# Outbreak of Beriberi Among Illegal Mainland Chinese Immigrants at a Detention Center in Taiwan

Kow-Tong Chen, MD, PhD<sup>a</sup> Shiing-Jer Twu, MD, PhD<sup>b</sup> Shu-Ti Chiou, MD, MS<sup>c</sup> Wen-Harn Pan, PhD<sup>d</sup> Hong-Jen Chang, MD, MPH, MS<sup>b</sup>

MARY K. SERDULA, MD, MPHe

### **SYNOPSIS**

**Objective.** The authors describe an outbreak of beriberi in a detention center in Taiwan and examine risk factors for illness.

**Methods.** A survey was conducted among a sample of 176 randomly selected detainees. A menu-assisted dietary recall method was used to obtain diet information from nine hospitalized detainees. A probable case patient was defined as an individual who had at least two of the following characteristics: leg edema, weakness of the extremities, poor appetite, and dyspnea. Possible case patients were those who had only one of these characteristics.

**Results.** Of the 176 survey respondents, 19% were classified as probable case patients and 40% as possible case patients. The mortality rate based on probable cases was 1.1%. Body Mass Index (BMI) was negatively associated with illness (p<0.0001), and length of stay in the detention center was independently positively associated with illness (p<0.05). The average intake of dietary thiamine among the nine hospitalized case patients who completed three-day dietary recall surveys was  $0.49\pm0.1$  mg/day. After thiamine administration, all symptoms and signs of beriberi resolved.

**Conclusion.** This outbreak is a reminder of the importance of ensuring adequate diets for poor, institutionalized, or refugee populations who are unable to supplement their diets.

Address correspondence to Shiing-Jer Twu, MD, PhD, Center for Disease Control, Dept. of Health, Taiwan, Republic of China, No. 6-8F, Lin-Shen South Rd., Taipei, Taiwan; tel. 886-2-2396-7764; fax 886-2-2321-0110; e-mail <a href="mailto:ktchen@cdc.gov.tw">ktchen@cdc.gov.tw</a>.

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<sup>&</sup>lt;sup>a</sup>Field Epidemiology Training Program, Center for Disease Control, Department of Health, Taiwan, Republic of China

<sup>&</sup>lt;sup>b</sup>Center for Disease Control, Department of Health, Taiwan, Republic of China

<sup>&</sup>lt;sup>e</sup>Health Bureau of I-Lan County, Taiwan, Republic of China

<sup>&</sup>lt;sup>d</sup>Institute of Biomedical Sciences, Academia Sinica, Taiwan, Republic of China

<sup>&</sup>lt;sup>e</sup>Division of Nutrition and Physical Activity, Centers for Disease Control and Prevention, Atlanta, GA

Beriberi is caused by thiamine (vitamin B1) deficiency. This disease was common during the 1800s and early 1900s, especially in Asia, where polished rice was and continues to be the major staple of most diets. The role of a polished rice diet in causing beriberi was first described in the late 1800s by Eijkman, who observed that chickens raised on a diet of refined rice developed acute head retraction that could be reversed by adding unrefined brown rice to the feed. Thiamine was isolated in 1934 and synthesized for the first time in 1936. Today, because of food fortification and a general improvement in living conditions worldwide, beriberi has become an extremely uncommon disease.

More recently, beriberi, although still extremely uncommon, has been reported in refugee populations as well as among alcoholics, those undergoing total parenteral nutrition without thiamine, and those on severely restricted diets.<sup>4–7</sup> Rare causes of thiamine deficiency include the ingestion of raw fish or bracken fern containing anti-thiamine factors, thiamine-responsive inborn errors of metabolism, and chronic febrile conditions.<sup>3</sup> In Taiwan, before the outbreak reported here, beriberi had not been described since 1979.<sup>8</sup>

# **Background**

Illegal immigrants from mainland China are held in detention centers in Taiwan until they are repatriated. We describe an outbreak of beriberi among illegal immigrants incarcerated at the I-Lan Detention Center, located about 150km from Taipei Metropolitan City. From June 1 through June 14, 1999, 12 previously healthy detainees were hospitalized because of leg edema, weakness of the extremities, poor appetite, and dyspnea. Detainees were treated symptomatically because the cause of their illness was not initially identified. Despite receiving respiratory and cardiovascular support, two of the patients died within 24 hours of hospitalization. The medical staff then sought consultation from physicians at nearby teaching hospitals. Infectious diseases were initially suspected, and antibiotics were administered. However, the patients' medical conditions continued to worsen, and further consultation was sought from Taiwan's Center for Disease Control. Researchers conducted a medical records review and found that from February through May 1999, 15 additional patients had been hospitalized and symptomatically treated for heart failure or renal dysfunction. In addition, the medical records review showed that some detainees who had been returned to China were unable to walk without assistance during repatriation.

Because hospitalized patients had a combination of high output heart failure, leg edema, and polyneuropathy, beriberi was suspected and thiamine treatment was initiated. Over the following days, hospitalized patients improved rapidly. From June 15 to June 18, an additional four detainees were hospitalized with a similar clinical picture; they, too, improved with thiamine treatment.

Because thiamine deficiency was suspected to be the cause of illness, several measures were implemented to treat the hospitalized case patients and prevent others from developing the disease. Thiamine (300 mg) was given intravenously to the hospitalized immigrants who were severely ill, and a lower dose (100 mg) was given orally to all detainees. With intravenous administration of thiamine, symptoms began improving within 10 to 22 hours.

When this outbreak occurred, 381 illegal immigrants, 82 police officers, and 6 cooks were at the detention center. Detainees participated in one hour of exercise each day. While the police and other staff members had access to outside food, detainees ate only food that was prepared by the detention center cafeteria. None of the police officers or other detention center personnel became ill or complained of symptoms similar to those of the detainees.

#### **METHODS**

#### **Epidemiologic investigation**

Researchers from Taiwan's Center for Disease Control obtained lists of all detainees at the I-Lan center and then selected study participants using systematic random sampling. In June, they selected a systematic random sample of 190 individuals from the list of detainees for interviews by trained public health nurses. Some of those selected had already been repatriated; these were replaced by individuals who were listed immediately before or after them. A total of 176 questionnaires were returned, for a response rate of 93%. Information was collected on age, residential location in mainland China, occupation, height and weight, length of stay in detention center, and history of illness including date of onset, symptoms and signs, and hospitalization. Body weight and height were measured by detention center personnel. Body Mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared and was used as an index of overall adiposity.9 The information on deceased subjects was abstracted from medical records.

# **Dietary information**

Using a menu-assisted dietary recall method,<sup>10</sup> researchers obtained information on dietary intake from nine hospitalized case patients. Daily meal menus were pro-

vided by the detention center kitchen. Hospitalized case patients were asked to recall, using a food item list, the foods consumed and their portion sizes from the menus of three selected days (one weekend day and two week days). 10 The nutrient content of the diet was calculated according to the recipe provided by the kitchen, using the Taiwan national food composition table,11,12 and reported intakes were compared with the Estimated Average Intake recommended by the U.S. Institute of Medicine.<sup>13</sup>

#### Case definition

For study purposes, a probable case patient was defined as one who had any two of the following clinical characteristics during the period from January to June 1999: leg edema, weakness of the extremities, poor appetite, and dyspnea. A possible case patient was defined as one who had only one of the above clinical characteristics during the same time frame. Weakness of the extremities was defined as being unable to walk or elevate the leg and was determined by history or physical exam.

### Statistical analysis

Statistical analysis was conducted using SPSS software.<sup>14</sup> Univariate analysis was used to identify factors associated with being a probable case patient or a possible case patient. In the univariate analysis, the association between illness and categorical risk factors was assessed for statistical significance by the chi-square test; the association for continuous variables was assessed using t-tests. Researchers also performed logistic regression analysis to identify covariates associated with case status. To be entered into the logistic model, variables had to be significantly associated (p<0.05) with being a case in the univariate analysis. Case status (probable or possible case vs. non-case) was the dependent variable. The independent variables entered into the model were occupation (farming, fishing, manual labor, business, other), residence in China (Fuchin township vs. other townships in Fukien Province), BMI (below median vs. above median), and duration of detention ( $<60 \text{ days}, 60-89 \text{ days}, 90-119 \text{ days}, <math>\ge 120$ days). The backward stepwise procedure was used to eliminate variables that were not significant at p < 0.05). A two-sided p-value < 0.05 was considered statistically significant.

#### **RESULTS**

# **Epidemiologic investigation**

Of the 176 detainees, 34 (19%) had probable beriberi, 70 (40%) had possible beriberi, and 72 (41%)

were healthy with no symptoms. The attack rate based on probable cases was 19.3% (34/176), and the mortality rate was 1.1% (2/176). All 176 detainees were male and residents of Fukein Province in mainland China. Their mean age was 30.4 years (range 22 years to 40 years). The first case of beriberi occurred in February 1999, and the epidemic peaked in June. The most common symptoms of probable case patients were leg edema (100%) and weakness of the extremities (77%). The most common symptoms of possible case patients were weakness of the extremities (56%) and leg edema (32%) (Table 1). Among 12 hospitalized patients, 4 (33.3%) had lactic acidosis. The majority of the 104 probable or possible patients had a BMI  $\geq$ 18.5 kg/m<sup>2</sup> and  $\leq$ 25 kg/m<sup>2</sup>, and 5% had a BMI  $\geq 25.0 \text{ kg/m}^2$ . (None of the respondents was underweight [BMI  $\leq 18.5$ ].) The mean BMI was  $21.5 \text{ kg/m}^2$ , and the median was 21.0 kg/m<sup>2</sup>. The average duration of stay in the detention center was three months.

Compared with non-ill subjects, probable case patients were more likely to be farmers (18% vs. 8%), reside in Fuchin township (34 % vs. 15%; p < 0.02), have a longer duration of detention (126±40 days vs.  $77\pm55$  days; p < 0.001), and have a lower BMI (19.8 $\pm0.7$ vs.  $22.4\pm1.3$ ; p<0.0001). Age was not significantly different between ill and non-ill individuals (Table 2). Compared with non-ill subjects, possible case patients were more likely to have stayed longer in the detention center (98 $\pm$ 55 days vs. 77 $\pm$ 55 days, p<0.03) and to have lower BMI  $(21.0\pm1.0 \text{ kg/m}^2 \text{ vs. } 22.4\pm1.3$  $kg/m^2$ ; p < 0.0001) (Table 2). In the logistic regression analysis, BMI was negatively (p<0.001) associated and length of stay was positively (p < 0.05) associated with

Table 1. Percentage of probable and possible case patients with selected symptoms and signs during an outbreak of suspected beriberi disease, Taiwan, February-June 1999

|                         | Probable case patients (n = 34) | Possible<br>case patients<br>(n = 70) |
|-------------------------|---------------------------------|---------------------------------------|
| Symptom/sign            | Percent                         | Percent                               |
| Leg edema               | 100                             | 32                                    |
| Weakness of extremities | 77                              | 56                                    |
| Poor appetite           | 29                              | 9                                     |
| Vomiting                | 27                              | 7                                     |
| Nausea                  | 18                              | 9                                     |
| Chest pain              | 18                              | 13                                    |
| Abdominal pain          | 15                              | 11                                    |
| Dyspnea                 | 9                               | 3                                     |

Table 2. Case status by various characteristics, outbreak of suspected beriberi disease, Taiwan, February–June 1999

| Variable                          | Probable case patients<br>(n = 34) | Possible case patients<br>(n = 70) | Non-ill subjects<br>(n = 72) |
|-----------------------------------|------------------------------------|------------------------------------|------------------------------|
| Mean age (years)                  | 29.4                               | 30.8                               | 30.5                         |
| Mean BMI (kg/m²)                  | 19.8ª                              | 21.0ª                              | 22.4                         |
|                                   | Percent                            | Percent                            | Percent                      |
| Educational level                 |                                    |                                    |                              |
| Illiterate                        | 9                                  | 7                                  | 4                            |
| <6 years                          | 53                                 | 64                                 | 57                           |
| 7–9 years                         | 29                                 | 20                                 | 36                           |
| ≥10 years                         | 9                                  | 9                                  | 3                            |
| Occupation                        |                                    |                                    |                              |
| Farming                           | 18 <sup>b</sup>                    | 9                                  | 8                            |
| Fishing                           | 24                                 | 29                                 | 46                           |
| Manual labor                      | 29                                 | 36                                 | 36                           |
| Business                          | 6                                  | 4                                  | 3                            |
| Other                             | 23                                 | 22                                 | 7                            |
| Dormitory                         |                                    |                                    |                              |
| A                                 | 35                                 | 23                                 | 33                           |
| В                                 | 21                                 | 33                                 | 32                           |
| С                                 | 44                                 | 44                                 | 35                           |
| Residence                         |                                    |                                    |                              |
| Fuchin township                   | 34 <sup>b</sup>                    | 14                                 | 15                           |
| Other township                    | 66                                 | 86                                 | 85                           |
| Mean duration of detention (days) | 126ª                               | 98 <sup>b</sup>                    | 77                           |

NOTE: As noted, results are means for continuous variables and percentages for categorical variables. For comparisons with non-ill subjects, t-tests were used for continuous variables and chi-square tests were used for categorical variables.

ap<0.001.

 $^{b}p < 0.05.$ 

BMI = Body Mass Index

illness (Table 3). Other factors, such as occupation or residential location, were not significantly associated with illness. (An analysis restricted to probable cases and non-cases found that BMI was negatively related to case status.)

### **Dietary information**

The detainees' diet was monotonous, with the same meals served repeatedly week after week. The food served included refined rice, gluten products (wheat-based items), fish, marbled meat, green vegetables, and fruits. No dairy products and very few beans or peas were provided. Among the nine hospitalized case patients who completed three-day dietary recall surveys, the average calorie intake was 1,781 kcal/day

(national average is 2,203 kcal for adult men<sup>12</sup>), and the average thiamine intake was  $0.49\pm0.1$  mg/day.

#### **DISCUSSION**

We describe a large beriberi outbreak in a population of illegal Chinese immigrants detained in Taiwan. Despite classic symptomatology and the occurrence of individual cases over a five-month period, beriberi was not initially suspected and was not recognized until 12 individuals were hospitalized and two died in a two-week period. Among those interviewed, 19% met the criteria for a probable case and 40% met the criteria for a possible case. The risk for illness among detainees with probable or possible illness was higher for

Table 3. Variables independently associated with illness for all cases (probable and possible cases) in logistic regression analysis, outbreak of suspected beriberi disease, Taiwan, February-June 1999

| Variable                     | OR               | 95% CI     |
|------------------------------|------------------|------------|
| BMI (kg/m²)                  |                  |            |
| ≤ median (≤21)               | 1.0              | (Referent) |
| > median (>21)               | $0.06^{a}$       | 0.02, 0.13 |
| Duration of detention (days) |                  |            |
| <60                          | 1.0              | (Referent) |
| 60–89                        | 3.7 <sup>b</sup> | 1.1, 12.5  |
| 90–119                       | 4.3 <sup>b</sup> | 1.4, 13.6  |
| ≥120                         | 4.1 <sup>b</sup> | 1.2, 13.9  |
|                              |                  |            |

 $<sup>^{</sup>a}p < 0.001$ .

OR = odds ratio

CI = confidence interval

BMI = Body Mass Index

those with lower BMI and longer stays in the detention center.

In this outbreak, beriberi was diagnosed for several reasons: (a) patients exhibited the typical symptoms of beriberi<sup>15–20</sup> without any other apparent cause and dramatically improved after administration of thiamine, and (b) the amount of thiamine in the diets (0.49 mg/)day) was much lower than the Estimated Average Requirement (1.0 mg) recommended by the U.S. Institute of Medicine for men ages 19-50 years. 13 Unfortunately, researchers were unable to confirm diagnoses of thiamine deficiency by laboratory analysis because the patients had been given thiamine treatment upon suspicion of beriberi. Our study showed a higher attack rate (19% vs. 9%) and lower mortality rate (1.1% vs. 2.3%) compared to a beriberi outbreak in the Gambia in a free-living village population after gradual replacement of traditional cereals with imported milled rice.21 Consistent with the Gambia study, most of the case patients in our study were free of leg edema within a few days of thiamine administration and many noticed a swift diuresis after their first dose of thiamine.

Thiamine in the form of thiamine pyrophosphate is essential for glucose metabolism in the body. In the absence of thiamine, pyruvate from the glycolytic pathway cannot be converted to acetyl coenzyme A—the necessary first step of the Krebs cycle. The excess pyruvate then accumulates and is converted to lactic acid. (This may explain the severe and even fatal metabolic acidosis<sup>22</sup> exhibited by our hospitalized patients.) The only definitive treatment of beriberi is immediate administration of thiamine, along with supportive therapy. With thiamine treatment, the clinical symptoms of beriberi may ease in minutes to hours and disappear completely within a few days.<sup>20</sup>

Subsequent to the identification of beriberi at the detention center, several measures were implemented to prevent others from developing disease, and the outbreak ended. Thiamine (100 mg orally) was given to all detainees. A dietician began assisting in designing meals and performing dietary assessment. Thiamine-fortified foods are now included in the diet, and no further cases of beriberi have occurred.

The outbreak in Taiwan was caused by a prolonged, monotonous diet low in thiamine. Unable to supplement their diet, detainees reported that they became tired of their food and decreased their food intake over time. The dose-response relation between days of detention and illness was consistent with the fact that a low level of thiamine was present in the diet of detainees. Thiamine intake was estimated based on detainees' menu-assisted recall of what and how much they had eaten. Researchers believed this method would provide a reasonable estimate of the thiamine intake because the menu cycle did not vary much from week to week. However, the amount of dietary thiamine may have been overestimated because the thiamine content listed in the food composition table was primarily for raw foods and no correction was made for thiamine loss during cooking.

Humans are dependent on exogenous sources of thiamine. Good sources of thiamine are wheat germ and yeast extract, pork meat and ham, peas, and asparagus.<sup>23</sup> When this vitamin is totally excluded from the diet, the body stores in previously well-nourished patients are depleted in about 18 days.<sup>24</sup> Therefore, one would expect to see signs of deprivation in about three weeks. In this study, the mean duration of stay was longest for case patients (126 days), intermediate for possible case patients (98 days), and shortest for non-ill subjects (77 days). Although none of the study subjects met the WHO criteria for underweight, the mean BMI value in detainees was lower than that reported for people living in nearby Penghu, Taiwan<sup>25</sup> (21.5 vs. 24.6; p < 0.001). Both BMI and length of stay in center were risk factor for illness. As would be expected based on the low caloric intake, the duration of stay was negatively correlated with BMI (r = -0.3; p < 0.001).

Although beriberi is historically important, it is now rare in general populations, primarily due to improved socioeconomic conditions and food fortification programs. However, outbreaks of thiamine and other vitamin deficiencies still occur, as illustrated by nutrition-

 $<sup>^{</sup>b}p < 0.05.$ 

related outbreaks of beriberi, pellagra, and scurvy among refugee populations in recent years.4 From a public health perspective, these outbreaks illustrate the need for vigilance in ensuring an adequate diet of both macro-nutrients and micro-nutrients, particularly among poor, institutionalized populations, such as prisoners and refugees, who are unable to provide for themselves. From a clinical perspective, the I-Lan outbreak illustrates the importance of considering vitamin deficiency in the differential diagnosis of illness, especially among patients whose diets are very restricted or unusual, such as alcoholics, patients reliant on total parenteral nutrition, or those on very severe weight loss diets. 5,6,7,26 Unless beriberi is considered in the differential diagnosis of neuropathy, high output cardiac failure, lactic acidosis, or shock, an easily treated, potentially fatal condition may be overlooked.

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