Effect of Vitamin Deficiency on the Heart and Circulation

By Marion A. Blankenhorn, M.D.

Not much clinical progress can be reported in a field in which little is known, not much work going on and few patients are being observed. The situation has changed little from that described by this author in 1950: "That except for beriberi heart disease, which is known to be caused by diets deficient in thiamine, the matter to be discussed is in the realm of speculation or else in interesting animal experimentation."

Beriberi was seldom described in American or in European literature. In Boston, New York, Philadelphia, Cincinnati and elsewhere, a few observers, having access to numerous patients, derelict because of chronic alcoholism, did describe a characteristic syndrome, which improved promptly after appropriate treatment. Before the pathogenesis of this syndrome could be discovered, it has practically disappeared, probably because of so-called diet reform and the better management of chronic alcoholism.

Where the disease was studied by elaborate physiological and biochemical methods, there was agreement about principal features in carefully selected patients. These features were "high output failure" with accelerated peripheral circulation, elevated venous pressure, elevated right ventricular systolic and end diastolic pressure, lowered total pulmonary resistance and lowered total peripheral resistance with edema and no cyanosis. When patients with this disorder were observed during failure and immediately after the cessation of failure, no mechanism was discovered to explain either the cause of failure or the effect of therapy with thiamine, except that the patient usually completely recovered.

In fact, a contradiction of terms develops from this study. The heart is said to "fail" while it is doing more work and is circulating more blood when in failure than when out of failure. Although these tests before and after treatment have been done with due regard to the function of thiamine, which usually cures the disease, the riddle remains much as Wenckebach stated it in 1929 and in 1934, in much simpler clinical terms. For a lively discussion of this riddle the reader is referred to the work of Burwell and his co-workers.

Wenckebach and others proposed that vagus neuropathy was the mechanism, but no such lesion was found in man or experimental animals. Furthermore, such myocardial lesions as do occur in man are of a sort that could be a consequence of failure and are perhaps not the cause of failure. However, this writer, finding lesions in the upper segments of the cervical spinal cord in two typical patients, has recently proposed that the mechanism is neurogenic, i.e. a disorder of vasomotion. This disorder of vasomotion is reflected in the circulation primarily and in the heart secondarily. When beriberi heart disease ends fatally, in the writer's experience, death is sudden and unexpected and no mechanism may be apparent at autopsy, especially, no great disruption of the heart muscle. No progress has
been made beyond this speculation and the recording of a few well studied examples of the "riddle".

In the diagnosis of beriberi heart disease one small item can be added to the stigmata of deficiency disease which have been useful in its clinical recognition; nutritional type cirrhosis should be added to pellagra and peripheral neuritis. The basis of this addition is a statement from Dr. Bernard Black-Schaffer of the Department of Pathology who restudied the case material previously reported from the Cincinnati General Hospital as beriberi heart disease. Of ten records available for such review, five showed nutritional cirrhosis, two in the very early stages; three others showed non-specific fibrosis of the liver and two showed neither fibrosis nor cirrhosis. He states: "There can be no doubt that the extremely high incidence of nutritional cirrhosis in this small group is of greatest significance." Because beriberi heart disease is the most clearly defined in the entire group of cardiocirculatory disorders, the diagnostic criteria, as published in 1946 and now generally accepted, are repeated below:

1. No other cause for heart disease found
2. Three or more months of thiamine-deficient diet
3. Signs of neuritis, pellagra or both
4. Enlarged heart with sinus rhythm
5. Dependent edema
6. Elevated venous pressure
7. Minor electrocardiographic changes
8. Recovery with decrease in heart size or autopsy consistent with beriberi heart disease, including nutritional type cirrhosis of the liver

If any new information about beriberi has come out of Korean prison camps, Brig. General Elbert DeCoursey of the Army Institute of Pathology has no knowledge of it. He reported, in a recent letter to me, that "the incidence of beriberi during World War II among American soldiers was negligible. There has been no revision of this statement".

In the difficult matter of deciding how much effect thiamine deficiency may have upon heart disease of any type, or perhaps all types, no clinical progress can be reported now. Biochemical testing of the patient to determine thiamine stores or thiamine needs is unsatisfactory. To prove the matter by giving thiamine or withholding it from the patient who has chronic failure is equally unsatisfactory in our experience. Recently, Wohl and his associates have shown increased urinary output of thiamine, given as a test load to patients, who received a mercurial diuretic for treatment of chronic cardiac edema. In individual cases the matter is usually disposed of by giving thiamine in all prolonged and debilitating illnesses, especially where weight loss and diuresis could possibly cause a deficiency of any nutrient.

Vitamin E, in relation to myocardial disease, has recently received considerably more attention than has thiamine. In medical literature, the use of vitamin E (tocopherols) has reached the stage where large groups of patients are helped according to some observers, and equally large groups are found not helped by other observers.

The metabolism of tocopherols in relation to muscle development and muscle function has long been studied by Karl E. Mason and others. In primates, made deficient by diet manipulation, he found no disorder of the heart and circulation. In autopsy material from patients of various ages, dead of myocardial disease, he found no reduction of tocopherol content in various tissues, especially in the heart muscle tissue. In advance of publication, he permits me to quote, from a personal communication: "These data in no wise suggest that tocopherols are useful in the management of acute myocardial failure." If the matter is to be settled by clinical trials already published, the most that can be said is "no progress." The interesting animal experiments, especially those dealing with the growth and development of skeletal muscle, do not throw light on the problems of heart disease in man.

Scurvy, although manifestly a disease involving capillaries in many sites with hemorrhage a conspicuous symptom, does not involve the heart and general circulation. In 1949 the author reported a ten year study of deficiency diseases in the Cincinnati General
Hospital, which included 33 cases of scurvy among adults. In this group there were six deaths. In none of the six did heart disease, that is so called "Scorbutic heart disease," cause or contribute to the death. Since that report, two other scorbutics were autopsied, as of June 1952, and in neither was there hemorrhage in the heart or pericardium. The incidence of degenerative heart disease among scorbutics is about the same as in the hospital population.

In the Cincinnati General Hospital we have seen several individuals in two attacks of severe and disabling scurvy but without any clear evidence of heart disease. Dependent edema is conspicuous; the nature of this edema in beriberi is not clear. Patients with scurvy die suddenly and unexpectedly in a manner suggesting vagal reflex and syncope. Such deaths are not associated with autopsy findings of heart disease. The vasomotor behavior of scorbutics is quite unlike that of beriberi patients except in this tendency to syncope. If any useful thing can be said now about the management of the heart and circulation in scurvy, it would be to guard against vagal stimulation.

In clinical and experimental study of such newer vitamins as folic acid, pyridoxine, vitamin B12 and even nicotinic acid, there is no hint that heart disease is caused, or preexisting heart disease aggravated, by them.

It should be pointed out here that pure forms of vitamin deficiency disease probably do not occur in nature and that more than one vitamin is usually concerned in any given patient. In nutritional failure, the effect on mineral metabolism is quite obscure. The patient's protein intake is often manifestly low and signs of hypoproteinemia are found. Tinsley Harrison has referred to this situation as "cardiac cachexia," a term that should call to mind the duty to study the patient's metabolic needs.

This report cannot consider low protein diets and heart disease, but it is inaccurate and misleading to write about the effects of vitamin deficiency on the heart and circulation when, in all probability, at least as far as can be proven, pure vitamin deficiency does not exist in nature and possibly not even under rigid experimental conditions. The writer is not aware of any clinical experiment that has attempted to apply such a grossly artificial approach to beriberi, scurvy, or any phase of heart disease as it occurs spontaneously.

There is, however, an increasing approach to the field of idiopathic heart diseases by searching for evidence of nutritional failure. In this class is endocardial sclerosis of infancy and "alcoholic heart disease" with mural thrombosis and postpartum myocardosis in young women.

The nutritional failure of the pregnant woman has been suspected as a cause of endocardial sclerosis of the infant as well as a cause of other forms of congenital heart disease. Postpartum myocardosis or myocarditis, as may be preferred, has been associated with multiple pregnancies and poor diets. This condition was described principally from the Charity Hospital in New Orleans, the Grady Hospital of Atlanta, the Cincinnati General Hospital and the Philadelphia General Hospital more than a decade ago. Now the several authors of such reports say, in personal communications, that the disease has become "very infrequent in recent years." This writer presumes that improved diets may be responsible for the disappearance of such idiopathic disease rather than that it has been renamed into some other entity.

Chronic alcoholism continues to be the main cause of nutritional failure in the United States. In a recent and personal communication, Dr. Hans Popper of the Hektoen Institute reports seeing idiopathic myocardial enlargement with mural thrombi in "repeated instances among chronic alcoholics." This disease, which is sometimes called alcoholic heart disease, is diagnosable but no specific therapy has been useful when the stage of endocardial sclerosis has developed. In this same class may be a disease described in South Africa and seen there in Bantus and other tribes, called cardiovascular collagenosis by Becker. Becker found no cause for what he considered a specific disease entity. In a personal communica-
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January 1954, he gave reasons why he did not conclude that the cause was “primarily nutritional,” but did consider that the nutritional aspects required further investigation. He had not seen it in Bantu children with kwashiorkor. Also in January 1954, a personal communication from Dr. V. N. Patwardhan, Director of the Nutrition Research Laboratories at Coonoor, S. India, reports that “endocardial fibroelastosis or sclerosis is a condition diagnosed very often at autopsy”. It is known to occur in children between the ages of 3 days to 6 years and in three clinical patterns, the outstanding features of which are (1) sudden death in children within 24 to 48 hours after onset of respiratory distress; (2) prolonged progressive increase in dyspnea followed by cardiac failure and death; (3) repeated episodes of respiratory distress and cardiac failure sometimes lasting for months or years and showing cardiac hypertrophy.

By searching those spots in the world where nutritional deficiency diseases are common we may gain some hint as to the cause of our own idiopathic diseases of the heart.

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