Some Remarks *rê* the Etiology of the Kakke Disease.

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Nowadays there are still some objections against the view that the kakke-disease prevailing in Japan and other oriental countries is produced solely by the deficiency of vitamin B₁ in the human body.

In the first place the objections are put forward from the view-point of epidemiology; while the deficiency of vitamin B acts to cause experimentally kakke-like disease all the year round and in the uniform severity without regard to seasons and individuals, people suffer from the kakke most frequently from summer to earlier fall, but only infrequently in winter, and young people suffer much in contrast to the aged and children. And among one and the same family, who are taking similar kinds of food, some suffer from the kakke, others do not.

In the second place there are a number of pathological papers in this country in which the authors claim the existence of differences in the patho-anatomical and patho-historical findings between the human cadavers died on the kakke and the animal bodies died on the experimental vitamin-B deficiency.

The heart, suprarenal capsules, and sexual organs, pancreas, liver, spleen, thymus, salivary glands, blood, nervous tissue, etc. were tested by Tomo. Ogata¹⁾²⁾ and Y. Hayashi³⁾, and some definitely different features were discovered there. Further Ogata came to witness some differences in the predisposition of hemorrhage and the resistance against infection as well. The content of the vitamin-B was not found diminished in the organs of cadavers died of kakke, while a large shortage is to be seen in the cases suffering from the artificial vitamin deficiency, as Ogata also related to.²⁾⁴⁾

Thirdly, there are also easily noticeable differences in degree between both the kinds of disease *rê* disturbances of the appetite and the digestion, and also *rê* the nutritious condition and body weight, as mentioned by J. Shimazono,⁵⁾ etc. The sufferings are incomparably serious in cases of the

vitamin B deficiency.

Now turning to the baby-kakke, it may be further pointed out: Nearly no signs of the baby-kakke are detectable among the babies fed with cereal powder only and consequently suffering from the vitamin deficiency. A baby can be recovered from the kakke readily and without exception if weaned even in the serious stage of suffering and then given food stuffs poor in the vitamin, such as condensed or powdered milk. (N. Hirota⁸⁷⁾ *et al.*). Interesting are the cases, though rather seldom, where in a mother, whose baby was suffering from the baby-kakke but no signs of kakke were detectable in herself, the signs became often suddenly manifest when suckling was discontinued. (T. Inagaki⁸⁾ and R. Ikeda⁹⁾). Further, basophile granules appear in red blood cells of babies with the kakke and of patients suffering seriously from the kakke (K. Takasu¹⁰⁾).

In such a manner various materials, observed by a large number of the pathologists and clinicians in this country seem to offer decided obstacles for taking the kakke and the vitamin-B insufficiency as completely identical.

Now, clinical, but experimental observations of the present writer seem to add some other supports to the non-identical theory, which will be given in the following pages.

I.

In summer of 1924, I had an opportunity to observe a group of students aged 19–20, 7 in number, who attended a college and were living in a boarding house together. While some of them were remaining quite healthy, others suffered from the kakke. They all graduated higher schools in March and entered that college in April. They took every day in the boarding house quite same amount of food of quite same quality, that is, no variations among the individuals, except the amount of rice cooked. Five students did not take any other physical exercise than the walk to and from school, say 600 meters. The two remainings took a moderate amount of recreation; they remained healthy.

Of the five persons, three suffered from kakke of a moderate degree and two only lightly.

The amount of rice taken by those kakke students were 1400–2420 g. per diem or 33–46 Calories per kilo body weight, per diem, while the two healthy took 1600 g. or 36–38 Cal. Two students who took somewhat large amount of rice, 2000–2420 g. every day, and suffered from the kakke of a moderate grade had taken more larger amount of rice, i.e. 600 g. more, when they studied in higher schools, but one used to walk from home to school and back, about 24 kilometers every day and the other was a base-ball player, and they then were quite healthy.

This story shows, it may be readily said, that while there were no material differences between two groups of students, 5 kakke students and two healthy, *rê* the amount of rice taken every day, the former had only a small amount of physical exercise contrary to the healthy students. The other conditions of nutrition and living manner were quite the same among them.

Among clinicians it is sometimes said, that the eater of a large amount of rice apt to suffer from the kakke, because of a relative deficiency of vitamine B. This view may be however readily disproved, for example, by the fact that a student (Miyata)⁹⁾ who took the smallest amount of rice (1400 g. per diem, namely 32.8 Cal. per diem, per kg.) suffered from the kakke, though lightly.

Further, that the absolute amount of vitamin is not responsible for bringing about the disease is deducible from the data that some suffered therefrom, while some others remained quite healthy, notwithstanding that the students took almost the same amount of vitamine every day.

II.

Since the three students suffered from the disease of a moderate degree took a little more rice than the other two suffered only slightly, and further some intimate relationship of the rice to the development of kakke is alluded, an over dose of carbohydrate diet has been tried as follows.

It is to compel a quite healthy person to take cooked starch or milk sugar in a certain amount.

Some individuals were selected from nurses or nurse-students lodging in the nurse boarding house in our hospital; they had never suffered from the kakke previously and obliged to take besides the ordinary diet as usual with the addition of 250 g. Japanese macaroni before the dinner and 500 g. before going to bed, or 214 g. milk sugar a day, i.e. divided into several portions and taken at the times at will.

It was very difficult to find such persons who were able to continue this kind of experimentation in a period extending for a week or longer. The ordinary diet does not bring about the disease in any person, and it was so in the boarding house in the period of the experimentation. And whether the persons under investigation have eaten up all the ordinary diets and the extra carbohydrate or not was strictly watched.

The test thus planned could be carried out without failure only in three nurses.

To take cane sugar or grape sugar in a large quantity for a period, longer than 2 or 3 days, was wholly intolerable to any. Milk sugar also apt to occasion diarrhoea; only a nurse was able to take it for two weeks in dose of 214 g. a day.

- (a) A secretary nurse, 21 years old, 55.5 kilos.

Ordinary diet 42.8 Cal. per kilo (Carbohydrate 36.2 Cal.)
 Extra carbohydrate 15.0 „ („ 14.4 „)
 (Macaroni)
 Total 57.8 „ („ 50.6 „)

- (b) A nurse-student, 17 years old. 43.7 kilos.

Ordinary diet 56.4 Cal. per kilo (Carbohydrate 49.0 Cal.)
 Extra carbohydrate 19.1 „ („ 18.3 „)
 (Macaroni)
 Total 75.5 „ („ 67.3 „)

- (c) A nurse-ment, 18 years old. 55.7 kilos.

Ordinary diet 39.5 Cal. per kilo (Carbohydrate 35.9 Cal.)
 Extra carbohydrate 15.7 „
 (Milk sugar)
 Total 55.2 („ 51.6 „)

The two nurses, who took macaroni besides the ordinary diet, suffered from the kakke, so that all the symptoms developed fully at the end of two weeks of extra feeding. A dilated heart was photographed by X-ray. Despite of the smallness of carbohydrate amount the secretary nurse showed more severe symptoms than the other, what is due surely to the smallness of physical exercise. All the symptoms disappeared almost entirely ten days after discontinuation of the extra feeding, without any other treatment.

The nurse student (c), fed with the addition of milk sugar in particular not only did not betray any trace of the disease, but also the pulse rate difference due to the exercise was counted as smaller and the heart-figure in X-ray photo appeared rather a little smaller.

This outcome might be taken as indicating that the excess of starch in the food is harmful as to occasion the kakke disease, while the disaccharide given in the amount as to correspond to the extra starch & the fuel value has no influence upon the health if any.

It may be added here by way of precaution the fact that all the nurses and nurse-students in our hospital boarding house, other than these three, did not suffer from the kakke for the period of the present experiment can be taken as the control for the latter.

What is responsible for this clear difference ?

Next I tried to feed persons with the starch digested by the diastase, for it has become manifest that there must be something hidden in the processes of digestion from polysaccharide to disaccharide in the digestive tract *in situ*.

Several trials were carried out, but finally from the technical point of feeding diastase was given in a dose of 2 g. Takadiastase mixed to 50 g. rice cooked, with a result showing some beneficial effect in 7 cases of kakke of a moderate severeness, but never comparable to that with milk sugar. It is now found difficult to trace the cause of the difference to the purely chemical processes of the digestion of polysaccharides.

III.

As is well known, the raw or unpolished rice cooked acts demonstrably to cure the kakke always with success. On the other hand it is, however, also well known that the raw rice cooked can not be eaten so much as the polished rice; the former of about only half the quantity of the latter can taken without difficulty.

If the polished rice cooked in the same amount of the raw rice taken be given, kakke patients apt to recover, though not much. Addition of be vitamin B acts to hasten it.

Here I wish to present an accidental observation that the unpolished rice, when it is boiled for a considerably long time with water in the form of gruel, could not develop an ability to cure a kakke patient, with poor teeth. Further coarse rice bran was made vitamin free by treating with 50% alcohol (Relatively large grain of rice-bran, remained on the sieve, was extracted by 5 volumes 50% alcohol for 12 hr. at the room temperature, sometimes being shaken. Of the residue, the same procedure was repeated. 5 times in all.), and 10 g. were given at each meal, whereby five persons suffering from the kakke of a light grade, recovered therefrom. Similar patients, 4 in number, were treated with coarse-grained Alsilin (animal-charcoal, plated with silver) with similar outcome to the cases of the vitamin free coarse rice-bran.

In passing other clinical experiences, well known, will be here mentioned for supplementing the present data.

The fact that persons working in sewing, printing, spinning manufactories are liable to suffer from the kakke, contrary to those who take a light walk, though the amount of physical exercise does not much differ from each other, and further the fatigue also accelerates the development of kakke; otherwise expressed, the existence of an insufficient digestion in such person must be taken into consideration. The influence of climate, particularly of the temperature and moisture is also well known.

SUMMARY.

The present observations were done on human beings, the healthy and the patients suffering from the kakke as well. The chief data may be

summarized as follows.

1. Youths, who neglect physical exercise, apt to suffer from the kakke, if the nutritious conditions, especially the amount of the vitamin B, be taken practically same to those who remain quite healthy.

2. Disaccharide, as milk sugar, does not effect any development of the disease, while polysaccharide as starch, taken in the amount to furnish the same amount of fuel value, acts to produce it.

3. Unpolished rice, if it will be cooked for a long time in the form of gruel, cannot effect to cure the kakke, while rice-bran, made vitamin B free by means of alcohol, acts to lessen the disease.

Such outcomes apparently give us some warnings against taking the deficiency of vitamin B as the sole cause of the kakke disease, as several authors commonly assume, the various materials, pathological and clinical as well, put forwarded by a number of authorities in Tokyo, etc. what are concisely presented above, being taken also into account.

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