STUDIES ON THE HEART IN NUTRITIONAL DISTURBANCES IN INFANCY *

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Infants who are suffering from nutritional disturbances and show signs of athrepsia may present various manifestations of circulatory derangements. Electrocardiograms have been made from a group of athreptic infants admitted to the St. Louis Children's Hospital, and it is my purpose to direct attention to certain observations made in the study of these cases.

Infants with athrepsia are in a state of partial starvation because the food they receive, for one reason or another, is not sufficient to supply the needs of the body tissues. An insufficient intake by mouth, an inability to completely digest and absorb food, or an inability on the part of the body tissues to completely utilize the food ingested are phenomena that lead to the development of this condition. Anatomic changes that might explain the symptoms associated with the condition have not been found in the body tissues, and it seems necessary to assume some alteration in the chemical and physiological processes and reactions of the body. Marriott¹ recently described the circulatory changes that occur in athreptic infants and brought out explanations for the various phenomena that occur in these infants. Briefly, the changes he describes are a slow, small and weak pulse; a surface temperature much below normal; a low hemoglobin and red blood cell count; concentration of the protein contents of the blood serum much lower than normal. The blood volume is much decreased, both absolutely and in relation to the body weight; the volume flow is often one-fifth, occasionally one-tenth of the normal; there is a constriction of the arterioles leading to a piling up of corpuscles in the capillary blood. The arteriolar constriction may be considered a compensatory mechanism to maintain blood pressure at its normal height; but despite this the blood pressure may fall below normal. He states that the evidence indicates that there is an increased tissue destruction throughout the whole body; the stored glycogen and fat are burned in preference to protein but when the fat and carbohydrate stores are exhausted, a general consumption of protoplasm occurs as is evident by a marked negative nitrogen and mineral salt balance.

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1. Marriott: Some Phases of the Pathology of Nutrition in Infancy, Harvey Lectures, Series 1919-1920, Am. J. Dis. Child. **20**:461 (Dec.) 1920.

These observations on infants have been substantiated by Uthheim,² working in Marriott's laboratory. By prolonged underfeeding, the blood volume of rabbits was decreased both absolutely and in proportion to the body weight and surface area; the volume flow was decreased, and the corpuscular count and volume were also decreased.

Burge and Neill³ studied the oxidative powers of various tissues in the bodies of animals before and after starvation by measuring the catalase content of those tissues. They consider that the catalase content of a tissue is directly proportional to the amount of oxidation in that tissue. The heart, which is not autolyzed during starvation, shows a normally high catalase content which is not decreased during starvation. While that of the fat and skeletal muscles which are autolyzed during starvation, is greatly decreased and at the end of periods of starvation these tissues have an exceedingly low catalase content.

Electrocardiograms from infants showing various nutritional states have been made previously by many observers. In those infants with a severe loss of water and body weight, the curves often have shown abnormal forms of the ventricular complexes. Noeggerath⁴ studied the electrocardiograms made from infants that were prematurely born, or who were suffering from disturbances of nutrition or from infection. He observed many curves with abnormal ventricular complexes and also noticed that severely atrophic infants show a slowing of the pulse due to a sinus bradycardia and not to a disturbed cardiac mechanism. He concludes that the electrocardiogram is of no value in estimating the degree of function of the heart in such infants, nor is the method of value in determining the prognosis; that its usefulness is restricted to the demonstration and analysis of disturbances of cardiac mechanism.

Czerny⁵ examined the hearts of athreptic infants by roentgenograms and found that the area of the heart shadow is much decreased in size. The condition exists independently of a loss in water content of the infant and it is most pronounced immediately preceding death. He is inclined to think that the heart is incompletely filled during systole, due partly to the decrease in total blood volume, but most likely to a disturbed action of the diaphragm.

2. Uthheim: Study of the Blood and Its Circulation in Normal Infants and Infants Suffering from Chronic Nutritional Disturbances, to be published in *Am. J. Dis. Child.*

3. Burge and Neill: The Effect of Starvation on the Catalase of the Tissues, *Am. J. Physiol.* **43**:58, 1917.

4. Noeggerath, C. T.: Elektrokardiogramme Schwächliche Säuglinge, *Ztschr. f. Kinderh.* **6**:396, 1913.

5. Czerny, Ad.: Zur Kenntnis der Zirkulationsstörungen bei Akuten Ernährungsstörungen der Säuglinge, *Jahrb. f. Kinderh.* **80**:601, 1914.

Fletcher and Hopkins⁶ studied the relation of acids, particularly lactic acid, to the activity of amphibian muscle, and conclude that the presence of acid products depends on how favorable the conditions that exist in the muscle are for oxidative processes. When the oxygen supply is adequate, there is no accumulation of acid products, but when factors are present which diminish the oxygen supply, the acid is increased and can be removed only slowly and with difficulty. Their experiments show that lactic acid formed in muscle from various causes follows this rule and its disappearance is dependent on the oxygen supply.

Burridge⁷ has shown that the rate of propagation of contraction^{*} in the frog's ventricle may be delayed by the addition of inorganic acids in sufficient strength to the fluid with which the heart was perfused. He states further that after treatment of the heart with a sufficient strength of acid to cause the heart to stop beating, by replacing such acid solution by Ringer's solution containing sodium bicarbonate, spontaneous beating will be resumed but with markedly delayed conduction of the impulse through the ventricles.

Mines⁸ concludes from his experiments that certain changes in the electrocardiogram which result from increased frequency of the heart beat may be due to changes in the hydrogen ion concentration in some region of the muscle. He states that it is only when the hydrogen ion concentration is raised above a certain value that the effect will appear. After a long pause the hydrogen ion concentration is certainly lower than after a period of activity. Oxidative removal of lactic acid is a slow process and during the pauses between successive contractions of the heart, the removal is certainly not complete. A long pause will mean more complete removal.

The work of Fletcher and Hopkins, of Burridge and of Mines offers experimental proof for the observations made by Robinson⁹ in this laboratory. He reports cases in which there were abnormalities in the form of the electrocardiogram due to faulty conduction of the cardiac impulse through the ventricles. This faulty conduction, he considers, depends on what has been termed "functional fatigue" rather than on anatomic lesions involving the intraventricular conducting system. He cites examples in which derangement of the ventricular

6. Fletcher and Hopkins: Lactic Acid in Amphibian Muscle, *J. Physiol.* **35**: 247, 1907.

7. Burridge: Propagation of Contraction in the Frog's Heart, *J. Physiol.* **45**: 6, 1912.

8. Mines: On Dynamic Equilibrium in the Heart, *J. Physiol.* **46**:349, 1913.

9. Robinson: The Significance of Abnormalities in the Form of the Electrocardiogram, *Arch. Int. Med.* **24**:422 (Sept.) 1919.

conduction has resulted from lack of time for conduction recovery after a ventricular contraction. In one case distinct improvement in intraventricular conduction followed slowing of the heart rate when longer diastolic pauses were present. The rate of recovery of conduction was observed also in this case to become more rapid with improved circulatory efficiency. He concludes, in part, that "lesions causing an insufficient blood supply to the ventricles are responsible for the presence of acid metabolites, which accumulate whenever the oxygen supply to the muscle is inadequate."

CLINICAL OBSERVATIONS

A group of sixteen infants who showed moderate or severe degrees of athrepsia were studied. Electrocardiograms were made on admission to the hospital and at subsequent times when the evidence indicated a material change in the clinical condition. Curves that were made within a period of twelve hours preceding death were not included since it was felt that any change in the electrocardiogram at that time might be due to the fatal cardiac failure rather than to the condition we are studying. Below are the curves selected from two of the cases which indicate functional changes in the cardiac mechanism.

CASE 1 (Children's Hospital No. 14454).—The patient was admitted to the hospital, July 21, 1919, for an acute intestinal disorder. He has been a normal baby, except for improper feeding, up to about one week previous to admission, when vomiting and diarrhea set in. The baby responded quickly to hospital care and was discharged well one week later. He began vomiting and having diarrhea again at home and returned to the hospital August 4. He was suffering then from severe athrepsia and anhydremia. Electrocardiogram 2760 was made shortly after his admission. Again he improved and was doing well when he developed ileocolitis and pyelitis. Electrocardiogram 2827 was made during this period. His lower resistance and nutrition were not sufficient to withstand the infection and he died September 24.

Electrocardiogram 2760 (Fig. 1), made August 17, shows no evidence of abnormal muscle preponderance. QRS time is 0.080 second, not abnormal. The complex is normal in form, except that the waves are low in amplitude. This is particularly true in Lead I. The P wave is not present in Lead I and III; it is low in Lead II. The T wave is not present in Lead I and III; it is abnormal in form in Lead II. Ventricular rate 95.7 per minute. PR time, 0.200 second, is a distinct delay in an infant.

Electrocardiogram 2827 (Fig. 2), made September 4, shows distinct improvement in the cardiac condition as compared with Electrocardiogram 2760. The QRS times is 0.080 second, but the amplitude of the waves is much increased and now seems normal. The T waves are well formed in all leads, the change being particularly noticeable in Lead I. The P waves likewise are easily made out in all leads. Ventricular rate 103.8 per minute. PR time, 0.160, a faster time than Electrocardiogram 2760.

Interpretation: The decrease in the time for auriculoventricular conduction, the faster heart rate and the improvement in the form of the QRS, and T and P complexes, coincident with the decrease in the signs of athrepsia, would indicate an improvement in the function of the heart.

Fig. 1.—The QRS complex is normal in form but the waves are low in amplitude. The PR time is 0.200 second, being slightly delayed. Ventricular rate, 95.7 per minute.

Fig. 2.—The amplitude of the QRS complex is much increased. Ventricular rate, 103.8 per minute. The PR time is 0.160 second, the conduction time being much faster.

CASE 2 (Children's Hospital No. 15063 and 15248).—Patient was admitted to the hospital, Jan. 22, 1920, suffering from marked degrees of athrepsia, anhydremia and acidosis. The findings in the study of the circulation were in accord with those described by Marriott. It is not shown how long she had been ill or what the previous feedings had been. She was discharged from the hospital in fair condition February 9. Electrocardiogram 3457 was made the day after her admission when her condition was at its worst. She was readmitted March 5 because of a return of her previous nutritional disturbance. Electrocardiogram 3711 was made at this time. Shortly after this admission she developed an acute otitis media which was followed by an erysipelas and she died.

Electrocardiogram 3457 (Fig. 3), made January 23, shows no evidence of abnormal muscle preponderance. The Q R S time is 0.060 second, not abnormal. The complexes are abnormal in form, particularly in Leads II and III. In Lead II the down stroke of the R wave is notched and in Lead III it is broadened out. Further, the waves are low in amplitude. The T waves are absent in all three leads. Ventricular rate, 150 per minute. The P R time is 0.160, an abnormal delay in an infant with such a ventricular rate.

Electrocardiogram 3711 (Fig. 4) was made March 7. As in Case 1 these curves show distinct improvement in the cardiac function. Q R S time is not shortened nor is the form changed, but the amplitude is much greater. The T waves are well formed though R T time, which is 0.240 second, seems much delayed. Ventricular rate, 138 per minute. The P R time is 0.120 second, a distinct improvement in the auriculoventricular conduction.

Interpretation: This curve was made at the time when the degree of athrepsia was not so marked and the patient seemed to be improving. It is probable that there was some improvement in the heart function.

In explanation of the alterations in the electrocardiogram reported by Robinson,⁹ he states that sclerosis of the coronary vessels furnishes the condition for the increased production of acid metabolites and it also tends to delay their removal. Myocardial lesions, such as fibrosis would, perhaps, also tend to produce these effects by lessening the efficiency of the blood supply to the cardiac tissue. In athreptic infants the heart muscle and coronary vessels on examination have not shown any recognizable anatomic fibrosis or sclerosis. But the marked decrease in the blood volume and delay in blood flow with low protein content would certainly result in a deficient supply of oxygen to the body tissues, with a resulting increase in hydrogen ion concentration. These changes would furnish the conditions under which alterations in the cardiac mechanism might occur. Alterations have been found as shown in the examinations made by previous observers and in the two cases reported above. The alterations in these two cases are not extensive but they are distinct enough to show that a profound influence has been exerted on the heart. In spite of the protective measures that have been set up to spare the heart, they have broken down. There has been a delay in impulse conduction from auricles to ventricles and when the nutrition of the body improved this abnormal delay disappeared and the impulses passed freely from auricles to ventricles. Coincident with this the form of the T waves was much improved and the amplitude of the Q R S complex was increased.

Fig. 3.—The QRS waves are low in amplitude. Ventricular rate, 150.0 per minute. The PR time is 0.160 second.

Fig. 4.—The amplitude of the QRS waves are much increased. Ventricular rate, 138 per minute. The PR time is 0.120 second, being much faster than in Figure 3.

The changes described occurred in infants who were markedly athreptic, as evidenced by the other examinations on the circulation, but other infants suffering from athrepsia of just as severe a type have failed to give evidence of any disturbance in the electrocardiogram. Nor does the length of time that the nutritional disturbance has existed seem to be a factor in the production of functional changes in the heart. It is not to be expected that these changes would occur constantly for we must consider that several important factors are present in athreptic infants which delay the failure of circulation in the heart itself. The observations on volume flow, total volume and protein content of the blood have been made on the peripheral circulation of the body surface and especially in the extremities. It is both conceivable and probable that these same changes make themselves felt in the internal organs of the body, though possibly not to the same extent.

Phenomena that occur in one area of the circulation need not occur to the same degree or of the same kind in all the circulatory areas. In a pathologic state in which the circulation is altered to such an extent as in these athreptic infants, it is hardly conceivable that the internal organs can escape wholly some alteration in their circulation; truly, in mild cases no change may occur, but in the moderate and severe cases the profound changes observed in the surface area must spread to the deeper structures. Furthermore, it is probable that nature makes every attempt to provide primarily for the vital structures, the heart, brain and internal organs, and will endeavor to protect those structures from damage as long as possible. If the volume of blood is diminished, if the oxygen content is low, the blood will be diverted as much as possible by surface vasoconstriction into the circulation of those organs whose functional activity is essential to life. By withdrawing fluid from the rest of the body tissues, more fluid may be made available for the heart and other internal organs. If sufficient food for body needs is not received the glycogen and fat in the body tissue is used up and finally the tissue protein. The organs which are most essential for life, such as the heart and central nervous system, are preserved as long as possible, while organs which are relatively nonessential, waste away. It is probable even then that the heart is one of the last structures in the body to feel the effect of tissue destruction, one of the last structures in which the oxygen supply is diminished.

The hearts of infants suffering from athrepsia may be further protected by the decrease in heart rate so commonly observed. The more activity in the heart muscle, the more rapid the rate and the greater the need for oxygen. In experimental study it is found that

when the surface areas become depleted of fluids and the blood vessels constricted to prevent further loss of heat, the animal becomes quiet and thus prevents muscular activity in those areas involved. The same phenomena occur in the heart. Functional fatigue appears to prevail if the oxygen supply is diminished and subsequently the cardiac mechanism is deranged. A slow heart rate acts as a compensatory mechanism to protect the heart muscle.

In making electrocardiograms from athreptic infants, we have found in most instances that the body resistance is very high and for this reason it is difficult to obtain satisfactory curves. The skin surface is dry and attempts to produce erythema and a moist skin with a high conductivity by rubbing with hot salt solution before applying the electrodes, is almost uniformly unsuccessful. It is common to find the body resistance as high as from 2,000 to 3,000 ohms, often higher. During convalescence in the favorable cases, coincident with the improvement in the circulatory conditions the body resistance is again lowered and the electrocardiogram may be obtained with the same ease as in a normal infant. Due to the withdrawal of fluid to other parts of the body the water content of the subcutaneous tissues is so much reduced that the electrical conductivity is lowered.

In some incompleting experiments we have attempted to produce alterations in the cardiac mechanism and in the form of the ventricular complex of animals. Up to the present time we have not succeeded in doing so.

We have no evidence that the alteration in the cardiac mechanism is dependent on structural change in the conducting tissue or the heart muscle. We think they are functional in nature resulting from an insufficient circulation of oxygen through the coronary vessels. Czerny's observation that the area of the heart shadow is decreased in size is probably due to incomplete filling of the heart chambers and coronary vessels.

CONCLUSIONS

1. Electrocardiograms were made from a group of sixteen athreptic infants, and in the case of two of these infants, alterations of cardiac mechanism were observed. The alterations consisted of a delay in auriculoventricular conduction, and changes in the form of the Q R S complex.

2. As an explanation of these disturbances we offer a suggestion that they are the result of alterations in the blood and body tissues in these infants suffering from nutritional disorders. It is probable that the changes which have taken place in the blood result in a deficient supply of oxygen to the heart, with incomplete or delayed removal of metabolic products (acid metabolites) from the cardiac tissue.

3. When improvement takes place in these athreptic infants the alterations in cardiac mechanism disappear. Measures adopted to relieve the nutritional disturbance seem to be the rational treatment for the cardiac condition as well.

4. We have not observed any phenomena indicating heart failure in these infants.