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. 

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 and rats. 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. These results were interpreted as suggesting that endogenous PRL is involved in blood pressure regulation. 

We have recently observed elevated blood pressures in 20 rats transplanted with PRL-secreting mammotrophic 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, 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.

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, I should like to comment on the discussion of Gruber vs Berecek and Crofton (Hypertension 4: 572-574, 1982). A moderate salt hypertension occurred in DI rats that were influenced by very high salt intake only in adulthood (250 mmol/kg/day for 14 weeks). This is not in apparent conflict with the findings of Crofton et al and Berecék et al. 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. 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 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 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, 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-

### Table 1

<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>132 ± 6.7</td>
<td>1623 ± 436</td>
</tr>
</tbody>
</table>

References


**JAMES R. SOWERS, M.D.**

Associate Professor of Medicine

UCLA School of Medicine

Sepulveda VA Medical Center

Sepulveda, California 91343
tomy was substantially increased if high salt intake started prior to the end of sexual maturation. Unin¬
ephrectomy carried out in adult DI rats, drinking 0.6% saline, elicited hypertension only in those ani¬
imals exposed to the high salt regimen from youth, 2-4 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, 4 DOC-salt, 10 triiodothyronine—
salt, 11 and salt hypertension of Dahl salt-sensitive
rats. 12 Our results demonstrated that vasopressinplayed no important role in the higher susceptibility of
young rats to salt hypertension.13 Thus, the age from
which high salt intake started must be carefully consid¬
ered 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 mecha¬
nisms 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 15 or of blood volume.14 The natriuretic ability
of rats matures gradually until the end of sexual matu¬
rature. 14 15 At this time the higher susceptibility of rats
to salt hypertension disappears. 1 Solomon et al. 10 ex¬
plained 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 frac¬
tional sodium excretion in young dogs,17 and the in¬
creased urinary sodium concentration persists in "in¬
fluenced" rats until adulthood. 18 18 The mechanisms of
this increased ability to excrete sodium are not defi¬
nitely 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.12 It is an open question
as to which "rat model" of hypertension is best appli¬
cable to humans, but age-dependent salt hypertension
has been observed in lower primates (baboons) as
well. 19

The relation between blood pressure and salt intake
was rarely observed in Western societies. 20 However,
in such societies the dietary changes during the develop¬
ment of the individual seem to be more profound
than in primitive tribes. Both blood pressure and sodi¬
um 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 sodi¬
um metabolism of adult humans are more dependent
on salt intake in youth than on the salt intake per se.

References
1. Dlouhý H, Křeček J, Zicha J: Hypertension in rats with heredi¬
tary diabetes insipidus. The role of age. Pflugers Arch 369:
177, 1977
2. Dlouhý H, Křeček J, Zicha J: Effect of age on hypertensive
stimuli and the development of hypertension in Brattleboro
3. Dlouhý H, Křeček J, Zicha J: Sodium metabolism in rats with
hereditary defect of vasopressin synthesis. In Hormonal Regu¬
lation of Sodium Excretion. edited by Lichardus B, Schrner
RW, Ponec J. Amsterdam: Elsevier/North Holland Biomi¬
edical Press, 1980, pp 129
and the injurious influence of salt in youth. Physiol Bohemos¬
lov 30: 531, 1981
5. Crofton JT, Share L, Shade RE, Lee-Kwon WJ, Mangu M,
Sawyer WH: The importance of vasopressin in the develop¬
ment and maintenance of DOC-salt hypertension in the rat.
Hypertension 1: 31, 1979
and vascular reactivity in the development of DOCA hyperten¬
sion in rats with hereditary diabetes insipidus. Hypertension 4:
3, 1982
7. Hatzinikolaou P, Gavras H, Brunner HR, Gavras I: Sodium
induced elevation of blood pressure in the anephric state. Sci¬
ence 209: 935, 1980
8. Saito Y, Yajima Y, Watanebe T: Involvement of AVP in the
development and the maintenance of hypertension in rats. In
Antidiuretic Hormone, edited by Yoshida S, Share L, Yagi K.
9. Skelton FR, Guillebeau J: The influence of age on the develop¬
ment of adrenal regeneration hypertension. Endocrinology 59:
201, 1956
10. Musilová H, Jelínek J, Albrecht I: The age factor in experi¬
mental hypertension of the DCA type in rats Physiol Bohemos¬
lov 15: 525, 1966
11. Willard PV, L-triiodothyronine and dinitro-phenol induced hy¬
salt intake in youth. Physiol Bohemoslov 15: 137, 1966
13. Crofton JT, Share L, Shade RE, Lee-Kwon WJ, Manning M,
Sawyer WH: The importance of vasopressin in the develop¬
ment and maintenance of hypertension in rats. 2-4
Gen 35: 113, 1969
15. Solomon S, Hathaway S, Curb D: Evidence that the renal
response to volume expansion involves a blood-borne factor.
Biof Neonate 35: 113, 1979
16. Steichen JJ, Kleinman LF: Influence of dietary sodium intake
on renal maturation in unanesthetized canine puppies. Proc Soc
17. Jelínek J, Kraus M, Musilová H: Adaptation of rats of different
ages to forced intake of a 2% NaCl solution without the occur¬
dence of salt hypertension. Physiol Bohemoslov 15: 137, 1966
High salt intake and blood pressure in lower primates (Papio
19. Simpson FO: Salt and hypertension: a sceptical review of the
on renal maturation in unanesthetized canine puppies. Proc Soc
on renal maturation in unanesthetized canine puppies. Proc Soc
22. Simpson FO: Salt and hypertension: a sceptical review of the

MUDr JOSEF ZICHA
Institute of Physiology
Czechoslovak Academy of Sciences
Prague 4 - Královské Vinohrady
CS-142 20 Czechoslovakia
The age factor and salt-induced hypertension in the Brattleboro rat.
J Zicha

Hypertension. 1983;5:156-157
doi: 10.1161/01.HYP.5.1.156

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/5/1/156.citation