



PROC ENDOCR SOC 1978; 60: 394

## THE ENDOCRINE SOCIETY

A NEW MECHANISM FOR NORMOTENSIVE PHEOCHROMOCYTOMAS. J.M. Feldman, J.A. Blalock\*, R.T. Zern\*, J.D. Shelburne\*, J.T. Gaede\*, R. Farrell\* and S.A. Wells, Jr. Departments of Medicine, Pathology and Surgery, Duke University Medical Center, Durham, N.C. 27710.

The majority of patients with pheochromocytomas (P) have either sustained or episodic hypertension due to excessive catecholamine secretion from their tumors; occasional patients with these tumors are normotensive. We recently evaluated a 28 yr old man with a 7 month history of abdominal pain and L suprarenal mass. Daily blood pressures during 5 wks of hospitalization were all normal. The patient had elevated urinary norepinephrine (NE)(250ug/d), vanilylmandelic acid (8.5mg/d) and homovanillic acid (HVA)(21.5mg/d) excretion. A Ladrenal and R extraadrenal P were resected. On light microscopy, both tumors were typical P; however, only occasional cells had a positive chromaffin reaction. Electron microscopy of both tumors showed electron dense neurosecretory granules with the typical appearance of NE. The table compares the P of this patient with P resected from 4 patients with hypertension (1 unilateral, 3 bilateral). These patients differed by having normal HVA excretion ( $\overline{X}$ =4.2mg, range=3.3-4.8). Although the P of the normotensive patient contained substantial amounts of dopamine (DA), the NE and E content was low. This was due to a marked deficiency of dopamine B-hydroxylase (DBN) and phenylethanolamine-N-methyltransferase (PMMT). Mixing experiments showed no enzyme inhibitors in the tumors. The large amount of HVA in the pre-op urine of the normotensive P patient suggests his tumor was secreting DA. Despite substantial amounts of the intermediate DA in the tumors of hypertensive P patients, their normal HVA excretion suggests that their P do not secrete DA. One mechanism for the absence of hypertension in P is a deficiency of DBH, with a resulting increased DA and decreased NE secretion.

	_WT_	UA	DBH	NŁ	NW.	t.
	<u>(g)</u>	(pg/g)	(nm/min/mg	$(\overline{\mu g/g})$	(pm/m1n/mg)	(pg/g)
Normotensive Pheo						1.0.0.
Right	15	20 <del>9</del>	0.8	11	7	0
Left	160	261	0.4	4	. 3	Ŏ
Hypertensive Pheos	;			•	, ,	_
Mean	3 <b>9</b>	922	14.0	4263	62	1150
(Range)	(1.8-113)	(406-1460)	(3.5-30.3)	(1241-8747		(0-2530)
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PROTEIN IODINATION IN THE BREAST AND THYROID OF RATS.

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We have measured  $^{125}$  iodide uptake and protein iodination in normal and lactating breasts and respective thyroids of rats in vivo. The organ homogenates were analyzed by gel filtration column chromatography in the presence of sodium dodecyl sulfate (SDS) two hours after I.V. injection of 3-6  $\mu$ Ci  $^{125}$ iodide. The protein subunit molecular size was determined by both gel filtration and polyacrylamide gel electrophoresis in SDS.

There was uptake (expressed as percent of injected  $^{125}$ iodide) of  $4.1^{\pm}1.5\%$  (SEM) and  $5.1^{\pm}1.4\%$  in the thyroids of control and lactating rats and  $0.2^{\pm}0.1\%$  compared to  $6.7^{\pm}1.7\%$  in the control and lactating breasts. Using  $^{51}$ Cr dilution techniques to measure vascularity, we estimate more than 95% of the tissue  $^{125}$ 1 radioactivity was extravascular. Lactating breast weighs 2.0 gms and the control 0.8 gms. The following chart shows the percent distribution of tissue  $^{125}$ 1 radioactivity. Column 1 represents iodide; columns 2 and 3 represent protein subunit molecular size ranges in daltons:

	125 I-iodide	1,000-50,000	> 50,000	
Thyroid (control)	9.0 ± 1.0	15.5 ± 2.5	75.5 ± 3.5	
Thyroid (lactating)	11.8 ± 0.6	15.0 ± 0.7	73.3 🛨 1.0	
Breast (control)	99.0 <sup>±</sup> 0.5	0.5 # 0.3	0	
Breast (lactating)	80.2 ± 5.7	19.8 <sup>±</sup> 5.7	0	

There was uptake of injected  $^{125}$ lodide into lactating breast tissue and organification to a protein of 10-20,000 daltons in subunit size. In contrast, the thyroid organified most of the  $^{125}$ lodide to a protein larger than 100,000 daltons (thyroglobulin) but 15% was to a 10-20,000 dalton protein. Iodinated protein did not appear in the serum. The percent of injected radio-activity remaining in the serum was 13.6  $^{\pm}$  1.6 in the controls compared to 12.4  $^{\pm}$  3.0 in the lactating animals. Rapid uptake and organification of iodide may be an important function of active breast tissue. (CA 14705, HL 19168)

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> Normal Range (ng Type of Control # of Determinati Mean I SD (ng/dl Range (ng/dl)

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\*p<0.005 (in

637 ACTION OF GLUCOC CYTES: EFFECTS O Anatomy, Univers Previous work adrenalectomized plasmic reticulu gested that the placed in SER me deposition. In t with puromycin a in liver cells w given a single i + DEX. Six rats hormone administ croscopy and fro of all groups of ADX rats the hep-6 hrs. a level of injected with DE untreated with Di overnight fasted treatment with DI associated with after hormone adm merous tubules ar were found in her those from overni experiments that upon protein synt lism or to the ac USPHS grant #AM-1