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B E R I - B E R I

A Consideration of the Theories advanced regarding
its Etiology, and a Careful Examination of its
Clinical and Pathological Phenomena.

During the past two decades the study of the Diseases of Tropical Climates has advanced more rapidly than ever before, with the result that at the present time, out of a large collection of clinical material, certain diseases stand defined and clear, as regards their Etiology and Symptomatology. Former hypotheses have exploded and former empirical modes of treatment have been replaced by others standing on a firm scientific basis.

These enormous strides have been accomplished by a greater realization at home of the importance of accurate study of Tropical diseases per se, by the establishment abroad of Clinical Research Laboratories efficiently equipped with every modern appliance and by the thorough investigation and publication of all types of disease by scientific men of every nationality.

The result gained is undoubtedly one of value in every direction, but one of its chief advantages must be the stimulus, which it gives to further effort in the elucidation of many diseases, which up till now have baffled the keenest research.

The longer one remains in the Tropics the greater one realizes the impossibility, with the knowledge to hand, to solve the many clinical riddles, that almost daily present themselves; diseases which refuse to be labelled and pigeon-holed in an orderly manner, and which present Pathological problems as yet unapproached.

The very frequency of such cases tends often to cause one to despair of ever placing them on a firm foundation and it is only the comparison of the extent of our present knowledge with that of ten years ago, that enables one to go on with what often seems a use-
-less labour, ever realizing that:

"New times demand new measures and new men,
The world advances, and in time outgrows
The laws that in our fathers' day were best,
And doubtless after us some purer scheme
Will be shaped out by wiser men than we
Made wiser by the steady growth of Truth."

Amongst the many diseases, whose causation is still an unsettled point Beriberi stands out prominently, theory after theory has been advanced only in the end to fail to be applicable to every case and so in turn to be discarded.

It seemed therefore, that as one has been for almost the last three years brought into close contact with a large number of cases of Beriberi, to be worth while recording the result of ones investigations, not so much with the idea, that one has solved, what has so long been of such paramount difficulty, but in the hopes, that a careful marshalling of the various theories with a thorough examination of the clinical and pathological aspects, as obtained from ones own personal experience, may bring our knowledge

of this most interesting of Tropical diseases up-to-date.

The majority of the observations recorded in this paper were made at Christmas Island (Straits Settlements), supplemented by work done on this subject during the last year in Singapore, Burma, India and Hongkong.

DEFINITION and DISTRIBUTION

The origin of the term Beriberi is hidden in obscurity. It has been said to have been first described by that name by Dr Malcolmson F.R.S. of the Madras Medical Service in 1835 and was identified by Fayrer as being the same disease as Barbiers, noted by earlier European travellers, and so possibly the Hindostani word for swelling ie: Bharbari is the most probable etimology.

The name has been officially and popularly recognized and its retention is justified in spite of its lack of definity, always provided, that it is clearly understood what is meant by the term, namely-----

--- A specific multiple neuritis, infectious or toxic, often accompanied by oedema and with a special tendency to involvement of the Vagus and Phrenic nerves, and endemic and epidemic in most warm regions of the world.

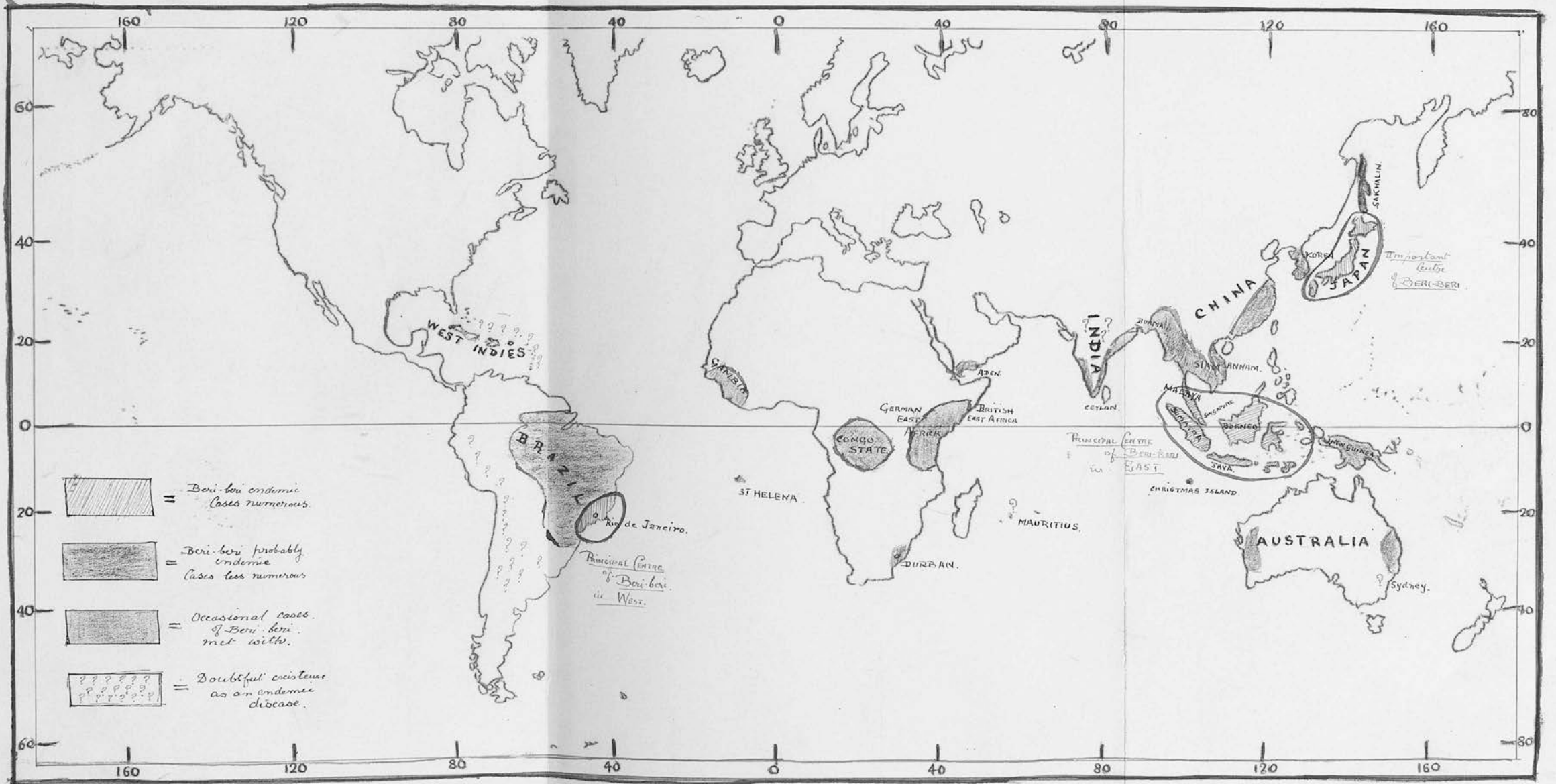
As shown later, laxity of a proper appreciation of this definition has frequently led to cases being recorded as Beriberi, which were really due to some other cause, such as Climatic Oedema, Ankylostomiasis, or of Post-Malarial origin. To obviate this many terms have been suggested, Scheube's "Neuritis multiplex endemica" or Baelz' "Pan-neuritis endemica" being possibly the most comprehensive, but they have never gained sufficient recognition to be of practical value. The disease known as "Kakke" (leg sickness) by the Japanese and Chinese, "Kaki Lembut" by the Malays and "Inchacao" by the Braziliáns are all considered to be identical.

As regards the History and Geographical Distribution of Beriberi, it is unnecessary in a treatise of this description to travel over such well known ground. It is sufficient to note that the disease is found endemically and epidemically in nearly ^{all} tropical and sub-tropical countries; the principal centres in the East being Malaya and Japan, and in the West Brazil. It has also been noted in temperate climates in isolated epidemics in ships and institutions.

The accompanying Map of the World will serve to show at a glance those areas of the globe, where the disease is most prevalent and where it is rare and of doubtful occurrence.

MAP
SHOWING

The Geographical Distribution of Beri-beri.



DISTRIBUTION OF BERI-BERI.

ETIOLOGICAL THEORIES

"Quot homines, tot sententiae".-----Terence.

"Opinionum commenta delet dies, naturae judicia
confirmat".-----Cicero.

In order to appreciate properly the relative importance of the various theories advanced regarding the factors at play in the causation of Beriberi, it will be as well first of all to state them numerically and then to consider, what can be advanced in support of each individually. It has been thought best to mention all the theories, that one has personally attempted to prove or disprove, and then to consider at greater length the two main theories, that are struggling for primary recognition at the present time.

1. The Miasmatic Theory.
2. The Theory of Arsenical Poisoning.
3. The Theory of Oxalate Poisoning.
4. Toxi-Infectious Theories.
 - A. Bacteria found in the Blood.
 - (a) Pekelharing & Winkler's Coccus.
 - (b) Gerard's Micrococcus.
 - (c) Dangerfield's Micrococcus.
 - (d) Okata & Kokubo's Kakkecoccus.
 - B. Bacteria found in the Urine.
 - (a) Herzog's Kakkecoccus of Okokubo.
 - (b) Tsuzuki's Micrococcus Beribericus.
 - C. Bacteria found in the Alimentary Tract.
 - (a) Hamilton Wright's Bacillus.
 - (b) Durham's Looped Organism.
5. Alimentary Theories.
 - A. Deficiency of Fat.
 - B. Nitrogenous Starvation.
 - C. Infected Fish.
 - D. Rice Theories.

D. Rice Theories.

- (a) Hose's Mouldy Rice.
- (b) Braddon's Specific Fungus of 'Uncured' Rice.
- (c) Saldanha's Arsin in Rice.
- (d) Fraser & Stanton's Phosphorus Deficiency.

Besides these there are several, which need not be considered at length:

The Drinking Water theory of Roll.

The Hoemamoeba Theory of Glögner.

That it is due to Anaemia, Over-crowding, or a form of Ankylostomiasis.

These show, what an enormous variety of hypotheses, the search for the true cause of Beriberi has inspired.

1. The Miasmatic Theory.

It is interesting to note here that, although probable references are made to Beriberi in Dio Cassius, which describes a Roman campaign in BC.24, under Aelius Gallus, and again in Kin Ki, a Chinese book of medicine written about 200 AD, yet the first full account is found in Sin Kiu Ho, written about 640 AD: by a Chinese doctor of the name of Si Bah Koh, who propounded the theory, that the disease was due to a gaseous poison set free from the ground by cold, heat, wind or moisture and as the feet are always in contact with the earth, so they are most liable to be most affected.

In more recent years Feibig came to the conclusion in his book on the Pathology and Therapeutics of Beriberi, that the disease was due to a microbe in the soil, which generates a gas of the nature of an evanescent ptomaine, and this by inhalation reaches the body and sets up the disease by its effect on the nerve tissues. The rise of this gas being determined by certain factors, such as moisture, atmospheric pressure and the position of the sun.

In a similar manner Manson, in his book on Tropical Diseases, suggests that the disease may be due to a germ in the soil, which liberates a volatile toxin. He draws a comparison between Beriberi and Alcoholic Neuritis, in the latter disease "the germ is the yeast, the culture medium the saccharine solution

and the toxin the alcohol," possibly the Arsenical Neuritis arising from poison papered walls would be more analagous. In the case of Beriberi the germ is in the soil, house or ship, and this under certain conditions becomes the culture medium with the result, that a toxin generates.

In support of this view he cites two facts:

- (1) Recovery is often immediate on leaving an endemic area, which would not be the case, if the germ was located in the body.
- (2) The disease clings to certain ships.

Both these statements are frequently made, but as will be shown later are not very reliably supported.

On the other hand several powerful arguments can be brought forward against the validity of this theory.

- (a) In the first place it would place this particular affection in an unique position, for in no known disease has a similar mode of toxin absorption been proved.
- (b) Again in ones own experience at Christmas Island, Beriberi occurred almost entirely in the coolie houses, (built on concrete, well raised above the ground and well disinfected) and practically never in the primitive ground built huts of the clearing camps, scattered over the island, and often inhabited for several months at a time.
- (c) Further this theory fails to explain certain well-established facts, why, for instance, on estates

employing mixed labour Chinese, Malay and Tamil, all of whom are living under the same external conditions, Beriberi should be confined, as it so often is, to only one section of the community. A number of such instances have been quoted by other observers and several have come under ones own notice. Since the recent Rubber Boom, in the Federated Malay States, has caused the opening up of large tracts of land for cultivation purposes, it has often been seen that, a short time after the Chinese emigrant coolies have arrived on an estate, which may have previously been for years occupied by Malay villagers, Beriberi invariably occurs; although it had never been known amongst the Malays, who as a race are almost if not quite as susceptible to the disease as the Chinese.

- (d) Again cases have repeatedly occurred in the cells of Gaols, which have been most thoroughly and constantly disinfected with Mercurial Solution.
- (e) Beriberi appears on ships far from land, ships too that have never touched at a port where Beriberi exists and none of whose crew have ever come in contact with a possible source of infection.
- (f) Lastly if such a mode of infection existed it would only be reasonable to expect to find certain pathological changes in the respiratory tract. Such however is not the case in ones own experience; a number of autopsies made with a view to proving this, having given absolutely negative results.

It therefore hardly seems probable that a theory, which fails to be efficient in so many different ways, can be accepted, as describing the real mode of the causation of this disease.

2. The Theory of Arsenical Poisoning.

This was first advanced by Ross, on the strength of an epidemic of Polyneuritis occurring after the consumption of adulterated beer. For there was a close analogy in many ways in the symptoms produced, and I mention it, because quite recently I heard it advanced during a Medical discussion.

The view is, that the disease known as Beri-beri is really due to a form of Arsenical poisoning, and I mention the following facts to disprove the same.

It is, of course, true that many of the Chinese in ~~their~~ work handle arsenical preparations. Natives employ manures containing Arsenic to improve the soil, and the tobacco used largely in the East contains traces of it, but on the other hand consider the following points:.....

- (1). Prisoners admitted into the ~~Cas~~ of the Straits Settlements have developed Beriberi after being there from three weeks to several months, and all the while any possible means of Arsenical introduction has been rigidly avoided, no tinned food or contaminated sugar has been used, and there has been no disturbance of the soil.
- (2). From a clinical point of view the pigmentation of

the skin, the plantar and palmar keratosis and the pruritis of Arsenical poisoning are all unknown in Beriberi. Further medicinally Arsenic can be given to patients suffering acutely from the disease, without increasing the symptoms, as one has often been able to demonstrate on patients under ones care.

- (3). A Royal Commission analyzed certain articles of food commonly consumed by coolies with a view to ascertaining the possible source of and amount of Arsenic present. Various kinds of rice came under inspection and it was decided, that Arsenic though present, was of such infinitissimal amount as to be absolutely negligable.

I have frequently seen quantities of weevils in bad rice actively on the increase, and the amount of Arsenic present was evidently insufficient to prevent their developement.

Dried fish, principally Bombay Duck and Norway Cod, were also found on careful analysis to contain Arsenic, but again only in a quantity too infinitely small to be of any importance.

- (4). An interesting point, brought before my attention, was the presence of Arsenic in the hairs of Chinese coolies, derived most probably from the kind of tobacco smoked. In order to substantiate this, I examined the hair of several coolies, both free from and suffering from, Beri-beri.

In order to estimate the amount of Arsenic present, the method employed was to dilute and filter the solution, and evaporate it with Sulphuric Acid. This was repeated several times, after the addition of a small amount of Nitric Acid, until the fumes of Sulphuric Acid appeared, and then to proceed in the usual way by Marsh's process.

It was found that in 70%, no trace of Arsenic was present at all, while in the remaining 30% it was infinitesimal and present equally amongst the healthy and the sick.

The following were the figures:---

CLASS of CASE	NO: of CASES	AS: pres:	AS:abs
(1). B-B present.	20	6	14
(2). B-B previously.	10	3	7
(3). B-B absent.	15	7	10

After completing this examination, I came across a reference to the work of two French observers, which, if correct, shows that the detection of Arsenic in the system is valueless; for they maintain, that it is a normal constituent of the tissues of nearly all animals, and Putnam affirms, that it can be found in the Urine of 30% of normal persons.

Braddon has pointed out, that Glucose, a possible medium of Beri-beri intoxication, sometimes contains more than mere traces of Arsenic: this combination might therefore greatly complicate the symptomatology of the disease. Very small quantities indeed of Arsenic

may set up paralytic and other symptoms, varying greatly with the idiosyncrasy of the consumer. This is mentioned not with a view of weakening the statements already made, because there is nothing in favour of the suggestion, that Tropical Beri-beri is ever due to Arsenic, but because, owing to the great difficulty arising in the differential diagnosis between certain forms of toxic polyneuritis, of acute ascending paralysis of the cord and of Beri-beri, as seen in England, it is not impossible, as Manson pointed out before the British Medical Association in 1898, that "many of the cases of so-called Peripheral Neuritis in Britain are really due to Beri-beri," such indeed as the notorious beer-drinkers epidemy in 1900.

3. THE THEORY OF OXALATE POISONING.

I mention this theory briefly, as it is based on a certain amount of experimental evidence.

Trentlein, on the strength of Maurer's experiments, who produced in fowls a condition closely resembling that of Beri-beri by feeding them with Oxalic Acid, carried out and amplified similar experiments by using oxalates and rice meal, as well as Oxalic Acid. He came to the conclusion from the results obtained, that Beri-beri could entirely be attributed to Oxalate poisoning. He held in the case of the fowls, that the action of Oxalic Acid or its Salts on the system was produced by the removal of the

Calcium Salts from the affected tissues, and further found he could stop all symptoms by giving an excess of Calcium Carbonate in the food and so forming the insoluble Calcium Oxalate.

He therefore concluded , that a similar excessive production of oxalic acid in man was the true cause of Beri-beri.

As will be seen later, when considering the Urine in this disease, I fairly frequently found Oxalates in excess more especially in the "moist" form of Beri-beri. As a result of this I carried out certain therapeutic experiments, also referred to further on, but in my own opinion the excess in these cases was most probably derived from the food and certainly Oxalic Acid plays no part in the production of the disease.

Under the heading "Experiments with Fowls" I shall refer to this matter and will show , that an attempt of mine to produce a condition analagous to Beri-beri in Fowls by feeding them on Oxalic Acid, proved absolutely negative. There were no evidences of Neuritis or Paralysis and, beyond a certain lack of energy and want of tone with loss of appetite and drooping of the comb, the birds showed none of the symptoms described by Maurer and Trentlein.

Let us now pass on to review at greater length the two more important theories, at present before the Medical world; as these embody a number of different postulates, I have decided to consider them under the headings of:-----

The Toxi-infectious Theory.

The Alimentary Theory.

Many supporters of both views exist and different schools hold more or less by one or the other.

The very fact, that such different theories can still be entertained, proves very clearly how far off either one or the other is from being incontrovertable.

At the meeting of The Society of Tropical Medicine and Hygiene held in April 1909, when the subject of Beri-beri was up for discussion, the final words of the President, Sir Patrick Manson, on the question were these:....."The weight of opinion amongst those, who have spoken in this discussion is opposed to the rice theory of the origin of Beriberi. Still many capable observers have deliberately adopted the hypothesis after having opposed it. The Society will hesitate to say, that these men are wrong, but until we have more facts at our disposal, my own position is one of suspended judgement."

Keeping then the dictum of such a high authority in mind, let us pass on to consider the different arguments, that have been urged in support of one or the other side.

4. THE TOXI-~~INFECTIOUS~~ THEORY.

Earth, Ground or Place infection have had many advocates. The constant recurrences of the disease in Ships, Prisons and Institutions have been urged in support of it, but so often cessation has occurred, without any Meteorological change to account for it, and with such suddenness, that it practically disposes of this, as a plausible possibility. Such a sudden cessation occurred, for instance, in the Singapore Gaol in 1904. Further, if infection were to arise from this cause, thorough dis-infection should be accompanied by extremely happy results, but this has been shown to be notoriously ineffectual.

It is always alleged, that removal from an infected area is followed by rapid recovery, this is often very strikingly true, but it must be remembered (a), That the cases, which are fit for removal, are not those, which are most seriously ill.

(b). That the locality, to which they are taken, is often a healthier one in every way.

(c). That there is frequently an accompanying alteration in the dietetic régime.

I do not think from my own experience, that place infection has anything to do with the disease. In Christmas Island the coolie houses were well-built, well-ventilated and dry, and were regularly dis-infected,

still cases of Beri-beri continued to occur in large numbers and were much more prevalent, than in many places, such as native villages in Malaya or the fo'cass-tles of ships, where the hygienic surroundings are anything but ideal.

From time to time several different observers have claimed to have discovered the micro-organism causative of Beri-beri and I will briefly refer to the more important of these.

They may well be divided into:-----

- A. BACTERIA found in the BLOOD.
- B. BACTERIA found in the URINE.
- C. BACTERIA found in the ALIMENTARY TRACT.

A. Bacteria in the Blood.

(a). Pekelharing and Winkler's Micrococcus.

These two Dutch physicians were probably the earliest to produce any really scientific work on the subject, for, as far back as 1890, they published the results of their labours in the Dutch East Indies---

Sumatra and Java---. They succeeded in isolating a micrococcus, which they considered to be the causal agent of Beriberi. Having exhaustively examined the blood, organs and tissues of subjects, who had died of this disease, they were unable to obtain any positive results. Then they turned to the investigation of the blood of those actually suffering from Beriberi, and were able to show, that in nearly every case,

bacteria could be demonstrated in the stained blood films. Then they endeavoured to isolate these by inoculating a variety of different media.

RESULTS.

Out of 80 cases in which the blood had been found to be infected, in 65 the media continued sterile, while on only the remaining 15 was a growth apparent. Out of these 15 only 9 were uniform and positive, 3 proved to be due to a bacillus, and 3 to different micrococci from which sub-cultures were unattainable.

The media employed was peptonized broth, and thickened with gelatin to which the blood was added, and then poured, while still liquid, over a cultivation plate. The micrococcus was described as having a white shining surface and liquefying gelatin. From sub-cultures, inoculations were made on rabbits and dogs.

In 6 out of 7 rabbits and in 1 out of 2 dogs certain nerve degenerations occurred, especially noticeable in those supplying the hind-limbs.

The conclusion they came to was, that this organism, which they termed "the white micrococcus", was the true cause of Beriberi, entering by the respiratory tract, infecting the blood and requiring repeated introduction to produce the disease.

CRITICISM.

The fact, that there were only 9 positive results out of 80 cases, in which blood infection was ascertained beforehand, casts grave doubts on the accuracy of their conclusions. Further in the inoculated animals

degeneration of certain nerves was considered positive evidence of the disease, while other clinical and pathological features were ignored or at least not recorded.

(b). Gerard's Micrococcus.

Later Gerard of the Federated Malay States Medical Service carried out similar experiments to the above and supported the observations of Pekelharing and Winkler. As a result of these he isolated two forms of micrococci, one forming a white colony, held to be the same as described by the two Dutch observers, and the other forming a golden-tan coloured colony. The two varieties, he held, being in some way connected with the two principal forms of the complaint.

(c). Dangerfield's Micrococcus.

Again in 1905 Dangerfield, published a treatise on the subject showing, how he had obtained cultures from the blood of Beriberics pricked through the skin. He maintained, that the disease was both infectious and contagious. As in the case of Pekelharing and Winkler, he sought to substantiate his conclusions by experimental inoculation of animals, and produced in some paralytic symptoms similar to those of Beri-beri. He also found the same organism in the Gastric contents, removed by the stomach tube, and later in the Sputum and Foeces, as well as the air and the soil. In his treatise on the subject he gave a full account of the morphological characteristics of this organism.

Dangerfield was especially struck by the constancy of digestive disturbances in all cases of Beri-beri, and by the presence of pathological lesions in the Gastro-intestinal Tract.

(d). Okata and Kokubo's Kakkecoccus.

The consideration of Bacteria found in the blood would be incomplete without a reference being made to the paper published by Okata and Kokubo in connection with work done on the subject of Beri-beri, amongst the sick during the Russo-Japanese War.

The material at their disposal was enormous, and it is not generally known, that at a minimum the cases numbered from 75,000 to 80,000: in fact the abrupt termination of the war, and the acceptance of terms scarcely in accordance to the position obtained, was entirely due, according to a high Japanese military authority, to the fact, that those in power realized that the rate of increase of cases of Beri-beri was getting beyond all control, and that it was this and not pecuniary difficulty, that decided the ultimate issue.

Kokubo's method of taking the blood was as follows, and as it is worthy of note I quote his own words-----"An area on the back over the Trapezius muscle was cleansed antiseptically and a puncture made with a sterile needle. A fold of skin was then raised, between two fingers of the operator's cleansed hand and firm pressure applied."

Although direct puncture of the median cephalic vein was suggested, Kokubo refused to employ this method.

These observers then isolated an organism, to which they gave the name of "Kakkecoccus". It was found in the blood of 129 cases, partly by microscopic examination, partly by culture and partly by both means, and was described as being both intra- and extra-cellular. Usually it was grouped as a diplococcus, but occasionally in bundles like staphylococci and even in streptococcal chains. The micrococcus was never abundant, being about one to a field; it stained well with Aniline dyes, such as Loeffler's Alkaline Blue and especially by the method of Semenowicz and Marzinowsky (a combination of Zeill and Loeffler's methods).

Cultures.

Agar-agar. Temp: 37°C, greyish growth visible in 12 hours, becoming yellow later.

Broth. Cloudy in 15 hours, later a very shiny grey deposit.

Celatin. Grey growth becoming yellow in 3 weeks, no liquefaction.

Blood Serum. Rich grey culture in 18 hours, spreading laterally in an arborescent form.

It does not ferment sugar, grows in Milk without coagulation of the casein, and does not alter litmus.

They succeeded in finding a similar organism in the Urine and Focces of patients suffering from Beri-beri, this will be referred to later under Herzog's experiments. In the Japanese military service autopsies can only be

done with the special permission of the dead man's family, this is rarely granted, and so the number of Post-mortem Examinations made by these observers was extremely limited. Okata however in one case isolated the Kakkecoccus from the Kidney and the Cerebro-spinal Fluid. Further they experimented with animals, injecting them intra-peritoneally and subcutaneously, but without very definite results: rabbits, pigs, and white mice were all tried and several died; (3 out of 19 rabbits, 17 out of 64 white mice), but the doses in the fatal cases were very large and no statement was made as to the condition of the peripheral nerves.

Finally Kokubo claimed to have prepared an antiserum from injected rabbits, which in two hours caused agglutination of 1 in 100.

Criticisms.

Many can be raised against the methods employed in this investigation. The mode of obtaining the blood by puncture through the skin, which is firmly squeezed, is altogether unsatisfactory. The absence of sufficient post-mortem data in cases that died, and the neglect to report on the state of the peripheral nerves in the animals, that succumbed, are also unfortunate omissions. Lastly it must be remembered, that acute pernicious forms of the disease did not come under observation, but died at the front.

Experiments at Christmas Island.

Before leaving the subject of the various bacteria found in the blood in cases of Beri-beri,

may I state briefly the experiments, that I carried out in
out in Christmas Island.

Working in the small laboratory at my disposal,
and using the strictest precautions, I was unable at
any time to obtain cultures from the blood; it is true
that occasionally a growth did occur in the media, but
this was proved to be accidental, being caused in al-
-most every case by the Staphlococcus Pyogenes Albus.

At the commencement of the investigation I
determined to approach the subject on the following
lines:-----

- (1). To make cultures from the blood, urine and
cerebro-spinal fluid of typical cases of Beri-
-beri of all forms and at various stages of the
disease.
- (2). To make several controls from the blood of
healthy persons.
- (3). To withdraw the blood from the Median Basilic
Vein, after careful sterilization of the skin
by means of Iodine. To do this with a sterile
needle, and to inoculate the media direct from
the needle without using a syringe.
To withdraw the urine by means of a sterile
catheter, and to obtain the cerebro-spinal
fluid by means of puncture between the second
and third Lumbar Vertebrae.
- (4). To use broth carefully sterilized and neutral-
-ized as the media, and to make sub-cultures
on Agar and Blood Agar.

(5). To inoculate animals and fowls with the subcultures and also directly with the blood and cerebro-spinal fluid.

By such means it was hoped, that should any causal organism be present in the blood, it would not be missed, and at the same time, that extraneous contamination would be avoided as far as possible.

I do not of course lay any claim to originality in these experiments, but, as shown already, so many observers have in the past discovered organisms in the blood, and this has been denied by so many others, that it seemed to me to be worth while to convince oneself by personal investigation of the matter.

In all 30 cases of Beri-beri were taken:

- A. 10 shewed only the very earliest symptoms of the disease::
- B. 10 were well marked cases:
- C. 2 were acute pernicious cases:
- D. 8 were cases of considerable duration, who had had previous attacks.

Controls were made from 12 healthy men.

Further the cerebro-spinal fluid was taken from 12 of these cases, the urine from 20 and the pericardial fluid from the 2 fulminating cases.

RESULTS.

BLOOD. Out of 30 cases the blood was sterile in 27.

Of the three cases, that gave a growth, 2 were chronic and only one was a well developed instance of the disease. The growths were alike and indistinguishable from that of Staph:Pyo:Albus.

Out of 12 healthy persons 10 tubes were sterile, and 2 were infected, one with Staph: Pyo: Alb: and the other with Staph: Pyo: Aureus.

CEREBRO-SPINAL FLUID. Growth was obtained in only 2 out of 12 cases, and was again due to the common pyogenic organisms.

PERICARDIAL FLUID. Sterile in both cases.

URINE. In 12 cases the media remained sterile and clear. In the remainder (8) cloudiness of the broth occurred, and subcultures shewed a variety of different organisms, Staph: Alb: and Aur:, Streptococcus, and Micrococcus Tetragonus being recognized.

It must be pointed out, in extenuation of the fact, that the results were not absolutely uniform, that in order only to employ suitable cases, these investigations were spread over a considerable period (18 mths). Also, though as far as possible freshly prepared media was used, it was not always possible to do so; and finally, that, working under somewhat amateur conditions, in a climate like that of Christmas Island, where all year round the temperature is almost that of an incubating chamber, the most careful technique is apt to be uncertain.

In any case I felt convinced in my own mind, that with due care the blood and cerebro-spinal fluid of cases of Beri-beri can always be shown to be sterile on ordinary media, and that the infected tubes in my experiments were due to some negligence on my part during the process of inoculation. This is further

substantiated by the fact, that the resulting growths were not similar to each other, and corresponded too closely to the appearances of well known pyogenic organisms to have any importance attached to them whatever.

These results did not encourage one to proceed with the further inoculation of animals, and no injections were given from the sub-cultures. Direct inoculation with the blood of well marked cases was however attempted. Fowls were injected sub-peritoneally with all aseptic precautions, and the results were absolutely negative: the birds showed no change at all though receiving repeated doses, and in a similar manner 2 Guinea-pigs proved to be unaffected.

A dog injected with cerebro-spinal fluid shewed distinct paresis of the hind limbs for a period of 12 days, which passed off completely; this experiment was unfortunately complicated by the fact, that he was bitten by the monkey referred to in the next paragraph.

The only really positive result was in the case of a monkey, inoculated with an emulsion, made immediately after death, from the affected nerves of a patient, who had died of the acute pernicious form. In this case a creeping paralysis occurred, similar in type to Landry's and terminating in death. However it is unfortunate, that in this experiment too, an opening for error to occur was allowed, for the animal was receiving at the time a "Beri-beri diet". This will be referred to again later on.

B. Bacteria found in the Urine.

(a). Herzog, as a result of seeing the work of Okata and Kokubo on their specific organism, carried out at Manilla a number of careful experiments on a variety of media. He isolated the "Kakkecoccus" from the urine, and inoculated 12 monkeys (*Macacus cynomolgus*) with absolutely no results, the animals remaining strong and well. Similarly experiments with guinea-pigs were negative; a number of rats treated in the same way however did die, but with none of the characteristic symptoms of Beri-beri.

Still he came to the conclusion, "that the disease is infectious and not due to nutritional disturbance, and that whatever the mode of axis to the body might be, it there produced a toxin, which caused the characteristic lesions." (Herzog)

access

(b). Another observer, Tsuzuki, has also found a diplococcus in the urine, and named it the "Micrococcus Beribericus".

It exhibits the following characteristics:---

On Agar small almost transparent colonies in a week, clots milk and ferments sugar. Is non-motile and stains with Gram.

He isolated the organism from the urine in 28% of cases and also found it present in the foeces. By means of inoculation of animals, he produced symptoms analagous to the disease in man, and proved microscopically after death certain degenerative changes in the nerves.

To a certain extent this theory is upheld, from a therapeutic point of view, in a paper published by Miller and Turner in the Transvaal Medical Journal, in which they pointed out, that their cases of Beriberi improved markedly under the administration of Urotropine in 5 grain doses well diluted in water three times a day.

I have referred already to my examination of the urine, which almost invariably proved to be sterile even after incubation for two weeks, and I ought to mention, that neuritis of a degenerative type may constantly be set up in these experimental inoculations by the presence of more or less long-standing septic processes.

C. Bacteria found in the Alimentary Tract.

(a). Hamilton Wright's Bacillus.

This author, from work done in the Federated Malay States published his results to shew, that the specific organism of Beri-beri gained entrance by the mouth and developed chiefly round the pyloric end of the stomach and the duodenum, causing a Gastro-duo-Duodenitis, from which a toxin was absorbed, which caused the characteristic nerve lesions. He also maintained, that it was passed in the faeces, lodged in the surrounding dust and under congenial conditions sustained its vitality, till it once more gained access to the body in the food. He was unable at any time to obtain the organism from the blood, but in a limited number of cases he found it in the tissues.

Wright described the organism, as a square-ended bacillus. He also sought to substantiate his theory by pointing out, that Beriberics invariably at the Onset of the disease complain of Epigastric pain and other abdominal symptoms; while Post-mortem Examination of cases, that die rapidly, always show injection and punctiform haemorrhages round the pylorus and duodenum.

He also fed monkeys on fruit, which had been rubbed on the floors of dirty cells, in which Beriberi patients had lived, and by this means did succeed in causing a polyneuritis in a certain number.

In 1906 the same observer published notes on a case of Acute Cardiac Beriberi, that died at the Seaman's Hospital in London, in which he found a similar necrosis of the gastro-duodenal mucosa, and from the sloughs of which he obtained the same organism.

This bacillus is described as being Gram-positive and staining with ordinary basic stains. Inoculated media showed a growth in 24 hours, the organism growing best on glucose agar stabs. Lastly injection of a guinea-pig subcutaneously with a Broth emulsion produced positive results. Paresis of the hind limbs occurred, ending in death, but on microscopical examination only a few degenerated fibres in the nerve twigs to the flexors of the hind limbs were discovered.

After studying the work done by Wright one is struck first of all by the fact, that the positive cases were all those of the Acute Cardiac Type. I think, that some such organism as he isolated may quite easily

be the causal agent of this type, for I have come to believe, that this complaint is not merely one of the forms of Beriberi, but is per se an entirely separate disease. If one has to consider this bacillus as the cause of all the forms of the disease now known as Beri-beri, I have no hesitation in denying, that it can be, and would offer the following criticisms on these deductions.

- (1). It is quite contrary to my experience to find, that all Beriberics complain of abdominal symptoms, it is almost more the exception than the rule. Many well marked cases never have any vomiting, nausea, dyspepsia or epigastric pain.
- (2). If this bacillus gains access to the body by dirt infection, why is it that the Tamil coolies so notoriously filthy in their habits escape, while the Chinese, who wash daily, are affected in such large numbers ?
- (3). If this bacillus is found in the stomach and upper duodenum, it must require an acid media for its growth and the developement of its toxin; how then can it be isolated from the foeces, after being so long in contact with alkaline surroundings ?
- (4). The polyneuritis found in the infected monkeys differed, according to Wright himself, from that found in man, and as Durham pointed out was probably due to septic absorption. For all the animals were in a most unhealthy condition and several in a similar state, that had never received the dirt-contaminated dietary developed

precisely the same degenerative changes.

(b). Durham's Throat Organism.

This investigator advanced the view, that the tonsils were the probable mode of entrance of the specific virus, for he noted, that in nearly all early cases, there was redness of the fauces unassociated with any tenderness or enlargement of the glands. Smears on Agar from the throats of such patients produced after 48 hours a large number of peculiar looped colonies, almost to the exclusion of any other growth. The organism was somewhat streptococcal in appearance, was non-motile, had a capsule and stained by Gram's method.

His attempts to obtain sub-cultures were failures, and he was unable to find the organism in the dust of prison cells or from the dead bodies of those, who had fallen victims to the disease. He came to the conclusion finally, that Beri-beri was communicated directly, as an actual poison, from patient to patient.

He attempted to produce the disease in monkeys (*macaceus nemestrinus*) by irritating the throat, and smearing over it the mucous, taken from the throats of Beri-beri patients, and also with prison dust. He also introduced into their food the scrapings of the alimentary tract, taken from an acute case of Beri-beri immediately after death.

All these proved absolutely negative.

I made it a routine practise to examine the throats of all cases coming under my care, and did not find redness of the fauces to be in any sense universal and often so slight, that it might well have been accounted for by some slight excess in smoking. Also the redness was present to quite an equal degree in those, who had not and never had had the disease. The failure too of all experimental inoculations detracts very largely from the plausibility of this theory.

Daniels, I may mention here, from work done at Kuala Lumpur, considered the disease to be an infectious one. He maintained, that there was no definite proof, that an intermediate host was required, but considered the disease was not carried by earth, air, water or food. He stated, that the last might have some effect on the susceptibility of a patient, but was not the causative agent. If an intermediate host was required, Daniels suggested, that it was either a Cimex or a Pediculus and most probably the latter.

Such then are the more important of the many organisms, that have from time to time been brought forward, as the specific cause of Beri-beri. Before discussing the relative importance of the toxi-infectious theory, it may be as well to propound the views of those, who hold by the alimentary theory, so that a comparative study of their respective claims may be better considered.

5. ALIMENTARY THEORIES.A. Deficiency of Fat.

This view has now, I think, been abandoned by everyone. It was first introduced by Laurent, because he found that two epidemics of Beri-beri, one at Chant-aboim in Siam and the other at Poulo Condor, ceased almost immediately on increasing the amount of Fat in the daily dietary. Experiments to substantiate this have since been tried by many observers in Japan and Malaya, and have invariably shown that there is nothing in this theory at all, and certainly it would fail to hold good for those cases which came under ones immediate care at Christmas Island; a glance at the Dietetic Tables being sufficient to show, that there was always abundance of Fat.

B. Nitrogenous Starvation.

Takaki introduced this hypothesis, on the strength of the enormous and extraordinary reduction of cases of Beri-beri in the Japanese Army and Navy after the alteration of the fixed diet by the introduction of a higher percentage of Nitrogenous substances. But unfortunately for this theory the diminution in the number of cases was universal, while the alteration in the diet was purposely local; further similar dietetic alterations were made in the Singapore Gaols, and were not followed by any such excellent results at all. Likewise at Kuala Lumpur Wright

increased the ratio of Nitrogen to Carbon in the food from the normal 1 in 15 up to 1 in 12, and continued this for 8 months. Cases of Beri-beri occurred just as frequently during the later months as before the alteration.

Again here, as in the case of the last theory, a glance at the appended Dietetic Tables (3) will show that as far as the coolies on Christmas Island were concerned, such a theory fails altogether to meet the case in point. It is interesting to note, that in this place we were occasionally, when communication failed, cut off from Singapore and the food supplies suffered accordingly, but at such times Beri-beri actually showed a diminution in the number of cases and not an increase.

C. Fish Theories.

Various workers have claimed, that in Fish was to be found the true cause of Beri-beri:-----

GULPKE thought, that certain forms of dried fish so much eaten by the Chinese, Malays etc was infected by a Trichina.

GRIMM that it was due to some sort of infected fish just dried in the sun until about to putrefy.

MIURA considered that it was the result of eating certain kinds of raw fish, blaming chiefly, that family known as the Scombres, of which the Mackerel is a common type.

VODERMAN, on the other hand, noted a brick-red sort of

pellicle on certain fish, which were being largely consumed by coolies amongst whom Beri-beri was rampant. This pellicle seemed to be of the nature of a parasite; Durham examined it, and found it to be a sarcinae of brick-red colour with quite non-pathogenic properties.

But, I think, that the question of Fish has now been definitely settled. As an article of diet it has been eliminated for months from the dietary of certain institutions, and yet cases of Beri-beri have continued to occur, unabated in the least degree. Such a trial was carried out by Wright at Kuala Lumpur, and has since been confirmed by many others.

I have seen coolies develop Acute Beri-beri, who to my certain knowledge disliked fish, both fresh and dried and never ate it.

It is interesting to note too as a minor point that this disease is rare amongst fishermen.

In 1880-1881 Le Dantec saw an epidemic of this disease cease altogether at Poulo Condor by the addition to the daily food supply of a small quantity of fresh fish.

D. RICE THEORIES.

(1). I think one of the earliest observers to advance the theory, that Rice was the fons et origo mali was Hose of Borneo, who had himself suffered from the disease. He held that Beri-beri was due to the ingestion of mouldy rice. He noticed that the women, who lived in the villages and ate freshly husked rice escaped, while the men, who went often on long expeditions into the interior in search of rubber, and who in consequence ate rice which was often very stale and mouldy frequently fell victims of the disease.

Hose made microscopic examination of this mouldy rice, and discovered a minute fungoid growth, which he thought was the probable causal agent. To prove this he carried out certain experiments with monkeys (*Macaceus nemestrinus*) and fowls, feeding them on bazaar rice. He produced in them certain symptoms of debility and weakness.

These experiments were substantiated later at Tokio.

While this theory is of great interest in the light of subsequent research, it cannot be said to be altogether satisfactory. Beri-beri constantly develops in communities where the quality of the rice is above reproach, also in gaols and elsewhere the method of cooking employed would be quite sufficient to destroy any activity of a mould on the rice: in a like manner natives do not eat uncooked rice.

Further his experiments on monkeys were quite inconclusive, because the principle symptoms of per-

peripheral neuritis were absent, none displayed any oedema and only two shewed "lack of energy". In the case of the fowls the results were more conclusive, but analagous conditions to Beri-beri can apparently be produced in fowls in a number of ways, I have already refered to Trentlein's experiments with oxalic acid and will have more to say on this subject later on.

(2). Braddon's Specific Fungus affecting 'uncured' Rice.

Braddon, independant of the work done by Hose, has for long held, that Rice is the chief factor in the production of Beri-beri and has most clearly and convincingly stated the reasons for his views in his book " The Cause and Prevention of Beri-beri ". In this he cites a large number of facts in support of his contention.

Stating it briefly Braddon was first struck by the extraordinary prevalence of Beri-beri amongst the Chinese coolies in the estates and mines of Malaya, while the Malay, Tamil and Kling coolies working in the same places to a very large extent escaped. Then he noted, that while all consumed rice as their principle article of diet, the kind of rice eaten differed. The Chinese ate a rice to which he gave the name of "uncured", while the Tamils, Malays etc used, what he termed "cured" rice.

That this immunity was not due to any racial

insusceptibility was at once proved by the fact, that both Malays and Tamils, when given "uncured" rice in gaol, develop the disease as readily as the Chinese.

The conclusion therefore was that Beri-beri could be shown to be due to the form of rice eaten; the probability being that a toxin was developed in it by a germ attacking the grain; the process of preparing the "cured" rice destroyed the germ, but ^{that} the toxin developed in the "uncured" rice was not destroyed by the process of cooking.

Varieties of Rice.

Before going further in the consideration of this matter let me describe, what is meant by the different terms applied to rice; a considerable amount of confusion has arisen in consequence of the varied nomenclature. The actual named varieties of rice are of course very numerous, and are only of interest to the expert, but there is another classification quite independent of this Botanical one, which refers to the process of preparation through which the rice passes subsequent to harvesting and prior to being cooked.

Rice is a single seeded grain consisting of an ovule covered by a layer known as the episperm, and outside of this comes the mesocarp and epicarp. These three layers (episperm, mesocarp, epicarp) form what is commonly known as the pericarp, and outside of all enclosing the whole are two glumes, which form the Husk. The surface of the ovary is covered by the

aleurone layer, where the gluten is stored.

The composition of different forms of rice vary; the following analysis for boiled rice is given in Hutchison's book

WATER	52.7 %
PROTEID	5.0 %
FAT	0.1 %
CARBO-HYDRATE	41.9 %
MINERAL MATTER	0.3 %

Rice is only moderately easily digested, but is absorbed with great completeness; its nutrient value is obviously much detracted by its poorness in proteid and fat.

Examination of rice in use nearly always shows the presence of various fungi, and in addition constantly contains weevils and lepidopterous larvae of different species varying according to the rice.

Form (1). PADI or the unhusked grain.

This is simply the grain that is dried after harvesting and stored in the villagers' houses in bins. When it is required for use a small quantity is taken, pounded in mortars and winnowed by hand. Before cooking, the rice is copiously washed with water to remove dust or anything that would tend to make the grain stick together; this also enables the cook to remove any diseased grains, that float, and also to pick out any badly coloured ones.

This method is largely employed by the poorer classes in India, and also in the villages in the

Malay States, and I believe I am correct in stating, that there has never been a case of Beri-beri reported amongst those, who eat rice prepared in this manner. Of course the disadvantages of this method, where large quantities of rice are in daily use, are obvious.

Form (2). "UNCURED" RICE.

This is also known as "white rice" or as "Siam rice", and is the form at present consumed by Chinese coolies all over the Malay States, the Straits Settlements, French Indo-China and the Dutch East Indies and also in such places, as Hongkong and Canton, which are easily accessible to shipping.

The grain is taken to the mills and husked by machinery between revolving mill-stones; it is then polished by rounded stones revolving rapidly against fine wire gauze, until it is of a clean white pearly appearance.

This method can be seen in daily use in the mills at Rangoon, Penang and Singapore.

As a result of this process two heaps are piled up on the ground floor of the Rice mills, one consisting of the white rice and the other of a fine brown bran, the rubbed-off pericarp, known sometimes as "rice meal" or "rice dust". This bran is largely exported from Rangoon to England to make cattle cakes and is sold extensively in Singapore as being the best pig's food.

The term "Siam" rice applied to this form is most misleading for the grain comes as much from Burma as Siam, and large quantities are grown in Province

Wellesley and the Federated Malay States. Therefore it is much less confusing to adhere throughout to a term, which can be used irrespective of where the rice was produced; hence the name "uncured" rice, adopted from Braddon's nomenclature, is probably as good as any.

Form (3); "CURED" RICE

This is also known as "red" rice or "Indian" rice or "parboiled" rice, and is prepared in the following manner:---

The 'padi' is soaked in water for ^{from} 12 to 24 hours, and then heated in vessels containing water over a slow fire until the husk bursts; it is then spread out in the sun and dried. After the drying is completed, it is husked by pounding (the husk separating very readily), or is sent to a mill where it passes through the revolving millstones, but not over the wire gauze.

The result is a grain, which has a distinctly reddish appearance due to the fact, that the aleurone layer, so rich in gluten etc, has not been removed.

The sole difference between these two forms of rice is that, one has been polished till nothing but the actual grain (ovule) is left, presenting a finished article white and pleasing to the eye, the whiter it is the more highly is it appreciated, while the other passing through a different process is not so highly polished, retains the aleurone layer and has a dirtier appearance.

Again I lay stress on the fact, that the term "Indian" is a misnomer and most ~~unfortunate~~

erroneous, for much of the so-called "Indian" rice is grown in Siam and elsewhere; in fact "Indian" and "Siam" rice may be seen growing together in the same field.

So the term "cured" though not altogether satisfactory, will be used as referring to rice put on the market after passing through this mode of preparation.

I have described the method I saw employed in India, but I believe there are some minor differences in other places. In Penang it was however very similar, but I should mention, that in this place the grain is often left soaking in water for a very long time, in fact I have seen it commencing to sprout, it is then heated or steamed for often no longer than 8 to 10 minutes.

Hence when one applies the term "cured" to this mode of preparation it is not intended to convey any idea of sterilization, though this has been claimed for it, because the rice is never heated to a sufficiently high temperature to kill any organisms. In fact it frequently looks mouldy and dirty and I was informed that innumerable moulds and bacteria have been cultivated from it.

Such then are the ways by which rice is made ready for consumption and the whole significance of the question of rice as the cause of Beri-beri depends on fully appreciating these initial differences in the mode of preparation.

To return then to Braddon's theory, it would serve no purpose to retail at length all the mass of facts he brings forward in support of it. All of which go more to prove the hypothesis, that rice is "uncured" is the actual mode by which the infection of Beri-beri is introduced into the system, than to uphold the corollary, which he advanced, that it is caused by a poison found in rice, which is the the result of the specific product of some organism, epiphyte or parasite.

Though unwilling to enter into the matter at greater length yet it may be as well to briefly recapitulate in order the points, which led up to his deductions:---

(a). Beri-beri must be due to a defect in the dietary, as all bacterial and infectious theories are incompatible with the known facts.

(b). It must be due to some form of grain intoxication----(note) the close analogy between Beri-beri and Ergotism----

(c). The only grain censurable is rice, because it is the staple food of the inhabitants of the area of endemicity of Beri-beri, and the distribution of the disease agrees generally with the distribution of grain drawn from those areas.

(d). All Beriberics eat rice and vica versa these who do not eat rice do not get Beri-beri.

(e). But all who eat rice do not get Beri-beri

for instance the disease is rare in China, where millions eat nothing else; and in India, where it forms the principle article of dietary of an enormous mass of the population the disease is very infrequent.

- (f). Therefore it must be due to a certain form of rice eaten.
- (g). The chief cause, in specializing the various forms of rice eaten, is the mode of preparation. The toxicity, therefore, must depend upon this and by a process of elimination "uncured" rice is the form which is most culpable.
- (h). The "uncured" rice is deprived of its natural protection, and so becomes an excellent medium for saprophytic growth, the poison being adventitious and only arising after decortification. On the other hand the "cured" rice retains this protection and its mode of preparation is such that any germs present--" would be made first to germinate and then in that vulnerable stage be destroyed by heating. The process is, roughly, and under open air conditions, in fact, such as is daily resorted to in every laboratory to sterilize or render free of noxious germs, various materials, which may contain them!

(BRADDON)

- (j). The incidence of Beri-beri varies with the quantity of " uncured " rice consumed, and the number of cases persists as long as this form of rice is eaten, and diminishes progressively

when it is discontinued:.

(k). As regards the nature of the toxic agent:---

(1)."The poison is probably an alkaloid stable and non-volatile!

(2)."The formation of the poison in stale rice is probably due neither to fermentation nor to bacteria, but to the growth in it of a special fungus!

(3)."The fungus is probably a surface parasite or epiphyte affecting the seed saprophytic-ally after decortication!"

(BRADDON)

Such then is the process of reasoning by which Braddon arrived at his conclusions and upon which he formulated his theory. The great value of the work lies in the enormous amount of evidence, which he accumulated to prove the all-important part "uncured" rice plays in the production of this disease. The conclusions arrived at in this respect are supported by definite facts, but the corollary to the theory, which explains what it is in the "uncured" rice, that is responsible for its toxicity, leaves the region of facts and enters that of the theoretical. There is one very strong objection, that can be raised against this explanation of the toxicity of this particular form of rice.

In the above summary I have at one point quoted Braddon's exact words in inverted commas, in which he

maintains, that the process, through which the "cured" rice passes, would be efficient first of all to germinate and then to destroy the specific growth, in fact a means of sterilization. But anyone, who has seen the process, while agreeing as far as the germinating part is concerned, would hesitate to acquiesce to the conception of sterilization; for as shown earlier in this thesis the rice, which has often lain in water until it is sprouting, is then heated often for only from 7 to 10 minutes and never to a height sufficient to ensure sterilization; the temperature being that of a comfortably warm poultice and tending rather to encourage than to exterminate the growth of any bacteria.

Amongst other observers, who have held that in rice is to be found the cause of Beri-beri, one should mention the names of two, who have done special work on the subject.

- (1). EIJKMAN experimented with fowls feeding them with rice and came to the conclusion that the poison was an inherent property of the rice seed as apart from the raw grain or 'padi', and that ⁱⁿ the pericarp a natural antidote was supplied to the poison of the seed.
- (2). Van DIEREN, who from the first held that the poison causing Beri-beri was contained in decorticated rice, published a book which embodied this view and substantiated

it by the quotation of a number of cases, in which the alteration in the dietary of "cured" for "uncured" rice was followed by surprisingly good results. He also laid stress on the close analogy between Beri-beri and such diseases as Pellagra, Lathyrism and Ergotism.

All these tend more and more to convince one of the undoubted culpability of "uncured" rice, but the reason of its toxicity is not shown satisfactorily by any of the theories we have considered.

(C). SALDANHA'S ARSIN THEORY.

In 1908 Saldanha published a paper giving his views as to why the "uncured" rice is so toxic. His work was done amongst the Chinese ^memigrants in the Transvaal. At first there were a large number of cases of Beri-beri with a high mortality, but after the introduction of "cured" rice there were practically no cases of the disease, although as many as from 50,000 to 60,000 coolies were being employed.

His theory is that rice is attacked by a fungoid disease, the active principle of which he called "ARSIN" (Tamil---arsin = rice).

This arsin during the "curing" of the rice undergoes fermentation and by doing so becomes inert. On the other hand the "uncured" rice retains its arsin in an active condition, chiefly in the fine bran which is not removed by winnowing,

When the "uncured" rice is eaten and especially

if the water it is cooked in is drunk as well, as it so often is, the consumer on each occasion takes into his system a small dose of arsin.

The result of this consumption of arsin in the food is, that in some cases diarrhoea is caused by which method Nature expels the poison and saves the system, or that in other cases the arsin accumulates ~~in the system~~ and eventually sets up all the symptoms of Beri-beri. This points to the poison being cumulative, and so in that respect this theory falls into line with the original bacteriological investigations of Pekelharing and Winkler, who laid particular stress on the fact, that the poison of Beri-beri must be constantly reintroduced into the system.

~~maintained.~~

Saldanha that the initial action of arsin is that of a cardiac sedative, further he asserts that rice containing arsin, when boiling, emits an alliaceous odour, the inhalation of which causes a sensation of fulness and exhilaration analagous to alcohol in small quantities.

The predilection of Beri-beri for certain ships is due to the fact, that, although the holds are emptied before a new supply of rice is stocked, the rice bran remains in the cracks and corners and infects the fresh consignment. I am unwilling at this point to enter into the discussion of Ship Beri-beri, but I cannot think that it can be explained by this method of reasoning. I am doubtful as to the existence of this so-called predilection, and in any case I have seen a

slight amount of arsin and a small quantity of rice-

ship's hold most thoroughly and conscientiously disinfecting in a manner that would have done justice to a surgical theatre and yet, I have learnt later, that Beri-beri has broken out amongst the crew.

But to return to the arsin theory, if one works on the lines of this hypothesis one will at once note that Beri-beri and Ergotism (from the eating of rye bread) lie in a much closer relationship to one another than Beri-beri and Scurvy.

This theory is in many ways an extremely plausible one, and it is certainly another positive proof of the value of eating "cured" rice, but, before accepting it as the actual cause of this disease, further research on these lines would have to be conducted with the isolation of this active principle "arsin", and inoculation experiments with the same. For as it stands the blaming of the fine rice bran, as harbouring the active principle, is in direct contradiction to the original results obtained by Eijkman with his fowls, and to the most recent of all researches conducted by Fraser and Stanton.

(D). FRASER and STANTON'S THEORY of PHOSPHORUS
DEFICIENCY.

These two observers first carried out a series of experiments to prove for themselves the truth of Braddon's theory, that it is the "uncured" rice that is at fault.

One of these experiments is of such great interest and so conclusive in its results that I will refer to it here at some length.

Two parties of men were placed under similar conditions, as to environment, and the food supply was under direct control.

To obviate any sources of error in the experiment it was desirable, that they should be working in an area previously uninhabited, where no Beri-beri had existed and removed at such a distance from any town or village, that infection could not occur in that way. For the same reason the men engaged in the work would be unable to obtain any additional food to that supplied to them.

These conditions were admirably obtained in the state of Negri Sembelan. Three hundred Javanese coolies were divided into two approximately equal parties and employed in road construction.

The quarters erected for their use were well made, well ventilated and dry; they were raised off the ground and on an open space prepared by clearing virgin jungle; in a like manner every care was taken to see that the sanitation was all that could be desired. The daily dietary was a full and generous one consisting of Rice, Salt Fish, Onions, Potatoes, Cocoa-nut Oil, Tea and Salt. All the men were examined carefully and Beri-beri excluded before they were allowed to go to work; also a suitable interval was allowed to elapse before the experiment was started.

Several conclusions were drawn from the results obtained.

RESULTS

20 cases of Beri-beri occurred out of the 220 men fed on " uncured " rice, this excludes a number which in ordinary practise would probably have been recorded as Beri-beri, for they shewed some of the symptoms of the disease but not very definitely.

.....

No cases of Beri-beri occurred out of 273 men fed on " cured " rice, nor did any of the slighter forms appear which have just been mentioned as being excluded from the list of those on " uncured ",

.....

Amongst the cases of Beri-beri none occurred sooner than 87 days after the commencement of the " uncured " rice; this of great interest in considering the incubation period of the disease.

.....

Further patients suffering from Beri-beri were brought into contact with those eating " cured " rice, but no cases occurred amongst the latter; this seems to be a strong point against the view that the disease is directly communicable.

.....

Again, patients suffering from Beri-beri, when removed from the place where they contracted the disease, showed no improvement, as long as they continued to eat the " uncured " rice; this is a distinct argument against

'place' infection having any influence on the development of the disease.

.....

Lastly, if Beri-beri broke out in a party and "cured" rice was substituted for "uncured", there was at once a cessation of the disease and no further cases occurred.

.....

This experiment is of the importance, because it was carried out in a manner, which excluded many of the possible fallacies urged against similar dietetic trials in the past, and throws a lot of extra light on the etiology of the disease.

Having thus satisfied themselves, that in "uncured" rice was to be found the cause of Beri-beri Fraser and Stanton determined to investigate this point more closely, and conducted a series of most interesting experiments with fowls. Personally speaking I had the pleasure of seeing these experiments at Kuala Lumpur and confess, that to ones own mind they carried with them the most absolute conviction.

Their first efforts were to see if they could possibly extract from "uncured" rice (which had been directly associated with an outbreak of Beri-beri) any substance, which by chemical means could be detected as poisonous: this they failed to do.

Then it struck them that there might possibly be some defect in the nutritive quality of this particular form of rice, and this induced them to carry out certain experiments with fowls; for it was found that rice, which caused Beri-beri in man, set up a polyneuritis

in fowls. They laid great stress on this, that in the meantime it is immaterial whether or no the disease in fowls (Polyneuritis Gallinorum) is analagous to that in man. The whole point being, that certain rice can be shown to set up a reaction in fowls, and that this can be taken as an indicator of the Beri-beri producing power of that rice in man. For rice which was actually being consumed during an outbreak of Beri-beri at the Kuala Lumpur Police Depôt was found to produce in fowls the distinguishing reaction.

A comparison of the analyses of the various forms of rice showed, that of the three main constituents of food, the only one that was materially at variance was the amount of Fat present; this being least in the "uncured" Siam rice. But Fat Deficiency, as already shown, had been proved to have nothing to do with the causation of the disease, so they turned their attention instead to the mineral constituents of the grain.

By a special method they were able to cut and stain sections of the rice of such thinness, that their histological characters could be studied. It could then be clearly demonstrated, that in the "cured" rice remnants of the pericarp remained attached to the grain, which in the case of the "uncured" had been polished away. The layer retained in the "cured" rice contained most of the aleurone and oily material present in the grain. Experiments then showed that whereas fowls fed on "uncured" rice developed the "reaction", those fed on "cured" rice or on "padi" milled by primitive

methods did not succumb. Further "cured" rice could be rendered as toxic ~~as~~ toxic as "uncured", if it were first subjected to exhaustion with alcohol and then carefully dried in the sun to free it from the alcohol. That is to say, that rice, which had previously been proved to be non-toxic, became after passing through this process toxic to fowls; something had been removed from the rice, which was essential to prevent polyneuritis in these birds.

Also fowls fed on the "uncured" rice from the same bag, as had set up the "reaction" in some other fowls, had this food supplemented by an emulsion made from the rice 'polishings', which was introduced into their crops, and none of them developed the "reaction".

In case the "reaction" caused by the "uncured" rice was due to staleness, fresh "uncured" rice was obtained daily with exactly the same results. This seems to discountenance at once the idea, that the harmfulness of "uncured" rice is due to the development in it of a poisonous substance subsequent to milling.

If now fowls were fed on "uncured" rice already proven to be harmful, and to this diet there were added the emulsified residue (extracted by-- and freed from alcohol) from the "cured" rice, it was found that no "reaction" occurred.

It might with justification be urged, that the use of alcohol to extract from the "cured" rice the properties, whose absence rendered it toxic,

and the nature of the substance by which the substance is

opened a possible means by which the subsequent polyneuritis was produced; but this contention is proved to be invalid, because the very substance, which was extracted by the alcohol, when freed from it by drying in the sun, was able to prevent the "reaction" occurring in fowls, who were eating "uncured" rice of known toxicity.

What then was the difference between the two forms of rice in use ?

After some attempts to estimate the lipoids, Fraser decided to turn his attention to the amount of Phosphorus as Phosphorus pentoxide (P_2O_5). The most interesting fact soon became apparent that the rices, which produced the greatest "reaction" in fowls were those which were most deficient in P_2O_5 .

A "cured" rice containing .46% of P_2O_5 never set up any "reaction"; an "uncured" rice with only .27% gave marked polyneuritis; and in the same way "polishings", whose admixture with a toxic rice prevented any "reaction" occurring, contained 4.2% of P_2O_5 .

Thus by the phosphorus estimation of a given rice its power to cause a polyneuritis in fowls can be readily gauged, and a very probable measure of its Beri-beri producing properties in man ascertained.

This then is the most modern of all the rice theories of Beri-beri and is of the greatest interest, supported as it is by so much experimental evidence, because it places Beri-beri in a position analogous to that of Scurvy, amongst the diseases due to faulty nutrition.

Recent Work done on Beri-beri and "Uncured" Rice

Fink in a recent paper described work done by him on this subject in which he tried an experiment with Parrots. Five young birds were fed on "uncured" rice green chillies and papaya. On the 18 th day one bird got ill and died on the 22 nd, with loss of power in the legs and dyspnoea. The next day the second bird died in a similar manner. A week later the third and a week later the last. The last bird was now very ill and its life was despaired of. At this time then its food was changed to RICE (still "uncured") plus POLISHINGS, within a few days a distinct change was seen and the improvement went on steadily till within 4 weeks it could sit on its perch and fold its wings naturally.

This experiment is of great interest and is another very convincing piece of evidence in favour of the value of rice "polishings" and so of the Phosphorus Starvation Theory.

In support of the work done by Fraser and Stanton a report was recently published (Oct 1910) of work done by Aron in the Physiological Laboratory of the Philippine Medical School. He summarises the result of his experiments as follows:--

(1). Certain food stuffs, especially rice, which are poor in Phosphorus (phytin) if used as the main or exclusive article of diet for any length of time, cause Beri-beri.

(2). The process of polishing removes the outer layers which are rich in Phosphorus, especially the soluble organic compounds of that element (phytin).

(3). A diet, which causes Beri-beri if given to animals for any length of time, is not sufficient to keep them in normal health.

(4). A polyneuritis is set up in chickens eating white ("uncured") rice, while the addition of organic phosphorus in the form of Phytin reduces the deleterious effect of this diet.

Before passing on to a consideration of the etiological factors of this disease let us determine, which of all the theories I have enumerated can be said to be most in consistence with the known facts.

When we come to describe the symptoms of the disease it will be seen, that those, that give to Beri-beri its typical aspect, are all secondary. The question arises, are they secondary to disease occurring in the same man, or to a poison formed outside man and

absorbed by him or simply to a want of something, which is essential for his well-being.?

Many observers continue to maintain, that the Infectious theory is the only plausible one; and yet both the causal agent and its mode of entering the body are entirely theoretical; not one of the many views advanced from time to time have been able to stand a thorough investigation.

The very fact, that in spite of rapid and facilitated interport intercourse districts where ~~BE~~ Beri-beri is epidemic do not alter to any great extent and the long and indefinite period of incubation are both strongly against any infectious theory of the disease. Further, though it is true that some of the epidemic features of Beri-beri may be explained by an infectious theory, yet it fails altogether to clear up many of its most obscure problems.

Direct contagion has never been proved, although there are some arguments that can be brought forward in favour of it, such as --- the close retention of an attack to a group of houses, or to one house where all were eating and living in the same way, but although such cases have been reported they are unusual and it has not been ones experience to come across any such selective propensity.

At Christmas Island the houses furthest along the coolie lines from the "kongsi" (store) always furnished the most cases, but this was undoubtedly due to the fact, that those particular dwellings were used by the "sinkhehs" (new comers, coolies under indenture), while

the "laukhehs" (coolies who had re-engaged after serving their indenture) occupied the houses nearer the store and incidentally the gambling tables.

It is only right however to refer to certain published facts, which seem to support the infective theory, though personally I do not see that they in any way detract from the validity of the alimentary theory.

(a), Scriba pointed out, that at the University Hospital at Tokio, Beri-beri constantly attacked the patients on one side of the ward and spared those on the other; and I was told in Batavia, that there used to be three beds in the Military Hospital there, that always gave Beri-beri to young soldiers occupying them.

(b), Vorderman noted that at Krakään in the Dutch Indies Beri-beri was unknown, until some of the prisoners were taken to work at Probonlinggo, where the disease was very rife. On the return of these men to Krakään Beri-beri broke out and has been endemic ever since. Also Major Grey some years ago reported, that Beri-beri was unknown at Penang until 200 prisoners were brought up from Singapore and that ever since then it has been extremely prevalent.

(c), It is undoubted that the disease follows the principle lines of traffic this has been claimed to support both theories by their respective advocates.

(d), Again those in favour of an infectious cause instance the introduction of Beri-beri into Australia by the Chinese and into Fiji and Diego-Garcia by the Japanese and into New Caledonia by the Annamites.

In the last case 800 coolies from Indo-China were landed on the island of Freyainet (a desert island used as a quarantine station). Soon after that Beri-beri broke out and the island was abandoned and 400 of the ^{72.}_A emigrants went to Noumea, the capital of New Caledonia. Shortly after their arrival Beri-beri became prevalent amongst them and 10 natives of the place died of the disease.

Jeanselme lays particular stress on these instances, as pointing indubitably to an infectious origin of the disease, but Braddon has dealt with each case individually, and has proved that rice can always be shown to have been at the bottom of the trouble.

For instance in the case of the immigrants to New Caledonia, their diet consisted of rice and a small quantity of salt fish and nothing more, when they were put in a position to buy their own food the disease disappeared. A number of Annamites with Beri-beri were retained on a moored vessel and close to this lay a lighter on board of which were living a party of Kanakas (natives of the New Hebrides who had never been known to have had Beri-beri). Ten of these developed Beri-beri and this was taken by Hagen, the medical officer in charge, as being proof positive of the contagiousness of the disease. But it is much more likely that as the ships lay so near one another, the Kanakas obtained rice from the Annamites. In any case the dietary of the Kanakas was not stated and there seems to be some reasonable doubt as to whether they

ever had Beri-beri at all; Hagen was in extreme doubt at the time and the described symptoms do not tally with those of the disease known as Beri-beri.

On the other hand consider a few of the arguments in favour of the RICE THEORY. Some of these I have already touched upon, but may be permitted briefly to recapitulate.

A. (A). All over Malaya the coolie class, who eat "uncured" rice, is the source from which all the cases of Beri-beri are drawn. In the same way on Christmas Island the disease was confined to the Chinese while the Tamils and Malays escaped. On the rare occasions on which a Malay did develop the disease I found, that he had been getting his rice from the Chinese store. The wealthy Chinese in Malaya eat "uncured" rice, but do not develop Beri-beri, this is readily explained because, as in the case of Europeans, rice forms only a subsidiary part of their daily diet.

B. (B). It is true that at the Gaol at Taiping in 1897-1898 and again in 1903-1904 though the rice in use was "uncured", yet there were no cases of the disease. But this is little evidence to balance all that can be brought in support of the theory, for it is quite possible that the "uncured" rice in use on these occasions had not passed through any very excessive polishing and still retained sufficient Phosphorus to prevent an outbreak of the disease.

ADDITIONAL NOTE.
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In 1897 in the Gaols of Bengal owing to a great scarcity in the Indian crop Burma rice was used instead and has been used ever since as it is usually cheaper. Thus the prisoners have been eating "uncured" rice and yet Beri-beri is not found, I mention this because stress has been laid on it, that here lies a direct proof against the Rice Theory. At first the lack of toxicity was attributed to the method of storing the grain, which consisted in mixing it with lime, which was washed out before it was cooked. The explanation is much simpler for the rice was never eaten to the exclusion of other forms of food, but only in conjunction with an abundant supply of pulses (dals), while in the Bihar District of Bengal more than half of the dietary consists in Wheat or Maize.

It is not hard to understand how the necessary proportion of Phosphorus is obtained.

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C. (C). In 1901 practically the only cases of Beri-beri, that occurred in the Indian Army, were amongst the regiment stationed at Rangoon and they ate "uncured" rice. Again in 1902-1903 it was the regiment at Sing-
-apore that supplied the cases for a similar reason.

D. (D). In Penang the Tamils eating "cured" rice, who work in the mines at Sungei Besi are immune, while the Chinese eating "uncured" rice and working in the immediate neighbourhood at mining-labour suffer severely.

E. (E). Buchanan has pointed out, that in Cal-
-cutta the natives who do not eat rice, but prefer millet, wheat and corn do not contract the disease; on the other hand there is a small community of Chinese chiefly shoemakers and carpenters, who eat rice and it is amongst them only that Beri-beri is found. This was the case in 1898, and when I was in Calcutta I was informed that it is almost equally true today.

F. (F). In Singapore Gaol from 1875-1885 Beri-beri was very prevalent, then the amount of rice was reduced and from 1886-1897 no cases occurred. Then the amount of rice was increased and from 1898-1904 Beri-beri again predominated. During all this time "uncured" rice was in use, but from 1904 up to the present time "cured" rice has been in use and the number of cases has steadily decreased, until an absolute minimum has been reached.

As regards the Lunatic Asylum at Singa-
-pore Ellis in his report states that from Oct 1903 to Oct 1904 the inmates were on "cured" rice and during

that time only one case of Beri-beri occurred, though endemic in the Gaol and formerly both institutions had been attacked to a similar degree. A return to "uncured" rice was very soon followed by an outbreak of Beri-beri, while none of those kept on the "cured" variety as a control developed the disease. This is of extra importance coming from Ellis, for in 1903 he had published a paper, in which he clearly stated his disbelief in the rice theory.

G. (G). One of the most striking examples is afforded by Manila. Before 1884 Beri-beri was unknown in the island, just previous to this date there had been an outbreak of Cholera, which devastated the country. The diet of the poorer Philipinos was rice, a little fish and some fruit; as a result of the cholera scare they did not dare to touch fish (as the rivers were polluted) or fruit and so were forced to rely on rice alone as their form of diet. AS a direct consequence of this Beri-beri broke out and hundreds fell victims to it, the disease being confined solely to those (Philipinos, Malays and even some Europeans) who subsisted entirely on rice.

H. (H). The geographical distribution of Beri-beri as a common disease is admittedly that of the distribution of "uncured" rice. In Japan according to Miura, who has long held the alimentary theory, Beri-beri was for years limited to the big sea-ports until, with the advent of railways and rapid locomotion rice was able to be cheaply imported up country, and then the disease became extremely prevalent in the interior.

In Hongkong cases of Beri-beri occur in great numbers, the same can be said of Canton and places up the river, wherever trade facilities enable "uncured" rice to be readily imported and sold cheaply. Once away from these districts the disease is practically if not absolutely unknown.

In the interior of China they employ what is probably the most primitive of all methods of preparing the grain for consumption: the woman places a handful of "Padi" on the floor, and then standing on it rolls it about with her foot, until the unhusked grain separates out; as much then as the chickens have not eaten is swept up off the floor and cooked.

I have seen coolies, who have developed typical Beri-beri in Hongkong, go inland to their homes, where they continued to live on rice, which was now home-milled, and return in quite a short time perfectly well. Some of these cases were so surprisingly complete, that had I not examined them myself both before and after, I could hardly have credited the results.

- I. (I). Women are singularly free from Beri-beri, but it has been constantly noted in the Philippines and amongst the Portugese in Malaya, that quite large numbers of women develop the disease during the puerperium, often with fatal results. The probable reason being, that it is the custom of these people to keep the puerperal woman often for weeks on an almost starvation diet, the only form of nourishment allowed being a thin rice gruel. Takaki has recognized the same to be the case in Japan, as referred to

in Bentley's book on Beri-beri.

There are so many instances which substantiate this theory, that I can hardly refer to them all, mere reiteration is of little value, but such as I have had first-hand acquaintance with are perhaps worth retail-
-ing.

K. (K). For instance in the Hongkong Gaol, since the use of a "coarse" rice, namely one with a large amount of adherent pericarp, out of a daily average of 500 prisoners no cases of Beri-beri have occurred. On the other hand a large number of cases of this disease are daily admitted to the Tung Wah Chinese Hospital. Enquiry shows that by far the greater number of these patients are "free" coolies. In other words the "contracted" coolies, who are given a rice which is not highly polished, do not develop the disease to anything like the same extent as those, such as the rickisha class, who buy their own rice and prefer to purchase the highly polished white variety.

L. (L). Campbell Highet M.O.H. for Siam in his 12th Annual Report instances the following:---
Owing to a severe outbreak of Beri-beri amongst the police, it was decided to make some experiments with "cured" rice. The first place chosen was the Lunatic Asylum, which was a hot-bed of the disease, and it was selected because the food supply was under complete control. At the time when the "cured" rice was commenced (Feb 1909) 22 patients were suffering from Beri-

Beri-beri, of these 4 died, the remainder improved steadily and not a case has since occurred, the result was really most striking. This rice was then supplied to the Hospital for Infectious Diseases, to the police prisoners and to the Reformatory at Koh Si Chang with like gratifying results. Hight reported that during 20 years service it was the most wonderful phenomena that he had come across-.

M.

(M). Van Andel, Army Surgeon in the Dutch East Indian Army in a paper on the Etiology of Beri-beri refers to the good results he has obtained in his practice by the substitution of a legumen to take the place of the rice in the daily dietary. The legumen chosen being known as the Java Pea --Phaseolus Radiatus-- locally called "Kadjang-Idju". Samples of this were shown to me in Batavia, and also its method of preparation, it being cooked to resemble a rice food as closely as possible, while its use is supplemented with fresh fish, vegetables and fruit.

It has been shown over and over again, if rice is absolutely cut out of the dietary and this pea substituted, that not only does Beri-beri cease but also cases that have developed advanced paraplegia or ^{are} absolutely water-logged ^{are} improve with marked rapidity. In the light of Fraser's experiments it would be of much interest to know the percentage of Phosphorus in this pea, everything points to the probability, that it is as high ~~as~~ if not higher than that of "cured" rice. This analysis is being carried out, but up to the time of writing I have not heard the result.

N.

(N). At Christmas Island coolies in Hospital got nothing but "cured" rice and no cases of Beri-beri developed. Outside much to my disappointment one had to be satisfied with half measures. The reason for this was two-fold, one was that the contractor, finding that he had to pay almost double the price for the "cured" rice, failed to see any reason why he should supply it to the coolies, and the other was, that on a previous occasion when they had been suddenly and without warning changed from "uncured" to "cured", the coolies had gone on strike en masse and so the manager refused to risk a repetition of this experience. As a compromise a certain amount of "cured" rice was mixed with the "uncured", at first in the proportion of 1 of the former to 7 of the latter, this was gradually increased until the proportion stood at 3 : 4. The results were encouraging for from the time the change was made the number of cases of Beri-beri diminished steadily and during the last year fell considerably as a glance at the charts will show. ^(page 216) Before leaving I recommended that the coolies at work in the quarries should be supplied with a thin soup made from the rice polishings, so that they could drink this in the place of plain water. This has been carried into effect but with what results I have not heard. But I am certain, that if it can be done properly the result will be eminently satisfactory: of course a much easier way of meeting the difficulty would be to insist on the consumption solely of "cured" (parboiled) rice, everything points to the conclusion that on such a régime

the disease could be completely stamped out. The Chinese are extremely suspicious of any sudden alteration in their diet, but I found that in Hospital they had no real dislike to the "cured" rice per se, but greedily ate as much of it as they were allowed to have.

Q. (O). In Muntok on the Island of Banka (Dutch) there are a large number of Chinese coolies employed in the mines. Beri-beri has been prevalent for many years, and was especially so amongst the prisoners in the Gaol. The dietary consisted of imported "uncured" rice, but after a mill had been introduced locally, husked "cured" rice was used in the Gaol and Beri-beri speedily disappeared. When at Muntok I was shown the process of milling, but it did not differ materially from that already recorded.

P. (P). Wellington of Sarawak has pointed out that in Simanggang Gaol and in Baram Beri-beri was very rife, but was checked by feeding the inmates on "fresh" rice.

Such then are a few of the instances that I would draw special attention to, as I do not think that it is saying too much to maintain, that taken collectively they form a strong positive evidence in support of the Rice Theory.

On the other hand what objections have been raised ?

OBJECTIONS to the RICE THEORY.

A consideration of ~~the more~~ important of these will be found to add rather than to detract from the

value of the rice theory.

(1). Many observers, who repudiate the rice theory do so on the grounds, that so frequently under a dietary which is physiologically correct, Beri-beri still continues. This is certainly the case and does not detract from the hypothesis at all; the point being, that it is not a deficiency in either Protein, Fat or Carbo-hydrate that causes the disease, but the use of a special form of rice.

Hamilton Wright instanced this fact as disproving the rice theory, namely that whereas a large number of cases occurred, while a group of men were on full physiological diet, the number diminished when the diet was reduced in value. This has really no bearing on the point in question for they continued to eat rice. Moreover as it happens it was a singularly unfortunate instance to have cited, for an inquiry into the medical records shows that subsequently on the reduced diet there was an enormous increase in the number of cases of the disease.

In the same manner after a careful consideration of the Alimentary Theory Prof: Jeanselme sums up against it in the following words:--"De tout ce qui précède, il result qu'une nourriture insuffisante ou de mauvaise qualité, ne peut pas être considérée comme la cause réelle du Béri-béri",

Several of the instances, which lead up to this remark, will now be considered and it will be shown, that in every case "uncured" rice was the probable causal agent.

(2). Fiji is constantly quoted as being a place, where the natives eat "uncured" rice and do not develop the disease.

Let us consider the facts for a moment. Prior to the advent of a number of Japanese coolies, there had never been any known cases of Beri-beri, but shortly after the arrival of these men, the disease broke out amongst them (Japanese) and steadily increased.

A full account of this outbreak has been given by Joynt, and it is very apparent, that of all the coolies at work--Japanese, Indians and Polynesians the first alone ate "uncured" rice and they alone developed Beri-beri. The Indians ate "cured" rice imported from Calcutta. Since the Japanese left, a certain number of Chinese have been employed, and at the present time it is only amongst this people that Beri-beri is found and they eat "uncured" rice.

The natives do not get the disease, but it is inaccurate to say that they eat "uncured" rice, for their grain is chiefly imported from Calcutta, and as well their dietary is largely supplemented by Yams, Maize, Vegitables and quantities of Fresh Fish.

(3). One of the strongest arguments was advanced by Feibig, who stated that in the Moluccas the natives eat Sago and not Rice, and yet Beri-beri occurs freely. The grounds for this belief were based on some very old reports and it is extremely doubtful if it is the case that no rice was consumed, and it is by no means certain

that the disease was really Beri-beri.

This seems rather an easy way of getting out of the argument, but even granting that the disease was true Beri-beri and that no rice was consumed, the theory that rice is at least the commonest of all factors in the causation of the disease is not in the least weakened. It is of the highest probability that a group of men subsisting solely on Sago would in a like manner suffer from a deficiency of Phosphorus.

A careful analysis would prove whether Sago is above or below the physiological limit, which Fraser has shown to be the guide to the potentiality of a given food stuff to produce Beri-beri. It has been shown that fowls fed exclusively on Sago develop a polyneuritis analagous in every way to that caused by Rice ("uncured"), which has been shown to be an "index" of its Beri-beri producing power in man.

(4). The outbreak of Beri-beri amongst the Boer prisoners at St Helena, who got no rice, has been described by Casey. The diagnosis was considered doubtful by most of his colleagues, and many of the symptoms described as being present are not found in Beri-beri, while others are more characteristic of Epidemic Dropsy. Besides ataxia and inco-ordination were present and the oedema appeared suddenly and disappeared suddenly. There were no gastric symptoms and no urinary symptoms and the patients often made rapid recoveries.

(5). Durham after his visit to Christmas Island raised certain difficulties, from his observations there, as regards the acceptance of the rice theory. One of these was that all the people, that ate rice got it from the same store and yet only the coolies suffered. As a matter of fact this doesn't represent the case. It is true that Beri-beri was and is far the most prevalent amongst the Chinese coolies, especially the contractor-fed "sinkehs", whose diet at the time Durham was there consisted almost entirely of "uncured" rice. The other Chinese who obtained their rice at the same store were the Companies servants, mechanics and the like, who received far better wages and were able to supplement their diet in a number of ways, namely, by the purchase of pork, pigeon, fish and vegetable. In fact those of them that lived like the better class Chinese do in Malaya escaped; those that did not frequently developed Beri-beri.

At the present day on Christmas Island there are two stores, the Kongsí Store, where the contractor keeps the coolies food, and the Company's store: The rice in the Kongsí store is served daily to the Chinese coolies, and the only other people, that obtain rice from this source, are the Chinese employed directly by the Company and paid by them. The rice in the Company's store is used by the Malays and Tamils, while the Europeans can purchase it there if they desire to do so.

Beri-beri only develops amongst those that

get their rice from the Kongsí store.

As already mentioned in Hospital nothing but "cured" rice is used, while a mixture is supplied to the coolies. On the other hand there is nothing to prevent a "tukang" (mechanic) buying "uncured" rice without any admixture of "cured" for their own use. While I was on the Island I found several did so and thus the explanation was forth-coming, why so many mechanics, who were paid well, developed Beri-beri out of all proportion to their number as compared with the number of coolies.

(6). Carnegie Brown found difficulty in the acceptance of this theory, on the grounds that a disease indistinguishable from Beri-beri was often seen in persons into whose dietary rice never entered. Considering the mass of evidence brought forward in support of the theory, one would require to know concrete cases of this. Again it has already been insisted on, that in the theory of Phosphorus starvation, it is quite possible, that any confined diet lacking in this essential and taken over a sufficiently long period might result in the production of a form of Beri-beri, as instanced in the case of Sago.

Further he claimed that in an endemic area large communities live on the incriminated rice and do not suffer from the disease. The question of the personal equation comes in here and will be considered very shortly, in most cases it will be found, that if "uncured" rice is the form eaten, the dietary is

supplemented in other ways, as in the case of Europeans and wealthy Chinese in Malaya.

It must be remembered, that for the disease to be caused by the method indicated, the process must naturally be a long one and will vary greatly with any extra articles of food taken.

I think that one may fairly claim that it is a proven fact, that if a man eat nothing but "uncured" rice with a low Phosphorus percentage sooner or later he will develop the typical symptoms of Beri-beri whatever his nationality may be.

Finally Carnegie Brown stated that Asylum neuritis and Ship Beri-beri were very possibly the same disease as True Beri-beri and if such were the case it would be hard to reconcile them to the Rice Theory, because for instance, on Italian Ships there is no Beri-beri and they eat largely of rice, while on Norwegian vessels they eat no rice and yet cases have been so numerous as to require the appointment of a special commission by the Norwegian Government to thoroughly study the matter.

The question of Ship Beri-beri will come up for consideration later on, but in the meantime I would point out that in the Italian vessels, at least on board such as I have enquired as regards their dietary, though rice figures quite considerably it does not in any way preponderate and is very largely supplemented by Macaroni, Vermicelli and the like.

(7). At the 1910 meeting of the Society of Tropical Medicine Biddoes found, that he was unable to accept the rice theory on the grounds that, no rice is eaten up the Amazon and yet Beri-beri is very prevalent in certain parts. There must, I presume, be places up this river where rice is not eaten, but considering Brazil as a whole this state of affairs can hardly be said to exist. The disease has been recognized in that country since 1860, and it was just at this time that its ports were thrown open to world-wide traffic. Moreover it has been recognized in Brazil, that the importation of rice into the interior has been systematically followed by Beri-beri, in fact the incidence of the disease goes hand in hand with the distribution of the grain.

The cases referred to by Biddoes, where no rice was eaten, are according to him nearly all of the Acute Malignant type and exhibit certain symptoms foreign to the disease as seen in the principle endemic regions of Malaya, the Dutch Indies and Japan. For some time I have wondered, if the sudden fulminating form seen in Malaya is really only a variety of Beri-beri and not a separate disease altogether, probably of Infective origin, and this report from Brazil seems to be a striking proof of the possibility of the same. The suddenness of its occurrence as compared with other forms of Beri-beri, the marked Gastro-intestinal symptoms so generally present, and the fact that it was only from this type of case that Hamilton

Wright was able to isolate his bacillus, taken all together seem to me to greatly strengthen this contention.

I should mention that up the Amazon the principle food is Cassava, which is prepared from the same root as tapioca. This is of interest, considering the experiments with sago that have already been referred to, and it would in a like manner be of additional value to know the Phosphorus percentage in this form of food.

(8). It is urged that the beneficial results, that accrue after a change to "cured" rice are due to the facts --:

(a). That the alteration is made when the worst of the outbreak is over and the more susceptible people have succumbed.

(b). That the alteration is accompanied by other hygienic methods all of which would equally lessen the chances of the introduction and spread of an infectious agent.

This is however most certainly not the case for in many instances solely by changing the kind of rice in use, without in any way improving the rest of the diet or the general hygienic conditions, an outbreak of Beri-beri has rapidly discontinued and further epidemics have been avoided.

(9). On the strength of the theory, that the disease is due to deficiency of Phosphorus one of the most common

most powerful arguments against the validity of the Rice Theory falls to the ground, namely that the process of cooking should render the grain sterile and prevent it being a means of introducing a poison into the system: for it is obvious that if the disease can be proved to be due to dietetic deficiency cooking will not overcome the difficulty, but will tend rather to increase it.

Finally it is only fair to demand that those whose experience leads them to discredit this theory should make special notes on the following points in their reports of outbreaks, or of experiments carried out to prove its etiology--:

- (a). The kind of rice in use with the Phosphorus estimation of the same.
- (b). The period over which the rice is taken.
- (c). The approximate daily quantity of rice eaten or at least its proportion to other articles of diet.
- (d). Should no rice be eaten, the nature of the grain taking its place, also with its Phosphorus Estimation.
- (e). Careful clinical study, so that no possible doubt can arise, as to the disease under consideration being True Beri-beri.

N.B. I mention this last clause, because I have seen cases diagnosed in Hospitals, especially those under native supervision, as Beri-beri, which lacked many of the most salient features of the disease and were apparently so called for the want of a better application.

SUMMARY

A fair number of instances from various quarters have thus been exemplified, and after a critical examination of these, coupled with the experience one has had of the disease, there seems to be some justification in the views, that one has arrived at on the subject, and these I would briefly summarize, as embodying at least a plausible possibility, as follows.

- (A). That the disease known as Beri-beri and shortly to be described as such is in the convincing light of Fraser's experiments due to PHOSPHORUS STARVATION, and that this is caused in nearly every case by the consumption of "uncured" rice, as the staple article of diet, but may possibly arise by the use of any other substitute, which is equally deficient in this essential.
- (B). That though acute symptoms may arise in True Beri-beri, the condition known as Acute Cardiac or Fulminating Beri-beri, is probably not an acute phase of the same complaint, but a totally different disorder of bacterial origin, invading the system through the gastro-intestinal tract. This brings Wright's observations

and the reports of cases from the Amazon, where no rice is eaten, into direct line.

- (C). That the disease known as Ship Beri-beri is closely allied to True Beri-beri, except that the Scurvy element is super-imposed, and is more predominant, there being deficiency of Citrates, Lactates and possibly Potassic Salts as well as Phosphorus in the dietary.
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ETIOLOGICAL FACTORS.

Certain factors are usually credited with playing a part in the production of Beri-beri, for the disease is more prevalent under certain conditions than others. Let us consider how much weight can be attached to these as being predisposing causes of this disease.

A. RACE and NATIONALITY

At first sight it would appear, that certain races of mankind are more susceptible to Beri-beri than others, and it is quite possible that a reduced form of resistance does exist, the personal equation may well be national as well as individual.

For instance the Japanese seem to be particularly prone and wherever they go the disease goes with them: that this is principally due to a dietetic cause has already been shown, yet it is interesting to note that in Korea, which these indefatigable people have so recently annexed, they do seem to succumb more readily than the Koreans themselves, though living in much the same way.

Again amongst coloured races aboriginals would appear to offer more resistance than ^{the} immigrants; during the construction of the Congo railway Bourguignon, who was medical officer in charge, noted that there were far fewer cases of Beri-beri amongst the natives of the

Congo, than amongst the Chinese or the coolies from the Barbadoes. Taking it all round I am doubtful, whether this has really any very great influence, the probability being that placed in the same environment and under the same dietetic conditions, any race, European included, would succumb to the disease just as readily as the Chinese, Japanese and Malays. An instance in point is afforded by the way the disease ravaged the European troops in the Dutch East Indies especially at Atjeh in the north of Sumatra.

B. SEX.

By far the larger majority of cases are Males. As regards the Chinese coolies in Malaya this is readily explained by their enormous preponderance, but in countries where the balance of the sexes is more even the male section still always returns far the greater number of cases. This may be explained by the fact that the males are away all day and take their portion of rice with them, while the women at home, as women all the world over will do, supplement their rice with many small additions.

If women live under the same conditions as men, they will develop Beri-beri quite as readily! such is often proved to be the case in prisons, and such was the case in the school at Tokio and in the convent at Choquan near Saigon, where out of a total of 40 female inmates, there were 31 cases of the disease.

In Hongkong one fairly often sees women suffering from Beri-beri, and inquiry into these cases always shows, that they have been at manual labour outside just like male coolies. In the Tung Wah Hospital at Hongkong every year the total Beri-beri admissions always contain a small but quite definite proportion of female cases. (In 1910-43 out of 871 = 4.9%).

4.9%

Hirota noted that children nourished by mothers suffering from Beri-beri sometimes also shewed symptoms of the disease, and rapidly recovered if nursed by a healthy woman or put on cow's milk, this observation is of considerable interest and is quite in line with what would be expected dietetically.

The reason for the liability of pregnant women to develop the disease has already been referred to (page 67) and is based on purely dietetic grounds.

C. AGE.

The period commonly quoted, as being the one during which the disease is most likely to develop, is between the ages of 15--35, it being rare in children and the very old. In the Tung Wah Hospital the number of admissions of the disease in children is very small indeed. (In 1910--10 out of 871). 1.1%. This period is certainly correct as far as cases in Malaya are concerned, for of course it is just between those two ages that by far the largest number of coolies are at work. Also anywhere else it is again between those ages that a man is out at labour all day, taking

his daily ration of rice with him most frequently with nothing else to supplement it. (See Chart page 99)

D. CONSTITUTION.

In an epidemic it is by no means the weakling that is prone to fall a victim more readily than his stronger brother, for one constantly sees men of fine physique with well developed muscles amongst the first to develop the disease.

According to Scheube 87% are robust, and both Baelz and Miura noted the same fact in Japan especially in those that developed the Acute Form, for instance in one outbreak in Tokio 593 were robust out of a total of 626.

This can like the other etiological factors we have been considering ~~be readily~~ be readily explained on dietetic grounds, it is absurd to suppose that, because a man is hale and well and above the physiological line of health, he should for that reason be more liable to develop disease.

One constantly sees cases developing as secondary to other Tropical diseases such as Malaria, Cholera and Dysentery, the reason being that frequently over a long period the only article of diet such persons have been allowed has been Congee (Rice water). In a like manner it occurs as secondary to such chronic complaints as Phthisis, Rheumatism, Syphilis and long-standing Suppuration.

The question of the "personal equation"

is very hard to judge, it has been shown to exist in other diseases and probably does so in Beri-beri. In the same way what part Heredity plays, if any, has hardly been touched upon. Amongst the many cases one has personally come in contact with, one never could get any sufficiently reliable facts from which to draw any deductions, but it is very likely, that to some is granted a natural immunity to others a natural predisposition.

E. SOCIAL CONDITIONS.

This disease is in Malaya one principally of the lower classes, though according to Scheube in Japan it is the middle class that is by far the most affected.

Another social condition, which seems to favour the disease is over-crowding in damp, badly-ventilated habitations, such as used to be found in prisons in the East, like those of Poulo Condore or Saigon, which were notorious. The Beri-beri incidence can in such places primarily be traced in every case to the form of rice consumed and the same reason explains the prevalence of the disease in big towns, especially those on the sea-board, and vica versa the immunity of villages up country.

Such causes of physiological depression, as fatigue and privation also play their part as predisposing causes.

F. METEOROLOGICAL CONDITIONS.

In countries where there is a cold and a hot season, Beri-beri is more prevalent during the latter, while cases in hospital improve and fewer are admitted during the winter. Where the temperature varies little all the year round as in Malaya, there is usually a marked increase during the wet season. This has been constantly noted in a number of places where the disease is endemic, for instance in Japan, which is one of the dampest countries in the world, there are two wet seasons, June and September, and it is between these two months that by far the most cases occur,-- this is shown graphically in the appended chart. (page 92)

Geyet at Poulo Condore always found there was a regular seasonal incidence, cases increasing each year during the cold damp N-E Monsoon.

In Java Vorderman noted its special prevalence during the season, and at Atjeh (Sumatra) Pekelharing and Winkler found a marked increase during the wet months: the same is reported by Leslie to occur in Burma.

On the other hand Braddon does not think that the rain-fall has anything to do with the incidence of the disease, but maintains that any seasonal variation, that is present depends on two factors:--

- (1). That rice is an annual crop and the new grain comes into the market early in the

year; the age of the rice having a direct relation-ship to its Beri-beri-producing power.

- (2). That immigration of "sinkehs", who are most liable to the disease, is brisker at the beginning of the year.

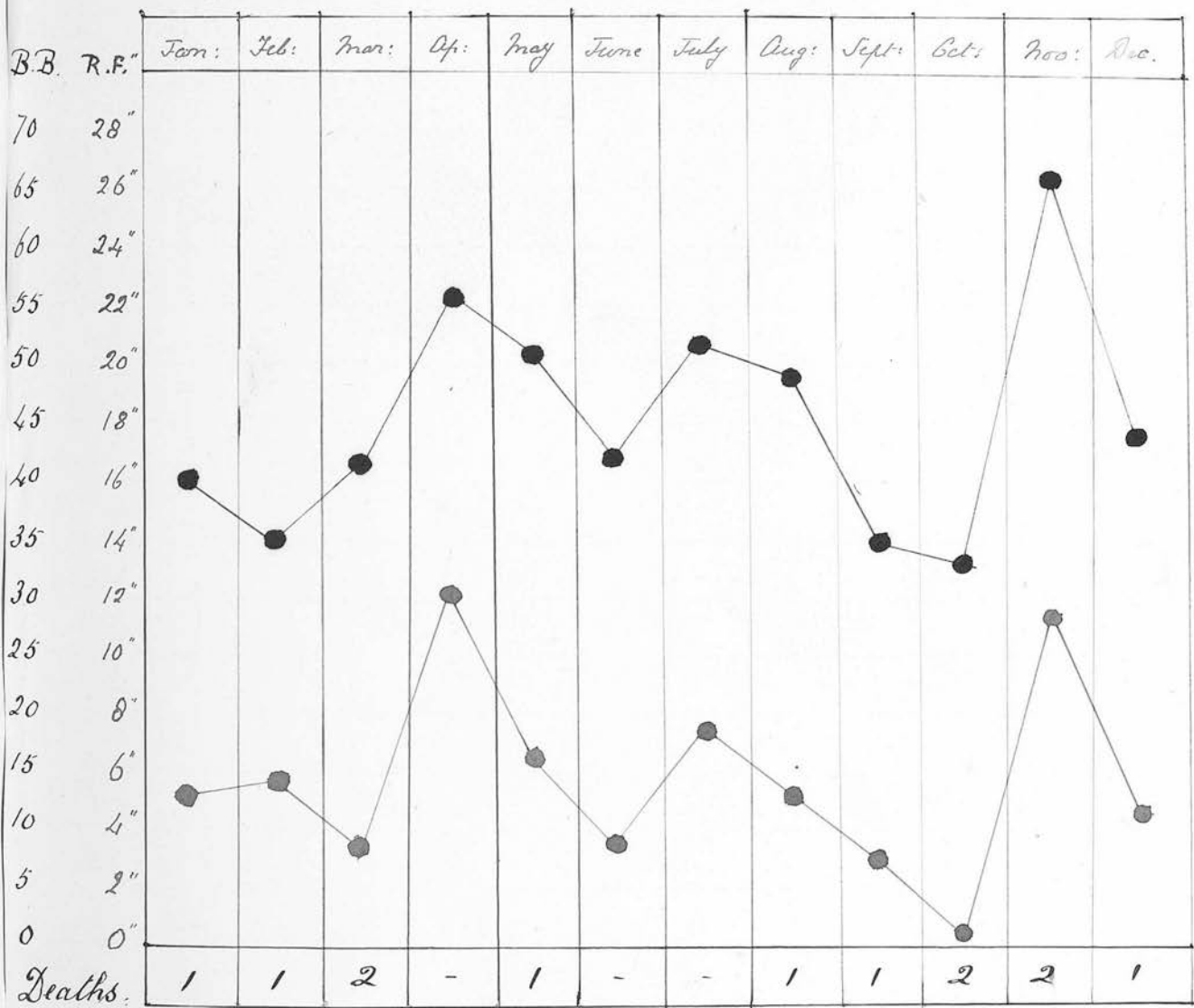
These two having a direct relation-ship; for the time when the rice is most potent to do mischief will correspond with the time when the coolies are most liable to develop the complaint.

Fraser's most recent experiments disprove the former, while the latter factor would have no weight in a number of places where little or no immigration takes place and indeed is scarcely true of Malaya since the commencement of the extraordinary boom in rubber, which caused a constant demand for coolie labour.

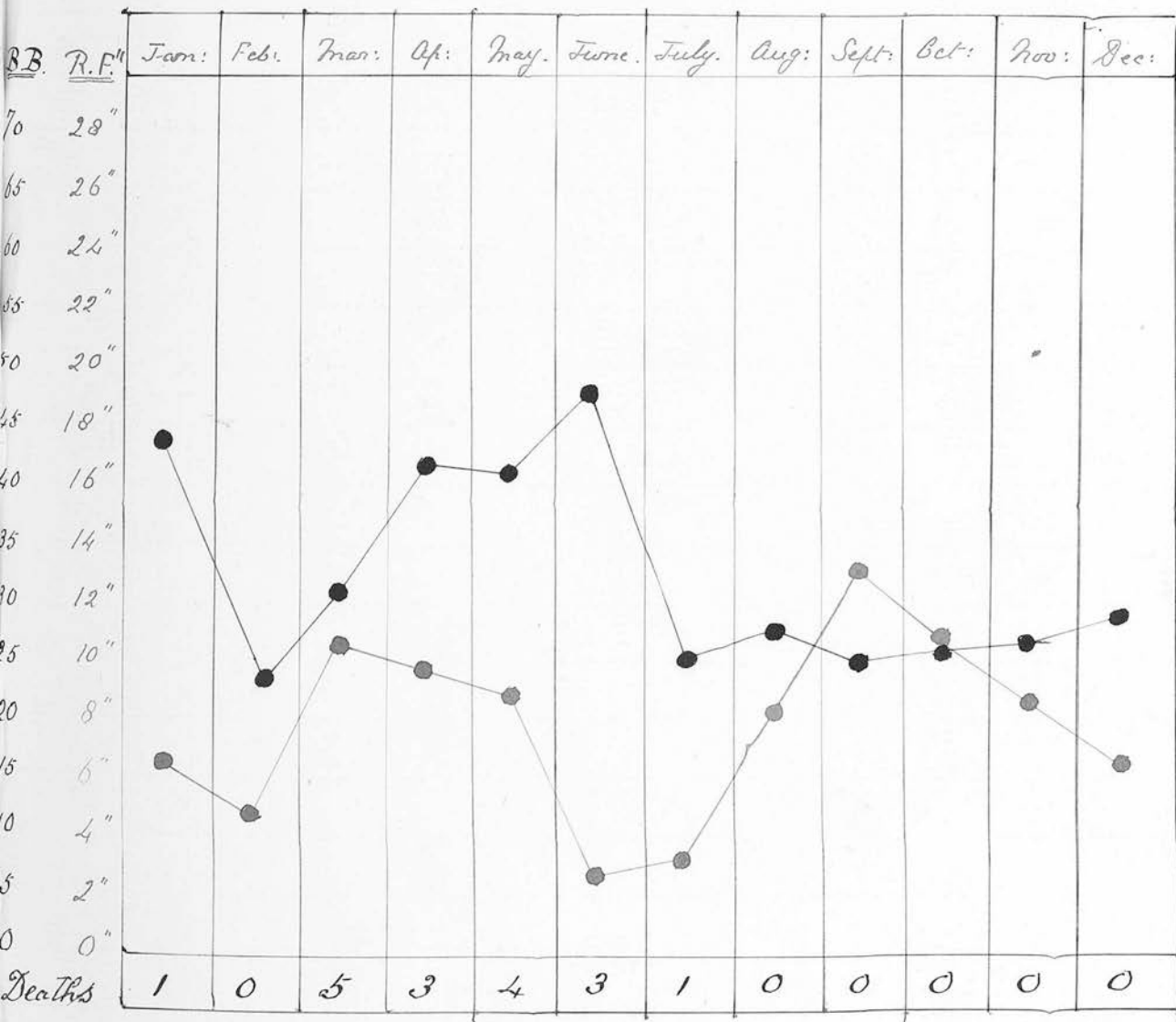
Braddon collected statistics, which extended over a considerable period to demonstrate that in the Malay Peninsular "there was no definite relation-ship between rain-fall and Beri-beri" and that "though independent of meteorological factors, the local variations in Beri-beri incidence coincided in time at different stations.

At Christmas Island I examined the records as far back as any were taken, and from the appended charts it will be seen at a glance, that though the case incidence does not in any way slavishly follow the rainfall curve, yet there is a distinct relation-ship between the two. (pages 93---97).

Monthly Beriberi Admissions compared.
with Monthly Rainfall
on Christmas Island.
1905



Monthly Beriberi Admissions compared.
 with Monthly Rainfall
 on Christmas Island
1906

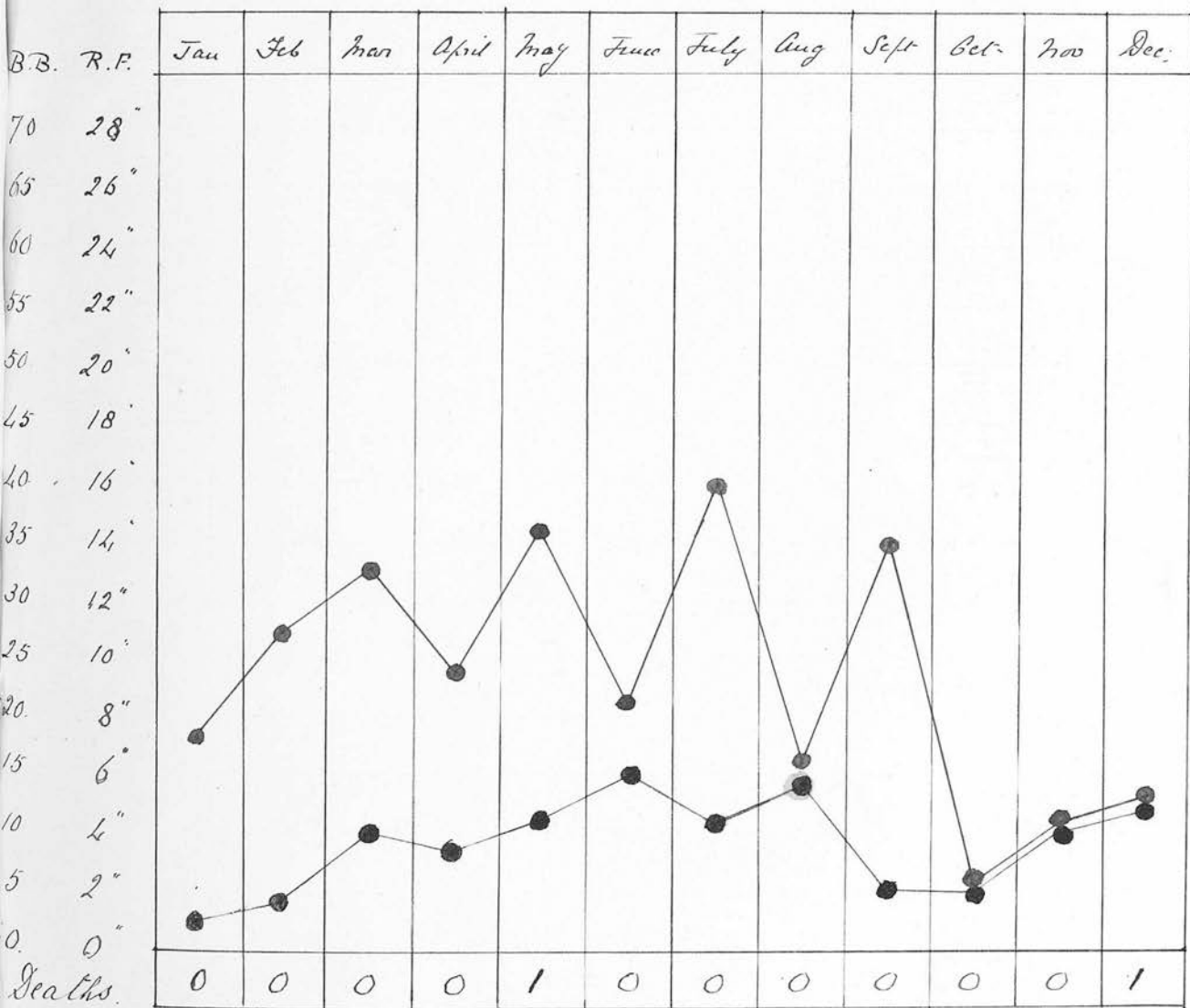


Monthly Beru-beri Admissions

compared with

Monthly Rainfall on Christmas Island.

1909.

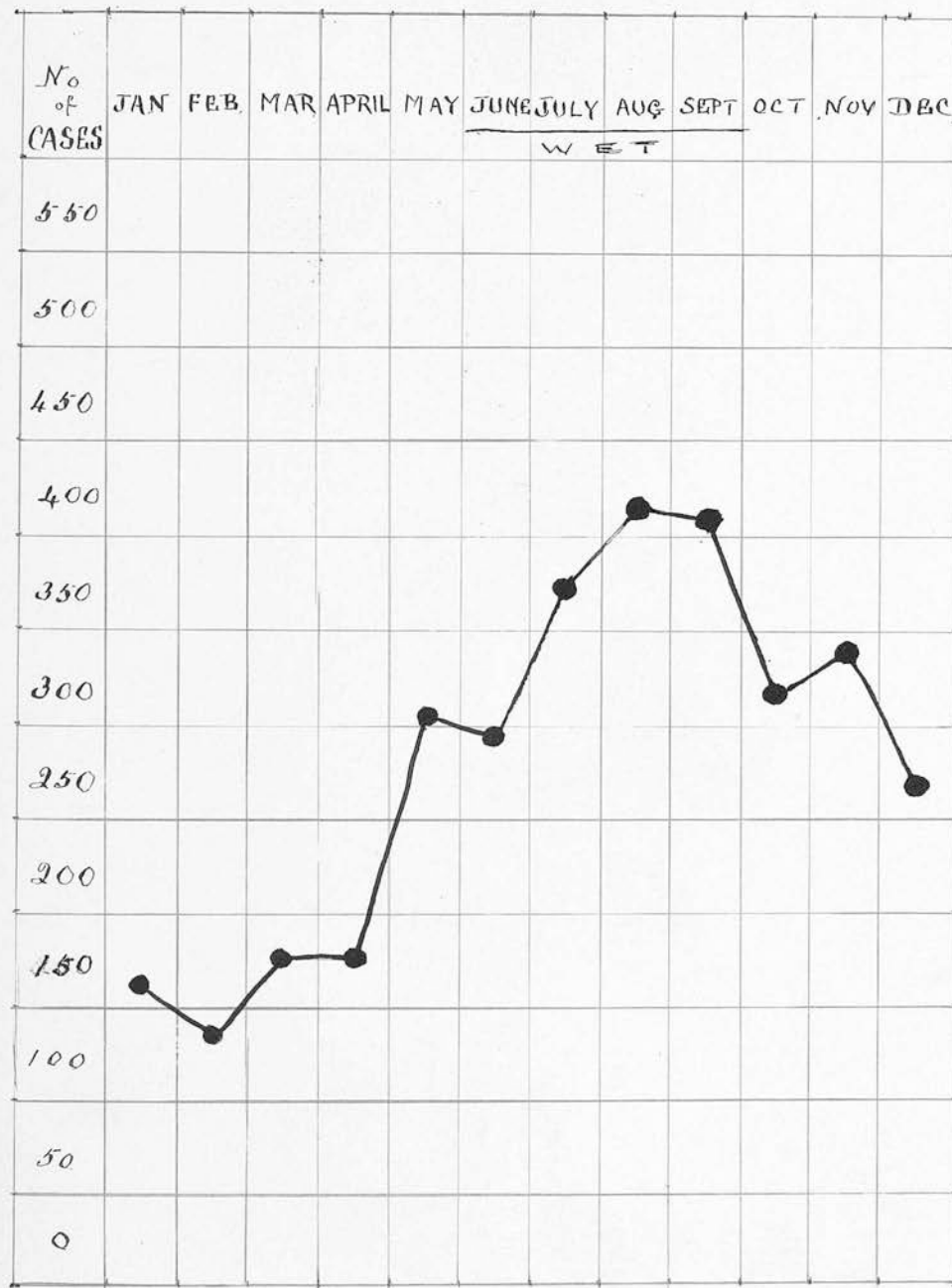


TUNG WAH HOSPITAL HONGKONG.

(From Government Reports)

CHART TO SHOW MONTHLY ADMISSIONS OF
BERI-BERI OVER A PERIOD OF 10 YEARS.

(The wet months being from June to September)



The Incubation or Latent Period.

Before entering into a discussion regarding the Forms and Symptoms of Beri-beri, it may be as well to see what conclusions can be drawn regarding the Incubation Period of the disease.

Infectious diseases are characterized by a definite incubation period, while those that are due to poisons or to defective nutrition, being dependent on a number of factors, are manifestly indefinite. Such indeed is characteristic of Beri-beri and ones difficulties are increased by never being able to say when "exposure" commenced.

As in the Etiology of this disease, so in the consideration of this point much difference of opinion has been expressed. Periods varying from 10 days to 7 months have been quoted as being correct.

Hamilton Wright seeking to bring this into line with his "Infective" theory maintained that the period was as short as 10 to 15 days. He based his conclusions upon a series of observations done on "sinkehs" arriving from China to work in the Mines of the Federated Malay States. However commenting on his conclusions, one has to remember, that he disregarded one important point, namely the period passed in the lodging houses of Singapore. These places are regular hot-beds of the disease and offer every opportunity for its development and coolies often remain in them three weeks or more.

On the other hand against this short period must be placed the view of Braddon, who believed it to be probably seven months. Pekelharing and Winkler in a like manner considered that the Latent Period must be a long one, infection being constantly and frequently incured.

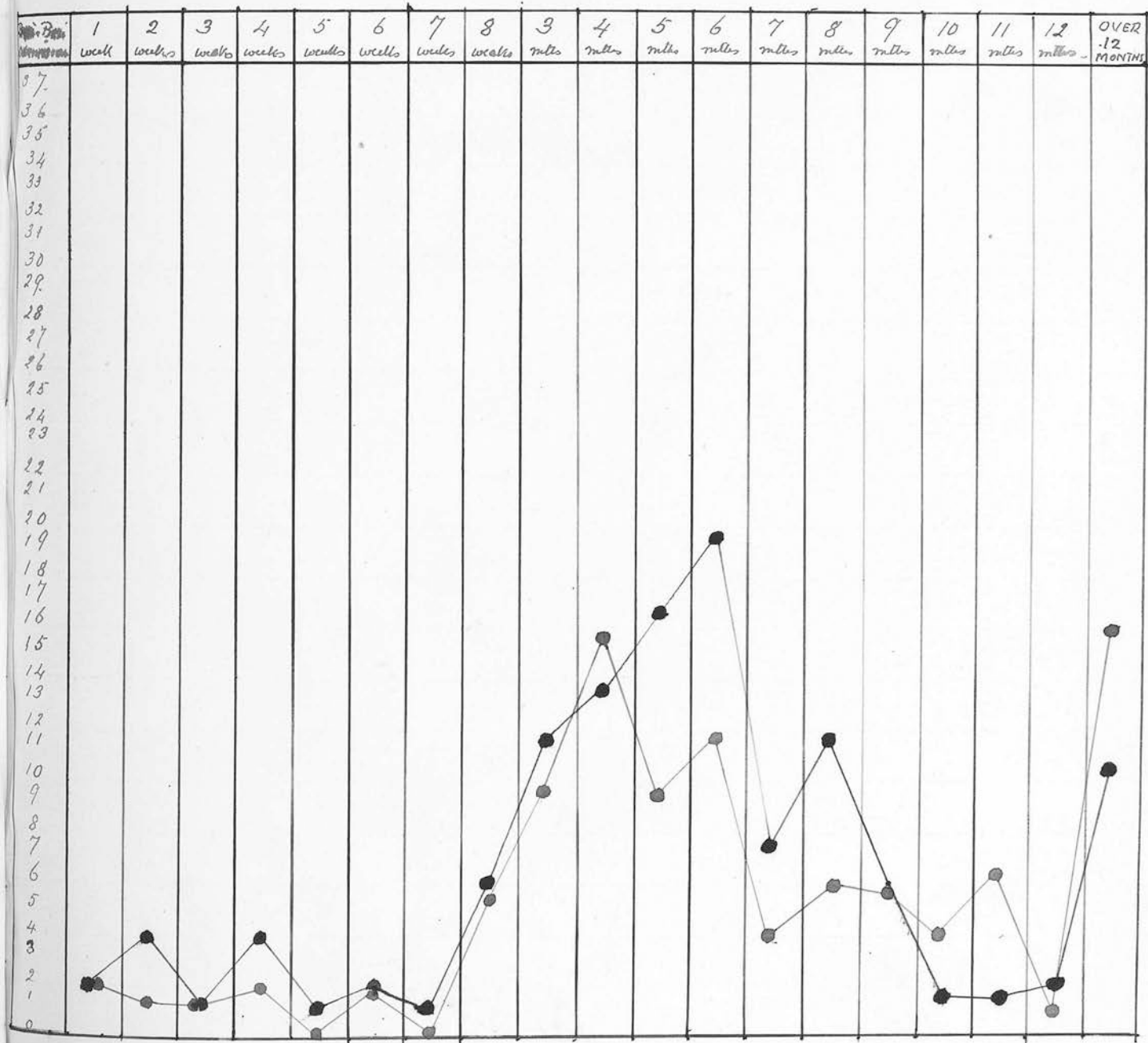
Travers has shown that in the Kuala Lumpur Gaol the commonest period is 3 months (amongst those that have not previously had Beri-beri) though it may be shorter. (For actual figures and Graphic Chart see page 106). Similarly in an outbreak in an Institute for Kidnapped Girls in Hongkong the average period as nearly as could be computed was 84 days --(Koch)--

In Fraser and Stanton's most recent experiment (page 55) the earliest case that occurred was after a period of 87 days.

In a same way a large number of reports from other sources could be quoted, as showing that the most frequent period, other conditions being the same, during which the disease takes to develop is from 3 to 6 months. I refer to such reports as those given by Voderman, Lasnet, Stanley, Dykes, Gerard and Ucherman.

There is always difficulty in getting accurate history from a Chinese coolie, especially if one is handicapped by having to do all interrogation through an interpreter. It seems to me however, that after all that has been said as regards the plausibility of the theory of Phosphorus Starvation, that it can be quite clearly demonstrated, that the closer the adherence is to a diet of "uncured" rice the speedier will be the onset of symptoms.

Graphic Chart showing the Period of Residence on Christmas Island before acquiring Beri-beri.
 thus giving possible Period of Incubation
 1907 - 1908

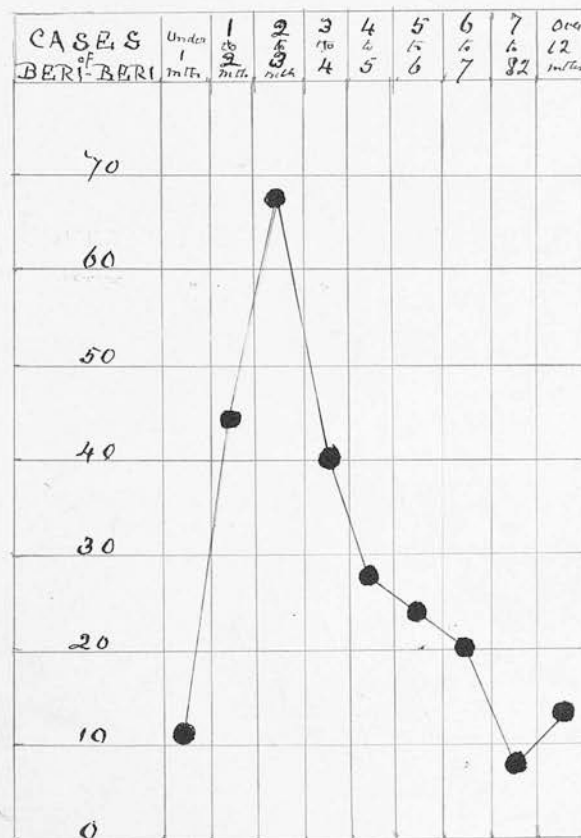


(1907 by Black Line) (1908 by Red Line)

The Incubation Period

Traver's Table compiled from 256 cases in Kuala Lumpur
Gaol.

Time between Date of Sentence and Development of Beriberi.	Number of Cases.
Under 1 month	11
1 to 2 months	45
2 to 3 months	67
3 to 4 months	40
4 to 5 months	27
5 to 6 months	25
7 to 12 months	8
Over 1 year	13

Graphically.

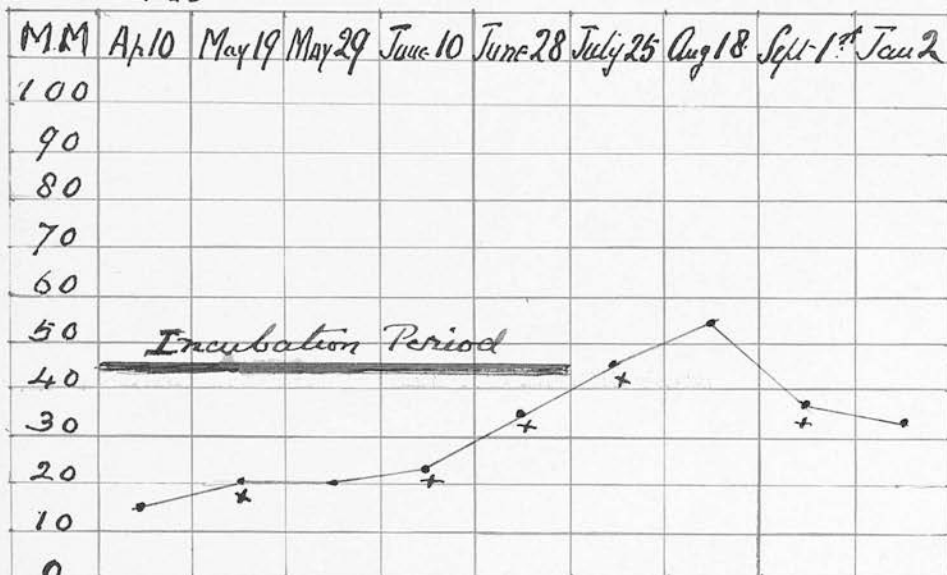
who felt quite healthy for they did not come to hospital. By examining several on their arrival to the Island, one had some data to commence with. Some of these eventually developed Beri-beri and a few prior to doing so were in hospital on account of some "other cause", thus a few occasional observations of a more or less continuous nature were recorded, and the charts of two of them are appended in a graphic form. (page 110).

Braddon less stress on this point that "the absence of perception of light cotton-wool touches over areas corresponding to the 3rd and 2nd Sacral segments of the cord is one of the earliest signs of incipient Beri-beri.

Charts of two cases showing graphically the Variations in the Tactile Sense over a considerable period prior to and during a Rudimentary attack of Beri-beri.

When testing, the same spot was always taken-middle of calf--.

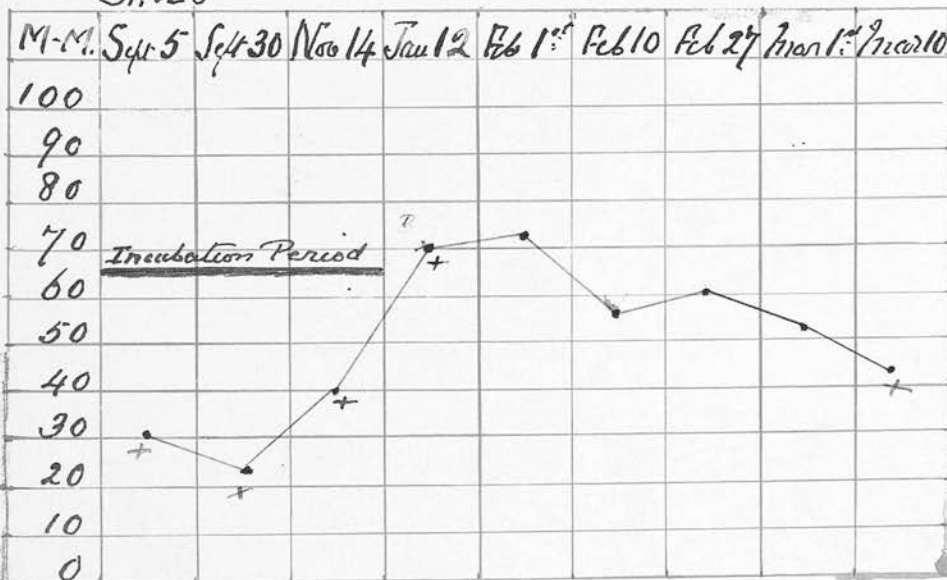
DATES



N.B.

- April 10 Arrived on Christmas Island.
- May 19 Admitted to Hospital with Septic Wound of Thigh.
- June 10 Discharged.
- June 28 Seen as Out-Patient.
- July 25 Admitted to Hospital with Beri-beri.
- Sept 1 Discharged.

DATES



N.B.

- Sept 5 Arrived on the Island, admitted with Gonorrhoea.
- Sept 30 Discharged.
- Nov 14 Seen as Out-Patient.
- Jan 12 Admitted with Beri-beri.
- Mar 10 Discharged.

Some oedema can always be made out along the crest of the tibiae and it is here and not around the ankles that one should first look for this symptom.

There is as well difficulty in the execution of certain movements such as going upstairs; a very useful method of proving this is that known in Malay as the "Jongkok" (squatting) Test. This consists in getting the patient to stand with his heels together and his hands clasped above his head, he then slowly goes down into the squatting position, (so that his buttocks are touching his heels) and rises without aid. Even an early case of Beri-beri is unable to perform this test and it will often be found of real diagnostic value. Careful testing by means of a feather will show that there is slight anaesthesia or rather paraesthesia of the legs below the knee. On exertion the cardiac action is too readily accelerated, while the apparent strength of the impulse of the apex beat is quite out of comparison with the actual force of the pulse wave. Later some increase of Cardiac dulness to the right will be detected with re-duplication of the second sound. The Knee Jerk is absent, no clonus is attainable and the other deep reflexes are impaired, but the superficial remain normal if not slightly exaggerated.

As the disease advances the symptoms become more pronounced and locomotion impaired. The anaesthetic area increases, and in by far the greater number of cases this spread is from below upwards .