STUDIES ON MYOCARDIAL METABOLISM

By

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ABSTRACT

Changes in cardiac metabolism in the normal fed, starved and alloxan-diabetic rat have been investigated by measuring changes in acetyl and acyl Coenzyme A (CoA) concentrations of cardiac muscle. It was found that the method with which the animals were killed contributed to differences in the absolute values of these CoA esters, especially acyl CoA, but changes within a given experimental condition were comparable. Acetyl and acyl CoA concentrations in correlation with corresponding blood glucose and total ketone body concentrations do not substantiate the hypothesis of Garland and Randle with respect to the "Glucose-Fatty Acid Cycle" in heart muscle. These investigations have shown that in the normal fed and the diabetic animal, acetyl CoA and acyl CoA remain unchanged demonstrating no correlation to changes in ketone bodies. On the other hand, in normal fed rats which had received insulin and in starved animals, the acetyl CoA remained unchanged but the acyl CoA concentrations became elevated as the blood glucose concentration was decreased.

Earlier work in cardiac lipid metabolism utilized total glycerol output as an index of lipolysis. Recent studies have demonstrated the existence of glycerokinase in the rat heart. Investigations undertaken here have attempted to assess the validity of total glycerol release from isolated perfused rat hearts as a lipolytic index. In the absence of glycerokinase, glycerol is a lipolytic end product. In the presence of the glycerokinase, glycerol is further metabolized to

α-glycerolphosphate and can enter the glycolytic pathway via dihydroxyacetone phosphate. α-Glycerolphosphate and lactic acid are considered to be end products of carbohydrate metabolism. In both cases the compounds would be derived from the Embden Meyerhof Pathway. Other sources, though minor, include phosphatidylglycerols and the pentose phosphate pathways. Increases observed in α-glycerolphosphate or glycerol in the presence of inotropic stimulation of the heart, could be derived from either glucose and/or lipolysis. This was studied in the isolated heart both in the presence and absence of glucose. Isoproterenol and glucagon were used to produce a positive inotropic response in the hearts. The inotropic response was accompanied by release of glycerol and α-glycerolphosphate. Agonists were also studied in the presence of l-isopropyl-p-nitrophenylethanolamine (l-INPEA) and nicotinic acid. It was found that α-glycerolphosphate contributed a relatively constant but small amount to the total glycerol release in the isolated perfused heart. Relative changes appear to remain the same whether total glycerol or true glycerol release is measured in heart perfusion studies.

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