eral observations. Treatment with the dopamine agonist bromocriptine causes parallel decreases in plasma PRL, sympathetic tone, and blood pressure in SHR and in patients with essential hypertension without lowering resting supine blood pressure in normotensive rats and humans. 4-7

Although it is likely that exaggerated PRL responses to TRH and stress in the SHR and hypertensive humans probably reflect altered dopaminergic regulation of PRL secretion and blood pressure, it is possible that PRL may have a direct role in the pathogenesis of hypertension in the SHR and in LREH. PRL administration has been reported to increase blood pressure in rabbits 4 and rats. 9 Recently, it was reported that postnatal administration of antiserum to rat PRL resulted in a significant lowering of pressure in SHR at 14 weeks of age. 10 These results were interpreted as suggesting that endogenous PRL is involved in blood pressure regulation. 10 We have recently observed elevated blood pressures in 20 rats transplanted with PRL-secreting mammothmic tumors (MttF4) compared to sham transplanted controls (table 1). Further, there was a positive correlation (r = 0.67) between PRL levels and blood pressures in these tumor-transplanted rats. These observations suggest a possible direct role for elevated endogenous PRL levels in the pathogenesis of high blood pressure in the SHR and in a subset of patients with essential hypertension. Since PRL levels rise in response to a variety of conditions including mental and physical stress, perhaps posture and isometric exercise and sleep, 7 it is possible that exaggerated PRL responses to these stimuli and secondarily elevated endogenous PRL levels could play a role in the pathogenesis and/or maintenance of hypertension.

**References**


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**Table 1.** Mean (±1 SEM) Arterial Blood Pressures (MAP) and Plasma Prolactin (PRL) Levels 3 Weeks after Either Subcutaneous Sham Transplantation or Transplantation of the Furth Transplantable Pituitary Mammatropic Tumor (MttF4) in 20 Wistar Furth Rats

<table>
<thead>
<tr>
<th>Transplantation</th>
<th>MAP (mm Hg)</th>
<th>PRL (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>105 ± 4.7</td>
<td>8.2 ± 0.6</td>
</tr>
<tr>
<td>MtTF4</td>
<td>123 ± 6.7</td>
<td>1623 ± 436</td>
</tr>
</tbody>
</table>

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**The Age Factor and Salt-Induced Hypertension in the Brattleboro Rat**

To The Editor: As a coauthor of papers on salt-induced hypertension in Brattleboro rats, 1-4 I should like to comment on the discussion of Gruber vs Berecek and Crofton (Hypertension 4: 572-574, 1982). A moderate salt hypertension was elicited in uninephrectomized DI rats exposed from prepuberty to high salt intake, while no hypertension occurred in DI rats that were influenced by very high salt intake only in adulthood (250 mmoles/kg/day for 14 weeks). 1 This is not in apparent conflict with the findings of Crofton et al. 2 and Berecèk et al. 4 The lower salt sensitivity of DI animals was confirmed when hypertonic saline was infused into adult nephrectomized DI rats. Only 50% of the blood pressure increase observed in Wistar rats was elicited in DI rats. 7 The existence of a vasopressin-independent component of increased blood pressure argues against the resistance of vasopressin-deficient animals to the hypertensogenic action of salt. Thus, the failure to induce DOC-salt hypertension in DI rats 5 need not be caused only by the use of adult animals. Relatively low salt intake (as compared to our experiments) and/or a difference in the stimulus provided by the DOC-salt regimen could be important factors, as well. Our data 6 indicated that vasopressin was not essential for the pathogenesis and/or maintenance of salt hypertension, but the data did not rule out an important modulatory role for vasopressin in this kind of hypertension. However, if dDAVP can substitute for vasopressin, 6 the direct pressor role of vasopressin seems to be of minor importance in DOC-salt hypertension.

Our most important finding was that the susceptibility of DI rats to the hypertensive effects of uninephrec-
tomy was substantially increased if high salt intake started prior to the end of sexual maturation. Uninephrectomy carried out in adult DI rats, drinking 0.6% saline, elicited hypertension only in those animals exposed to the high salt regimen from youth. Only minimal blood pressure elevation occurred in animals that were kept on a normal salt intake in youth. Higher susceptibility of young rats to hypertensive stimuli was demonstrated in various kinds of experimental hypertension in which salt intake is increased — adrenal-regeneration, DOC-salt, triidothyronine-salt, and salt hypertension of Dahl salt-sensitive rats. Our results demonstrated that vasopressin played no important role in the higher susceptibility of young rats to salt hypertension. Thus, the age from which high salt intake started must be carefully considered if different experiments are compared. The DI model seems to me to be very valuable in this respect.

Even if there are complex interactions of the mechanisms regulating volume and circulatory homeostasis, we must be aware of the fact that young rats (and other animals) as compared with older rats excrete less water and sodium after the expansion of extracellular fluid volume or of blood volume. The natriuretic ability of rats matures gradually until the end of sexual maturation. At this time the higher susceptibility of rats to salt hypertension disappears. Solomon et al. explained the lower sodium excretion after blood volume expansion in terms of the lower natriuretic activity of the blood in young rats. Although this finding appears to be contradictory to recent ideas on the role of the "natriuretic factor" in hypertension, this need not be the case. High salt intake from youth increased fractional sodium excretion in young dogs, and the increased urinary sodium concentration persists in "influenced" rats until adulthood. The mechanisms of this increased ability to excrete sodium are not definitely known.

We never tried to extrapolate our data to humans, although Dr. Lewis K. Dahl did point out the possible relevance of his data in young salt-sensitive rats to human hypertension. A short exposure of these rats to high salt diet in prepuberty was sufficient to induce a life-long severe hypertension. It is an open question as to which "rat model" of hypertension is best applicable to humans, but age-dependent salt hypertension has been observed in lower primates (baboons) as well.

The relation between blood pressure and salt intake was rarely observed in Western societies. However, in such societies the dietary changes during the development of the individual seem to be more profound than in primitive tribes. Both blood pressure and sodium excretion (at least in the rat) can be modified by the dietary salt regimen in youth. Therefore the possibility cannot be excluded that the blood pressure and/or sodium metabolism of adult humans are more dependent on salt intake in youth than on the salt intake per se.

References


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