THE HEXOSE MONOPHOSPHATE PATHWAY IN ARTERIAL TISSUE

Anthony J. Sbarra, Robert F. Gilfillan, and Wadi A. Bardawil

Department of Pathology and Medical Research, St. Margaret's Hospital and Tufts University Medical School, Boston, Mass.

Received September 6, 1960

The metabolism of carbohydrate by normal and abnormal arterial tissue impinges on every phase of basic and medical physiology. Kirk, Wang, and Brandstrup (1) have demonstrated the presence of glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase in homogenates of human aortic, pulmonary artery, and coronary artery tissue. This significant finding indicates the functioning in these tissues of the hexose monophosphate (HMP) pathway, which may be either the principle or an alternate pathway of glucose dissimilation. The presence of a pathway that appears to have a major role in supplying TPNH for reductive synthesis by arterial tissue may be highly important in the elucidation of the role of lipids in arterial disease such as arteriosclerosis We have confirmed and extended this observation in experiments employing glucose-1-C^{14} and glucose-6-C^{14}.

Using intact thoracic aorta from guinea pigs, we have been able to show that this tissue will produce, under different conditions, a greater amount of CO_2 from carbon one of glucose relative to glucose carbon six. Table I shows the results obtained from a typical experiment in which intact thoracic aorta, stripped of adventitia, was allowed to respire in the presence of glucose-1-C^{14} or glucose-6-C^{14}. From the table it can be seen that there is an increased appearance of C-1 of glucose as CO_2 relative to C-6 with a C-1:C-6 ratio of 6.6. The addition of autologous sera produced an increase in the C-1:C-6 ratio from 6.6 to 17.3, almost a threefold enhancement. In the presence of yeast extract,

the resulting C-1:C-6 ratio is increased to 27.6. In unstimulated and stimulated tissue, the greater C-1:C-6 ratios are produced by an increased liberation of CO_2 from C-1 of glucose while the CO_2 from C-6 remains relatively constant.

The increased C-1:C-6 ratios observed by the addition of either serum or yeast extract would indicate that this tissue has the necessary enzymes to metabolize glucose through the phosphogluconate pathway, however, co-factor concentration may be limiting. These co-factor (s) are shown to be present in autologous serum and yeast extract. The involvement of the HMP pathway in lipid synthesis of other tissues (2) makes this finding extremely attractive. From these observations, it may be implied that the extent of glucose available from participation in the HMP pathway and lipid synthesis is controlled by availability of co-factor (s). At present, a systematic study of this finding and its relationship to lipid synthesis and arteriosclerosis is being made.

TABLE I

Oxidation of Glucose by Arterial Tissue[1]
Under Different Conditions

Addition	Activity in CO_2 C.P.M.[2]		Ratio
	C-1 [3]	C-6 [3]	C-1:C-6
None	33	5	6.6
Autologous[4] Serum 1 ml.	121	7	17.3
Yeast Extract[5] 50 mg.	165	6	27.6

Intact aorta (25-50 mg.), yeast extract or autologous serum were placed in the main compartment of Warburg vessels. 30 μ moles of glucose in Krebs Ringer Phosphate medium was added from the side arm. The total volume in each flask was adjusted to 3.0 ml. with the Krebs Ringer Phosphate medium pH 7.4. Incubation was carried out at 37^0 C.

[1] 300 g. guinea pigs of either sex.

[2] Radioactivity data are "normalized" to 1×10^6 C.P.M. added as glucose and results are based on mg. of tissue dry wt. per 120 minutes.

[3] $C^{14}O_2$ was trapped with KOH (0.2 ml. 20% with a filter paper fan in center well) and the carbonate was ppted. as $BaC^{14}O_3$. Activities of samples of glucose used as substrate were determined on their osazones and all measurements were

carried out as previously described (3).

4 1.0 ml. of fresh autologous guinea pig serum.

5 Bacto Yeast Extract (Difco), a water soluble portion of autolyzed fresh yeast.

This work was supported by grants from USPH B1962 and A2168

References

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