Effect of Prolonged Glucose Infusion on Serum Protein-Bound Glucosamine and Protein-Bound Hexose in Non-Diabetic and Diabetic Patients.* (31352)

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The relationship of glycoproteins to the vascular lesions in the diabetic state is a problem of great interest(1). Histochemical studies have established that glycoproteins are present in normal capillary basement membranes, and electron miscroscopic studies have shown that basement membrane abnormalities are found in capillaries of the glomerulus, retina, subcutaneous tissue, and muscle of patients with diabetes mellitus(2). Basement membrane changes have been noted very early in the clinical course of diabetes(3), suggesting a fundamental relationship with the metabolic disturbances.

Recent studies have been aimed at the biosynthesis of the sugar constituents of glycoproteins. Spiro(4) has demonstrated in the alloxan-diabetic rat that the biosynthesis of protein-bound glucosamine from glucose is not impaired in insulin deficiency, despite an almost complete failure in glycogen synthesis. The possibility of the shunting of glucose into non-insulin dependent pathways in diabetes might be relevant in glycoprotein synthesis.

This study attempted to examine changes in serum glycoproteins by measuring two of the sugar constituents of these molecules, protein-bound glucosamine and protein-bound hexose. These measurements were made during prolonged glucose infusions in non-diabetic and diabetic subjects, at a time when an abundant glucose load was available for metabolic disposition.

Materials and methods. Four non-diabetic subjects and 6 maturity-onset diabetic patients were studied. Each patient received a continuous intravenous infusion of glucose (6 g/kg/24 hr) for 5-7 days, in addition to a small daily diet (20 cal/kg/24 hr, with 40% carbohydrate, 20% protein, 40% fat, divided into 3 equal meals). Pre-breakfast blood specimens were obtained before and periodically during the infusion. Measurements of the serum protein-bound hexosamine (glucosamine) were by the method of Boas(5), and those of the protein-bound hexose were by the method of Winzler(6), using a galactose-mannose standard.

Results. Levels of serum protein-bound glucosamine and protein-bound hexose are shown in Tables I and II. Before the infusion, the mean levels of both of these substances were slightly higher in the diabetics in this small sample of patients; however, there was marked overlapping of values. During the infusion there were negligible changes in either of these substances in both groups.

Discussion. The observation that serum protein-bound glucosamine and protein-bound hexose remained relatively constant in both groups during the glucose infusion should be considered in relation to the observed glucose metabolism. During the infusion the normal subjects did not develop hyperglycemia or glucosuria and, therefore, metabolized all the administered glucose (10). Each diabetic developed marked hyperglycemia and glucosuria, and therefore abundant glucose was available for alternate routes of metabolism.

Although serum levels of protein-bound glucosamine and protein-bound hexose did not change remarkably, changes in the turnover rates of these compounds are not excluded by these studies. In addition, the lack of change in the levels of these protein-bound sugars does not preclude changes in tissue glycoproteins during these infusions. It is also possible that changes occurred in other sugar constituents which were not measured in this study, such as fucose, sialic acid, etc.

Winegrad and Burden(7) have shown recently that l-xylulose, a nonphosphorylated intermediate of the glucuronic acid pathway, is elevated in serum of fasting diabetic patients. In addition, Miller *et al*(8) have sug-

* This work was supported by USPHS grants AM-02456 and T1 AM 5020-12.

TABLE I. Protein-Bound Glucosamine (mg/100 ml serum).

Patient	Before infusion	Day of infusion 1	2	3	4	5	6	7
			Non-Diabetic Subjects					
V.L.	94.5, 101		111	88	118	83		
W.J.	77	84	79	74	68	68		
F.A.	71	68	77	80	77	78		
R.F.	135	118			128			
	Mean 95 Range 71-135							
			Diabetic Subjects					
M.C.	109.5	98.5		103.5				
E.F.	114, 127, 129	124	118	114	112	121		
J.B.	87	84	87	85	83	87		
D.W.	101				90		107	
C.H.	92	95				97		91
F.W.		133	137		115	136		
	Mean 108 Range 87-129							

TABLE II. Protein-Bound Hexose (mg/100 ml serum).

Patient	Before infusion	Day of infusion 1	2	3	4	5	6	7
			Non-Diabetic Subjects					
*V.L.	94	90	93	90	88	89		
W.J.		62	68	55	60	57		
F.A.	83	86	86	72	73	75		
R.F.	120	107	105			102	107	103
	Mean 89 Range 83-120							
			Diabetic Subjects					
E.F.	68, 63, 68	70	73	73	75	70		
J.B.	110	113	110	105	110	105		
F.W.	107	110	115	114	116	119		
D.W.	125				126		125	
	Mean 104 Range 66-125							

* 10:00 a.m. instead of before breakfast.

gested that the increased activity in diabetic serum of β-glucuronidase reflects greater utilization of the noninsulin-sensitive glucuronic acid cycle in these patients.

Further study is needed to explore the complex interrelationships between carbohydrate and glycoprotein metabolism in both normal and diabetic states.

Summary. Serum protein-bound glucosamine and protein-bound hexose were measured during prolonged glucose infusions in non-diabetic and diabetic subjects. Negligible changes in either of these substances occurred in either group.

We are indebted to Miss Lindsay Fiske for technical assistance.

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Received May 2, 1966. P.S.E.B.M., 1966, v122.