A Study of Nutritional and Bio-geochemical Factors in the Occurrence and Development of Keshan Disease

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Keshan disease is a chronic endemic cardiomyopathy, which was first discovered in the rural areas of China. The author proposes that Keshan disease is a nutritional bio-geochemical disease.

The differences between the endemic and non-endemic areas consist of the water-soil factors (bio-geochemical elements) in the natural environment. The etiological factor of the natural environment in the endemic region acts on the human body by way of the food consumed. Those who lived on a “single type of food”, which was produced from their own fields, were liable to suffer from Keshan disease. Young females of child-bearing age and children after lactation were the most frequent victims of the disease. The use of soy-beans to improve the diet and oral administration of sodium selenite will prevent Keshan disease. Experiments on animals fed on cereals and vegetables from the endemic areas have shown that there might be some myocardial necrotizing factor and/or growth inhibition factor in the water-soil elements.

Keshan disease is a chronic endemic myocardial disease which was first discovered in 1935 in Keshan County, Heilongjiang Province, China. Since 1953, the author and co-workers have surveyed a population of more than 60,000 persons in endemic and non-endemic areas of 160 counties of the following provinces: Heilongjiang, Jilin, Liaoning, Hebei, Henan, Shandong, Shaanxi, Gansu, Hubei, Shanxi, Sichuan and Yunnan, and of two autonomous regions (Neimeng, Xizang). Of these, 3,500 individuals were found to have Keshan disease. They were examined systematically, given first aid treatment and follow-up observations. Keshan disease was also found in 479 of 600 autopsied cases.

In 1965, a long-standing prevention and observation unit was set up in a district with a population of 160,000. In two endemic areas, 371 families were experimentally put on an improved prophylactical diet for 3–5 years and were observed for the same length of time. Also 1,800 animals were studied by experimental procedure. In the provinces where the disease occurred extensively, the diet was investigated and analyzed. In 326 samples of foodstuffs taken from the endemic and non-endemic areas, the presence of the trace elements Se, Cu, Zn, Mn, Fe and Mo was investigated.

**Clinical Types**

On the basis of our work mentioned above,

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**Key Words:**
- Keshan disease
- Epidemiology
- Nutrition
- Bio-geochemistry
- Prophylaxis

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Fig.1. An autopsied heart (600 g in weight) from a case (24 year old male) with chronic Keshan disease. The left ventricle is highly dilated and old myocardial scars are widely scattered.

Fig.2. Histopathology of the myocardium from a case of chronic Keshan disease. Disseminated necrotic foci are characteristic (HE stain).

we believe that Keshan disease can be divided into the following four clinical types:
1) Latent type: this is the most common type. It is seen at the early stage of the disease or in the chronic recurrent form. In this type, the cardiac function is in compensation.
2) Acute type: this has an abrupt onset. Severe arrhythmia and cardiogenic shock are seen.
3) Chronic type: the cardiac function is severely impaired. This may be an intermediate form of the other types.
4) Subacute type: predominant in children with general edema and heart failure. At present, this is the most prevalent form of the disease.

**Autopsy Findings**

Typical pathological changes seen in autopsied hearts are as follows:
1) Marked ventricular dilatation and a comparative increase in heart weight (Fig. 1).
2) Diffuse myocardial degeneration, with old and new lesions co-existing (Fig. 2).
3) The main changes are in the parenchyma of the myocardium; the inflammatory change is only secondary.
4) Scattered and focal myocardial necrosis.
5) Involvement of the conduction system.
6) Thrombosis and infarction are frequent; the incidence of mural thrombi in the ventricles

Fig.3. Monthly incidence of the acute type of Keshan disease in Heilongjiang Province during 1955–1966.

and the auricles is 21.5%.

**Characteristics of Epidemiology**

There was marked difference in the incidence according to the location, season, year and

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Fig. 4. Incidence of the different types of Keshan disease in Heilongjiang Province (%).

Fig. 5. Incidence of Keshan disease in Heilongjiang Province.

Fig. 6. Distribution of Keshan disease in China.

Fig. 7. Distribution of Keshan disease in Wuyuer River basin. The endemic areas are distributed in the higher areas.

In view of the above facts, Keshan disease may be defined as a chronic endemic cardiomyopathy of unknown etiology. The epidemiological characteristics are prevalence in particular districts, years, seasons and among specific socioeconomic groups of people.

occupation of the victims.

Prevalent area: Keshan disease predominated over all other cardiac diseases in the endemic districts.

Prevalent time: In some prevalent years, the incidence reached a peak (year of peak incidence), but in the other years, the incidence was much lower (ordinary year). Prevalent season (where the incidence of the disease was high) was winter in northern China and summer in the south-west part of China (Figs. 3 and 4).

Prevalent population: peasant women of child-bearing age and peasant's children after lactation (Fig. 5).

Definition

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Fig. 8. Incidence of Keshan disease in Heilongjiang Province during 1955–1966.

Fig. 9. Keshan disease in children in Dazhu County of Sichuan Province during 1973–1977. Incidence during different months. The incidence in children after lactation (2–7 years old) is 94.6%.

Epidemiology of Keshan Disease
The characteristic distribution of Keshan disease is belt-like, i.e., from north-east to south-west, identical to the ploughing area, where the trace elements in the soil were washed away (Figs. 6 and 7).

The incidence rate of Keshan disease diagnosed in an endemic area may be as high as 11%, e.g., in Huanglong County of Shanxi Province. During outbreaks, Keshan disease had the highest incidence of all heart diseases; in Beian County of Heilongjiang Province in 1962, it reached 42% of all cardiac diseases. In a prevalent season (August, 1972), as many as 50% of the patients hospitalized were suffering from Keshan disease,

TABLE I DIFFERENCES IN INCIDENCE OF MORTALITY BETWEEN PEASANTS AND EMPLOYEES IN AN ENDEMIC AREA OF KESHAH DISEASE (SHANGZHI COUNTY IN 15 YEARS).

<table>
<thead>
<tr>
<th>Kinds</th>
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<th>Population</th>
<th>Incidence</th>
<th>Mortality</th>
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<td></td>
<td></td>
<td></td>
<td>families</td>
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<td>859</td>
<td>33</td>
<td>18.9</td>
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<tr>
<td>EMPLOYEE</td>
<td>188</td>
<td>1076</td>
<td></td>
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</tbody>
</table>

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Fig. 11. Dietary composition of the population in the endemic area (15th brigade in Fuyu County) during different years (%). In the prevalent year, the diet was very simple.

Fig. 12. Mean dietary proportions of staple and subsidiary foods of peasants and railway workers (1975). The peasants, who ate the agricultural products from their own fields, had a very simple diet as compared to the railway workers.

Fig. 13. Necrotic foci of papillary muscle (X240, HE stain). Albino rat (No. 1014) fed on grains from the endemic area.

In the northern mountainous districts of Korea, which is in the neighborhood of one of the endemic districts of our country, there are reported occurrences of Keshan disease. However, in Siberia which also borders our country, no case has ever been reported. In Equatorial Africa a similar myocardial disease has been encountered, but its relationship to Keshan disease is not yet clear.

Regularity of the Outbreaks of the Disease: According to our yearly observation, we noticed that in some years, Keshan disease was prevalent and in others it was rarely seen. For example, in 1955 in Heilongjiang Province, the prevalence rate was 32.7/100,000, but in 1961, it was only 1.9/100,000. Sometimes during a prevalent year, several counties in one province, or several communes in one county were attacked by the disease. During large outbreaks, the prevalence rate in one county could be as high as 980/100,000, e.g., in Shangzhi County of Heilongjiang Province in 1969 (Fig. 8).

In the northern endemic area where Keshan disease is mainly of the acute type, 90% of the patients had attacks in winter (from Nov. to
Feb.). In the south-western endemic area where the disease is mainly of the subacute type, 80% had episodes from June to August (Fig. 9).

**Prevalence among Certain Groups:** Ninety-nine percent of the patients lived on grains from their own fields, and 80% of these were young females of child-bearing age and infants after lactation. In the south-western area, child-bearing female were the main victims (Fig. 10). However, coal miners, foresters, railway workers and others living in the same endemic area as the peasants, who ate commercial agricultural products rather than food produced by the peasants, did not have Keshan disease (Table I). Thirty percent of the patients, all from poor families, had a family history of Keshan disease.

In addition to Keshan disease, endemic goiter and Kachin-Beck’s disease are also common in the endemic areas. However, there is no interrelationship among these three conditions. In the endemic areas, no animals were found to be suffering from Keshan disease.

From the view of epidemiology, it seems apparent that the etiology of Keshan disease is related somehow to the characteristics of the natural environment, that is, some geo-chemical elements act on the body by way of water and soil, resulting in Keshan disease.

**The Relationship between Water-soil, Conditions of Food and the Prevalence of Keshan Disease**

Following an investigation of the type of food consumed in endemic and non-endemic areas of Heilongjiang, Jilin, Shandong, Shanxi and Yunnan Provinces, as well as of Xizang autonomous region, the author and co-workers examined not only the contents of trace elements in the soil, water and the hair of inhabitants of the endemic area, but also various organic and inorganic chemicals in the food. The content of selenium in the internal and external environments of the patients was low, and the staple food was simple, e.g., in Fuyu County of Heilongjiang Province, 90.16% of the diet was maize (Figs. 11 and 12).

In the non-endemic area, only 28.1% of the patients’ food was maize, 11.3% was wheat flour, 58.6% millet and 1% sorghum. As for the non-peasant population in the endemic area, the staple food was of a mixed type (Fig. 12). The author therefore suggests that people who had been living for a long time on a “single type of food”, which was harvested from their own fields in the endemic area, with its particular background of water-soil conditions were liable to suffer from Keshan disease.

**Improvement of Prophylactic Diet in Experimental Districts**

Since 1965 the author and co-workers supplied 1,500 individuals from 371 families in two observational areas in Dedu and Fuyu Counties, with home-made soy-bean preparations (doufu and soy-bean powder). In one of the areas, each person ate 250 g doufu daily, and in the other each individual was supplied with soy-bean flour which amounted to 10% of his staple food. During the following 3 to 5 years while the families were on the improved diet, no Keshan
disease was reported in these places, but in the neighboring control areas, new patients with Keshan disease were often reported. This experiment proves that in the endemic area the supplement of soy-bean products to improve the diet can prevent the occurrence of Keshan disease.

Animal Experiments

The experimental results of using maize or raw oats and potatoes from endemic and non-endemic areas to feed 1,800 albino rats showed that the incidence of myocardial necrosis in the endemic area was within 6–13%, whereas in the non-endemic area the condition was non-existent (Fig. 13).

When the food from the endemic area was supplemented by other kinds of food, such as soy-bean powder, the incidence of myocardial necrosis in the animals was lowered. In some places, a selenium supplement gave the same results. Likewise, the use of sodium selenite showed good results in the prevention of Keshan disease (Fig. 14).

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