PATHOGENESIS OF LOW PLASMA RENIN ACTIVITY (PRA) IN THE SYNDROME OF HYPORENINEMIC HYPOALDOSTERONISM (HRHA). S.C. Gulati*, J. Jain*, and A.R. Arnstein. Department of Medicine, Wayne State University, Detroit, Michigan.

In HRHA, which has been observed in elderly patients with renal disease, the pathogenesis of low PRA is unknown. Elevations of cyclic adenosine monophosphate (CAMP), under certain conditions, are associated with increased renin release. In order to evaluate this mechanism of renin release, urinary CAMP and PRA was measured in two such patients and four control subjects before and 4 hours after administration of furosemide (F) (80 mg p.o.), theophylline ethylenediamine (T) (250 mg I.V. slowly), and isoproterenol infusion (I) (20 ng/kg/min over 4 hrs). Mean creatinine clearance and serum potassium of the two patients were 60 ml/min and 7.1 mEq/L respectively. Mean urinary aldosterone excretion of 1.9 mcg/24 hrs (n, 5-20 mcg/24 hrs), which did not respond to ACTH infusion (40 units I.V. over 8 hrs), increased two to three-fold following angiotensin infusion for 6 hours.

Results of cyclic AMP (measured by RIA method of Steiner) and PRA (measured by RIA method of Haber) determinations are as follows:

	CAMP (μmole/gm creatinine)				PRA (ng/ml/hour)			
	B*	Post F	Post T	Post I	B*	Post F	Post T	Post I
Pt. #1	2.3	4.3	3.8	3.5	0.3	.3	0.3	.3
Pt. #2	1.6	3.2	3.2	3.2	0.5	0.7	0.8	.6
Control (4)	3.2± 1.0	4.3± 0.5	4.0± 1.1	-	1.5± 0.5	5.6± 1.6	5.9± 1.4	-

*B=Baseline

These data suggest that there is a defect in cyclic AMP-mediated renin release in this syndrome.

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HYPOGLYCEMIA, A POTENT STIMULATOR OF THE HYPOTHALAMIC-PITUITARY-THYROID AXIS. Y. Leung,* A.R. Guansing,* K. Ajlouni* and T.C. Hagen (intr. by P.S. Rosenfeld). Department of Medicine, Wood VA Center, Medical College of Wisconsin, Milwaukee, Wisconsin.

Recent studies indicate that hypoglycemia induces thyrotropin (TSH) release in growth hormone deficiency states. To elucidate the controlling mechanism(s) involved in this phenomenon, studies were carried out in adult female Holtzman rats in whom hypoglycemia was induced by the intraperitoneal injection of insulin. Serial measurements of blood sugar, thyrotropin releasing hormone (TRH), TSH, T3 and T4 were performed over a period of 3 hours as indicated in the table. Each time period represents experiments performed in 6 rats. TRH and TSH were measured in crude extracts of the hypothalamus (SME) and pituitary (pit). Blood sugar levels decreased from a basal value of 122.5 ± 8 mg% to 39.3 ± 3.7 mg% within 15 minutes post-insulin, and returned to normal within 60 minutes.

Time (min.)	0	15	30	45	60	90	120	180
SME TRH (ng/SME)	3.3	1.5#	5.6	4.6	4.1	4.4	4.5	3.5
Pit TSH (mU/pit)	320	312	104#	209	59#	113#	194	347
Serum TSH (uU/ml)	6.7	4.6	16.2	18.4##	8.4	3.9	2.8	2.6
T3 (ng%)	108	181	184	190	144	783#	265	251
T4 (mcg%)	4.1	3.9	4.0	4.6	3.8	4.6	3.9	4.7

# $p < 0.01$ ## $p < 0.001$

Simultaneous with the fall in blood sugar is the significant decrease in SME TRH followed within 30 minutes by the peak increase in serum TSH. Circulating T3 did not rise until 90 minutes post-insulin injection. We conclude that hypoglycemia induces TRH release with a subsequent cascade in the secretion of TSH and T3.