

Alterations in Renal Threshold for Sugar by Oral Administration of Cortisone Acetate. (21942)

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Because of widespread clinical use of ACTH and cortisone, their influence upon renal threshold for sugar is of more than academic interest. Holten and Lundbraek(1) noted glycosuria without appreciable rise in fasting or maximum blood sugar levels in well controlled patients by administration of 100 mg of ACTH daily. These findings were confirmed by Kass(2), whereas Fillipis(3), working independently, found the renal threshold for glucose to be significantly increased after use of ACTH in single doses not higher than 40 mg. The effect of DOC glucoside on renal tubular reabsorption in dogs was investigated by Despopoulos and Kaufman(4), who found a reversible depression of renal reabsorption capacity for glucose. To obtain such data after the use of cortisone, renal threshold determinations were made in 8 patients.

Methods and procedures. Four patients were studied, 2 men and 2 women, aged 75, 77, 59, and 64, respectively. One had a diaphragmatic hernia and no other pathology. The other 3 were objects of custodial care without any obvious pathologic conditions, except a degree of arteriosclerosis compatible with age. None of the patients had ever had evidence of diabetes mellitus. After 10 P.M. of the evening preceding each test, food and fluids were withheld. An indwelling catheter was inserted 15 minutes before the test and the bladder emptied. After a fasting blood sugar specimen had been taken, infusion of a 20% solution of glucose in water was started. The infusion was allowed to flow at a speed of 10 ml per minute. The blood and urine were examined for glucose at 5-minute intervals, the infusion stopped as soon as a positive reaction for sugar was found in the urine. For each of 6 immediately consecutive days, the patients were given 200 mg of cortisone acetate orally and their regular ward diets

were kept at an isocaloric level of 2200 calories. On the 7th day, the above procedure was repeated. Before, during and after the test, patients were on a regular ward diet. This method provided us with some rather strikingly uniform data about the "breakdown" of the kidney threshold, as a result of administration of glucose and glucose in conjunction with cortisone acetate. In a second group of 4 patients, we determined not only the point at which the renal threshold was exceeded, but also the point of its restoration after treatment with glucose alone and glucose plus cortisone acetate, respectively. The technic remained essentially the same as for the first study, except that values for glucose in blood and urine were determined after stopping the infusion until the urine was found to be aglycosuric. The subjects of the second group, 2 of whom were men, 69 and 76 years old, respectively, and 2, women, 70 and 72 years old, respectively, were free of any active organic disease, other than the vascular changes compatible with age.

Results. Study I. In all 4 patients of the first group, we found a lowered threshold for glucose following treatment with cortisone. Glycosuria occurred at definitely lower level for blood sugar. The difference between values before and after cortisone varied from 52 to 132 mg per 100 ml (Table I and Fig. 1). The average decrease in the threshold for glucose was 86 mg per 100 ml. Administration of cortisone was associated with a shortening of the time necessary to exceed the renal threshold for glucose in 2 subjects, a lengthening in one, and no change in the fourth (Table I).

Study II. In the second group of 4 patients, we confirmed the findings of Study I, although in case No. 7 (Table I) the decrease in the threshold was not as evident as in the other subjects. In this individual, during the first test, glucose appeared in the urine between

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TABLE I. Influence of Cortisone on Renal Threshold for Glucose in 8 Normally Aging Subjects. Determinations of glucose in blood (mg/100 cc) and urine at periodic intervals (min.).

Before and after treatment with cortisone																		
Pt. No.	Sex	Age (yr)	B*	Time in min.														
				0	5	10	15	20	25	30	35	45	50	55	60	65	70	75
1	♀	75	Blood	98	120	206	253	240	364	416	478	560	544	630				
			Urine	0	0	0	0	0	1+	1+	2+	2+	3+	3+				
2	♀	77	Blood	101	89	236	253	369	305	437	358	518	415					
			Urine	0	0	0	0	0	3+	3+	3+	4+	4+					
3	♂	59	Blood	142	115	229	183	370	248	434	287	443	327	495	334	438		
			Urine	0	0	0	0	0	0	0	0	2+	0	3+	1+	4+		
4	♂	64	Blood	99	66	144	152	234	166	282	220	344	290	368	302			
			Urine	0	0	0	0	0	0	1+	1+	3+	3+	4+	4+			
5	♂	69	Blood	102	100	205	187	306	322	347	330	395	372					
			Urine	0	0	0	0	0	0	2+	2+	4+	4+					
6	♂	76	Blood	121	90	334	281	501	346	532		451						
			Urine	0	0	0	0	2+	1+	3+		4+						
7	♀	70	Blood	70	91	220	218	327	358	346								
			Urine	0	0	0	0	0	3+	3+								
8	♀	72	Blood	122	108	154	172	196	311	345	370	428	403	512				
			Urine	0	0	0	0	0	1+	2+	3+	3+	4+	4+				

* B = Before; A = After.

Solid underline shows point of break in tolerance. Dotted underline shows point of restoration of tolerance.

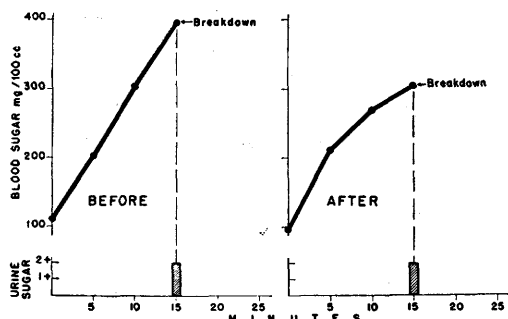


FIG. 1. Breakdown of the renal threshold for sugar before and after treatment with cortisone acetate—200 mg orally daily for 6 days (arithmetical averages for cases 1-4).

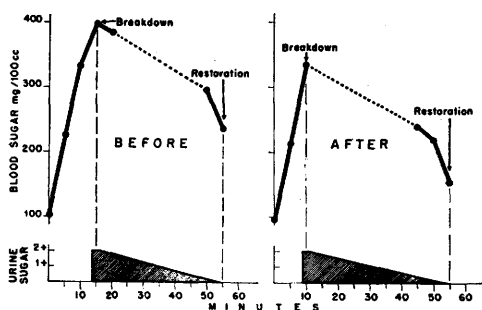


FIG. 2. Breakdown and restoration of the renal threshold for sugar before and after treatment with cortisone acetate—200 mg orally daily for 6 days (arithmetical averages for cases 5-8).

blood sugar levels of 327 and 346 mg per 100 ml, while after administration of cortisone acetate this occurred between 218 and 358 mg per ml. During the 5-minute span, it seems likely that glucose may have been excreted into the bladder before the higher level of 358 mg per 100 ml was reached.

In addition to confirmation of the previous findings, we determined the "restoration" of the kidney threshold in these 4 subjects. In all of them, there was a marked decrease in the blood sugar level at which restoration of the threshold occurred following the use of cortisone acetate (Table I and Fig. 2). The dif-

ferences before and after the use of cortisone acetate varied from 35 to 116 mg per 100 ml with an average of 89 mg per 100 ml. Not only was the renal threshold for sugar lowered by cortisone, but also all values for blood sugar seemed to be depressed, thus producing a depressed or low glucose tolerance curve (Fig. 2). Following administration of cortisone acetate, the time necessary to exceed the renal threshold for sugar was unchanged in 2 and shortened in 2 (Table I). The time required to "restore" the renal threshold for sugar was not altered by the amounts of cortisone given in these studies (Table I and Fig. 2).

Summary. A simple method is described for determination of the renal threshold for glucose in untreated and cortisone-treated individuals. In 4 patients the "breakdown" of the glucose-threshold was investigated and was found to be markedly decreased after 6 days of orally administered cortisone, 200 mg daily. The decrease amounted to an average of 86 mg per 100 ml of blood with a range from 52 to 132 mg per 100 ml. In another group of 4 patients, both the "breakdown" and the "restoration" thresholds were determined. The breakdown values for the first group were confirmed and in addition the restoration of the threshold was also found to be at a lower level for blood sugar, averaging 68 mg per 100 ml less after cortisone than before it with individual variations from 35 to 116 mg per 100 ml.

1. Holten, C., and Lundbrack, K., *Scandinav. Clin. and Lab. Invest.*, 1950, v2, 317.
2. De Filippis, V., *Lancet*, 1951, v1, 856.
3. Kass, E. H., *Proc. Soc. Exp. Biol. and Med.*, 1950, v73, 669.
4. Despopoulos, A., and Kaufman, E. H., *Am. J. Physiol.*, 1952, v170, 11.

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