CLINICAL PROGRESS

Beriberi Heart Disease

By Reverdy H. Jones, Jr., M.D.

Two cases of beriberi heart disease are presented together with a discussion of the history, diagnosis, and treatment of this condition. Special emphasis is given to the broadened concept of the diagnosis of beriberi heart disease, particularly as it occurs in the Occident.

DURING THE PAST several decades significant advances have been made in the diagnosis and therapy of various types of heart disease. Intensive investigative studies have now assigned specific causes to certain cardiac disorders that formerly, for want of a more accurate classification, were loosely grouped under the category of "arteriosclerotic," "coronary," or "idiopathic" heart disease. Beriberi heart disease is one such abnormality and it is the purpose of this communication to describe the clinical manifestations, the diagnosis, and the treatment of this condition as illustrated by 2 cases.

Although classical descriptions of the polyneuritic form of beriberi have been available in Japanese and Chinese literature for many centuries, it was not until 1929 that Aalsmeer, a Javanese physician, and Wenckebach\(^1\) presented an adequate description of the cardiovascular manifestations of this disorder. These authors emphasized the bounding pulse, pistol-shot sounds over the larger arteries, predominant right heart failure, venous engorgement, and frequent syncope and shock. They thought that there was peripheral vasodilatation, described the rapid circulation, and noted that improvement often occurred after the administration of thiamine. It has been this striking symptomatology as described in the Orient which has, until recently, dominated the clinical impression of beriberi heart disease.

While sporadic reports of cardiac manifestations in beriberi appeared in the United States from 1925 to 1928,\(^2\)\(^3\) the relationship of thiamine deficiency to the cardiovascular manifestations of this disease, as found in this country, was not fully appreciated until the investigations of Weiss and Wilkins in 1936.\(^4\) These authors described 97 patients with "wet beriberi," all of whom had been on vitamin \(B_1\)-deficient diets and most of whom were chronic alcoholics, and concluded that the same types of beriberi described in the Orient existed in this country. Like Aalsmeer and Wenckebach, they emphasized the clinical manifestations of rapid circulation in the presence of heart failure. However, left ventricular failure with dyspnea, orthopnea, and pulmonary congestion were observed as often as pure right-sided failure. A predilection to circulatory collapse and shock was noted, particularly in the presence of respiratory infections. Severe polyneuritis was found only in cases of mild congestive failure. In some patients electrocardiographic changes with tachycardia but without other abnormalities were seen. Weiss and Wilkins\(^5\) concluded that the "cardiovascular disturbances caused by nutritional defects do not form a rigid clinical syndrome."

In 1945 Blankenhorn\(^6\) of Cincinnati commented on the few references to the cardio-
vascular manifestations of beriberi in this country and stated that the condition was not at all rare in hospitals where other deficiency diseases occurred. He thought that too strict adherence to the criteria of beriberi heart disease as described by Aalsmeer and Wenekebach had much to do with the failure to observe this disorder more frequently, and he stated that the well-known Oriental concept of the disease probably hindered rather than helped to establish the diagnosis in many cases in the United States. Keefer in 1930, in describing cases of beriberi heart disease in Peiping, China, found that only 30 per cent exhibited a rapid circulation. Goodhart and Jolliffe in studying the cardiovascular complications in chronic alcoholism observed no acceleration of the circulation or conspicuous enlargement of the right heart. Blankenhorn also thought that rapid peripheral circulation and prominence of the right heart were often absent in the Occidental type of beriberi heart disease. In an effort to facilitate the diagnosis of beriberi heart disease, Blankenhorn proposed the following criteria: (1) enlarged heart with normal (sinoatrial) rhythm, (2) dependent edema, (3) elevated venous pressure, (4) peripheral neuritis or pellagra, (5) nonspecific changes in the electrocardiogram, (6) no other cause evident, (7) gross deficiency of diet for 3 months or more, and (8) improvement and reduction of heart size after specific treatment or autopsy findings consistent with beriberi.

Following this expansion of the criteria for the diagnosis of beriberi heart disease by Blankenhorn, many more case reports appeared in the literature. Some of these cases have failed to fulfill even the above criteria. Dock particularly commented on the great variety of clinical findings in beriberi, depending upon the region, type, and habits of the patients studied. Hussey and Katz concluded that the symptoms and signs of beriberi heart disease show no important variation from those of heart failure due to other causes, and therefore the diagnosis depends mainly upon evidence of a deficient diet, on the exclusion of other etiologic types of heart disease, and on the therapeutic response to the administration of thiamine chloride.

Thus since the original description, the concept of beriberi heart disease has become considerably broadened. Although the originally described Oriental cases and some of the cases in the United States demonstrate the picture of hyperkinetic circulation in the presence of congestive failure, many other cases fail to present this vivid picture. Occidental beriberi heart disease is undoubtedly more prevalent than the number of cases diagnosed at the present time would seem to indicate.

Etiology

Considerable evidence indicates that thiamine deficiency is the primary etiologic factor. Cardiac disturbances produced in animals fed thiamine-deficient diets disappear following the administration of thiamine chloride. Likewise, electrocardiographic abnormalities similar to those observed in beriberi can be produced by giving a thiamine-deficient diet to healthy persons; these changes return to normal following the restoration of an adequate diet. Thiamine is essential in carbohydrate metabolism, and consequently the amount of carbohydrate in the diet is an important contributing factor in the pathogenesis of beriberi. That an increase in carbohydrate consumption may predispose to beriberi by increasing the metabolic demands for vitamin B₆ is shown by the consistent inability to produce thiamine deficiency in pigeons on a vitamin B₆-deficient diet that is high in fats rather than carbohydrates.

In the Orient beriberi occurs primarily in those individuals whose chief food is polished rice, which is deficient in thiamine but high in carbohydrates. In the Occident beriberi heart disease occurs chiefly in chronic alcoholics. Alcohol, like polished rice, is particularly low in vitamin B₆, but has a high carbohydrate content. That alcohol itself is a contributing rather than a primary cause of the cardiovascular manifestations of beriberi has been proved by the complete reversal of the clinical picture following the administration of large doses of thiamine to patients.
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who maintain their usual intake of alcohol. Physical exertion is likewise a contributing factor; cardiac manifestations of beriberi are more frequent and more rapidly produced by regimes of strenuous physical exertion. Some of the cardiovascular characteristics of thyrotoxicosis and of pregnancy may be caused in part by the increased thiamine requirement. Similarly, infectious diseases, particularly pneumonia, with their increased thiamine requirements, may precipitate fulminating beriberi in subclinical, deficient individuals. Another etiologic factor may be faulty gastrointestinal absorption of vitamin B1 due to chronic gastrointestinal disease and occasionally following operation.

Finally, and quite important, thiamine deficiency may influence the course of other etiologic types of heart disease, a fact recognized by Weiss as early as 1936. Some of the signs and symptoms in such patients may be caused by a coexistent vitamin B1 deficiency rather than by the primary cardiac abnormality itself.

Signs and Symptoms

The clinical manifestations of beriberi heart disease vary considerably with the severity and rapidity of the onset of the condition. The signs and symptoms of heart failure are most frequent. The picture of the severely dyspneic, flushed, orthopneic, diffusely edematous patient as commonly described in the Orient has already been discussed. Such patients may be observed in the United States and may develop syncope and shock, with sudden death.

In the Occidental type of beriberi heart disease, however, the clinical manifestations are not usually so dramatic. Dyspnea, weakness, swelling of the ankles, and a nonproductive nocturnal cough are the most common complaints. Examination of the heart reveals tachycardia, gallop rhythm, and often a systolic and less frequently a soft diastolic murmur that may lead to the diagnosis of incompetency of the aortic valve. With treatment and relief of the decompensation these murmurs disappear. There is usually moderate dependent edema, enlarged liver, and prominent and engorged veins. The systolic blood pressure is often slightly elevated and in the more severe cases the pulse pressure is decreased and pistol-shot sounds are heard over the large arteries. The circulation time may be shortened, but is usually moderately prolonged. In the 22 cases reported by Benchimol and Schlesinger, for example, 11 had a prolonged circulation time; in the other 11, the circulation time was normal.

X-ray of the chest usually reveals cardiac enlargement with prominence of both the left and right ventricles and pulmonary congestion; on fluoroscopy, cardiac pulsations can be readily distinguished and the cardiac shadow may be differentiated from pericardial effusion. Pleural effusion is not uncommon.

Nonspecific electrocardiographic changes are common though not necessarily constant in occurrence. The main abnormalities consist in low voltage or inversion of the T waves and prolongation of the Q-T interval. Low voltage of the ventricular complex occurs and, although conduction defects are rare, bundle-branch block has occasionally been reported. Significant arrhythmias are characteristically absent. The enlarged cardiac shadow on x-ray and the abnormal electrocardiographic changes characteristically return to normal after the administration of thiamine. Usually clinical improvement occurs much more rapidly than disappearance of the electrocardiographic abnormalities; in advanced cases these abnormalities and cardiac enlargement may persist indefinitely.

Clinical evidences of vitamin deficiency are usual but not invariable. It has been emphasized that severe polyneuritis is present only in the milder cases of congestive failure because the presence of such neuritis interferes with locomotion and work and thus protects the heart. Anesthesias and paresthesias of the extremities, chelosis, decreased or absent knee jerks, painful glossitis, anemia, hyperkeratinized skin lesions, and hypoproteinemia have all been described as evidence of thiamine and associated vitamin deficiencies.
Pathology

Pathologically the heart in cardiac beriberi is most often hypertrophied and dilated, with involvement of both the right and left chambers. Gould describes the heart as globular with marked dilatation particularly of the right ventricle. In adults the heart frequently weighs 500 to 600 Gm. Microscopically edema and hydropic degeneration occur, particularly of the subendocardial muscle fibers and the conduction bundle, together with marked edema of the interstitial connective tissues. Dock stated that mural thrombi are often attached to the trabeculae carneae of the ventricles. No evidence of inflammation is found. Weiss emphasized that the observed histologic changes are neither specific nor characteristic and can be found in other diseases.

Diagnosis

When the classical hyperkinetic syndrome associated with predominantly right-sided failure occurs in beriberi heart disease, the diagnosis is not difficult. With bilateral failure and in the absence of a rapid circulation, as so often occurs in the Occidental variety, the clinical manifestations may be quite similar to other forms of heart failure. Of great importance is the history of dietary thiamine deficiency. In America the vast majority of cases are chronic alcoholics, predominantly males; a few occur in diet faddists and in patients with gastrointestinal disorders. The absence of other etiologic factors increases the possibility of cardiovascular beriberi. Other signs of vitamin deficiency usually are present. Finally, of great diagnostic significance is the favorable therapeutic response to thiamine administration.

Mention has been made of the coexistence of beriberi with other organic types of heart disease. In a patient with heart failure of known etiology, particularly when there is a history or evidence of an inadequate diet, when signs and symptoms of failure fail to respond to the usual therapeutic regime, an additional factor of thiamine deficiency should be strongly considered.

Therapy

Specific therapy for beriberi heart disease consists in the administration of thiamine chloride. Milder cases require 10 to 30 mg. 3 times a day, whereas the more severe cases may require 100 mg. thrice daily. Intravenous or subcutaneous administration should be used when associated gastrointestinal or liver disorders may interfere with the absorption of thiamine. In markedly edematous or severely dyspneic patients digitalis, oxygen, salt restriction, and diuretics should be used. As Blankenhorn and co-workers have pointed out, there is considerable doubt regarding the dictum that digitalis is without value and that if the heart responds well to this drug the diagnosis of beriberi is eliminated. In the acutely ill patient, therapy should be immediate and no time should be lost with diagnostic studies or test thiamine-deficient diets, since some patients may rapidly develop terminal shock.

Report of Cases

Case 1. W. B., a 51-year-old white man was admitted to the hospital on November 17, 1953. He complained chiefly of shortness of breath, weakness, and swelling of the ankles, associated with a severe nocturnal cough and sense of substernal congestion. These complaints were of 6 months' duration but had markedly increased in the month prior to admission.

The patient had consumed large quantities of alcohol, chiefly in the form of beer. A grossly deficient dietary history was also elicited. He was a rural mail carrier and stated that he rarely ate during the day and at night was fatigued but readily revived himself with 6 to 8 bottles of beer, which with several drinks of whisky constituted his main caloric intake. There was no past history of rheumatic fever, high blood pressure, serious illnesses, or any known cardiac disorder.

Physical examination revealed a worn but not emaciated, dyspneic, ruddy, chronically ill-appearing man. The blood pressure was 100/80, the pulse 92, the temperature 98.6 F., and the respirations were 20 per minute. The weight was 139 pounds. There were fissures in the corners of the mouth. The neck veins were distended. Examination of the lungs was negative. The second pulmonic sound was accentuated, and the cardiac tones were of poor quality. The rhythm was regular. There was a distinct, moderately loud, low-pitched, apical systolic murmur. The liver was
felt 2 fingerbreadths below the costal border, and there was moderate pitting edema of the extremities. The reflexes were active.

Laboratory studies revealed a red-cell count of 3.9 million, 10 Gm. per cent of hemoglobin, and a white-cell count of 7,300, with a normal differential count. The urine was normal except for a trace of albumin. The serum protein was 6.75 Gm. per cent, the alkaline phosphatase was 2.3 units, and the cephalin flocculation test was 2+. Urobilinogen in the urine was not increased. Repeated examinations of the sputum for acid-fast bacilli were negative. A bromsulphalein test showed dye retention of 13.2 per cent. A Wassermann test was weakly positive. The spinal fluid examination was normal.

An x-ray of the chest (fig. 1A) revealed gross diffuse cardiac enlargement with pulmonary congestion and some fluid in the left base. An electrocardiogram showed low T waves (fig. 2). The venous pressure on November 19, 1953, was 195 mm. of water, and the circulation time was 24 seconds.

The diagnosis of cardiovascular beriberi was made and the patient was kept at bed rest, placed on a high-carbohydrate, high-protein diet, and was given 200 mg. of thiamine chloride subcutaneously 3 times a day.

The patient's response was slow but definite. He lost weight, edema disappeared, and there was relief of dyspnea and cough. The urinary output was very satisfactory, and on November 23, 1953, 4 days after the administration of thiamine, the heart had decreased somewhat in size and there was diminished pulmonary congestion (fig. 1B). On November 27, 1953, the heart was still large and globular, but fluoroscopic examination failed to show any left atrial enlargement and the pattern was not consistent with pericardial effusion.
he was much more active. Examination revealed no edema, the liver was barely palpable, and the heart examination revealed normal tones but no murmurs. The electrocardiogram (fig. 2) showed marked improvement and was considered normal. He was advised to continue taking brewer’s yeast for several months and was cautioned against poor dietary habits and alcoholic consumption.

This case has been presented as an instance of Occidental beriberi heart disease. Important diagnostic factors were the easily elicited history of dietary deficiency, the signs and symptoms of heart failure, and the excellent clinical response to thiamine chloride. It is true that, aside from cheilosis, general appearance, and anemia, there was no other evidence of vitamin deficiency, but, as has been pointed out, this is often the case. Characteristically, the enlarged heart and the abnormal electrocardiogram returned to normal some time after the relief of the symptoms of congestion.

As has been shown, the original concept of beriberi heart disease has been considerably modified and broadened. In the Occident particular emphasis should be placed on the signs and symptoms of congestive failure in a patient on a known vitamin B-deficient diet, with demonstrable improvement after thiamine chloride therapy. The case presented illustrates many of the present concepts of beriberi heart disease and emphasizes that a more liberal diagnostic approach on this subject will undoubtedly permit one to identify and to treat successfully more patients with this condition.

Case 2. E. B., a 48-year-old white man was admitted to the hospital on March 31, 1955.

His main complaints were dyspnea and ankle edema of 3 weeks’ duration. He had had chorea at the age of 10. There had been no known rheumatic fever. At the age of 15 the patient had been told he had a “heart condition.” Fifteen years before admission the patient had been told he had “high blood pressure” and subsequently it was “as high as 210” and caused his rejection by the Army. Ten years before admission the patient developed rheumatoid arthritis, which so limited his activities that for several years he could scarcely walk alone and could only shuffle about the house. The patient admitted to a grossly deficient diet and stated that he had eaten only 1
meal a day for the preceding 10 years. Previous records revealed that the patient had been hospitalized in July 1954 with severe epistaxis and that the blood pressure was recorded as 170/104 mm. Hg.

Approximately 3 weeks before admission, the patient first noted slight ankle edema followed by increasing shortness of breath on exertion. One week prior to admission the patient developed orthopnea. He had been given some unknown diuretics, without benefit, but no digitalis. Because of the increasing severity of these symptoms, the patient was sent to the hospital.

Physical examination revealed a pale, dyspneic, acutely and chronically ill-appearing man. The blood pressure was 190/120, pulse 98, respirations 20, temperature 97.8 °F, and weight 140 pounds. The tongue was red and there were fissures in the corners of the mouth. The eyes appeared puffy. Moist rales were present at both lung bases, although there was no dullness on percussion. The heart was markedly enlarged with a forceful apex beat noted in the seventh intercostal space in the midaxillary line. A loud, rough systolic murmur was heard at the apex, transmitted to the axilla. The second pulmonic sound was accentuated. The liver was felt 2 fingerbreadths below the right costal border. No ascites was noted. The fingers and ankles revealed arthritic deformities and there was extensive pitting edema of the legs and ankles.

Laboratory studies revealed a red-cell count of 4.3 million per mm.³, 13 Gm. per cent of hemoglobin, and a white-cell count of 8,100, with a normal differential count. The blood urea was 50 mg. per cent. The urine was normal, with a specific gravity of 1.025. The serum protein was 6.5 Gm. per cent, with a normal albumin-globulin ratio. A serologic test for syphilis was negative. An electrocardiogram was essentially normal. The circulation time (arm-to-tongue with Decholin) was reported as 15 seconds, and the venous pressure was 140 mm. of water. An x-ray of the chest on admission (fig. 3A) revealed marked cardiac enlargement with a globular heart and engorge-ment of the pulmonary vessels. The patient was considered to have chronic rheumatic endocarditis with mitral insufficiency and congestive heart failure as well as rheumatoid arthritis, essential hypertension, and malnutrition.
On the succeeding 6 days the patient was given 6 mg. of digoxin as well as ammonium chloride, 2 Gm. 4 times daily, and 2 injections of a mercurial diuretic. This treatment produced no diuresis; in fact, the patient grew worse as evidenced by a 6-pound gain in weight and increasing heart size and pulmonary congestion (fig. 3B).

At this time the possibility of a coexisting thiamine deficiency was considered, and on April 4 the patient was given thiamine chloride, 100 mg. 3 times daily, subcutaneously. On April 6 the thiamine chloride was raised to 100 mg. 4 times daily and aminometradine (Mictine), 200 mg. 3 times daily, was added to the therapeutic regimen.

Diuresis and weight reduction were immediately produced and in the next 6 days the patient lost weight, from 146 to 109 pounds, a total of 37 pounds, as seen in table 1. The pulse slowed, edema vanished, and symptoms of dyspnea and orthopnea disappeared.

An x-ray of the chest on April 9 revealed a marked decrease in the heart size and absence of pulmonary edema. On April 12 there was still further reduction in the cardiac size (fig. 3C). The patient was maintained on digoxin, 0.25 mg. daily, and a high-carbohydrate, high-vitamin diet with supplementary thiamine chloride. A final x-ray of the chest on April 18 (fig. 3D) revealed still further reduction in the cardiac size. The patient was discharged from the hospital on April 20, 1955, with the above medications and diet.

This case has been presented as an instance of chronic rheumatic endocarditis with congestive failure, complicated by thiamine chloride deficiency. At first the factor of thiamine deficiency was overlooked. However, because of no response to digitalis, ammonium chloride, diet, and mercurial diuretics, vitamin B1 was added to the therapeutic program with very gratifying results, characterized by diuresis, weight loss, a subsidence of symptoms, and a reduction of cardiac size and pulmonary edema. Although a proprietary drug, aminometradine, was given at approximately the same time, it is hardly conceivable that this drug could have caused such a response when a number of other cardiac drugs had failed to influence the edema or clinical course. Although the therapeutic response to thiamine is moderately slow, several of Blankenhorn’s cases responded to parenteral medication very rapidly and dramatically. Undoubtedly in a number of cases of organic heart disease with congestive failure there is a contributing factor of thiamine deficiency, thus in effect constituting a form of beriberi heart disease. Failure to recognize this factor in the management of some cases of organic heart disease with congestive failure will result in an insufficient control of symptoms and an inadequate clinical response.

CONCLUSIONS

An outline of the development of the current concept of beriberi heart disease, particularly as it occurs in the Occident, has been presented.

The etiology, symptomatology, diagnosis, and treatment of this condition have been described.

Two cases of Occidental beriberi heart disease with a typical therapeutic response to thiamine chloride have been presented.

It has been emphasized that some patients with known organic heart disease in congestive failure may have a coexisting factor of thiamine chloride deficiency that will influence the clinical manifestation of failure and necessitate supplementary vitamin B1 therapy.

Classical beriberi heart disease as originally described in the Orient was graphically por-
trayed as predominantly right-sided heart failure in the face of a hyperkinetic circulation. In the Occident, and particularly in America, many cases of beriberi heart disease do not conform to this dramatic syndrome. A broader diagnostic concept has permitted the recognition and treatment of an increasing number of patients with beriberi heart disease who respond to thiamine after having been refractory to all other measures.

**SUMMARIO IN INTERLINGUA**

Es delineate le discollamento del concepcion currente de beriberi cardiae, specialmente como illo occurre in le Occidente.

Es describite le etiologia, symptomatologia, diagnostique, e tractamento de iste condition.

Es presentate 2 casos de beriberi cardiae occidentale, con un typic responsa therapeutic a chloruro de thiamina.

Es signalate que certe patientes cognoscite-mente con organic morbo cardiae in disfallimento congestive ha etiam un co-existente carrentia de chloruro de thiamina, influentiante le manifestacion clinic de disfallimento e rendente necessari un therapia de vitamina B1 supplementari.

Classic beriberi cardiae, originalmente descritte in le Oriente, esseva representate como disfallimento cardiae predominantemente dextero-lateral in le presentia de circulation hyperkinetic. In le Occidente, e particularmente in America, multe casos de beriberi cardiae non corresponde a ille tableau dramatic. Un concepcion diagnostic plus liberal ha permitite le recognition e le tractamento de un crescente numero de patientes con beriebri cardiae qui responde a thiamina post haber essite refractori a omne altere mesureas.

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REVERDY H. JONES, JR.

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