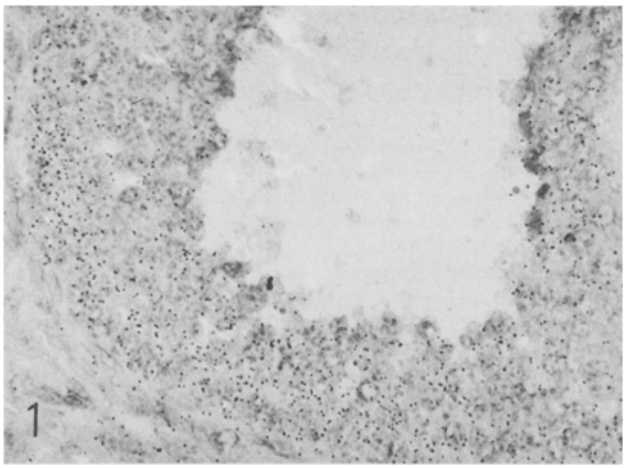

Figure 1. Autoradiograph of a section of a mouse ovary, 48 h after PMSG injection, showing radioactivity from incorporated 125_I-FSH in the peripheral granulosa and cumulus cells. Note negligible number of grains in the theca and interstitium.

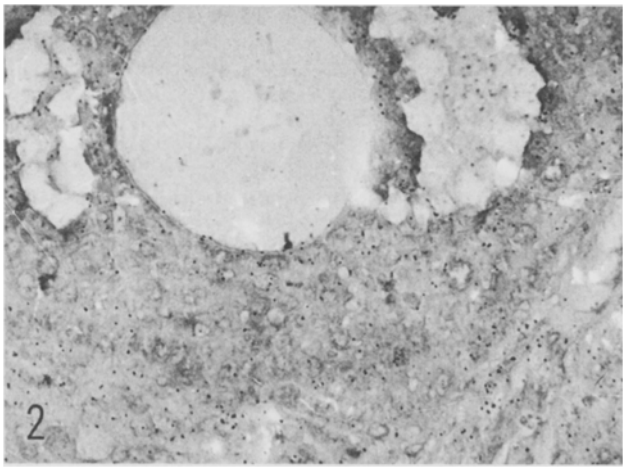

Figure 2. Autoradiograph of a section of a mouse ovary, 72 h after PMSG injection, showing radioactivity from incorporated 125_I-FSH. Dispersed sliver grains are seen all over the follicle.

The remaining cell types of the ovarian compartment did not show any uptake of labeled FSH. These results are in agreement with earlier reports[5-7].

Recently we were able to demonstrate that, morphologically, 10% of the antral follicles were atretic 48 h after PMSG injection and 90% by 72 h after PMSG treatment. Thus the decreased binding of FSH to granulosa cells, 72 h after PMSG, is presumably due to degenerative changes, possibly reducing the number of FSH-receptors in the granulosa cells of atretic follicles.

The distribution of silver grains in the peripheral granulosa cells situated near the basement membrane was higher than in the cumulus cells loated centrally in the 48 h group. This differential uptake has been reported earlier with labeled luteinizing hormone (LH[8,9]).

McNatty[10] has shown that FSH concentration in the fluid of atretic follicles is significantly reduced compared to that in normal antral follicles. The reduced FSH-binding to granulosa cells of atretic follicles, observed by us, could also be due to decreased availability of FSH in the follicular fluid due to a change in the permeability of the basement membrane. Recently, Farookhi[11] postulated that the basement membrane changes its permeability during atresia of the follicle. However, he presumes that this change in membrane permeability permits even large molecules, such as globulins (antibodies to granulosa cells) to enter the follicle and probably destroy it.

It is therefore necessary to elucidate further whether the changes in the binding of FSH to granulosa cells during follicular atresia are due to a decrease in 1. the number of FSH receptors on the granulosa cells 2. in the availability of FSH due to changes in the permeability of the basement membrane and/or 3. passage of antibodies to granulosa cells through the basement membrane, causing degenerative processes in these cells.

1 We are grateful to Dr A.F. Parlow, California, USA for the gift of PMSG. Reprint requests to T.D.N.

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Norepinephrine level in the hypothalamus of the genetically hypertensive mouse[1]

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Summary. The norepinephrine content of the hypothalamus of young mice with high blood pressure was statistically lower than that of mice with low blood pressure. The difference was not evident in older mice from these same strains. No differences in dopamine content were found suggesting a genetic difference in the activity of the converting enzyme.

There are presently a number of potential animal models for human hypertension[2,3]. The cause of the hypertension in these models is still unknown and there is still some question as to whether or not any of these models will be a suitable paradigm for human hypertension. As determinants of the elevated blood pressure in animal models are

uncovered, one would seek similarities among the models. This is not meant to imply that all forms of hypertension have a common cause, but rather that the number of mechanisms are limited and, as the number of animal models increase, common determinants should be found in some. Norepinephrine (NE) content of the hypothalamus has been found to be lower in young hypertensive rats than in normotensive controls for the spontaneously hypertensive rat (SHR)[4-7] and for the Sabra hypertensive rat[8]. This paper will report a similar finding in the young genetically hypertensive mouse.

Materials and methods. The mice were males sampled from the 25th and 26th generations of selective breeding for high (HBP) and low systolic blood pressure (LBP). About half of the mice in the HBP have blood pressures exceeding 140 mmHg and are considered 'genetically hypertensive mice'[2]. Details of the genetic selection program have been published elsewhere[9].

Blood pressures were determined indirectly by tail occlusion in restrained but unanesthetized mice (Narco Bio Systems physiograph)[9]. Beginning at 09.00 h, mice were sacrificed by cervical dislocation, hypothalami removed and catecholamines of individual hypothalami extracted as described earlier[10]. After desorption of catecholamines from alumina, 50 µl were injected into a high pressure liquid chromatography system using an Ultrasphere C_{18} ion pair column (Altex No. 256-13). Mobile phase was 0.05 M citric acid, 0.1 M sodium phosphate, 0.1 mM EDTA, 0.3 mM sodium octyl sulfate and 10% methanol. Flow rate was maintained at 60 ml per h with a back pressure of 2000 psi. Dihydroxybenzylamine was used as the internal standard. Detection of catecholamines and calculation of catecholamine amounts were accomplished as previously described[10].

Statistical significance was ascertained by a Student's t-test comparing HBP and LBP at each age.

Results and discussion. The table summarizes the catecholamine data for the 2 strains. Statistically significant differences were found in the NE content of the hypothalamus at 5 weeks ($p<0.05$) and 7 weeks ($p<0.02$). Mice at 12 weeks and at 10 and 11 months did not show statistically significant differences ($p>0.05$) but the differences, small as they were, were in the same direction. There were no significant differences in DA content between HBP and LBP at any of the ages.

Mean blood pressure of the generation from which the older mice were sampled was 137 ± 2 ($n=55$) in the HBP and 83 ± 1 ($n=48$) in the LBP. It is difficult to measure the blood pressure of unanesthetized young mice of these strains, but preliminary data suggests that the HBP may be around 100 mmHg, while the LBP may average 60 mm Hg at 6–8 weeks of age. These averages are based on small numbers of mice for which repeatable measurements were obtained.

We have previously reported no difference in NE content of the hypothalamus of older mice of these strains[10]. The present data confirms that finding. Differences in NE content between young mice of the HBP and LBP is in agreement with reports for the SHR[4-7] and Sabra hypertensive rats[8]. In each of these cases the young animal with the elevated blood pressure had lower NE concentration in the hypothalamus than normotensives. This difference may or may not persist. Saavedra[11] reported differences in 14-week-old SHR compared to WKY normotensive controls. Yamori et al.[6] and Wijnen et al.[7] reported similar differences at 10 weeks, but LeQuan-Bui et al.[5] did not find this directional difference at 12 weeks. Not all young hypertensive animals have lower hypothalamic NE. Young rats of the genetically hypertensive (GH) rat from New Zealand show no difference[12] and in the Dahl Salt-Susceptible and Salt-Resistant rat the rats who became hypertensive after chronic salt-ingestion have higher hypothalamic NE than resistant rats at 5–17 weeks of age[13].

NE is formed from DA by the action of the converting enzyme dopamine-β-hydroxylase (DβH) and is itself converted to epinephrine by phenylethanolamine-N-methyltransferase (PNMT). If the concentration of DA is the same in our lines of mice, but the NE is lower in the HBP compared to LBP, the difference in NE concentration could be due to a decrease in the activity of DβH or an increase in the activity of PNMT. Saavadra et al.[4] found a decrease in DβH activity in some hypothalamic nuclei (but not in others) in the SHR which may relate to the lower NE concentration. They postulated that the decrease in NE concentration was probably due to diminished synthesis.

Dopamine (DA) and norepinephrine (NE) content of the hypothalamus of the high blood pressure (HBP) and low blood pressure (LBP) strains

Age	Strain	n	ng DA/g	ng NE/g
5 weeks	HBP	4	581±24	1518± 32*
	LBP	4	587±48	1731± 62
7 weeks	HBP	4	960±69	1633± 40*
	LBP	4	1015±59	1922± 79
12 weeks	HBP	4	1212±92	1647±146
	LBP	4	1025±64	1700± 52
10–11 months	HBP	10	977±45	1596± 39
	LBP	10	847±76	1601± 72

*Difference between strains statistically significant by a t-test at $p<0.05$.

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