A CONTRIBUTION TO THE ETIOLOGY OF POLYNEURITIS as met with at SINGAPORE.

A THESIS for the DEGREE of M. D. by
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A CONTRIBUTION TO THE ETIOLOGY OF POLYNEURITIS
as met with at SINGAPORE.

A. The following Thesis is based upon a series of Notes kept by the writer relative to cases of Polyneuritis, admitted to the Hospital for Beri-Beri, Singapore, during the year 1914-15, while he was Medical Officer in charge.

During the period of eleven months, in which observations were kept, 211 cases were under treatment, male patients only being admitted. All cases dealt with were those of natives.

The sum total with regard to nationality was made up as follows:—

<table>
<thead>
<tr>
<th>Nationality</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>180</td>
<td>84.9%</td>
</tr>
<tr>
<td>Japanese</td>
<td>19</td>
<td>8.0%</td>
</tr>
<tr>
<td>Tamils</td>
<td>3</td>
<td>1.4%</td>
</tr>
<tr>
<td>Malays</td>
<td>4</td>
<td>1.8%</td>
</tr>
<tr>
<td>Javanese</td>
<td>3</td>
<td>1.4%</td>
</tr>
<tr>
<td>Arab</td>
<td>1</td>
<td>0.47%</td>
</tr>
<tr>
<td>Bengali</td>
<td>1</td>
<td>0.47%</td>
</tr>
</tbody>
</table>

It occurred to the writer that a sub-division of cases admitted to hospital might be made under two different categories:—

(a) patients affected with the disease soon after arriving in the colony, and those affected after some considerable residence:— or

(b) patients suffering from Polyneuritis uncomplicated, and those in whom/
whom, in addition to Polyneuritis, some other well marked diseased state existed at the same time, or had existed previously.

As it was found that the two categories, (a) and (b) showed several points in common, it was decided to classify all cases of Polyneuritis as:—

(1) Primary, and

(2) Secondary.

The former, with slight exception, comprised newcomers healthy with the exception of Polyneuritis, whilst the secondary cases comprised, not necessarily newcomers, but those in whom the affection of Polyneuritis existed as a complication of another disease. It must be stated, however, that a sharp distinction could not be accurately drawn, as in a small number of cases there existed some doubt as to whether what might be considered Primary Neuritis had not been engrafted as a complication of another existing disease. On the basis of Primary and Secondary Neuritis the sum total of cases could be subdivided as:—

(1) Primary Neuritis .159 or 78.3%

(2) Secondary Neuritis 53 21.7%

Apart from Trauma, the causes of Neuritis are generally assigned as:—

(1)/
(1) Acute Toxic States - Diphtheria - Scarletina - Influenza - or Typhoid.

(2) Chronic Toxic States - Tuberculosis - Leprosy - Syphilis - Anaemia.

(3) Introduction of poisons from without - Lead - Mercury - Alcohol - Ether and Carbon Bi-sulphide.

Although somewhat loosely referred to as Beri-Beri, the writer is of opinion, from the evidence at his disposal, that cases falling into the group of Primary Polyneuritis, should alone be classed as true Beri-Beri. The remaining cases - of Group (2) - should, in his opinion, be grouped under the name of Secondary Neuritis.

The leading symptoms of true Beri-Beri can now be referred to in detail, and later contrasted with those found in the group known as "Secondary Neuritis" or False Beri-Beri. As already mentioned, true Beri-Beri accounted for 78.3% of all cases under observation, during the period stated.

The writer feels justified in emphasising the importance of the clinical fact that, while Peripheral Neuritis affecting the lower extremities is at once the most obvious symptom of true Beri-Beri, a more important feature of the disease is a Neuritis affecting the Splanchnic Nerves, and principally among these the Vagi and Phrenic, and that/
that in the majority of cases these visceral nerves show involvement prior to those distributed to the skeletal muscles.

In regard to the secondary group of Neuritis, visceral nerves are very infrequently involved, except in cases where both types of the disease may co-exist. Vagus Neuritis being then kept in view, as a very early manifestation of true Beri-Beri, the chief symptoms of the disease may be considered in detail in regard to their etiological significance. Beri-Beri has been divided into the following sub-groups:

- Fulminant
- Atropic
- Rudimentary, &
- Oedematous.

From the clinical point of view, the writer would regard all cases as Acute or Fulminant, and Chronic, the latter including the remaining sub-groups which do not seem clinically distinct, but tend to pass from one to the other.

Acute Fulminant cases are rare, and very infrequently form admissions to Beri-Beri Hospitals. Three out of four cases, seen by the writer, were admitted to the native wards of the General Hospital, Singapore: three of the cases being Chinese, the fourth a Japanese.

The principal features of these cases were/
were those of acute cardiac failure, urgent dyspnoea and at times a peculiar gasping for breath. Severe epigastric pain was complained of, and cyanosis tended to be an early manifestation. The pulse was rapid and intermittent, the blood pressure low, and, of the 4 cases observed, three proved fatal within an average of forty-eight hours. A certain amount of cardiac dilatation could be made out in every case.

An important point in connection with acute Beri-Beri, is the liability to sudden death. The writer was present at three post-mortem examinations ordered by H.M. Coroner, Singapore, in cases of sudden death, all of which were found to have died of this disease. All were Chinese, and all examinations showed the dilated left ventricle with commencing fatty change, the dark red fluid blood, the lungs and spleen congested, and pathological appearances of the liver and kidneys indicating the existence of cloudy swelling—a very usual post-mortem finding after toxic states. Superficially, the appearances after death bore some resemblance to those met with in cases of toxic diphtheria.

That/
That a visceral neuritis plays the principal rôle in Acute Beri-Beri can thus be clearly seen. The rapid, irregular heart, with evidence of fatty change after death, the lowered blood pressure, and the stasis and congestion of the lungs, in themselves contain convincing evidence of an acute involvement of the pneumogastric nerves, tending progressively and frequently to a fatal termination.

Reference may here be made to the unpublished researches of Ellis, late P.C.M.O. Straits Settlements, that the inflammatory degeneration in Beri-Beri involved not only the peripheral nerves, but included the participation to the arteries, the splanchnics and the solar and renal plexuses.

The writer has never seen an example of Acute Fulminant Beri-Beri develop from any of those of the Chronic type while under his charge.

With regard to the symptoms of the Chronic variety of the disease the writer found that all cases conformed more or less closely to what may be called the "Beri-Beri Syndrome":

(1) Dyspnœa
(2) Paræsis or paralysis of the lower extremities
(3) Diminished urinary secretion approaching an almost anuria in a certain number of cases.

Anaemia/
Anaemia of the chlorotic type is present in a large number of cases, but the writer is not inclined to regard it as a symptom so much as probably a pre-existing and predisposing cause of the disease. Chlorotic Anaemia is frequently met with among peoples subsisting largely on polished rice as a result of the almost exclusively starchy diet, and proportionate diminution of the other essential food stuffs and mineral constituents.

The writer is of opinion that all of the above manifestations, except anaemia, are explainable on the basis of a degenerative polyneuritis affecting certain nerves or plexuses, viz; the lumber plexus, the branches of the vagus to the Cardiac plexus, and the renal plexuses.

(1) Dyspnoea is so common at all stages of Beri-Beri, that the writer made it a rule in no case to diagnose Beri-Beri unless Dyspnoea on exertion, accompanied by a certain amount of existing Cardiac Dilatation could be elicited.

The apex beat was found to be, generally speaking, just internal or external to the mid-clavicular line. In most cases a recurring mitral systolic Bruit was present, and the second sound might be re-duplicated. The pulse, which always showed a certain amount of irregularity, might beat from/
from 180 to 130 per minute after such slight exertion as a convalescent patient walking to the end of his ward. Blood pressure was as would be expected, continuously low, but no exact figures can be given as no recording instruments were made use of. By section of the vagi in rabbits similar symptoms can be produced, a fall of blood pressure: a rapid and irregular heart, and a tendency to atrophic changes in the myocardium.

As further evidence of vagus involvement one may mention the frequent occurrence of gastric atony and dyspepsia, with, in many cases, gastric dilatation. Paresis may extend further, giving rise to intractable constipation occasionally also met with and due likewise to vagus degenerative changes.

Dyspnoea in some cases may be the first symptom complained of, as in the case of a Chinese Coolie, under the care of the writer in the General Hospital, Singapore, who while convalescing from what at first appeared to be heart strain, developed suddenly paresis of the lower extremities, and was later discharged to the Beri-Beri Hospital, a typical case of the disease.

(2) Paresis or paralysis of the lower extremities is usually complete within a few days and as a point of distinction between other forms of/
of Polyneuritis, the knee jerk is quickly lost, remaining absent in many cases, when the patient is otherwise fit and able to leave hospital.

Sensory changes are almost invariably present, — areas of anesthesia, paraesthesia and tenderness on deep pressure over the calf muscles, remaining practically in every case till convalescence is well established.

A curious, and to the writer an inexplicable phenomenon, is the occasional presence of a Babinski extensor reflex in one, or both feet. Pre-tibial oedema, — referred to as being frequently present, — was, in the writer's experience a rare phenomenon.

Atrophic forms of Beri-Beri were merely advanced cases of the Rudimentary, and due to muscular degeneration:— colloid and fatty, of the skeletal muscles, as the result of nerve degeneration and loss of trophic influence. The so-called Wet or Oedematous type, has been shown to be due to a Neuritis affecting the vaso-motor plexus, and occurs most frequently in respect of the lower limbs. In 4% of cases seen by the writer, this condition was present. In one case considerable ascites developed, but the condition eventually improved. In the writer's experience the occurrence of Wet Beri-Beri has been distinctly rare.

There/
There was no evidence in any case to show that such dropsy was in any way due to pronounced cardiac inefficiency. The oedema usually improved while the cardiac condition remained in statu quo, when such cases were under treatment. Cardiac dropsy per se. is occasionally present.

Three cases were under treatment in whom neuritis, in addition to the lower had affected the upper extremities. In all three cases well marked wrist drop was present. All three cases belonged to the Atrophic type of Paralysis and exhibited loss of the Triceps reflex. No case of secondary neuritis involving the upper extremities was ever met with.

(3) Accurate results as to renal efficiency presented difficulties, principally in regard to the fact that the class of patients dealt with,—usually ignorant Chinese Coolies,—could not be induced to realise that their urine was to be kept, and not thrown away. In the case of a few only, more or less bed-ridden cases, could accurate results be kept. In such cases there was determined a lessened daily urinary secretion. The quantities varied, being on an average 10 to 15 to 20 or 30 ounces per day, compared with the usual 30 to 40 ounces or more usually passed by patients, not/
not Beri-Beri, in the General Hospital, Singapore.

Pressure of other duties did not permit time for exhaustive urinary examinations, except that Albumeninuria in uncomplicated Beri-Beri was practically always found to be absent.

Brooke, in his Manual of Tropical Medicine, under "Beri-Beri", draws attention to the almost invariable presence of Oxaluria in Beri-Beri, and at the same time to the diminished excretion of Chlorides. The latter point is of importance as linking Beri-Beri with the Infective Fevers, as such is known, also to be the case, especially in acute Pneumonia and Enteric, during the acute stage, and prior to defervescence commencing. It is reasonable to suppose with Ellis, that the diminished functional activity of the Beri-Beri kidney is associated, as he has shown to be the case, with a Neuritis, involving the Renal Plexuses and Ganglia; and not entirely, as others have suggested, with the permanently lowered blood pressure so characteristic of this disease.

B./

*Ellis' unpublished researches on Beri-Beri.
B. In contrast with cases of true Beri-Beri, which the writer considers formed a majority of cases of Tropical Polyneuritis met with at Singapore, the remaining cases which were not true Beri-Beri, though they presented the usual symptoms of Neuritis of the lower extremities, will now be considered.

It has already been mentioned that True Beri-Beri is etiologically a disease of new comers, while False Beri-Beri is not necessarily so.

Of this latter group 29 patients were found, in addition to Neuritis, to be suffering from Chronic Amoebic Dysentery; 9 from Syphilis; 13 from Malaria; 1 from Ankylostomiasis, and 1 had recovered from what had been presumably Enteric.

As, in most cases, the cause was more or less persistent, no great improvement resulted from the Secondary Neuritis unless the previous disease showed signs of definite improvement at the same time. Syphilitic Neuritis showed marked improvement under anti-syphilitic treatment.

As would be expected, the exhibition of unpolished rice in such cases, was followed by no such pronounced amelioration of symptoms as resulted in the case of true Beri-Beri, and what improvement did result, could only be reasonably attributed to consequent/
consequent improvement and relief from the primary disease, rather than that from any special dietetic treatment of the Secondary Neuritis resulting therefrom.

While loss of knee jerks and early paresis or paralysis occurs constantly in true Beri-Beri, no such marked distinction is met with in Neuritis secondary to other affections. Knee jerks may persist to a modified extent for weeks or even months, while one knee jerk may be absent, and the other present.

Atrophic muscular changes are not, moreover, here met with to the same extent as in true Beri-Beri except in old standing cases.

While the degenerative nerve changes in Beri-Beri are, in reality, a parenchymatous neural degeneration, affecting various nerves and plexuses distributed to the voluntary muscles and viscera, the changes in Secondary Neuritis, though pathologically similar, are almost entirely limited to those nerves distributed to the skeletal muscles. Cardiac changes consequently are so inconstant that they were as previously stated, used by the writer as the important criterion between these two groups of Polyneuritis, and again this distinction may be further emphasised at this point. Where/
Where the primary cause is persistent, as in the case of chronic dysentery of malaria, the Secondary Polyneuritis that has developed only improves in proportion as the Primary disease shows improvement, as already stated. True Beri-Beri improves rapidly during the exhibition of unpolished rice as a food, while in Secondary neuritis or false Beri-Beri, improvement is not so marked. This distinction the writer found of use at times from a diagnostic point of view.

There are rarely Cardiac complications in Secondary Neuritis as described in true Beri-Beri, and the exhibition of unpolished rice, apart from its more nutritive and tonic properties generally, is not followed by the same rapid improvement as in the case of true Beri-Beri, although unpolished rice, from its high phosporous and proteid content, is a valuable asset in all cases of disease where nervous degeneration is being recovered from, or where presumably, it is due to such dietetic deficiencies.

Oedema of the extremities in Secondary Polyneuritis, when such develops is, in the writer's experience, cardiac in origin and usually accompanied by other signs of failing compensation such as albuminuria, etc.

While true Beri-Beri again, is roughly limited to the age groups 25 to 35, the writer found the types/
types of Secondary Polyneuritis in most cases, not so limited, but including a number of older age groups. This matter will be further referred to later, but it is here mentioned to explain that urinary changes could not be included to contrast with those already referred to, as met with in cases of Beri-Beri, with any degree of accuracy.

Of the many theories of recent years brought forward to account for the occurrence of Beri-Beri, two only will be considered in this paper, namely:—

(1) that of Manson — that it is due to a volatile or stable toxin, — earth, floor, or house, — of which the inhalation or ingestion is the main cause of the disease, and —

(2) that of Von Eykemann and Funk, later elaborated by Fraser and Stanton of Kwala Lumpur, that Beri-Beri is one of the "deficiency" diseases and due to the absence of a vitamine or vitamines, through the use of a diet more or less restricted to polished rice.

During two and a half years residence at Singapore, the writer did not meet with a case of true Beri-Beri among Europeans or Eurasians, As afore/
afore mentioned, the great majority of cases occurred in Chinese of the Coolie and working classes, and these almost entirely, with the exception of a few, recurrent cases, in the case of new comers to the colony. In regard to age all cases seemed to occur under 35 years of age, although allowance had to be made in a number of instances, where apparently patients were quite ignorant of their ages. No case of true Beri-Beri was met with under the age of twenty.

One very significant fact elicited by the writer was that, so far as could be determined, the disease did not attack Straits-born Chinese, but was confined, almost entirely to immigrants, a fact, which in his opinion, militates at once strongly against a rice diet as the main cause of Beri-Beri, since both classes partook largely of polished rice as a staple article of diet.

In regard to sex, in the writer's experience, the incidence of the disease seemed almost exclusively to attack the male sex. The writer does not remember having seem more than some four cases of true Beri-Beri among female patients at the General Hospital, Singapore, whilst males attacked by the disease, were seen at the rate of several cases per/
per week. At the same time, there could be made out little, if any difference between the respective diets of Chinese men and women with regard to the consumption of polished rice, whether Straits born or immigrant.

To consider MANSON'S theory more particularly, the writer found that the theory of a volatile toxin inhaled or ingested seemed to have much to commend it. Apart from other considerations, it was definitely established of the existence of "Beri-Beri houses" in parts of Singapore, and of particular coolie lines on rubber estates and pine-apple farms, and of certain ships conveying coolies from Chinese ports to Singapore, which appeared to bear a greater endemic incidence of Beri-Beri than others.

As a result of exhaustive enquiries no evidence of a greater consumption of polished rice could be found among coolies on rubber estates where those housed, in certain coolie lines suffered to a greater degree from Beri-Beri than others on the same estate, housed in different lines.

As far as enquired into, the same held good for the occurrence of the disease in different parts of Singapore itself. These facts, and the comparative rarity of the disease among the female sex/
sex, appeared to indicate that something more than a merely food origin must be necessary to account for the occurrence of Beri-Beri, and that a locality or endemic toxin of some sort must at least play, besides food, a not inconsiderable part, — considering the endemic influence which residence in certain parts of Singapore seemed to exert in furthering the incidence of Beri-Beri among those so exposed.

Among saw-mill coolies admitted to Hospital suffering from Beri-Beri, 75% were found to have been employed at one particular saw-mill in Singapore, although polished rice had been the staple diet of all saw-mill coolies admitted.

Occasion was taken to visit several of the poorer lodging and rest houses in Singapore, which were known to have accommodated natives who were subsequently admitted to hospital for Beri-Beri. Speaking generally, these places showed much to be desired from the sanitary point of view. In fact, the "closely barred and locked lodging houses of Singapore" are referred to by Brook in his "Manual of Tropical Medicine", as a probable pre-disposing cause of Beri-Beri. Such houses were badly ventilated, unclean, and oppressively hot, while the atmosphere inside smelt foul and stuffy at all times, even/
even when unoccupied. When overcrowded, conditions of existence could only have been most insanitary for the occupants.

In many such places as these, Coolies or "Sinkers", landed at Singapore, were confined for days, or it might be weeks, until finally despatched to the different estates, etc., for which they had been indentured. Of the total admissions to hospital for Beri-Beri, rubber estate Coolies from Johore accounted for the outstanding total of 70% of all Coolies admitted, while of the remaining cases, tailors accounted for 19%, being of occupied males, the most represented class and double those of any other occupation affected. In regard to tailors, we have evidence of a heavy incidence of Beri-Beri in those confined to close, damp, artificially heated and badly ventilated workshops, as occupied by many of the low class tailors of China Town, Singapore.

To realise the inadequately sanitary status of the low class Chinese tailor, in many instances, one had but to visit his dwelling and workroom to gain further re-assurance of the fact, were such necessary.

The writer cannot speak personally as to the/
the ships then used for the transportation of Coolies, but he has been assured by officials belonging to the Protectorate of Chinese, how inefficient in every sense such ships often were, necessitating overcrowding and diminished scope for proper cleanliness and air space, with all its attendant evils during a voyage of, from often two to three weeks in a humid, hot, tropical climate.

At Kudat, in British North Borneo, in 1899, of patients admitted to the old native hospital there, a large number, after three or four weeks stay, developed Beri-Beri. (About three weeks would appear to be the usual time of incubation in Beri-Beri, though it was found to be almost impossible to come to any definite conclusion on this point.)

The hospital was said to be in an insanitary and unsatisfactory state. So clamant did the need become for reform, that eventually it was, accidentally or otherwise, burned. A new Hospital was built on more sanitary lines generally than the former, and upon an elevated site, with the result, we learn, that the incidence of Beri-Beri among hospital patients, almost entirely ceased, though no change was made with regard to dietary. The above/
above information was supplied first hand to the writer by a former resident in British North Borneo, at Kudat at that time.

(1) On the basis of a so-called place or Endemic toxin, the non-incidence of the disease can thus be more satisfactorily explained, than upon a theory of diet entirely, as in the case of Straits-born Chinese and Chinese females generally, who were not so exposed to the same conditions of livelihood as had obtained in the case of immigrants of the Coolie and working classes of the male sex.

(2) Environmental conditions do not, however, account for the incidence of Beri-Beri entirely. Among rice eating communities, a probable deficiency in respect of diet also exists and may play a predisposing part in the production of the disease. The writer will attempt to explain this further in subsequent parts of this paper.

Enquiries into the pre-social conditions of nationalities, other than Chinese affected with Beri-Beri, owing to pressure of other work, could not be undertaken, although what facts were available did not but lead to the conclusion that insanitary conditions had played some important part in the final production of the disease.

Although indefinite, the writer at this stage feels justified in recording here, certain results/
results obtained by him while attempting to elucidate whether anything of a noxious nature could be found in the air of so-called "Beri-Beri houses". In two such houses which were used as temporary rest houses or lodging houses in Singapore, the writer is of opinion that gaseous sulphur compounds were present in the atmosphere of these houses.

The method employed was simply to expose filter papers impregnated with a solution of lead acetate in the house for twenty-four hours. In both cases a slight brownish discolouration of the filter papers used, was obtained, indicating the presence in the air of gaseous sulphur compounds of some sort, probably sulphides. (As sanitary conveniences in these houses were frequently in a neglected state, the prevalence of volatile sulphides must in great measure be ascribed to such cause.)

The experiments were repeated in the well ventilated wards of the Beri-Beri Hospital, Singapore situated on the sea front, with entirely negative results, proving that the mere presence in such a building, of Beri-Beri patients, was not associated with any increased prevalence of atmospheric sulphides. Further experiments were attempted, of the same nature, in low native Malay dwellings, where it must be admitted slight evidence of sulphides was indicated.
indicated, though in somewhat similar Chinese houses, no presence of sulphides could be satisfactorily proved. All were houses considerably overcrowded, and in which many other sanitary defects were obvious.

Under favourable conditions, such as in a hot, humid climate as that of Singapore, organic matter of all kinds easily and readily decomposes, breaking up into many varied stable and unstable, gaseous or liquid bodies of simpler constitution. It is known that among these, several gaseous sulphur compounds, — from such as sulphide of hydrogen, sulphide of ammonium, and bisulphide of carbon, to more complex organic compounds of sulphur, etc. — are elaborated. What these other special compounds respectively formed were, the writer had no means of determining.

To carry further this connection, it is of interest to note that workmen exposed to the fumes of bisulphide of carbon, such as in india-rubber works, etc., suffer from Polyneuritis, as a species of chronic bisulphide poisoning. Oliver, who has made a special study of the subject, records in his work on Dangerous Trades, (pp. 77–79) results of experiments of exposing animals to atmospheres charged/
charged with certain percentages (unstated) of carbon bisulphide vapour. Evidence of Polyneuritis in these cases was obtained, and in those proving fatal, remarkably similar appearances in the heart and kidneys to those described under Beri-Beri, were found post mortem.

As the writer was obliged to leave the colony and proceed to England to join the R.A.M.C., April, 1915, animal experiments in Beri-Beri houses which he had intended to undertake with monkeys, had necessarily to be relinquished.

It is not suggested that the occurrence of Beri-Beri was associated in any way with carbon bisulphide poisoning, but that in many cases residence in an insanitary environment was the probable inciting cause of the disease. The connection with the prevalence of sulphides is mentioned merely as a point of interest in the probable etiology of Beri-Beri.

Before leaving this part of the subject, however, reference may be made to a series of experiments undertaken by Prof. Noël Paton of Glasgow, as related in the British Medical Journal, December 1918, with regard to the causation of Rickets, a disease which, until recently, like Beri-Beri, was considered/
considered to be one of the "deficiency" diseases, and believed to be due to a lack of fat and deficiency of the milk-vitamines in milk, which had been condensed. Paton has shown that by subjecting puppies to lack of sunlight and inadequate ventilation, though at the same time providing ample fats in their dietaries, signs of Rickets were produced during life and confirmed post-mortem. A second series of puppies, though given a poorer dietary, but ample ventilation, sunlight, and exercise in the open air, remained free from the disease.

To pass to a consideration of the theory of Beri-Beri as a "deficiency disease" and due to lack of vitamines in the polished rice grain, as elaborated by Fraser and Stanton, we are now confronted by the positions taken up by the advocates of this theory as follows:—

The disease is stated to occur in those who subsist on a vitamine free, or exclusively polished rice diet. Polished rice, in the process of polishing, has been rendered vitamine free: the unpolished rice grain contains the full compliment of vitamine. The feeding of animals on polished rice causes a disease analogous to Beri-Beri, but the substitution of unpolished for polished rice, arrests, and finally cures the disease. Finally, when polished rice is replaced/
replaced by unpolished rice as an article of diet, Beri-Beri does not occur.

As a result of enquiries into the former dietaries of Beri-Beri patients, in a number of cases (18% so far as examined) no evidence could be got that unpolished rice had been the exclusively staple diet. On the other hand, polished rice had been supplemented by various vitamine containing substances, such as vegetables, fish, seaweed jellies, or a preparation known as "kweh-chow" prepared from germinating grain, and curiously enough, similar to a recipe advocated recently by the Lister Institute, as affording a very rich vitamine supply to dietaries, which from any cause may be considered deficient in vitamine containing food stuff. (British Medical Journal December 1918. "Dietary Vitamines")

The fact that those subsisting on such a diet in China should, a few weeks after landing in Singapore, develop Beri-Beri, requires further elucidation and explanation. Why again, females should be so exceptionally spared compared with males, leaves the argument still more unconvincing from the point of view of a dietary cause.

Families of Straits born Chinese who partake largely of polished rice, nevertheless, remain apparently free from the disease. Of this there was abundant evidence in Singapore. The fact that again/
again Beri-Beri occurs in non-rice eating countries (Scheube) such as Brazil, the Moluccas, etc., where vegetables, sago, fish and game are the staple articles of diet, (Fiebig), all substances, it will be observed, vitamine containing - if lack of vitamine accounts for Beri-Beri, - and where also the disease attacks Europeans who have never eaten rice (Voortman) militates strongly, in the opinion of the writer, against a polished rice diet as being chiefly responsible for the disease, or of its being due to a loss of any special rice vitamine.

Funk has published in the British Medical Journal, 1913, an article, wherein he stated that pigeons fed from ten to twenty-one days on a diet of polished rice, developed the characteristic symptoms of Avian Beri-Beri, proving fatal in, from six to twelve hours afterwards. Funk further stated that he had isolated in more or less pure state, from the rice polishings or bran, a vitamine body which on intra-muscular injections in doses of 8 milligrammes into the Pectoral Muscles of the affected birds, was followed, two hours later by a bird, instead of being dead, being able to fly to its perch, although previously paralysed in wings and legs, and apparently

* Browkes Manual of Tropical Diseases - Beri-Beri.
apparently unable to move.

Although put forward by such an eminent authority as Dr. Casimir Funk, the writer, with all due respect, entertains doubts as to the production of a genuine Polyneuritis, as in Beri-Beri which is a true parenchymatous degeneration of the nerves and ganglia. In the case of the human subject, and presumably also in pigeons, recovery can only take place by regeneration of the degenerated paths, a process known to physiologists and pathologists alike, to take, till complete, some six weeks, and dependent upon the degree of degeneration attained, as to completeness of ultimate recovery.

All Beri-Beri patients admitted to hospital were given unpolished rice entirely, besides other extras, but nevertheless, in spite of this, were not, if admitted bedridden, able to get about even with the aid of a stick, within an average, of nine days. Such cases were often two and three months in hospital before being actually fit for discharge. In view of the ordinary pathology of Neuritis and time taken for its recovery, Funk's claim to the production and cure of the disease as thus produced in pigeons, after a few hours, can hardly be warranted and supported on scientific data.

One/
One point of dissimilarity which presented itself, with regard to Funk's experiments and his inferences drawn therefrom, relating to the human subject, was that his pigeons were fed on uncooked polished rice, while cooked rice was, and is, invariably that eaten by rice eating communities.

While the writer consistently questions the production of Polyneuritis, produced by Funk in pigeons, fed on raw, polished rice, in view of the astoundingly rapid recovery, - in the space of a few hours, - from a degeneration of the peripheral nervous system, through an injection of an extract from the polishings of the rice husk, he is yet prepared to admit that the consumption of uncooked rice may give rise to loss of weight and other toxic symptoms, which he has, however, been unable to verify or substantiate in experiments undertaken with properly cooked, polished rice. The cheaper grades of Siam, unpolished, or "bazaar" rice, are, at times adulterated with mouldy rice, which may give rise to pathological states, and similar to conditions produced in animals, such as Pellagra, by feeding with damaged maize. This difficulty can, however, be overcome by properly cooking the article before its exhibition as a food.

As before stated, unpolished rice differs
from polished rice, merely in that the husk or pericarp has not been removed in milling. It is in consequence, after cooking, yellowish and of a somewhat mawkish taste, while the polished rice is quite white and more palatable, and consequently more popular as an article of diet, with rice-eating peoples.

The rice bran is undoubtedly the more nutritious, part of the grain, being richer in mineral salts, proteid, and especially organically combined phosphorus, in which the polished grain is markedly poor, containing practically no phosphorus at all, and over ninety per cent of starch, with only proteid traces. In addition, the husk or bran is credited by its advocates, as possessing the active principle or vitamine, which prevents Beri-Beri. This "principle" is said to be thermo-labile, and to be dissociated at a temperature maintained for a few minutes beyond 100° C. On such an assumption, this vitamine, in the process of cooking unpolished rice, — which now obtains in Government Institutions in Singapore, — in large iron steamers, under a pressure of nearly two atmospheres for about an hour and a half, must, of necessity, suffer destruction or dissociation!

From what has been previously stated, it will be seen, that Beri-Beri is not necessarily associated/
associated with a vitamine-free diet, as in many cases sufficient vitamine had been taken in other articles of food, if deficient in the rice. As before-mentioned, Beri-Beri is practically unknown among Straits-born Chinese, who are, nevertheless, a largely polished-rice eating community.

To carry the analogy further, the writer has, during two and a half years' experience in the Tropics, only met with six cases of Scurvy complicating, some 400 or more cases of Beri-Beri in all. During the latter two and a half months before leaving Singapore, the writer, carried out a number of feeding experiments on chickens at the Beri-Beri Hospital, Singapore. Two chickens were fed upon cooked polished rice, and two upon cooked unpolished rice. Those fed upon unpolished rice thrrove much better than the other two, as to general condition, increase of weight, and laying. The two chickens fed upon polished rice did not increase in flesh to the same extent, showed a lack of energy and vitality, and laid badly, but up to the time when the writer left the Colony, had shown no outward or visible sign of Neuritis and contrasted strongly with Funk's experiments, where signs of Polyneuritis were observed in ten to twenty-one days in/
in the case of pigeons, as recorded by him in his recent articles on this subject, as already mentioned. So far as could be determined, all the chickens remained free, to the last, from intercurrent disease of any kind.

In January of the present year, a pigeon was fed on an exclusive diet of boiled, polished rice. Feeding was begun on the 4th instant, and the pigeon being confined in a cage, no other food of any sort, was, or could be supplied. The pigeon eats well, is in good health, active and energetic, and to all outward appearance, is still free from disease of any kind, excepting a loss of about two ounces in weight. The bird has been and is kept in a well ventilated and airy room.

Before concluding this part of the article, the writer may be allowed to express his own convictions as to what, in the case of rice eating peoples, the disadvantages from polished rice are, and to what extent he believes them operative in the production of Beri-Beri. Shortly, it may be put that the predisposing cause is a phosphorous-protein shortage to the peripheral and central nervous systems in particular, through the use of polished rice, the main phosphorous-protein content being in the husk, which has been discarded. Phosphorus is an essential/
essential element in the nutrition and well being of the nervous systems, and its absence leads to an increased vulnerability to external inciting causes of disease. It may well be that that vulnerability is influenced under conditions of over-crowding, and defective sanitation, where the inspired air is apt to become tainted with sulphides and other known and unknown toxic products of decomposition.

The making good of these deficiencies, - phosphorus, proteid, etc., - through the use of unpolished rice before the disease is actually established, may serve to re-adjust the balance, and thus probably act as a prophylactic. When the disease is actually established, by its tonic properties and building up that into the nervous system which is specially lacking, recovery is promoted.

In this way, the substitution of unpolished rice for polished rice may be both, to some extent prophylactic, and to a great extent curative. Where native races have substituted unpolished rice for polished, Beri-Beri is now unknown, as among certain classes of Tamils.

Finally, as to the question of the so-called vitamines, considerable doubt as to whether they play such a prominent part in dietetics, has lately/
lately been raised by experiments on the use of dried milk for infant feeding, by the Local Government Board, and investigated principally by Dr. Janet Lane-Claypon and her co-workers. (Special L.G.B. Reports - Dried Milk 1918)

Reference has already been made to the experiments of Professor Noël Paton, in the production of Rickets by subjecting puppies to defective sanitary conditions in spite of a vitamine containing diet.

Lane-Claypon has shown that over half a million babies already have been brought up exclusively on dried milk (Glaxo, Cow and Gate), which presumably cannot then contain vitamine, with the production of Scurvy or Rickets in less than one per cent of all cases. In such cases, the production of Rickets or Scurvy is now attributed to the insanitary environmental surroundings of the child, as lately demonstrated by Noël Paton.

Further and more detailed feeding experiments are required to establish satisfactorily whether Funk's results, after feeding pigeons with polished rice, were genuine cases of Polyneuritis, and analogous to those met with in the human subject in Beri-Beri, or merely toxic states, resulting from/
from the uncooked grain.

Such results throw little light on the real production of Beri-Beri in rice eating communities, where uncooked rice is never eaten.

In another direction, experiments might be undertaken as to the susceptibility of groups of animals fed respectively on polished and unpolished rice, to Polyneuritis, when later submitted to adverse sanitary conditions.

The prevalence of Beri-Beri among non-rice eating people at all, as lately in Spain, again raises an interesting point in the further etiology of the disease, as being primarily of dietary origin. A short reference to above was made in British Medical Journal January 1919, attributing the disease to an almost exclusive potato diet. Potatoes contain little else than starch and water and the article is of interest in correlating the predisposition to the disease through a diet lacking in proteid and fat with that in the case of rice-eating communities. The article is, further, of interest, in view of the fact that potatoes contain a considerable amount of vitamine. The writer has been unable to find any reference to a distinction having been drawn between true and false Beri-Beri, as he has/
has attempted to do in this paper from cases in his own experience, and is inclined to consider so-called outbreaks of Beri-Beri among non-rice eating peoples, especially when mixed diets have been indulged in, as in all probability belonging to some or other of the many forms of Secondary Neuritis, except in instances where the dietary has, from any cause, been particularly carbohydrate.

In conclusion, the following extracts may be quoted from a paper published in the British Medical Journal, February 15th, 1919, by Lieut. Colonel R. McCarrison, I.M.S., entitled, "The Pathogenesis of Deficiency Disease". -

"The manifold toxic influences to which human beings are subjected under conditions of food deficiency must play an important part in further depressing the functional activities in these organs and tissues on which normal metabolism is dependent. The toxic products of intestinal bacteria may thus assume a role of high importance in the genesis of morbid states, which are, no doubt initiated by the dietetic defect".

"Pigeons fed on a diet consisting solely of polished rice (uncooked?) i.e. on a diet composed solely of starch with less than ten per cent/"
"37.

"cent protein, in addition to showing signs of Polyneuritis Avium, in ninety-four out of 142 cases examined, showed, when bacteriologically examined, post mortem, septicaemic infections of various kinds. Four out of 142 had tuberculous disease of the lungs or abdominal viscera or both".

"The absence of certain accessory food factors from the dietary, - improperly termed Anti-Neuritic, - leads not only to functional and degenerative changes in the Central Nervous system, but to similar changes in every organ and tissue of the body. The morbid state to which their absence gives rise is not a Neuritis".

"The Central Nervous System atrophies little, paralytic symptoms, when they occur, are due mainly to impaired functional activity of the nerve cells, much more rarely to their degeneration. The bones are thinned and there is a loss of bone marrow. The red cells of the blood are diminished by about 20%.".

"Finally, although deficiency of certain accessory food factors is the essential etiological agent in the genesis of Beri-Beri, it is held that infectious and parasitic agencies are often important causes determining the onset of symptoms."

The/
The above extracts corroborate the writer's previously expressed opinion that a starchy diet, to the almost total exclusion of the other essential groups of food stuffs, predispose the nervous system to the inciting cause or causes of Beri-Beri, in those so predisposed.

The use of dried milk alone, which comprises the essential food elements, proteid, carbohydrate, and fat, in proper and adequate proportions, as an infant food, affords ample evidence of the only secondary importance of the so-called vitamins and of the full importance of a diet containing the adequate physiological requirements in food stuffs essential for the needs of the organism.

CONCLUSIONS/
CONCLUSIONS.

(1) Polyneuritis as met with at Singapore presented two distinct types, the two types co-existing in a small proportion of cases.

(2) 78.3% of cases belonged to true Beri-Beri, while 21.7% were of the false or spurious type and were instances of Peripheral Neuritis supervening as a secondary complication after Malaria, Dysentery, Syphilis, etc.

(3) Among rice eating communities, the consumption of polished rice leads to diminished functional activity in the cells of the Central Nervous System, through what has been termed "nuclear starvation", besides changes in the Ganglia and Central Nervous System, of a quasi degenerative nature, in some cases. These effects are mainly the result of an excessive starch diet, with disproportionate diminution of all the other essential food elements, proteid, fat, and mineral salts.
(4) Unpolished rice is more nutritious from the greater presence of proteid, phosphorus, and mineral salts in the husk or bran which is discarded on polishing.

(5) The exact inciting causes of Beri-Beri in those so predisposed, may be inhaled or ingested toxins. Beri-Beri is usually associated with over-crowding and other attendant sanitary defects, which may be in such localities, influences of an endemic character, and of "Beri-Beri Houses".

(6) Unpolished rice is not a predisposing cause in the production of Beri-Beri, but is both curative and prophylactic.

(7) The so-called vitamines probably play a very unimportant part in the production of the disease, as Beri-Beri is very unusually associated at the same time with scurvy. (The question of the etiology of Scurvy is not discussed in this paper).

(8) A vitamine containing diet with polished/
polished rice may be followed by Beri-Beri. In the case of Straits born Chinese an almost exclusive rice diet is not associated with Beri-Beri in numerous instances.

(9) Avian Beri-Beri is probably not true Beri-Beri, but a toxic process due to uncooked polished rice which may be mouldy, etc., or may contain toxic substances dispersed by boiling.

(10.) Perfectly cooked polished rice may be given for long periods without any signs of Polyneuritis, though birds so fed may show a lack of vitality, and loss of flesh, and exhibit a predisposition to intercurrent disease, chief of which may be Neuritis and Tuberculosis.

(11) Apart from such lack of vigour etc., in birds, a vitamin free diet is not associated with any definite diseased state, their predisposition to intercurrent disease being the direct result of a diet lacking in the essential food requirements of the organism.
Provided the essential food elements be present, as in the case of dried milk, it has been abundantly proved that the further addition of vitamine containing elements such as orange juice or raw meat juice are unnecessary.

An excessive carbohydrate diet to the exclusion of other essential elements, is the predisposing cause of Beri-Beri in rice-eating communities and peoples.

The inciting causes of Beri-Beri, among those so predisposed, in the writer's experience, were the various adverse influences arising from an insanitary environment; this, also, may explain the apparent freedom from the disease in the case of women and Straits-born Chinese, who, at any rate were not required to use the various coolie lines, rest-houses, etc., mainly used by immigrant Chinese of the male sex, after arrival in the Colony.

The efficacy of unpolished rice is due to the/
the fact that it is a more nearly perfect food, as typified in the case of dried milk. The so-called vitamins, if present, are, as in the case of dried milk, destroyed in the process of cooking or preparation and would appear to be of only little importance in dietetics.