THE PRE-BERIBERI CONDITION.

WITH SPECIAL REFERENCE TO ITS EXISTENCE IN JAPAN.

By EGERTON CHARLES GREY, M.A., D.Sc., M.R.C.S.

(*From the Biochemical Institute, Cambridge.*)

(With Plates I–III.)

A PRE-SCORBUTIC condition has been described, but not, as far as the writer is aware, a pre-Beriberi condition, to the existence of which it is the purpose of this communication to draw attention.

THE PRE-BERIBERI CONDITION TO BE EXPECTED.

We may consider in the first place the *à priori* grounds for expecting to find such a condition. A disease attributable to one cause only, as for example one of the specific infectious diseases, could not have a pronounced preparatory period. The disease starts with the entrance of the virus, however long the effects may outlast elimination of the causative agent (and diathesis is rather a passive than an active condition, so far as the production of the disease is concerned, and is not yet sufficiently understood to be considered here). But with deficiency diseases it is certain that in no case can the condition be attributed to the absence of one factor only, and moreover the body has the ability to replace or synthetise at least some of the factors of which it may be in need. There is a continual destruction, resynthesis and redistribution of various factors, and as to the accessory food factors or vitamins their complexity is becoming more and more manifest (Funk (1922), Berg (1927), Chick (1927), Drummond (1927)). A better conception of the Aetiology of Rickets, for example, has only been obtained by the recognition of the cooperation of several factors in its causation and prevention. See discussion on deficiency diseases (1919), Mellanby (1921), McCollum (1925), Berg (1927), Stepp and György (1927).

Curiously enough while rickets has been so successfully studied, Beriberi has continued a puzzle. In Japan there is certainly no clear opinion about the disease (see Ogata (1924) and Shimanozo in Stepp and György's *Avitaminosen* (1927)). Possibly the cause of such vagueness is to be found in the fact that the disease is supposed to be cured with ease, by, for example, a little fresh food, or restricting the polishing of the rice, and the matter there ceases to evoke interest.

If, however, it becomes recognised that there is a latent or pre-Beriberi condition which is much more general and widespread, further interest may be aroused.

Most writers on the subject of Beriberi seem to think themselves duty bound to give judgment in favour of one or other factor as productive of the disease, and to relegate the others to unimportance, but this in the writer's

opinion is not the attitude which should be taken towards the group of diseases which we call deficiency diseases. When the cause of a disease is something added from without, as in the case of a specific infection, we need not look to more than one agent, for it is unlikely that two would enter simultaneously, but when the cause is something missing from within, it is clear there may be as many causes as there are things to be missed, and to imagine that a deficiency disease can result through the absence of one factor only, is to picture a very unlikely state of affairs. And even those who pin their faith on vitamin B as the agent solely responsible for the protection of the body against Beriberi, have now to face the fact that vitamin B is a mixture. The fault lies in too slavishly adapting to the study of deficiency disease the ideas learned from the study of the specific infections. The latter are positive, the former are, so to speak, negative diseases.

The essential point to emphasise here, however, is that the cause of the deficiency disease is multiple, and not single as with the specific infection. And such being the case we shall expect such deficiency diseases to blend into one another, as for example in the classical disease described by Barlow (1894). We shall expect the same deficiency to affect different animals differently, as indeed is found to be the case (Holst and Fröhlich (1911), Schaumann (1910)), and as McCarrison (1919) has found and the writer has himself confirmed, differences in race, habit, age, climate, and other causes materially alter the type of disease produced both in man and in animals, and therefore we shall expect to find leading up to the condition of obvious deficiency of a certain factor, other conditions due to the absence of one or more associated factors, in other words we might anticipate a preliminary condition leading to the deficiency disease in its characteristic form. In the case of Beriberi, a pre-Beriberi condition.

The following factors, as the writer (1927) has recently pointed out, must certainly be taken into account in explaining the cause and prevention of Beriberi in Japan:

Beneficial factors:

(1) Fixed factors in the tissues (diathesis).
(2) The proportion of body building material in the food (organic and inorganic nutritional factors).
(3) The vitamin B complex (at least two factors).
(4) The cooperation of vitamin A (especially in growing animals).
(5) Efficient removal of products of metabolism (circulation, aeration, excretion).

Harmful factors:

(1) Excessive energy exchange in the tissues.
(2) Toxic effect of metabolic products.
(3) Effect of heat.
(4) Effect of humidity.

The extent to which these various factors, beneficial, or harmful, are operative, would obviously depend upon the circumstances, and would probably be sufficient to account for the varieties of Beriberi observed clinically, without postulating any superadded infection.

It will be wiser not to discuss for the moment the function of the vitamin B complex, because although certain of the German school (see Abderhalden (1922), Berg (1927)) have definite views on this matter such views seem hardly yet to have found acceptance in this country. Opinion, however, appears almost unanimous in attributing to the vitamin B complex an important rôle in preventing and curing all types of Beriberi disease. But even if one attribute to it the chief function in protecting the tissue machinery against collapse, it is clear that unless the necessary food factors are present out of which the tissue machinery can be built, the vitamin would be powerless to perform its function. For the vitamin is present in amount relatively so minute that we cannot regard it as replacing damaged bioplasm, but as aiding in the process of replacement, much as the late Sir William Bayliss suggested, as a catalyst aids a chemical reaction.

Clearly therefore for the vitamin catalyst to work there must be material for it to work upon, in other words a diet balanced within reasonable limits.

It is also important to point out that although a reasonable proportion between nitrogenous material and carbonaceous material in the food is essential for the maintenance of health however much vitamin may be present, the converse does not necessarily hold. Thus it may well happen that when there is plenty of protein in the food there is deficiency disease in the absence of vitamin. Both conditions are essential, the accessory factor and the factor to which it is accessory. On this view, therefore, it becomes no longer difficult to reconcile the apparently opposing views of those, on the one hand, who hold that lack of protein is at fault as a causal factor in the production of Beriberi, as for example Takaki (1887), and, on the other hand, who hold that protein deficiency has nothing to do with the matter, basing their conclusions on the observation that in certain cases the disease has arisen when there was protein in plenty in the diet. For it seems to the writer, and others, for example Ragnar Berg (1927), have expressed the same view, that it is not so much a question as to how much food is given to the animal as it is as to how much is absorbed. There will be clearly a vicious circle established when the food is poor in quality, in the absence of the vitamin the food will not be utilised and the tissues will atrophy, and subsequently even when the vitamin is replaced recovery may be exceedingly slow owing to the weakened condition of the tissue which it is the business of the vitamin to stimulate. One recalls in the analogy of whipping a tired horse, the danger of an attempt at a too rapid cure. It is probable that the sudden outbreak of Beriberi which has been observed following a change to an apparently better diet, may be explained in this way, namely the stimulation of a tissue which is not in a fit state to be stimulated.

It thus becomes clear that although an adequate supply of vitamin B may

serve to hide the defects of an ill-balanced diet, there must be an inefficient working of the metabolic processes, and hence an underlying source of weakness in the organism, and this may make itself felt with dramatic suddenness when the vitamin is withheld.

We should expect, therefore, in such a country as Japan, to find considerable evidence of this underlying weakness, or in other words a pre-Beriberi condition.

Such a condition we should expect would develop into true Beriberi disease without any lowering of the standard of the diet, as the result, for example, of any adverse condition such as excessive heat or humidity, lack of exercise, or fatigue from excessive physical or mental work, lack of proper ventilation and rest, or from superadded intoxication of any kind.

Evidence of the pre-Beriberi Condition in Japan.

There is doubtless a good deal of evidence in other countries of what may be called general malnutrition, but it does not pass abruptly into Beriberi as in Japan, where every year during the months of July, August, and September there is an increase of this disease, which would be alarming in any country which was not used to its appearance.

The causes of death in Japan, as published by the bureau of vital statistics of the Imperial Cabinet, in Tokyo 1924, for the whole of Japan proper, are given as follows:

Deaths per 100,000 *of the population*:

Diarrhoea and enteritis	273·7
Pneumonia	201·7
Heart, blood vessels, malacia ...	227·7
Tuberculosis of the lung	152·7
Decrepitude	135·6
Meningitis	122·0
Deformity and congenital feebleness	114·5
Nephritis and Bright's disease ...	108·7
Cancer	71·3
Chronic bronchitis	57·7
Diseases of the stomach	52·8
Intestinal tuberculosis	46·4
Beriberi	34·2
Typhoid fever	23·6
Influenza	22·6
Suicide	20·6

Thus Beriberi is about half as common as cancer as a cause of death.

In an uncivilised country, an outbreak of malnutrition following famine, would be intelligible, but in an advanced country such as Japan, where there are so many doctors, and so much attention is paid to sanitation, the persistence of Beriberi as a cause of death in normal times must be interpreted as meaning that the condition of many people is, prior to their admission to hospital, much worse than is commonly imagined by the medical profession. In other words that many are in the pre-Beriberi condition before it is recognised that their condition is serious.

It is difficult to form an idea as to the number of people suffering from this condition in Japan, but it is undoubtedly large. When there is an outbreak of Beriberi in the summer it is said that the disease has begun, but the fact is that it has become obvious where before it was hidden, and besides the large number of pronounced cases of the disease, there is a still larger number in the preliminary condition.

The writer had an opportunity of visiting the central telephone exchange in Tokyo in June 1927, that is to say about the time when the Beriberi season begins. The conditions of work in the department were extremely good, much better than in the factories and shops, the hours of work being on an average eight per day, whereas in the latter they may be as much as fourteen, the accommodation was also good, and as far as could be ascertained the average diets of the workers were normal for Japanese people, yet of the five hundred women workers employed at the time the writer visited the premises, eighty were incapacitated from work by a condition which was either diagnosed or about to be diagnosed as Beriberi disease. An examination of these women revealed the fact that they were in an exhausted condition without apparent cause, they were incapable of physical effort, if prolonged beyond a few minutes, such effort causing acceleration of the heart, a feeling of faintness and difficulty in breathing. The employees found it necessary to come very slowly up stairs, pausing about every ten steps, and ultimately had to declare themselves unable to work. The bodies of these women were not at all emaciated, the skin was in many cases rough, and a coarseness or brawny condition of the extremities was obvious, yet there was in most cases nothing which amounted clinically to oedema. Neither were the cutaneous sensations impaired in any marked way. The sense of balance was perfect, reflexes were normal and the memory good.

In most cases the heart was found to be enlarged and soft, the apex beat diffuse, the heart sounds tending to be equalised, the heart rate accelerated and irregular, frequently missing beats, there was evidently distension of the heart rather than hypertrophy. The wrist pulse was soft and rapid and irregular. The temperature was about 36·5–37° C., *i.e.* normal for Japanese people or only slightly above normal.

The only positive signs, therefore, were general weakness of the body, and varying degrees of affection of the heart, from an accelerated and obviously enfeebled heart to one definitely congested and possibly hypertrophied (the latter were cases which were supposed to have had Beriberi each of the two previous summers). In many cases there was loss of appetite, and often constipation. In practically all cases there was anaemia.

These cases were all classified by the Japanese medical officer as Beriberi, but it appears to the writer they would be better recognised as a pre-Beriberi condition. A condition which does not merely start with the cardiac symptoms but which already exists as a result of the faulty mode of nutrition. Thus the seasonal outbreak of this disability should be regarded as not merely the

initial stage of Beriberi beginning in previously healthy persons, but as an exacerbation of the condition of pre-Beriberi which already existed. The recognition of this fact would make all the difference in the attitude of the medical authorities towards the disease.

The case of the Japanese army seemed likely to offer a good opportunity of testing the idea of a pre-Beriberi condition, for recruits to the army are submitted to a careful medical examination, and only a small proportion of the fit are actually enrolled for training. The diet in the army cannot be considered as worse than that of the average civilian, and the life is certainly healthier, the men moreover are at the ideal age. If therefore during the course of military training many should develop Beriberi, it would surely point to the existence of a hidden condition of deficiency disease prior to the outbreak, or of something very closely akin to it. Through the kindness of Colonel L. R. Hill, and of the Japanese Military authorities the following facts were obtained:

Rations:

Each soldier receives per day:

	Pints
White rice	1·34
Barley	0·58

Extras:

	Ounces
Hard biscuit or bread	24·00
Tinned meat	5·25
Salt	0·50
Soy bean extract	0·65
Pickled vegetables	1·32

The bread and tinned meat twice per week, the other items each day.

Statistics of Sickness.

It will be most instructive to consider firstly the recruits and then men actually in training.

In 1923 there were 554,273 young men of conscriptional age. The exact number conscripted was not given, but may be taken at about 300,000.

The following facts were supplied with regard to the number of men who fell sick, died, or were exempted, subsequent to their enlistment in 1923.

Table I. *Recruits.*

Number of patients, death roll and exemption from service.

1923	No. of patients 207,939	Death roll 278	Exemption from service, 4512
Infectious and general	20,001	136	1114
Brain	4,166	23	274
Respiratory	25,736	31	2593
Circulatory	2,679	4	77
Nutritional	**82,429**	**40**	**83**
Reproductive ...	949	2	60
Venereal	4,650	—	18
Eye	3,401	—	50
Ear	1,413	—	26
Skin	22,882	—	23
Muscles	5,911	1	48
Injuries	33,660	25	143
Miscellaneous... ...	62	16	3

The Japanese army is trained on Spartan principles, and apparently everyone is a patient sometime or other in the first year. Yet the seriousness of such a high incidence of sickness amongst men of ideal age, and leading a healthy life cannot be ignored. As will be seen from Table I, forty per cent. of the sickness is recognised as "nutritional," and we may safely consider much of the other sickness as indirectly attributable to under-nourishment also.

And the point which the writer wishes particularly to emphasise, is that these cases of sickness have appeared in men who have previously been submitted to a careful medical examination, and considered fit for recruiting, and they have been fed in a manner considered by the authorities as satisfactory, at any rate no worse than they were fed prior to enlistment. The ration of barley which is obligatory and is mixed with the rice prior to issue, is supplied with the idea of preventing Beriberi, and so far as the majority are concerned the rations appear to contain sufficient vitamin B complex. However, 40 deaths and 83 exemptions from service on account of nutritional disease, which we may take as Beriberi, with 82,429 others reporting sick on the same grounds, seems a very convincing argument that even if there is not obvious Beriberi there is certainly a condition which is leading to it and which may be described as the pre-Beriberi condition.

One has only to observe some of the stronger men before and after recruitment to realise that on the whole the army conditions have improved them greatly, they have filled out, have lost their original pallor, they stand well and do not feel fatigue as before. Therefore it is clear that the sickness results not merely because the diet of the army is poor but because so many of the men though apparently well, as judged by Japanese standards, when recruited, are in reality under-nourished, and in many cases actually in the pre-Beriberi condition.

That this condition is deep rooted is further seen from the fact that it continues in the second two years of military training, as will be seen from Table II.

Table II. *Soldiers in Training.*

Statistics of sickness.

1923	Old patients		New patients		Total	Number of deaths
	Barracks	Hospital	Barracks	Hospital		
	1,553	1,475	211,651	37,444	252,123	306
Infectious and general	99	276	17,472	8116	25,963	184
Brain	38	45	3,742	1116	4,941	24
Respiratory	220	417	21,616	9598	31,851	45
Circulatory	21	30	2,162	1033	3,246	5
Nutritional	**345**	**205**	**92,902**	**6616**	**100,068**	**43**
Reproductive ...	6	15	617	520	1,158	2
Venereal	40	121	2,145	3394	5,700	—
Eye	33	32	3,326	578	3,969	—
Ear	23	14	1,278	379	1,694	—
Skin	259	52	24,925	1646	26,882	—
Muscles	74	36	6,125	797	7,032	1
Injuries	395	232	35,332	3594	39,553	2
Miscellaneous ...	—	—	9	57	66	—

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The number of men in the second two years of training, though not actually given may be taken as about 500,000. The incidence of sickness, therefore, though less than among recruits is remarkably high, and what concerns us most is to note that half of such cases are classified as nutritional. We shall probably not be wrong in considering the 6616 hospital cases as in large part Beriberi, and the 92,902 cases in barracks as being in many cases in the pre-Beriberi condition.

Indirect Evidence of the pre-Beriberi Condition.

There seems little doubt that the chronic catarrhal condition of the upper respiratory passages, which leads to adenoid growth, as well as directly or indirectly to the permanent opening of the mouth for comfortable respiration, and hence to tonsilitis and chronic bronchitis, is to be attributed to under-nourishment. Some have considered these conditions as resulting from lack of vitamin B complex (see Findlay (1922) and (1923)). Under-nourishment is almost certainly an important causative factor. The writer has made careful observation of the mode of respiration in Japanese people and observed that seventy-five per cent. habitually breath through the mouth. Children do not appear worse than adults. Men, however, appear worse than women in this respect. It is less obvious in the upper classes who are better fed, and may be trained to close the mouth. The open mouth is one of the most striking features to be observed amongst the working Japanese people. The attitude is seen both in the picture of the man making hoops (Plate I), and of the girl grinding rice (Plate II), which latter picture also serves to emphasise the view held by the writer that the rice food is the underlying cause of the chronic respiratory troubles.

Imperfect eyesight from which the population suffers greatly is probably also an outcome of under-nourishment, and together with anaemia and the habit of oral breathing referred to gives to the children, especially of the poorer classes, a characteristic drawn or pinched expression, which might be described as the pre-Beriberi facies. Some of such cases are to be seen in the picture of a typical group of poor children (Plate III). Here too, at the back especially, will be seen many mouths in the characteristic open attitude. This picture however, though it shows the type of face of ill-nourished people, does not give an adequate idea of the frequency of the open mouth, for these children are standing still. When any sort of effort is made the mouth opens at once, as is seen in the other two pictures of persons at work.

The picture of the hooper at work (Plate I) serves also to call to mind the fact that Japanese people prefer to sit than to stand. This is not mere habit, but represents a weakness of the legs and of the body generally, and incidentally it may be mentioned that sixty to seventy per cent. of young men rejected from the army are classed under the term "general weakness."

It is quite a common sight in Tokyo in the morning to see a large pro-

portion of adults, both men and women, dozing or even asleep in a public conveyance, and other people showing very obvious signs of fatigue.

Taken together, these many signs of weakness give a very definite impression of an under-nourished population, and support the view that there is a widespread pre-Beriberi condition.

ORIGIN OF THE PRE-BERIBERI CONDITION.

In the writer's opinion[1] the cause is to be sought in the inadequacy of the Japanese food as a whole, in respect of quality, and not merely an insufficiency of vitamin B. For an examination of the average diet of the Japanese people shows that it is ill-balanced in many respects. There is too much starch, and too little of nearly everything else, for example, protein, fat, lipoid, extractives, and of mineral constituents, phosphorus, lime, iron, potash, are lacking, while magnesium may be in excess. There is very little animal fat in the country so that there must be an inadequacy of vitamin A. Moreover the artificial treatment to which most of the food is submitted robs the food according to the writer's calculations of about ninety per cent. of vitamins before it reaches the consumer.

In order to obtain sufficient nourishment the Japanese people are obliged to consume large quantities of food, as may be seen from the amount of rice and barley allotted each soldier (see p. 262). Nine bowls of boiled rice per day is quite a common allowance. There is thus a large amount of work thrown upon the digestive system and upon the tissues generally, with consequences which are in part apparent in the list of the causes of death given on p. 260. In part, however, these consequences are not observed but act as a hidden source of evil undermining the health of the people.

PREVENTION AND TREATMENT OF THE PRE-BERIBERI CONDITION.

Once the widespread character of this condition is recognised the Japanese authorities will undoubtedly introduce measures to improve the average standard of diet in the country, aiming not merely at supplementing the supply of vitamin B complex, but adding the many other factors which are deficient, for a list of which the reader is referred to the writer's report to the League of Nations on this subject.

The pre-Beriberi condition has been defined as one which passes into Beriberi even without change of diet; it is obvious however that it has itself resulted from prolonged lack of proper nourishment. It is necessary, therefore, to go far back in the course of treatment, and begin with the child or even with the mother. The bulk of food given the child should be reduced, and percentage of protein raised. Milk and eggs would be valuable in Japan for this purpose, though at present very scarce. More natural and less artificial food must be employed.

The evils brought about by the present industrialisation of the country,

[1] Expressed in a report to the League of Nations on *The Food of Japan.* (In print.)

such as overcrowding, irregularity in meals, bad cooking, and monotonous dietary, fatigue, insanitary conditions, and worry, must as far as possible be alleviated by education, legislation, and medical supervision.

It must however be recognised that so long as rice represents such a large proportion of the total food, it will be exceedingly difficult to combat malnutrition in Japan, for in Japanese rice there is one part of protein to ten parts of starch, and in polished rice one part of protein to eleven parts of starch (to say nothing of other deficiencies), so that in order to get the equivalent of nourishment obtained by a European living on bread, as chief food, the Japanese must burn up in his body double the amount of starch, and this in the writer's opinion causes undesirable wear and tear of the tissues. The gradual introduction into the rice-eating countries of a staple food richer in protein will therefore do much to combat the malnutrition.

Conclusions.

1. A pre-Beriberi condition is described, and is considered to be very prevalent in Japan.

2. Much of the sickness at present classified as Beriberi is probably the pre-Beriberi condition.

3. The importance of the distinction lies in that its acceptance will lead to the recognition of the fact that widespread outbreaks of mild Beriberi are not merely the first symptoms of this disease, but are the last symptoms of pre-Beriberi disease, which is a chronic condition, with acute exacerbations, mistaken at present for the beginnings of Beriberi.

4. The pre-Beriberi condition arises from a prolonged use of a diet deficient in essential factors, as well as accessory factors, and in particular one too low in protein and too high in starch, though there is sufficient vitamin B complex to prevent, under ordinary circumstances, the appearance of Beriberi. It is, therefore, a condition to which the rice-eating peoples are liable whether the rice be polished or not.

5. When the pre-Beriberi condition is present Beriberi may appear as the result of many causes without any diminution in the quality of the diet, for example, as the sequel to fatigue, heat, or intoxication, and it is conceivable that a too sudden improvement in the quality of the diet might even act harmfully, in stimulating the body too quickly to activity.

6. Prophylactic treatment is by far the most important since the condition is slowly acquired, and difficult to cure. Diminishing quantity and increasing quality are the two great needs in Japan. Milk, eggs, meat are especially recommended, and natural instead of artificial foods. The detailed recommendations are given in a special report to the League of Nations.

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EXPLANATION OF PLATES I–III.

PLATE I.

Japanese hoop maker at work. Illustrating the habitual method of oral respiration, and the sitting posture for work, adopted by the rice eating people.

PLATE II.

Japanese girl grinding rice. Illustrating the habitual oral breathing especially when at work, and the stooping attitude due to general weakness.

PLATE III.

A group of typical Japanese faces. Illustrating the general condition of under-nourishment, the habitual open mouth, pinched expression of face, strained accommodation due to bad eyesight, and vacant expression due to poor development.

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