations. In these cases it sometimes happens that cardiac symptoms suddenly appear; acute and considerable dilatation of the righth cavity of the heart sets in and is almost immediately accompanied by asystolia, and death supervenes sometimes immediately and sometimes after some days.

It is clear that the words of the two doctors coincide. They coincide also with the facts which came under my notice in the north. There is a superposition of symptoms in beriberi, according to the kind of nerves attacked. As long as the great sympathetic and the vagus are not attained the disease may have a comparatively benign course, but at a given moment the cardiac affections intervene, and all cases of beriberi end in the same way, by an attack of acute asystolia.

Oedema in beriberi may attain all the organs. The subcutaneous cellular tissue may assume enormous proportions, as in anasarca. Diffusion in the serous cavities coincides with cutaneous infiltration. A very frequent phenomenon is hydropericardium.

In 256 cases, VEDDER found pericardiac effusion in making autopsies, in the proportion of 66 %. Hydro-thorax and ascites are rarer. The diagnosis of hydro-pericardium is very difficult, it is generally only revealed at the autopsy.

Oedema of the lungs is very rare in the initial stages of beriberi, and is generally one of the final symptoms. Beriberi cough, slight and tiring, accompanied by sanguinolent expectoration, according to some of our classical authors, has never come under my notice, even in the most acute forms of the disease. Dyspnoea comes from the weakness of the myocardium because percussion and auscultation do not reveal anything wrong in the lungs, except in the final stages of the disease. PEDRO DE MAGALHÃES attributes the cardiac affections of beriberi to a constriction in the pulmonary network, caused by the excitation of the thoracical ganglia and of the sympathetic ganglion on which depend the vasomotors of the lungs.

In the acute forms of beriberi I have met with real states of orthopnoea. Breathing is only effected with indescribable anguish. Paralysis of the diaphragm and the muscles of the thorax help to aggravate the situation of the patient. Sitting with his arms as if he were nailed to the bed, with distended neck and cyanotic lips, the sufferer tries to aid his inbreathing with his lips. Profuse cold sweat covers his face on which is imprinted the most anguished image of despair. SAMPAIO VIANNA counted from 50 to 60 respirations a minute in the acute stage of beriberi.

Beriberi girdle. This is a frequent symptom. The patient feels squeezed, constricted, the sensation beginning in the epigastrium and reaching round the sides. SILVA LIMA describes the girdle as "a feeling of being tied in, with a feeling of fulness and hardness, as if you were weighed upon by a plane

or an iron bar". I think that this is because the phrenic nerve is attacked, and thus causes paralysis of the diaphragm. As we are told by SILVA LIMA, TORRES HOMEM and AZEVEDO SODRÉ this sensation may extend to the armpit when the intercostal muscles are paralysed. In the north I found that this makes the prognosis serious. The sensation of the girdle is always accompanied by dyspnoea and precordial anguish.

Vomiting. Is often found in the beginning stages of the disease and ensues from gastric perturbations. Out of 61 patients, SAMPAIO VIANNA noticed vomiting in 13. In severe cases it is a very bad sign. VEDDER considers it as an indication that the disease is entering on an acute phase. SILVA LIMA tells us that the patients vomit oftener when their liver is very much congested. He is of opinion that the liver is always congested in oedematous cases, as the circulation in the veins is embarrassed. In this case the liver is very sensitive to the touch.

According to carefully taken measures by SAMPAIO VIANNA and PEDRO A. DE MAGALHÃES, the size of the liver is always increased (100 %). The spleen is also swollen according to SAMPAIO VIANNA and SCHEUBE.

It is very rare for the sense organs to be affected by beriberi, but Brazilian literature on the disease is full of notes on this subject. SILVA LIMA quotes cases of strabism and diplopia and even a case of blindness which appeared in 24 hours, eight days before the death of the patient.

Cases of amblyopia, diplopia and amaurosis *sine materia* of one eye, while the other one was not affected, were diagnosed and examined ophthalmoscopically by HILARIO DE GOUVEA, and observed by MIRANDA AZEVEDO in 1874. Touch seems to be most frequently affected. The patients are even often unable to hold anything in their hands, button their clothes, or even to put on a slipper, unless guided by their sight. (SILVA LIMA).

Convulsions. SILVA LIMA made observations on several patients who had slight convulsions, or choreic movements of the hands and arms. VEDDER thinks that convulsions are rare, but may be provoked by cerebral oedema. In experimental beriberi, however, convulsions are of common occurrence as will be seen later on in the account of my experiments. The rareness of convulsions is used as an argument by many scientists to prove that beriberi in man is not an illness of the same nature as that of birds.

The blood. WERNICH found constant hyperglobulia. From the studies of MARTINS COSTA, P. S. MAGALHÃES and WOLFERSTAN THOMAS a general rule may be established, that there is no considerable diminution in the red corpuscles nor increase of white globules in beriberi, especially in the early stages of the disease. As ankylostomiasis is a very common disease in Brazil, some beriberi patients may have been anaemic from the beginning of their illness, the anaemia being considered as proceeding from ankylostomiasis.

The urine does not show anything abnormal in its chemical constitution. SAMPAIO VIANNA found traces of albumen in some of his patients, and in others glucose. Albumen is not found as a rule. The urinary secretion is diminished. In some of the most oedematous cases the quantity of urine passed is very much less, in some cases only 200 to 300 grammes and even as little as 75 grammes in 24 hours.

The urine may stop altogether. FRANCISCO DE CASTRO was the first to call attention to beriberi uremia, without albuminuria. SAMPAIO VIANNA met two patients with frank symptoms of uremia. The diminution of the urinary secretion is due to vaso-motor *oedema* of the cortical part of the kidney, and as the tissues of this part are inextensible, the pressure applied to the afferent vessels explains everything (NINA RODRIGUES). The density of the urine always increases.

Pulse. The pulse is characterized by its frequency, irregularity and lowered tension.

In the acute cases it attains 150 a minute, and sometimes is too rapid to be counted.

Heart. The examination of the heart is of the greatest interest, as the alterations observed are almost sufficient to distinguish this polyneuritis from all others. In the beginning of the disease palpation indicates the increase of cardiac impulse, naturally due to the resistance in the network of pulmonary circulation. In the later stages, when the heart is dilated, the cardiac impulse is of course always diminished.

Percussion always gives an increase of precordial dullness especially on the right side, which is increased in size and reveals a larger zone of dullness of 2 or 3 centimeters to the right and deviation of the point to the left (a few centimeters). This increased dullness was observed by SAMPAIO VIANNA in 70% of his patients, and is not only due to the swelling of the organ, by dilatation or hypertrophy, but may also be attributed to hydro-pericardium, always met with in the final stages of the disease. The dilatation, in the beginning confined to the right ventricle, then it spreads over all the right half of the heart. SAMPAIO VIANNA says that a very certain sign of beriberi cardiopathy is the coinciding of epigastric pulsation with the absence of precordial shock which is an immediate consequence of the dilatation of the right side of the heart. Unfortunately, this modification of the shock of the apex is not absolutely constant; in the majority of cases it is only weakened, as is ascertained on touch. SAMPAIO VIANNA affirms that in all the patients observed in the hospital at Copacabana, he found the diastolic pulsation was greatly diminished or almost absent.

Palpitations. These constitute a symptom from the very beginning; at first, they are brought on by the least exercise or effort, even by a moral impression. Later on, tachycardia is a permanent phenomenon. The acceleration is accompanied by palpitations and is, according to PEKELHARING and WINKLER, simultaneous with the first manifestations of the disease. The slowing down

of the rhythm is rarer; I have never met with it. SCHEUBE often observed it, especially some hours before death. The palpitations also cause the precordial pain, which in slight cases is only a feeling of oppression, though in very acute cases it assumes the proportions of *angina pectoris*.

FRANCISCO DE CASTRO was the first to describe the beriberi *angina pectoris* «with excruciating retro-sternal pains, which extend to the neck, back of the neck and left arm». PEKELHARING and WINKLER describe similar observations. In the cases that came under my notice, I saw that the pains were far more excruciating than those of simple *angina pectoris*. The attendant dyspnoea, pains, the livid countenance contrasting with the cyanotic lips, the groans, the anxiety, the wild look of the patient together form a picture of as dramatic and pungent intensity, as the worst attack of *angina pectoris*. Under such conditions of well-defined asystolia it is impossible to obtain any clear account of his feelings from the half-unconscious patient.

Auscultation reveals other most important signs of heart affection. One cannot deny that SILVA LIMA deserves all the honour of the discovery of the predominance and gravity of the cardiac phenomena in beriberi. He calls attention to the perturbations of rhythm: «*a complete disorder in the succession and frequency of the systolic and diastolic movements, which render it impossible to count the cardiac revolutions and the pulse*». He also called attention to the reduplicating of the second sound, «thus giving rise to three distinct sounds; the first is the ventricular systole and after a short interval, in comes the diastole sound which is re duplicated and followed by a long pause». Reduplication of the first sound, although mentioned by SILVA LIMA, TORRES HOMEM and FRANCISCO DE CASTRO, is almost denied by PEDRO DE ALMEIDA MAGALHÃES and SAMPAIO VIANNA. The reduplication of the second sound has been met with and well described by all the Brazilian medical men who studied

beriberi cardiopathy, from SILVA LIMA down to the present day. AZEVEDO SODRÉ and PEKELHARING say the point of the heart is the best place for hearing the doubled sound; ALMEIDA MAGALHÃES and SAMPAIO think that the best point for auscultation of the second sound is the focus of the pulmonary artery.

There is no doubt that these latter observers are right. MAGALHÃES says that of the two sounds, the aortic precedes the pulmonary. SODRÉ denies this invariability. However all Brazilian pathologists agree that there is accentuation and reinforcement of the pulmonary sound, a fact to which FRANCISCO DE CASTRO called attention for the first time, and which was confirmed by SCHEUBE, PEKELHARING and WINKLER, AZEVEDO SODRÉ, PEDRO DE MAGALHÃES and SAMPAIO VIANNA.

Galloping sound. This sound was first mentioned by PEDRO ALMEIDA DE MAGALHÃES, SAMPAIO VIANNA noticed that the adventitious sound, whose addition to the normal sounds, causes the sound, of galloping is localised in the epigastric region and is sometimes more distinctly heard at a certain distance from the left margin of the sternum (margin of the right ventricle).

Murmurs. The murmurs are according to F. A. MAGALHÃES and SAMPAIO VIANNA generally mezzo-systolic, rarely systolic. «These sounds are soft, superficial, variable and not lasting.» SAMPAIO VIANNA heard them distinctly in 24 patients out of 24.

Pathogeny of the cardiac alterations. SCHEUBE says they ensue from the alteration of the vagus. AZEVEDO SODRÉ and LACERDA attribute them to the alterations of the sympathetic system. NINA RODRIGUES, without denying the influence of the alterations of the vagi, is of opinion that the lesion of the sympathetic is the chief factor in the cardiopathy observed in beriberi.

PEDRO DE MAGALHÃES thinks that the cardiac alterations ensue from the vasomotor disorders in the pulmonary circulation «the constriction of the pulmonary network

of vessels causes an increase of pressure on the pulmonary artery”.

“The pulmonary circulation having its tension increased, the pulmonary sound becomes accentuated, the ventricle is dilated, and by breathing, on the increased its pressure becomes hypertrophied. The right ventricle being dilated, the fibres of the myocardium lose their tenacity; hence the galloping sound. The right ventricular cavity becomes dilated, so that the diastolic aspiration is lessened, and the pulmonary valve, closing after the aortic, causes the doubling of the second sound”. This explanation is reasonable and logical. MAGALHÃES is of opinion that tachycardia is provoked by the irritation of the sympathetic system and the degeneration of the vagus.

We avoid dividing beriberi into different forms as one cannot separate well-defined varieties. Sometimes beriberi progresses slowly and becomes chronic; at other times it progresses swiftly and becomes very acute, with the intervention of the serious phenomena above-described. Often however the evolution of the disease takes place in a few hours or days; it is then known as galloping. Beriberi nearly always terminates in asystolia, either by direct attack or by the degeneration of the nerves innervating the heart. The degeyeration of the vagi and the lesions of the great sympathetic explain the evolution of the symptoms which have been noticed by many pathologists.

VEDDER does not accept the classification of clinical forms, but establishes a list of three kinds of principal symptoms: 1st) symptoms of peripheric neuritis 2d) cardiac insufficiency 3d) general tendency to oedema.

On comparing Brazilian studies with those of the Eastern authors I came to the conclusion that there is no difference between brazilian beriberi and they Japanese, Malayan or Philippine kind. No description could fit the galloping forms of the Amazonas better than that of the most acute forms seen in Japan by SCHEUBE. There is no difference between some of the chronic, torpid, attenuated forms observed by me in the Amazonas province, and the Segel-schiff beriberi of

NOCHT. The experimental cases in men, recently described by STRONG and CROWELL, might be pictures of those described by SILVA LIMA and SODRÉ.

We therefore conclude that the beriberi in Brazil is the same as Eastern beriberi as SILVA LIMA recognised.

Experimental beriberi.

In 1890 EIJKMAN noticed for the first time, that the birds fed with polished and cooked rice in his laboratory in Batavia (Java), showed ataxic symptoms, paralysis and convulsions after some time; in short, they revealed symptoms of an illness resembling human beriberi. His communication was received either with absolute indifference or, with complete unbelief. He did not however allow himself to be discouraged, but went on with his studies. At first he thought that *polynevritis gallinarum*, as the new disease was called, was a toxic polyneuritis caused by a substance that poisoned the nerves and resulted from fermentation or change in the rice when shelled, and which harmed birds when it remained in their crop. Since the birds showed no signs of illness when they were fed on unshelled rice, he thought that the pericarp protected the seed from the germs of fermentation.

In another series of investigations EIJKMAN renounced this hypothesis of intoxication as he saw that the shell of the rice contained a matter essential to the nourishment of birds and that without it they had polyneuritis. This substance is found in the red pellicule which encloses the seed. The pigeons nourished with unpolished rice with the pellicule, did not get polyneuritis even when the rice was cooked in the ordinary way. Consequently he realised that the illness was caused by a defficient nourishment. EIJKMAN therefore came to the conclusion that in the pellicule of rice there is a substance of such nutritive and protective value to the nerves that when it is wanting they became disintegrated because their structure is attacked.”

Another great advance was made when EIJKMAN verified the fact that excessive heat destroys the protective action of the rice-pellicle as well as that of all other cereals. He fed birds on unshelled, rice, heated to 120° C. for two hours, and saw that they died of polyneuritis. Oats, barley and millet eaten raw prevent polyneuritis. Cooked in the ordinary manner these cereals do not lose their protective action, but if they are kept two hours in the autoclave at 120°, they lose it and provoke polyneuritis. EIJKMAN therefore arrived at the conclusion that cereals contain a substance of special nutritive quality with a neuro-protective power, which is lost when the cereals are submitted to high temperatures.

These observations were elaborated some years afterwards by SCHAUMANN, who proved that long storage in the hold of hot and damp ships, or in laboratories in glass jars destroyed this protective substance. It was proved also that the birds attacked by polyneuritis were cured, if fed on meal of rice-husks, or if their insufficient alimentation was supplemented by other foods of greater protective value such as oats, barley, millet, etc.

No sooner was the existence of a highly nutritive and protective substance in the rice-husks known, than scientists in all parts of the world began to investigate the nature of it. As the rice-husks are rich in phytin, EIJKMAN went on to prove that phytin does not cure, nor does it prevent the illness, but that the substance sought for, is present in the watery extract of rice-meal after phytin was extracted.

These observations were confirmed by FRAZER and STANTON, also by CHAMBERLAIN and VEDDER and were the basis of the method used in extracting the *Protective substance* from the remains left after cleaning rice. A substance rich in phosphate was also extracted from rice-flour; it did not however protect the birds to which it was given by EIJKMAN in their polished rice food.»

Carrying his observations still further, EIJKMAN came to the following conclusions. "An apparently physiological diet may provoke the disease and even lead to death" and "although *polyneuritis gallinarum* is not in all points identical with beriberi in men, it is nevertheless caused by the same conditions. Human beriberi can be prevented and cured by the same diet as that which protects and cures birds.

In his thesis ARLINDO DE ASSIS, a pupil of FRAGA, proposes that the *polyneuritis gallinarum* be called EIJKMAN'S disease in homage to the important services rendered to science by the Dutch professor. I do not follow his example, but am of opinion that the name of beriberi ought to be kept, even if it be insufficient to express all that is meant by polyneuritis, brought on by insufficient alimentation. This I think due to SILVA LIMA, who chose this one, from amongst all other names for the same disease in use at the time in which the disease was observed in our country, and which has remained in scientific terminology. I am also convinced that there is not such a wide difference between experimental beriberi (*polyneuritis aviary*) and human beriberi and I think we should adopt a generic denomination for both.

GRIJNS demonstrated that sago, tapioca and meat, heated in an autoclave to 120°, provoked polyneuritis, almost as easily as polished rice. In 1901 he found that beans of the kind called *Katjangidjo* have a protective and curative action on the birds fed on polished rice. He however adopted the opinion that the disease was a real poisoning which could be neutralised and even prevented by feeding on rice-husks or *Katjangidjo*. GRIJNS however discarded the idea of infection.

In 1910 SCHAUMAN, in a series of experiments on *polyneuritis gallinarum*, came to the conclusion that it is a disease of metabolism, provoked by the absence of certain not determined organic combinations of phosphates in the food. He even determined that good rice ought to contain 0,4 penta-

oxyde of phosphorus ($\frac{P}{2} \frac{O}{3}$). SCHAUMANN believed that these organic combinations of phosphorus would be multiple and diverse: phosphatides, nucleic acid and probably many other substances which would act as stimulants, provoking and stimulating organic changes; they would be activating substances.

However, in 1911 FUNK isolated a substance from rice-husks which had a specific curative power on the experimental beriberi of birds. This discovery was a landmark in the study of the question. By means of phospho-tungstenic acid and also by means of nitrate of silver in the presence of baryte, he managed to precipitate an active substance of great curative value from the extract of rice-husks. Combining the two methods, he obtained an organic crystalline basic substance which melted at 233° C. FUNK gave the chemical formula ($\frac{C}{17} \frac{H}{20} \frac{N}{2} \frac{O}{7}$) to this basis. This substance was obtained from yeast and from many other alimentary substances. The small dose of 2 centigr. was sufficient to cure pigeons attacked by aviarian beriberi. FUNK thought that the substance thus isolated "was of complex structure and analogous to amides and because of its great biological functions named it VITAMINE, as this vital amide is one of those nitrogenic substances, infinitesimal quantities of which are indispensable in food, for the integrity of the nervous system of birds, men and other animals. "These studies were confirmed in Manilla, by VEDDER and WILLIAMS, who, by the same methods, isolated the same crystallisable substance, which was effective in curing a pigeon attacked by polyneuritis, in a dose of only 30 milligrs.

In March, 1912, EVANS, SIMPSON and WEBSTER, managed to isolate from yeast an organic basis which they called TURULINA and which also cured experimental beriberi, and for which they gave the formula : ($\frac{C}{7} \frac{H}{17} \frac{N}{2} \frac{O}{5}$).

In 1912 TZUSUKI extracted from rice meal a substance which he called antiberberina. This was only an alcoholic extract identical with that which CHAMBERLAIN

and VEDDER used for curing the disease in men. *Orizanina* found by SIMARUM and ODAKO (July 1912), obtained from the alcoholic extract of rice-meal by means of tannic acid, also cured beriberi in birds.

FUNK'S discovery gave rise to an infinity of interesting studies and although chemists are not all agreed about the exact formula and the chemical constitution, the name vitamine ought to be kept for the substance, which will doubtlessly latter on be found by means of more perfect analysis. The term VITAMINE ought even to become a generic name, not only for the substances found in rice-husks, yeast, Katjangidjo and other food-stuffs such as ox-brains, milk, horseflesh, the testicles of bulls etc. which have a protective action against beriberi, but also for the substances in food which act against scurvy.

Birds are not the only animals who show symptoms like those of beriberi in men. SCHAUMANN, in 1910, was successful in provoking polyneuritis in guinea-pigs, rats goats and a monkey. A dog, fed on meat sterilised at 120° , became completely paralysed. A goat fed on polished rice, became paralytic 3 or 4 months afterwards. HULSHOFF POL demonstrated the disease studied by SCHAUMANN in these animals to be the same as polyneuritis of birds and human beriberi.

SHIGA and KUSANA, in spite of their being at first opposed to the identification of human beriberi with the experimental beriberi of SCHAUMANN, made some interesting experiments on monkeys.

The first monkey fed on cooked rice died of tuberculosis at the end of a few weeks. The second, having lost in weight, showed paralysis of the legs at the end of 37 days. At first the turn the disease would take was uncertain, but afterwards the paralysis progressed and became complete. Anaesthesia of the legs was present. The reflexes were at first augmented and ultimately abolished. Auscultation showed accentuation of the aortic sound and the pulmonary sound. The slightest exercise brought on palpitations and there was considerable dys-

pnoea. In the last days oedema of the legs set in. At the end, cardiac troubles increased. Cardiac energy diminished. The pulse was weak and soft. The temperature went down, and death took place, 10 days after the illness declared itself. (Apud VEDDER).

We see that the monkey had all the symptoms of human beriberi: paralysis of the legs, gradually ascending, anaesthesia, loss of reflexes, oedema and cardiac symptoms. In other observations these scientists found the same typical lesions of beriberi and hypertrophy of the heart.

KUSANA and SHIGA drew the following conclusions from their studies: "It is a recognised fact that the dilatation and hypertrophy, essentially of the right side of the heart, are very characteristic of beriberi, so that this disease is very easily distinguished from polyneuritic intoxications. The illness of the monkeys was the same as human beriberi".

TSUSUKI also provoked experimental beriberi in dogs, cats, guinea-pigs, rabbits, rats and monkeys by feeding them on polished rice. ANDREWS (1912) also provoked the disease in newborn dogs. He had noticed that the disease "Taon" which causes great mortality amongst babies before they are weaned, is nothing else but infantile beriberi and that "Taon", was caused by the poor milk of the mothers who lived on polished rice. He put some little dogs to the breasts of the mothers whose children had died. The puppies were nourished thus for one month, at the end of which time they began to show incoordination of their movements, weakness of the extremities, especially of the hind legs, in many cases followed by paralysis. All had oedema of the subcutaneous cellular tissue. Marchi's method, showed degeneration of the peripheric nerves in all of them.

In 1906 WEILL and MOURIQUAND published an important work on experimental and clinical diseases caused by insufficient food in the "Revue de Médecine". This work, as well as the counter-proof, was made in the Lyons Laboratory. WEILL and MOU-

RIQUAND called the diseases caused by the want of vitamins, diseases of want. These diseases were provoked experimentally or observed clinically and came from want of a certain ferment of which the smallest dose is necessary for normal nutrition. This new denomination was adopted by ARLINDO DE ASSIS, pupil of FRAGA, in his thesis in 1918. The english writers had already given the name of deficiency diseases to this group of illnesses. FUNK had proposed the name of AVITAMINOSES which I find euphonic and expressive.

WEILL and MOURIQUAND'S work was another brilliant confirmation of that of EIJKMAN, FRAZER and STANTON, SUZUKI, SHIMAMURA, SCHAUMANN, FUNK, VEDDER, STRONG and all the others. He reproduced beriberi in birds and studied the symptomatology of the disease practically and systematically. He also produced scurvy in rabbits and polyneuritis in cats by destroying the vitamins of their food by long sterilisation in the autoclave. It was he who invented the expression that vitamins are living substances which can be destroyed by long sterilisation, saying that: "Life is necessary to life". WEILL and MOURIQUAND concluded that avian polyneuritis and human beriberi are caused by alimentary insufficiency. Though there are some differences in certain manifestations, one cannot expect the same reactions in men and animals in all points. Looking through all this enormous amount of literature, we notice that this highly interesting experimental beriberi did not awaken much enthusiasm amongst Brazilian authors.

The first Brazilian work on experimental beriberi was published by ARLINDO de ASSIS. Following the method of WEILL and MOURIQUAND, he made a series of most interesting experiments on deficiency. His work deserves to be read by all who are interested in such. As homage to EIJKMAN, he proposed to call experimental beriberi EIJKMAN'S disease. I have already explained my reasons for differing from him. As these studies are of great national interest they ought

to be written in simple language, so that the general public may be made cognisant of them. Thus the expression experimental beriberi is more suitable and shows the connection between it and human beriberi, allowing the reader to draw the right kind of conclusions and to learn what is of practical use to him.

In August of this year, (1919) I resolved to make a series of experiments on experimental beriberi with the cereals that are used for food in the north and the interior of Brazil. Dr. CARLOS CHAGAS was kind enough to allow them to be carried out in the aviary at Manguinhos. The library and the laboratories were also placed at my disposal.

The cereals chosen for the experiments were polished rice, fresh indian corn sterilised (1) by indian corn sulphurate of carbon; fresh and first class surui flour; mouldy Surui flour kept stored for a long time; farinha d'agua (mandioc flour specially prepared), polished rice sterilised in the autoclave at 120° during an hour; Surui flour of the best quality sterilised in the autoclave at 120° during an hour; first class maize-flour sterilised in the same way.

The object of these experiments was first to get to know *polyneuritis gallinarum* de visu, by provoking the disease in fowls and pigeons and then to verify the analogy or the differences between this disease and beriberi in men: secondly) to ascertain the quantity of vitamins in Surui flour and in mandioc meal and whether the exclusive use of these substances causes *polyneuritis gallinarum* quicker or more slowly than polished rice; thirdly) to find out if the sterilization processes in use in Rio de Janeiro be hurtful to the health; fourthly) whether lengthened sterilisation of nutritive substances or their getting old by long storage causes the destruction of vitamins thus provoking beriberi.

(1) Indian Corn was supplied by the Empresa Este de Cereales.

In spite of the fact that the work of ARLINDO DE ASSIS is worthy of all confidence, new contribution on the subject may throw new light on it, especially on those of its aspects which are not absolutely clear; it may also resolve some unsolved problems concerning the diseases caused by deficiency. It is enough to mention all there is still to be investigated as to the nutritive value of the milk used in Rio de Janeiro and the sterilized milk used de larga maxima in The Amazonas province.

The high infant mortality amongst us must be ascribed as in a great part due to the bad quality of food, to the milk deprived of its nutritive qualities by being over frozen or hypersterilised, to the flour of doubtful nutritive value, especially of that which comes from foreign countries and has been kept for an unknown length of time.

I began my observations on the 15th of August 1918, chose carefully examined, healthy animals, and had their compartments rigorously disinfected.

Those on which the experiments were to be made came from the same place as the witnesses, which were plentifully supplied with Indian corn.

The first group were fowls fed on Amazonas flour (farinha d'agua), of good quality, sterilised at 120°.

The fowls resisted from the 15th. of August until the 21st of October, without manifesting any symptoms of *polyneuritis*. They lost weight, and lost appetites but showed no signs of beriberi.

My technique was modelled on that of WEILL and MOURIQUAND. The animals were weighed every day and their food was changed and measured also every day. One of the fowls was artificially, fed as it would not eat, but it died of asphyxia during the process.

The conclusions drawn by me from these experiments do not agree with those of WALCOTT and ARLINDO DE ASSIS.

WALCOTT obtained *polyneuritis* by using Amazonas flour, but his experiments lasted

much longer than ours and he does not tell us how they were made. ARLINDO DE ASSIS, who modelled his experiments on those of MOURIQUAND, obtained *polyneuritis* with the mandioc flour commonly used in Brazil, but did not make experiments with Amazonas flour.

Amazonas flour must be subject to a process of preparation which deprives it of its nutritive value which seems to be less than that of white flour used in Brazil. However it may be, my experimental animals, which were fed on nothing else, did not show any symptoms of *polyneuritis*.

We might therefore conclude that Amazonas flour is not a deficient food; when fresh and good, is even better than polished rice. As my experiments were not long or complete, other experiments should be made the same direction.

Another group of fowls (3) was fed on old white flour. Two succumbed with all the symptoms of *polyneuritis*, the third resisted all the time the experiment lasted only manifesting loss of weight and want of appetite. We here give the details of the observations made on one of the fowls.

"Cock. No. 4 Weight: 1,880 gr. On the 16th it got a ration of 120 gr. of white flour of the Surui kind, of very bad quality; it ate 75 grs. of the ration in 24 hours.

During the first days it ate well, averaging 60 to 80 grs. of flour a day. From the 24th. to the 30th., in spite of not showing any outward symptoms of disease, it lost weight and appetite.

It continued to lose weight, being only 1,800 grs. on the 26th and eating only 20 grs of its ration a day. On the 30th. it weighed only 1,660 grs. From the 30th. on, it would hardly eat, taking only about 3 or 4 grs. of flour a day and on some days would not even take any. On the 5th. it weighed only 1,490 grs. it was sad its wings drooping while it lay down and, seemed apathetic.

On the 6th. and 7th. it could hardly walk, showing the characteristic beriberi stepping. On the 8th. it weighed 1,290 grs. The wings and

legs were paralysed. When strongly excited, it made incoordinated movement of the feet and legs. On the 9th. the paralysis was complete, the movements convulsive and tetaniform: the weight fell to 1185 grs. and the fowl died.

A third group was fed on national polished rice, of the kind here called needle rice, of the best quality, sterilised at 150°. This group was composed of pigeons.

After some days the classic symptoms of *polyneuritis* declared themselves.

Pigeon n. 8, shown in photograph n. 1, became paralysed after a few days.

Pigeon, n. 9, (fig. n. 2) died after being fed on polished and sterilised rice for 20 days; all the classic symptoms were present.

Heating in an autoclave destroys the vitamins and increases the already existing deficiency.

These observations only serve to corroborate those already made and published.

We still wanted to know whether the immunisation of cereals as done here, is harmful by destroying the vitamins.

For this purpose, a fourth group of pigeons was fed exclusively on Indian corn purveyed as sterilised, by the Companhia Esterelisadora de Cereales. Their sterilisation is effected by means of sulphurate of carbon steam. The Indian corn keeps its natural appearance and its germinative power.

The feeding of these pigeons went on for 2 and 1/2 months; they all increased in weight, had good appetites in spite of the monotony of their food, and none showed any symptoms of *polyneuritis gallinarum*.

As pigeons resisted the diet of polished rice better than gallinaceous birds, I resolved to make experiments with the latter, feeding them exclusively on polished rice, raw or heated in the autoclave at 120°.

I herewith give the description of a cock as type observation. On the 29th. of August, I began the experiment. The weight of the bird was 1260 grs. and its food was national polished "needle" rice given in rations of 120 grs. I must here say that national rice

is not so smooth as that which comes from foreign parts, there being always a vestige of the red shell in each grain.

The weight and the alimentation were as follows:

On the 21st. of August—weight:	1.260	grs.	ate	80	grs.
22nd. " — "	1.250	" "	"	55	"
23rd. " — "	1.220	" "	"	55	"
24th. " — "	1.230	" "	"	100	"
25th. " — "	1.225	" "	"	40	"
26th. " — "	1.195	" "	"	60	"
27th. " — "	1.220	" "	"	80	"
28th. " — "	1.170	" "	"	40	"
29th. " — "	1.175	" "	"	40	"
30th. " — "	1.160	" "	"	40	"
31th. " — "	1.160	" "	"	60	"
1st. of September—	1.140	" "	"	50	"
2nd. " — "	1.140	" "	"	40	"
3rd. " — "	1.115	" "	"	35	"
4th. " — "	1.080	" "	"	20	"
5th. " — "	1.055	" "	"	5th.	"
6th. " — "	1.040	" "	"	0	"
7th. " — "	1.020	" "	"	0	"

The bird found great difficulty in flying and seemed very sad.

On the 8th. of September the weight was 1999 grs. It ate 5 grs. and was still sad. It could not fly, when greatly excited, but ran. It tried to lie down continuously showing great weakness in the legs, as is seen in fig. 3. It stepped like people with beriberi.

On the 19th. of September the weight was 980 grs. It ate nothing and kept lying down, walking with great difficulty as can be seen (fig. 4,) opening its legs very wide to walk.

On the 10th. of September the weight was 965 grs. it ate nothing but was fed by *gavage* on 18 grammes of rice to avoid inanition.

On 11 th. of September—weight	955	grs.	<i>gavage</i>	40	grs.
12 th. " " "	975	" "	"	40	"
13 th. " " "	985	" "	"	40	"

The ataxy phenomena were accentuated. The food stayed in the crop without being digested.

On the 14th. of September the weight was 995 grs. No *gavage* was made; the crop was still full of food.

On the 15th. of September weight 995 grs. No *gavage*. Crop full.

On the 16th. of September weight 990 grs. *Gavage* 40 grs. Increase of paralysis. Kept lying down.

On the 17th. September weight 980 grs. *Gavage* 40 grs.

On the 16th. of September weight 980 grs. No *gavage*. Crop full. Food not digested.

On the 19th. of September the weight was 980 grs. No *gavage*. The extensors were completely paralysed, the feet permanently bent. Crop quite full of food administered before.

On the 20th. of September the weight was 980 grs. No *gavage*.

On 21st. September the weight was 960 grs. No *gavage*. Crop still full of food. Total paralysis. Cyanotic crest. Slight convulsions of the wing-muscles. Death.

Fig. 5 the photograph of a hen dieted with polished raw rice. (Hen n. 15).

From this we deduce that the birds eat raw rice for some days with a good or even exaggerated appetite. From the 20th. day on, the want of appetite increases, becoming quite absolute between the twentieth and thirtieth days when the morbid phenomena become accentuated.

Fowls get *polyneuritis* more quickly than pigeons when fed on polished rice sterilised at 120° for an hour. Their want of appetite is almost absolute in the first 19 days. The loss of weight is also considerable. The beriberi symptoms appear on the 15th. day, paralysis on the 17th and death on the 19th. Death may be said to ensue from inanition, for the fowls refuse to eat.

As the fowls seemed to find rice disagreeable, we resolved to feed them on Indian corn which they seem to like better, and which, though sterilised, does not lose its organoleptic qualities.

A group of fowls was dieted on Indian corn sterilised in the autoclave at 120°: The morbid phenomena of beriberi appeared after the 20th. day, the want of appetite ap-

pearing much later than is the case with sterilized rice flour.

Figs. 7, 8 show the different phases of *polyneuritis* in cock no. 13, dieted with sterilised Indian corn. The experiment began on the 22nd. of August, the fowl dying on the 27th. of September.

On the 23rd. day of treatment there was great weakness of the legs; the fowl lay down on its thighs all day; it stepped high and could run only with a great effort. Complete want of appetite. To avoid death from inanition, it was fed by *gavage*. On the 24th. it could not walk (as shown in fig. n. 8.)

The three last days before death there was complete paralysis, and only when strongly excited could it move or contract its legs and wings.

Another group was dieted on the finest mandioc flour. The results confirmed the observations of ARLINDO DE ASSIS.

I thus proved that a diet of fine and good mandioc flour is less deficient than a diet of polished rice. Amazonas flour is less deficient, and is less likely to induce *polyneuritis gallinarum* than white flour of the Surui kind.

Polyneuritis aviarum and beriberi have so many symptoms in common that we have no hesitation in joining those who accept their etiological and symptomatic identity.

Our experiments though incomplete, corroborate this conviction as well as the authority of those of SHIGA, SCHAUMANN, WEILL and MOURIQUAND.

Etiology of beriberi.

Since the time of SILVA LIMA until now, the idea that beriberi is an infectious disease was prevalent amongst our best-known Brazilian doctors. Even SILVA LIMA, though we find passages in his works which support the alimentary theory. was obliged by the force of circumstances to admit the hypothesis of infection. This hypothesis was adopted by all the well-known Brazilian doctors who studied beriberi; leaving some aside, we only call to mind the names of TORRES HOMEM,

MARTINS COSTA, SARAIVA, FRANCISCO DE CASTRO, SODRÉ, LACERDA, FAJARDO, PEDRO ALMEIDA MAGALHÃES, SAMPAIO VIANNA and AUSTREGESILO.

FAJARDO and LACERDA even discovered pathogenic micro-organisms although latterly, LACERDA came to accept the ideas which came from the East.

MIGUEL COUTO, repudiated the alimentary theory as the cause of our beriberi; he believes that the etiology of Brazilian beriberi is as yet unknown. Amongst those who believed in the alimentary theory we must count SILVA LIMA, in whose book we find proofs against the transmission of the disease and who speaking of its propagation says: "Not to presume to affirm anything certain about the diffusion of the disease, that is without getting away from facts, I must say the disease does not seem to propagate itself by contagion or infection, but to depend on a widely spread morbid cause and unknown serious hygienic conditions".

For a long time it was thought that beriberi depended on malaria. ALMEIDA COUTO in his competition thesis in 1871, says that he does not consider beriberi as a malarial disease on account of its being apyretic. He points out as causes, inferior food, alcoholism. SILVA LIMA, also repudiating the idea of malaria, wisely observes: beriberi epidemics have always been very frequent and fatal in unhealthy places, but for causes which have nothing to do with malaria, and particularly on board high seas, ships, in urbane prisons, penitentiaries, etc.

TORRES HOMEM recognizes that "insufficient nourishment both in quantity and quality is an important factor in provoking the appearance of beriberi, which more frequently attacks persons who are convalescent and have a great struggle for life."

MIRANDA AZEVEDO in 1874, was courageous enough to attack all the old theories in his inaugural thesis in which he defends the insufficient nourishment theory. At that time, the malarial etiology of beriberi was supported by the best-known medical

men of the country such as TORRES HOMEM MACEDO SOARES, A. FARIA, SARAIVA and others. On this occasion, LE ROY DE MÉRICOURT thus expressed his opinion: Beriberi breaks out amongst the crews and passengers of ships after long long journeys, amongst soldiers after a campaign, miners, prisoners, orphans (of course he is referring to homes) especially amongst the poorer classes, who have been living on a meagre and uniform diet, which either from circumstances or for the sake of economy is insufficient for their needs.

MIRANDA AZEVEDO was struck by this passage and the allusions to the forms observed in Paraguay, and encouraged by his own observations, was not afraid to criticize the most celebrated medical men of the day in his thesis and affirmed that insufficient nourishment is the cause of beriberi. He says:—"I understand by insufficient nourishment, not only the lack in quantity of food necessary to keep one in health, but also the want of variety of food, a pernicious uniformity, for varied nourishment is imperiously called for to sustain the organism. He afterwards says "Reading and study of the different hypotheses as to the origin of beriberi induced me to pay attention to popular beliefs and to think that rice is the cause of beriberi in Brazil and in India.

The only class of diseases in which this strange one can be classified, is that of the diseases called, by JACCOUD and other modern pathologists, constitutional distrophy on account of the etiology and the special symptoms.

JAYME SILVADO wrote some very interesting memoirs of Brazil in 1907: "*Beriberi in the Navy of Brazil*". In spite of his being influenced by the theory of infection he gave some good advice to the Superior Administration of the Navy, which, had it been taken, would have hastened the disappearance of the disease amongst our sailors. Referring to the question of rations he speaks of the sailors throwing their bread into the sea either because it was bad or because they

did not like it. He also says: As to the food, our rations are not what they ought to be neither as to quantity nor as to the way of cooking the food. The sailors do not get good food as the purveyors want to make as much profit as they can and purvey bad food for the price of good. With great discernment JAYME SILVADO, in his monograph, calls attention to the monotony of the food and the great want of variety in same.

Speaking of the Indian corn meal given on board ship (1907) three times a week, as obligatory food, he says: "Only people who are used to Indian corn meal can like it, and the kind sent on board ship is enough to make anyone sick of it. It is already sour when provided, and gets even more sour in the hot damp holds of the ship, becoming absolutely uneatable."

In this work, Dr. SILVADO draws the attention of the government to the food in the Japanese Navy, where by the advice of TAKAKI, barley-meal was added to the rations, so as to counteract the bad effects of rice. SILVADO refers to the communication read at the Congress in Paris in 1900 by Baron SANEIOSKI, and though he did not believe all that was therein, and did not believe beriberi was caused by eating rice, he avows that bad rice brings on polyneuritis.

He shows however a tendency towards adopting the nourishment theory, by giving the statistics which show the difference in the Japanese Navy before and after the adoption of TAKAKI'S theory.

Statistics of the decrease of beriberi beginning in 1884, when the changes were made in the rations of the Japanese Navy.

BERIBERI.

Years	1880	1881	1882	1883	1884	1885	1886	1887	1888	1889
Cases	1725	1163	1929	1236	718	41	3	0	0	3

As we see from these statistics, if the necessary attention had been given to them,

the greatest practical results would have been obtained, and beriberi would already be no more in our Navy.

In 1914, Professor AUSTREGESILO published a most important monograph on an epidemic of beriberi in the National Lunatic Asylum, which he called scorbutic polyneuritis, in the *REVUE de NEUROLOGIE*. Analysed by the light of the new doctrines, this work enlightens the etiology of the other epidemics of beriberi which have been noticed there. Studying all his magnificent observations in detail, we see that beriberi and scurvy broke out at the same time, and were most likely both caused by deficient alimentation! The polyneuritis described by Professor AUSTREGESILO had all the characteristic symptoms of beriberi.

Let us take for instance one of his observations: "D. Igl. I do not know when the illness began, as the patient is insane but on the 24th. of February he was shown to me, had attacks of dyspnoea tachycardia, difficulty in walking, oedema of the lower limbs; he looked like a very weak person, with *ptyriasis versicolor* on his neck, acne on the back, petechias on the lower limbs, scorbutic signs, echimoses in the popliteal space and also purpura spots on his legs; the general oedema was more accentuated in the lower limbs. The patient stepped high; the rotular reflexes were exaggerated and lasted a fortnight. Afterwards the reflexes diminished without disappearing. He had anaesthesia in his lower limbs, and hyperaesthesia of the trunk. Examination of the faeces revealed eggs of *ankylostomum*. There was reduplication of the first and second sounds of the heart. The murmur of the pulmonary artery vibrated more than in health.

This patient was put in the infirmary of the Asylum, but his family removed him so as to nurse him. He then escaped from the vigilance of the family after he was cured of the intercurrent disease.

We see that this was a classic form of beriberi, where there were symptoms of

scurvy caused by of deficient food, which were almost cured by a change of diet.

2nd. Observation. L. M. years old, Brazilian etc. 16th. of May 1916. During the slight epidemic of scurvy this year, he had classic symptoms of the disease. After treatment, cleansing the blood, rigorous disinfection of the mouth with ferruginous injections, change of diet etc. there appeared classic phenomena of polyneuritis; walking was impossible; there was high-stepping, *pes equino varus*, great weakness of the lower limbs, with muscular atrophy and pain in the *gastrocnemius* on being touched. Rotular and plantar reflexes were absent; there was progressive anaesthesia of the roots of the lower limbs and paraesthesia of the upper limbs. Tongue dirty and trembling. Hyperphonia of the pulmonary sound and some times of the second murmur. Pulse weak, 74 times a minute. Microscopical examination of the excrementa revealed eggs of *ankylostoma*; they are common amongst the insane in Brazil. The patient had a tendinous retraction of the right leg, on account of a scorbutic ecchymosis on the popliteal region. The muscles and nerves, especially those of the inferior limbs, did not answer to faradisation, and only irregularly to the galvanic current, mostly showing Erb's reaction of degeneration (D. R. incomplete). Extreme weakness and cachexy were noticeable: the patient weighed 22 kilos and 900 grs. He was transferred to another ward. After faradisation, galvanisation, massage, strychnine and change of diet the patient, put on weight till he weighed 43 kilos; the morbid phenomena disappeared in 6 months, leaving him almost cured.

Although the author thought of the possibility of a new affection (scorbutic polyneuritis), his observations form a valuable document in favor of modern doctrines. From his observations we may conclude that scurvy and beriberi are two different diseases caused by deficient nourishment; they were found in the same individual, mingling their symptoms, so that they seemed to be a new disease. And as their principal symptoms come from the want of certain vitamins, being at

different times accentuated or aggravated, an infinity of modulations may result, so that each patient seems to have a different morbid disease.

EDUARDO MEIRELLES studied the last epidemic of beriberi in the prison, in 1915 and although he almost denies the hypothesis of its being due to the alimentation, he owns that the disease disappeared almost entirely after disinfection and after better food was given to all the patients who were treated in the Prison Infirmary.

In 1916 I was called upon to present a memento of my ideas on the etiology of beriberi in the province of Amazonas, to the General Director of the Board of Health. In this work, which by kindness of Dr. CARLOS SEIDL was published in the "Jornal do Comercio", I tried to prove by my observations that beriberi showed a tendency to disappear since the suppression of the importation of rice from the East (polished Rangoon and Carolina rice) and by the diminished importation of flour and beans, which only used to arrive after a long journey and the nstay in damp and hot storehouses.

I take this opportunity to transcribe the table of mortality due to beriberi in Manaus from 1897 to 1917.

Years	Deaths due to Beriberi	Total Montality
1897	75	
1898	100	
1899	99	
1900	137	
1901	53	
1902	59	
1903	103	
1904	204	
1905	175	
1906	121	
1907	63	1429
1908	119	1692
1909	83	1603
1910	149	2196
1911	135	2328
1912	80	1915
1913	61	1681
1914	20	1305
1915	12	1204
1916	7	1595
1917	3	1070
1918	1	2170

Formerly, there were often on the ships navegating the Amazonas river, cases of death among individuals who felt ill and embarked for the capital. With the aid of data supplied by the Board of Commerce, I included, in the above-mencioned relatory, comparative tables of the importation of the cereals, which form a great part of the food of the inhabitants of those regions, and of the cases in the capital and on board the vessels coming from the interior which were registered by the Board of Health of the Port. In this paper, I called the attention of the Government to the necessity of a legislation regulating the improvement of rice, similar to that which exists in the Phillippine Islands. Convinced, as I was, that our beriberi is the same as Eastern beriberi, I tried to prove by documents from SCHAUMANN, Japanese and American authors, that what I

Year	Importation of Rice	Beriberi Obituary in the capital	Obituary on board	Total
1911	29.998 bags	135	54	189
1912	24.179 «	80	17	97
1913	12.189 «	61	20	81
1914	5.640 «	20	2	22
1915	3.639 «	12	4	16

Year	Importation of flour from Rio Grande	Beriberi deaths in the capital	Beriberi deaths on board	Total
1911	13.137 bags	135	54	189
1912	5.563 «	80	17	97
1913	2.270 «	61	20	81
1914	5.211 «	20	2	22
1915	2.191 «	12	4	16

Year	Importation of foreign beans	Beriberi deaths Capital	Beriberi deaths on board	Total
1911	77.539 bags	135	54	189
1912	85.021 «	80	17	97
1913	64.021 «	61	20	81
1914	51.610 «	20	2	22
1915	14.687 «	12	4	16

said was true, claiming the attention of competent persons to judge in the matter.

In July 1916, appeared MIGUEL COU-TO'S masterly work "Lessons on Clinical Medicine" in two lessons of which the author analyses and criticizes the current doctrines.

In the same year THEOPHILO DE ALMEIDA published his thesis on Beriberi. This contains all the modern theories in vogue, and discusses the development of beriberi in several provinces of Brazil. It deserves to be better known as the ideas defended deserve to triumph.

In his historic memoirs, presented in 1917 to the Faculty of Medicine, AFRANIO PEIXOTO discusses, in clear and elegant language all the different questions of pathogeny in the Amazonas province, and shows himself a partisan of the alimentation theory. In 1917, CLEMENTINO FRAGA published a synthetic study on "Beriberi or beriberi syndrome."

In this work, FRAGA analyses the epidemics of beriberi in Bahia, from 1866 to 1916. The beriberi epidemics in St. John's Asylum, the Pentenciary, the Palm Barracks, the Hospital of St. Elizabeth are all carefully studied. For FRAGA, beriberi is endemic in Bahia, and in the places where there are many cases, it has become from time to time epidemic; for this reason he believes in the infectious etiology of the disease. For him beriberi is an illness and not a syndrome.

In 1918 ARLINDO DE ASSIS' thesis appeared in Bahia; it was written under the direction of CLEMENTINO FRAGA, and is quite a remarkable work, both because of the doctrine and the experiments and because it is probable [that after having seen those experiments Professor FRAGA should have modified his opinions.

As I said before, there are very few medical men in Brazil who have studied this disease. On the other hand, since EIJKMAN'S discovery, a great many English, Japanese and Americans authours have published much valuable work on this subject.

We must remember that in the East het

idea of beriberi being caused by insufficient nourishment is not a new one. Even before there were any experiments mady, the practitioners had noticed this. In 1867 VAN LEENT said: "The principal cause of beriberi is an uniform and insufficient diet of bad quality." The organism being deprived of the indispensible elements for the formation of the blood, nutrition is impoverished by degrees. WERNICH in 1878 declares: "Kaki is a constitutional chronic disease of blood formation and of the vascular system."

"The rice, exclusively used as food, is chiefly responsible for the disease, not because it is of bad quality, (as one supposes) but because it is very satisfying so that the power of assimilating other food is reduced; and however good it may be, it is not sufficient for alimentation and blood formation."

TAKAKI obtained brilliant results in the Japanese Navy. He was not however able to cope with the opposition with which he met, nor to introduce his proposed reforms in the Army.

Everyone knows how great was the mortality amongst the Japanese army from beriberi during the Russo-Japanese war (80.000) and how small the proportion amongst the marines. Round Port Arthur, there was not a single death amongst the marines of the Naval Brigade, whilst the soldiers were decimated, though both endured the same conditions of climate and temperature while feeding differently. TAKAKI'S theory was true, but he erred in thinking that the defficiency was in nitrogen. For this reason his theories were not generally accepted by his countrymen.

BRADDEN (1907) for many years sustained the theory that the cause of the disease was not the rice as an article of diet, but that there was an alteration in it by germs or spores; these spores either existed in the husk and were mixed with the rice during the process of cleaning, or they developed after the shelling.

In 1908—1909 FRAZER and STANTON

made direct experiments on men for the first time. These belonged to an agricultural establishment in Malay. 300 javese were divided into 2 groups. To group "A" polished rice was given as principal food; to group "B" was given rice in the husk, brown rice, as principal diet. At the end of more or less 90 to 100 days, cases of typical beriberi appeared in the group "A" whilst group "B" remained quite well. If group "A" had its diet changed, the patients got well and beriberi disappeared. Several subjects from group "B" were mixed with those of group "A"; if they ate brown rice, they remained healthy, but if they ate polished rice, they presented symptoms of the malady after some time.

Thus was proved the non contagiousness of the disease and its alimentary origin. All precautions were taken, to avoid any error in the observations. At the same time, many well known scientists made the same experiments in animals and the conclusion of the etiological and symptomatic identity of the two diseases was reached.

FLETCHER in 1909 treated 123 inmates of the Kuala Lumpur Lunatic Asylum with polished rice and 123 with rough rice; in the first group there were 43 cases of beriberi, in the second none at all. The two groups changed from one building to the other but no case occurred in those who ate brown rice. Then they changed the rice food of each group. No new cases arose amongst the first group but there were cases amongst the second group, then feeding on polished rice.

In the Health Bulletin no. 12 published by the Department of the Interior, of the American Government in the Phillipines, the same results were obtained amongst the American scouts. There were very many cases amongst these soldiers. In one year there was a return of 600 cases. After giving them brown rice, the disease diminished and there were no new cases. The Governor then decreed that no polished rice was to be used in the Government Institutions.

And says the report, the disease disap-

peared everywhere. It was then proved that the few cases that occurred ensued from some department not having exactly obeyed the rule about polished rice. In this same Bulletin the government asked all the better classes to use unpolished rice, to give an example to the uneducated classes. The Board of Health proposed a tax of 4 centavos on the kilo of polished rice, so as to exclude the poor from making use of it; if the richer people used it there was not so much danger for them as they have other foods sufficiently nutritious to prevent the rice from harming them.

In 1913 STRONG and CROWELL published the result of their investigations in Spanish language and this work is so rigorously scientific that I consider it as the greatest and most definite argument with regard to the alimentary etiology of beriberi. The principal value of this work lies in the record of experiments on man, investigating the problem from all points of view and thus completing the studies of FRAZER, STANTON and FLETCHER. Convinced that MANSON, SCHEUBE, LE DANTEC, MARCHOUX WRIGHT, CASTELLANI, SHIBAYAMA did not bring forward sufficient proofs of their theory of infection, STRONG and CROWELL tried to reproduce the illness, excluding the influence of specific micro-organisms. They acknowledged the importance of the studies of *polyneuritis gallinarum* as the experiments on the birds were very clear and elucidated many problems in the aetiology and the cure of beriberi. They thought however that without identical experiments made on man, nothing absolute could be positively affirmed from a scientific point of view. These wonderful experiments were made in the prison of Bilibid in Manila, in which the hygienic conditions are almost ideal. With the Governor's permission, a certain number of criminals under sentence of capital punishment were chosen for the experiments.

To these men, STRONG and CROWELL explained with the utmost frankness, in the

Philippine dialect, the nature and danger of the experiments which would be made on them. They were told that the disease might end fatally for them, but that all that they were required to do was to eat certain kinds of rice. In compensation, they would receive as much tobacco and as many cigars as they liked. Twenty-nine offered themselves voluntarily. They were made to sign a document declaring that they had offered themselves of their own free will, and promised to continue until the end. They were divided into 4 groups: three of these groups were taken to one side of the building and the 4th group to the other side.

The sanitary conditions were excellent, and extreme vigilance was exercised to prevent the men receiving the slightest portion of food, outside that which was given them for the experiment. Their food was prepared by a special cook, and carefully weighed out for them at each meal. When cooked, the food was served out to them in equal portions. Each person received his ration in a bowl separated for him, with his number on it. For each meal, fresh rice was cooked and was given hot.

Diet used.

Slight repast called little breakfast:—
Bread—100 grs.—Coffee 500 cc. Sugar 15 grs. First Breakfast: Rice 300 grs.—Bacon 50 grs. Second Breakfast: Rice 300 grs.—Onions 100 grs.—Butter 15 grs. Third Breakfast—Rice 300 grs.—Bread 100 grs. Fourth Breakfast—Rice 200 grs.—Bread 150 grs.—Bacon 30 grs.

First Dinner: Rice 50 grs.—Onions 150 grs.—Butter 20 grs. Second Dinner: Rice 300 grs.—Bacon 50 grs; Third Dinner: Rice 300 grs.—150 grs.

This diet was given alternately to groups I, II and III. On the ninety—seventh day, and on the eighty first day for the third group 30 grs of codfish and 100 grs of potatoes were added, served with 300 grs of rice and alternated with the other food. The diet was the same for all except in the quality of the rice used.

The plan for the experiments was as follows.

Group I.—Polished white rice with meal from the rice husk.

Group II.—White rice and alcoholic extract of the cuticle.

Group III.—Polished white rice.

In spite of all, after some days some of the prisoners would not eat rice mixed with meal of the cuticle or prepared in a manner that made their food palatable. For instance Group I would not eat rice with meal and they were given dark rice (brown rice not polished) which is called *pinawa* in the Philippine Islands. The extract of bran was made by Dr. FELIX OCKSON of the laboratory of the College of Medicine by the process of VEDDER and CHAMBERLAIN.

These experiments are worthy of being copied in totum but unfortunately it would draw out our paper to an undue length. We will therefore make a synopsis and give the conclusions.

STRONG and CROWELL drew the following conclusions:

1. Beriberi in these men was due to their diet and therefore the disease has a dietic origin.

2. Beriberi appears when there is a want in the food of one or more substances necessary for the normal physiological processes of the organism.

3. When these substances are not found in the diet beriberi ensues. The substances exist in brown rice and in smaller quantities in the alcoholic extract of rice-bran, so that when one of these things are added to a diet physiologically appropriate, it prevents the appearance of beriberi symptoms.

4. In some cases though this substance forms part of the diet, the latter not being varied and being limited in kind, the patient loses his appetite and weight. These patients may present beriberi symptoms. The symptoms can however be stopped by changing the diet or adding other nutritive foods to it.

5. It is evident, say STRONG and CRO-

WELL, that the disease is not infectious but due to diet.

7. It is not probable that the patients could have been infected through the food, as it was always freshly cooked at a temperature to which only a sporogenous microbe could resist.

Besides this, if the infection had been introduced by the food, it would have been the same in all groups.

8. None of the rice used fermented, a fact which excludes the action of certain bacteria.

9. There is no proof to suggest the idea of beriberi being an infectious disease and it is certain that in the Phillipine Islands beriberi is due to a prolonged diet in which certain substances necessary to the normal physiological functions of human organism are wanting.

10. The disease studied was really beriberi as proved by the autopsy of the patient who died.

11. More observations should be made on the chemical properties and nature of the substance which prevents the disease; from a practical point of view however the etiology is known; prevention and cure are easy.

12. To prevent and cure the disease in man, nothing is wanted but liberal nourishment of the best quality adapted to the physiological necessities of the organism.

COBB, in a report on North Borneo written in 1916, says that beriberi has been long known there, but there has never been a serious epidemic. Those who are most liable to contract beriberi, are the poor, opiumsmokers and coolies employed in the rubber and tobacco plantations. A minutious investigation of the slight epidemics among them revealed that they were always arising from deficient nourishment and in two cases from the use of Saigon rice. COBB speaks of the great trouble there always is in the East to get the natives to use unpolished rice. The disease could have been eliminated. Everything depends on the food of the working classes.

In 1917 CHICK and HUME made an interesting communication to the LONDON SOCIETY FOR TROPICAL MEDICINE AND HYGIENE about beriberi amongst the English troops during the siege of Kut-el-Amara. The disease entirely disappeared with the change of food.

The British, who at first received a ration of white flour, afterwards received only a third or a half of this ration which was substituted by barley-meal or coarse wheat flour. They were protected against scurvy, being fed on ample rations of horseflesh. The Indian soldiers were supplied with cereals and beans rich in anti-beriberi vitamins. The Indians refused the horseflesh, and as there were no vegetables nor fruit in the region, they became an easy prey to scurvy. The authors made the following deductions:

1. To prevent beriberi, it is imperious that the germen (embryo) and the bran should not be separated from the flour used for making bread and biscuits for the soldiers on active service.

2. This is still more important when the troops are far away from all resources of fresh food, and live chiefly on tinned food which is deprived of vitamins by sterilisation at high temperatures.

3. To prevent scurvy, if there be no possibility of their obtaining fresh fruit and vegetables, they ought to be given seeds of leguminous plants which are already beginning to sprout.

It has been clearly proved by many of these who have studied the matter and by many experiments made on man, in the Philippines and in Malacca, that the origin of beriberi lies in the alimentation. One more argument must be cited here. I refer to the efficacious cure with Katjangidjo. This kind of beans from which HUSCHOLFF POLL extracted an acid substance which he calls X-acid, is not only useful to prevent the disease but also to cure it.

Vitamins are still very difficult and expensive to extract but the alcoholic extract of rice-bran can be given as a curative of

great efficacy. The celebrated case described by VEDDER ought to be known, and we here-with give a summary of it:

CIRILLO TAQUINEZ entered the General Hospital of Manilla on September the 5th. On the 9th. VEDDER found him in bed suffering from an intense dyspnoea, breathing with the greatest efforts. The pulse was 150 a minute; respiration 45 and the heart-beat violent. It was the typical history of a chronic case of beriberi with acute cardiac exacerbation. All the muscles were attacked and extremely painful when touched. For several days the patient had not eaten, on account of his vomiting. The assistant-doctor thought he could not live through the night and as the case was so serious, resolved to give it over to VEDDER. The latter ordered alcoholic extract of rice-bran which was given at 11 o'clock in the morning of the 9th. Fortunately the patient retained it. In the afternoon he got better, his pulse fell to 80 and respiration to 30. The next day he had a fresh exacerbation and was again given the alcoholic extract of a kilo of rice-bran. The dose was administered daily for a fortnight. The cardiac symptoms did not reappear; the hyperaesthesia of the muscles diminished a great deal, he did not vomit any more and regained his appetite improving greatly in appearance though the paralysis remained.

Similar results were obtained in other cases so that it was clearly proved that the disease was human beriberi (dropsical form), easily cured by this process. In the dropsical form and for cardiac trouble this remedy is therefore useful.

For the paralysis dependant on the lesion of the nerves and muscular fibres there exists no sure remedy; it can only be cured slowly, and by intelligent and careful dieting of the patient. This is easy to be understood as the restoration of important elements in the structure and the restitution *ad integrum* of a cell, such as the striated fibre or neuron can only be effected with comparative slowness and only if the destruction be not definite and total.

An objection of great scientific value against our arguments was emitted by the well known Brazilian doctor MIGUEL COUTO, in his book published in July 1916. He cannot believe that rice is the principal factor in causing beriberi, as was proved by BRAD-DON at the Congress of London, since rice does not cause beriberi as often in Brazil as in Asia and Oceania; he resumes all his objections in the following conclusions reproduced here textually:

As to symptomatology and as to clinical forms, evolution, anatomic substratum our beriberi is the same type as asiatic beriberi but it differs in aetiology, as is proved by the following facts.

1. The rice consumed by the people in the North is *the same* (1), both raw and cooked, as that eaten in the South; we have no reason to believe that it differs much in the quantity consumed, yet in the North beriberi is endemic and abundant and in the south almost unknown. (2)

2. In Brazil beriberi is more prevalent, in some States, and in these it is found in certain localities and in certain buildings, where there are agglomerations of human beings, while on the other hand the rice eaten by all is the same.

3. Rice is one of the staple articles of food in our country; it is not used so as to exclude other foods but it is eaten by all classes, and the vitamine esse quid is wanting to all, whilst some people are attacked with beriberi and others not.

4. Whilst there must be a receptive organism for infections to develop, intoxications have a universal action; but of all the people in our country who eat rice, some contract beriberi and others not.

Note 1. The italics are mine. Certainly Professor COUTO did not know that most of the rice eaten in the north comes from Rangoon and the Caroline Islands.

Note 2. In a previous paper, I noted that the india-rubber workers eat only, for months at a time, dried meat, flour, rice and beans all of which are imported, and make long journeys also remaining stored for some time.

5. Traditional observation has shown that the best remedy for beriberi is the removal of the patient from the centre where he contracted the disease; a half-dead patient embarks here and arrives quite well in Europe or in Buenos-Ayres; this feat is not compatible with the idea that he has had an alimentary intoxication, because, even changing his diet, he would have died if he had been left where he contracted the disease. (1)

6. Traditional experience has also proved that, even if the patient be cured, he may have a relapse, if he returns to the place where he fell ill, although he may eat no rice; whereas, if he remains away, there will be no relapse.

7. The rice furnished to the Navy is the same for one and all, and some vessels are more devastated than others, though the same store purveys rice to all. It is certainly the prisoners in the gaols who suffer most.

8. The rice sent to the troops in the Paraguayan war was the same as that consumed by the civilians who admired the valour of their compatriots from afar; these latter enjoyed good health while the soldiers were victimised in numbers by this fell disease. The same will be said by the Japanese, who lost 80, or (according to some opinions) 150 thousand soldiers in the with Russia war, who also ate the same rice as those who stayed at home.

9. Finally, my patient always eat about the same amount of the same kind of rice, and only fell ill once, whilst all the rest of his family were in the same condition.

Carried away by the logic of these arguments MIGUEL COUTO concludes thus:

"The disease by which our patient is attacked, is the same as the disease reigning in India and Japan under the name of beriberi. PATTERSON and SILVA thought they had discovered it in Bahia in 1894; the cause of the former is now discovered but that

Note 1. Observations made by AUSTREGESILO, MEIRELLES and myself (in Amazonas) prove that it is possible to cure beriberi *in loco*, if the symptoms are not yet fatal.

of ours is not. We erred therefore in the interpretation. Our beriberi is not beriberi."

We admit the plausibility of these arguments, until it was found that it is not only polished rice that causes the illness. Now we know that all cereals contain vitamins which can be destroyed by various conditions, as is proved by the experiments of SCHAUMANN, of SHIGA and others. The food may seem to be perfectly good and yet for multiple causes the protective substance may have been destroyed, and thus the food may have lost its most important biological qualities.

Latterly, new studies have shown that prolonged sterilisation deprives it of the properties indispensable for perfect nutrition and to the development of the organism.

SCHAUMANN saw beans enclosed in glass jars in Hamburg in a laboratory, looking as if they were quite perfectly preserved, but they had lost the power of curing *polyneuritis gallinarum*, which the same kind of beans possess when fresh.

ARLINDO DE ASSIS proved that beans sold on the Bahia market were deficient and deprived of their preventive substance against experimental beriberi.

It is a fact that all the beans imported in the State of Amazonas for the use of the men employed on rubber plantations come "roasted" as a preventive against weewils.

The observations made by JAYME SILVADO in 1907 do away with the objections made against the superior quality of the food furnished to the Navy.

A more or less uniform diet kept on for a long time, becomes deficient; the first sign the disease is want of appetite; the deficiency grows from day to day, provoking all the most grave symptoms. As a proof of this, we need only cite the beriberi attacking the British troops at Kut-el-Amara. For this reason, in the beginning the patients may be cured by sending them on a journey, thus changing their food entirely.

In the East the problem is very difficult on account of the numerous poor people, but here no such difficulty exists. Except

in the indiarubber plantations, in Brazil, beri-beri is a disease of barracks, ships, asylums, penitentiaries and hospitals. The purveyor is the first cause. He ought to be, permit the expression, eliminated by decree.

In the rubber plantations, the disease became rarer lately, owing to the war and the consequent depreciation of Brazilian indiarubber, as was proved to me by indisputable statistics. Through the agency of an intelligent and infatigable propaganda made by the Sanitary authorities in the North, it might be eradicated.

VEDDER, STRONG and CROWELL ask for the education of the people in the East and the Health Bulletins of the Philippine Islands began a propaganda for this end by exposing the matter in simple language. VEDDER speaks of the want of energy in the Eastern nations and in their persistence

in their ancient customs. And what people are more like the Orientals, with their fatalism, their indifference and resistance to modern ideas than our people of the North?

Measures ought to be taken. Already in 1916 I asked the Government to decree laws to prevent the exclusive use of polished rice, or at least to put a prohibitive tax on it, so that only rich people could use it.

Mandioc flour ought to be rigorously fiscalized, so that it be only used in the best state of preservation. But then my ideas on alimentation must be confirmed. The disease and its causes must be discussed and in these debates the voices of the princes of science must be heard at the side of the murmur of their humble disciples. And if the alimentary theory be true, the diffusion of these ideas will ensure the carrying out of the least costly and most necessary prophylactic needs of the country.

Explanations of the Plates 34—36.

Plate 34.

- Fig. 1. Pigeon, no. 8.—Food: polished rice sterilized at 120 C.—Paralysis of the right wing. High stepping.
- Fig. 2. Pigeon no. 9.—Food: At first raw polished rice, afterwards rice sterilized at 120.—High stepping. Paralysis of the legs and wings.
- Fig. 3. Cock no. 10.—Food: Raw polished rice.—Weak legs. High stepping.

Plate 35.

- Fig. 4. Cock, no. 10.—Food: raw polished rice. Difficulty in walking, paralysis of the extensors.
- Fig. 5. Hen no. 15.—Diet: national raw polished rice.—Paralysis of the legs on the 30th. day of observation.

- Fig. 6. Cock no. 16.—Diet: polished sterilised rice.—Paralysis on the 17th. day.—Died on the 19th. day.

Plate 36.

- Fig. 7. Cock no.—Diet: Indian corn autoclaved during an hour at 120.—Beginning of paralytic phenomena.
- Fig. 8. Cock no. 13.—Diet: Indian corn sterilised in the autoclave for one hour at 120.—Paralysis of the extensors almost preventing it from walking.
- Fig. 9. Diet: Sterilised Indian corn. Food administered by gavage to prevent death from inanition.—This state lasted for three days before death.