Urinary Excretion of Prostaglandin E\(_2\), Prostaglandin F\(_{2\alpha}\), and Thromboxane B\(_2\) in Normotensive and Hypertensive Subjects on Varying Sodium Intakes

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SUMMARY A deficiency in renal prostaglandins has been implicated in the pathogenesis of essential hypertension, particularly low renin hypertension. Previous studies of urinary prostaglandins as influenced by sodium balance and in essential hypertension have been handicapped by problems with assay methodology, inclusion of male subjects, and/or failure to standardize daily fluid consumption. We compared urinary excretion of prostaglandin E\(_2\) (PGE\(_2\)), prostaglandin F\(_{2\alpha}\) (PGF\(_{2\alpha}\)), and thromboxane B\(_2\) (TXB\(_2\)) in black and white normotensive and low-renin and normal-renin hypertensive women during two protocols producing sodium depletion (10 mEq sodium diet) and sodium loading (200 mEq sodium diet plus the fludrohydrocortisone Florinef, a synthetic mineralocorticoid). A constant fluid, potassium, and caloric intake was maintained throughout. Changes in plasma renin activity, urinary aldosterone excretion, and urinary kallikrein excretion were simultaneously assessed.

As sodium intake decreased from 120 to 10 mEq sodium/day, increases in urinary PGF\(_{2\alpha}\) (502 ± 60 to 1222 ± 176 ng/24 hr, p < 0.01) and TXB\(_2\) (99 ± 33 to 216 ± 77 ng/24 hr, p < 0.05) excretion were observed in normotensive subjects. These increases were not observed in the hypertensive patients, possibly because less renin stimulation was achieved during the low sodium diet. Alternatively, subnormal prostaglandin production may have contributed to the lesser renin stimulation. Furthermore, urinary PGF\(_{2\alpha}\) excretion in hypertensive patients during sodium depletion indicated strong influences of race and renin status; namely, black and normal-renin hypertensives increased urinary PGF\(_{2\alpha}\) excretion during sodium depletion whereas white and low-renin hypertensives did not. When white hypertensives and normotensive subjects consumed either 120 or 200 mEq sodium diet, there were no consistent differences in urinary excretion of PGE\(_2\), PGF\(_{2\alpha}\), or TXB\(_2\). With sodium loading, urinary PGE\(_2\), PGF\(_{2\alpha}\), and TXB\(_2\) excretion did not change, whereas urinary kallikrein excretion increased. Urinary excretion of these prostanoids was therefore independent of mineralocorticoid and kallikrein effects upon the kidney. Thus, we found no evidence for a role of renal PGE\(_2\), PGF\(_{2\alpha}\), and TXB\(_2\), in natriuresis in humans. Urinary excretion of these prostanoids was decreased in hypertensive patients only during sodium depletion. (Hypertension 4: 735-741, 1982)

KEY WORDS · prostaglandins · thromboxane · kallikrein · renin · aldosterone · natriuresis · mineralocorticoid escape · sodium loading

RENAL prostaglandins have been implicated in the pathogenesis of essential hypertension in several ways. Prostaglandin E\(_2\) (PGE\(_2\)) and prostacyclin have both vasodilating and natriuretic activity when infused into the renal artery.\(^1\)\(^2\) Since renal prostaglandins are released into the renal vein, a deficiency of renal prostaglandins has been postulated\(^1\) to cause essential hypertension by a loss of this systemic vasodilating activity. In addition, even if a systemic effect were not operative, local renal effects might alter renal vascular resistance\(^3\) or renal tubular sodium excretion\(^4\) and thus lead to diminished natriuresis and sodium-mediated low-renin hypertension.\(^1\)\(^4\) The ini-

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tial fashion in patients with essential hypertension.

The relationship between renal prostaglandin and kallikrein vasoconstrictor, has been assessed only in an initial fashion in patients with essential hypertension. Although animal studies have suggested a relationship between renal prostaglandin and kallikrein production, the changes in urinary kallikrein and prostaglandin excretion remain undefined in essential hypertension with changes in sodium status and during increased mineralocorticoid activity upon the kidney. In addition, black subjects have been noted to have increased mineralocorticoid activity upon the kidney.

The PGF excretion rates are of interest in hypertension, however, not only because of the possible suppressive effect of PGF upon renin release but also because alterations in the ratio of PGE/PGF reported with changes in dietary sodium, may reflect alterations in the activity of PGE-9-keto reductase, an enzyme that may metabolize PGF. Thromboxane A2, a potent vasoconstrictor, has been assessed only in an initial fashion in patients with essential hypertension.

Although animal studies have suggested a relationship between renal prostaglandin and kallikrein production, the changes in urinary kallikrein and prostaglandin excretion remain undefined in essential hypertension with changes in sodium status and during increased mineralocorticoid activity upon the kidney. In addition, black subjects have been noted to have lower plasma renin activity (PRA) and urinary kallikrein excretion than white subjects. Assessment of urinary prostaglandin excretion in black vs white subjects is thus of interest. To evaluate these factors, we performed the following study in normal subjects and patients with essential hypertension during regular sodium balance, normal vascular event during this time of antihypertensive medications. To assess changes in prostaglandin excretion during alterations in sodium balance, normal subjects and hypertensive patients were admitted on two occasions to the General Clinical Research Center of the University of Texas Health Science Center at Dallas. During this time the patients drank 3000 ml total fluids per day and ate the same food each day, thus maintaining a constant caloric intake. Sodium loading was accomplished during one admission by having the patients consume a daily diet of 200 mEq sodium and 70 mEq potassium for 6 days. During the last 3 days of this diet, the patients were given Florinef (fludrohydrocortisone, FHC) 0.5 mg twice daily. During a second admission the patients consumed a 120 mEq sodium, 70 mEq potassium (regular sodium) diet for 3 days and 10 mEq sodium, 70 mEq potassium (low sodium) diet during the following 6 days. These two admissions were separated by at least 2 weeks.

Daily 24-hour urine samples were collected and refrigerated, for sodium, potassium, and creatinine determinations. The patients stood or walked at the end of each of these diets, at 0600-0800 hours during the high sodium-FHC protocol or 0600-1000 hours during the regular sodium-low sodium protocol. After walking, blood samples were collected in 7 ml tubes containing 7 mg disodium EDTA for determination of PRA. The blood samples were immediately iced and centrifuged under refrigeration before the plasmas were separated and frozen. Renin status was classified by PRA response to sodium depletion with the low sodium protocol. Urinary aldosterone, kallikrein, and prostaglandin determinations were performed on the 24-hour urine samples collected at the end of each of the different dietary sodium periods. Urine samples for kallikrein were stored refrigerated under toluene until the time of assay. Urine samples for PGE, PGF, and TxB determinations were stored frozen without thawing until the time of assay.

Methods

Patient Studies

For these studies, 16 female hypertensive patients and 15 age- and race-matched normotensive female subjects were used. The hypertensive group consisted of nine white and seven black patients, whereas the normotensive group consisted of seven white and eight black subjects. The average age of the normotensive and hypertensive groups were 49.6 and 45.1 years respectively. All patients gave written informed consent to participate in these studies after an explanation of the study in lay language. All study protocols were approved by the Human Research Committee of the University of Texas Health Science Center at Dallas.

The diagnosis of essential hypertension was established after history, physical examination, blood chemistry studies using an automated sequential multiple analysis system (SMA-12), urinalysis, urinary metanephrine, and rapid-sequence intravenous pyelogram revealed no evidence of secondary forms of hypertension. All patients had been off antihypertensive medications for at least 3 weeks prior to study, and had diastolic blood pressure greater than 90 mm Hg during the time of study. No patient had any untoward cardiovascular event during this time off antihypertensive medications. To assess changes in prostaglandin excretion during alterations in sodium balance, normal subjects and hypertensive patients were admitted on two occasions to the General Clinical Research Center of the University of Texas Health Science Center at Dallas. During this time the patients drank 3000 ml total fluids per day and ate the same food each day, thus maintaining a constant caloric intake. Sodium loading was accomplished during one admission by having the patients consume a daily diet of 200 mEq sodium and 70 mEq potassium for 6 days. During the last 3 days of this diet, the patients were given Florinef (fludrohydrocortisone, FHC) 0.5 mg twice daily. During a second admission the patients consumed a 120 mEq sodium, 70 mEq potassium (regular sodium) diet for 3 days and 10 mEq sodium, 70 mEq potassium (low sodium) diet during the following 6 days. These two admissions were separated by at least 2 weeks.

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Prostaglandin Radioimmunoassays

The PGE, PGF, and thromboxane B2, excretions (TxB) were measured by the method of Dray et al., as modified by Campbell et al. The antisera were produced in our laboratory in rabbits immunized against a prostaglandin-thyroglobulin conjugate. The conjugate was prepared by the mixed anhydride method.

The prostaglandin (Upjohn Pharmaceutical, Kalamazoo, Michigan, 6-10 μmoles) was dissolved in 0.5 ml of dioxane along with 150,000 cpm of the 3H-prostaglandin. Tributylamine (Sigma Chemical, St. Louis, Missouri) was then added in twice the molar amount of the prostaglandin, followed by isobutyl-chloroformate (Sigma Chemical, St. Louis, Missouri)
in an equimolar amount to the prostaglandin. This mixture was incubated for 10 minutes at 4°C with stirring. After incubation, it was added to 5 mg of porcine thyroglobulin (Sigma Chemical, St. Louis, Missouri), dissolved in 0.1M NaHCO₃ (pH 7.4), and the mixture was stirred at 4°C for 4 hours. The conjugate was then dialyzed for 24 hours against 4 liters of phosphate buffered saline, pH 7.4, and then stored at −20°C until used.

With this method, incorporation of PGE₂ into the thyroglobulin molecule was 36 moles of PG/mole thyroglobulin. An aliquot of the conjugate (0.5 mg) was dissolved in 0.5 ml of normal saline and mixed with 4 ml of Freund’s complete adjuvant (Gibco, Grand Island, New York). This emulsion was injected in multiple subcutaneous sites in a rabbit. The injections were repeated at 6-week intervals. After the second injection, the rabbits were bled from their central ear artery at weekly intervals. The serum was removed and stored at −20°C. The specificities of the antisera obtained is illustrated by their low cross-reactivity with other known prostaglandins (table 1).

The assay consisted of adding 1000 cpm of 3H-PGE₂, 3H-PGF₂α, or 3H-TxB₂ (New England Nuclear, Boston, Massachusetts) to 2 ml of urine, acidifying the urine with glacial acetic acid to pH 3.0, and extracting with 10 ml of ethyl acetate/cyclohexane (50:50). The lower aqueous phase was quick frozen in a dry ice alcohol bath and the upper organic phase decanted. The organic phase was evaporated to dryness at 30°C under nitrogen and reconstituted in 1 ml of phosphate buffered saline containing 0.1% polyvinylpyrrolidone. The extract was reconstituted in a toluene:ethyl acetate:methanol (60:40:5) mixture and placed on an 0.8 x 10 cm silicic acid column (Bio-Rad Laboratories, Richmond, California; Biosil). The prostaglandins were then eluted with solvents of increasing polarity: toluene:ethyl acetate; toluene:ethyl acetate:methanol:water (60:40:5:1); and toluene:ethyl acetate/methanol:water (60:40:20:1) eluted PGF₂α. These eluates were dried at 30°C under nitrogen and reconstituted in 1 ml of phosphate buffered saline containing 0.1% polyvinylpyrrolidone. The radioimmunoassay was performed in duplicate and consisted of adding 0.1 ml of the unknown to 3000 cpm of 3H-PGE₂, 3H-PGF₂α, or 3H-TxB₂, and 0.1 ml of the diluted antisera. After incubating overnight at 4°C, the bound and free prostaglandins were separated by the addition of dextran-coated charcoal. The bound counts were estimated by liquid scintillation spectrometry (Beckman Instruments, Fullerton, California). The results were corrected for recoveries and expressed as ng/24 hr. The recovery of 3H-PGE₂, 3H-PGF₂α, and 3H-TxB₂ averaged 73% ± 2%. The interassay and intraassay variabilities were about 9% and 6% respectively, for each assay. Recovery studies were done on two occasions by addition of 0, 50, 100, and 200 pg/ml of PGE₂, PGF₂α, and TxB₂ to a control urine sample. Average PGE₂ determined was 50, 104, 141, and 223 pg/ml. Average PGF₂α determined was 57, 97, 196, and 288 pg/ml. Average TxB₂ determined was 44, 83, 138, and 234 pg/ml.

Changes in urinary prostaglandins induced by diet were compared statistically within the two protocols of admission to the Clinical Research Center with analysis of variance for a two factor (normotension vs hypertension, black vs white) or one factor (low-renin vs normal renin) experiment with repeated (paired) measures on a third factor (diet). Logarithmic and rank transformation of the data were performed to better satisfy the assumptions of the analysis of equal variance among the groups.

In addition, comparisons of urinary prostaglandin excretion in the baseline phases of the sodium depletion and sodium loading protocols in normotensive vs hypertensive subjects were performed with Student’s t test for unpaired observations. Changes in plasma renin activity, urinary aldosterone, urinary kallikrein, and urinary electrolytes during sodium loading or sodium depletion were performed with Student’s t test for paired observations.

**Results**

The effects of sodium depletion and sodium loading on the urinary excretion of PGE₂, PGF₂α, and TxB₂ in normotensive subjects and hypertensive patients are summarized in figure 1 and table 2. Eight (four black, four white) of the 16 hypertensive patients had low-renin hypertension. Seven of 15 normal subjects and 11 of 16 hypertensive patients completed both protocols of admission to the General Clinical Research Center. Sodium and water balance achieved in the baseline phase of the sodium depletion and sodium loading protocols was similar in normotensive vs hypertensive subjects (table 3). Urinary PGE₂ excretion did not differ significantly in normotensive vs hyperton—
Urinary excretion of PGF$_{2\alpha}$ did not differ significantly in normotensive vs hypertensive subjects during the baseline phase for the sodium loading protocol, but it was significantly higher ($p < 0.05$) in hypertensive patients during the baseline phase for the sodium depletion protocol. The difference appeared to be produced by unusually high PGF$_{2\alpha}$ excretion at this time in three of four white low-renin hypertensive subjects. One of these three patients maintained a high level (1125 vs 1436 ng/24 hr) in the baseline of the sodium loading protocol, one had a considerable fall (904 to 618 ng/24 hr), and one did not participate in the second protocol.

Urinary excretion of PGF$_{2\alpha}$ significantly increased ($p < 0.001$) with sodium depletion in white and black normotensive subjects (fig. 1 and table 2). With the response to sodium depletion in hypertensive patients, however, there were interactions of both race ($p < 0.05$) and renin status ($p < 0.01$). Low renin patients had no increase in urinary PGF$_{2\alpha}$ excretion during sodium depletion, whereas normal renin patients had a sizable increase (table 2). Likewise white hypertensives had no increase in urinary PGF$_{2\alpha}$ excretion with sodium depletion whereas black hypertensives had a modest increase. When the responses of normotensive subjects and hypertensive patients were compared, urinary PGF$_{2\alpha}$ excretion was significantly greater ($p < 0.05$) in the normotensive subjects after sodium depletion. Urinary PGF$_{2\alpha}$ excretion did not change significantly in either normotensive subjects or hypertensive patients during sodium loading, and there was no evidence for an interaction of race or renin status on urinary PGF$_{2\alpha}$ excretion during sodium loading.

Urinary excretion of PGF$_{2\alpha}$ did not differ significantly in normotensive vs hypertensive subjects during the baseline phase of the sodium depletion protocol. In hypertensive patients, however, it was significantly higher ($p < 0.05$) during the baseline phase of the sodium loading protocol.

Urinary thromboxane B$_2$ excretion increased ($p < 0.05$) in normotensive subjects but not hypertensive patients during sodium depletion (fig. 1 and table 2). There was no evidence for an interaction of race or renin status on TxB$_2$ excretion during sodium depletion. During sodium loading, however, hypertensive white patients maintained higher ($p < 0.05$) levels of urinary TxB$_2$ excretion. There was no evidence for an interaction of race or renin status on urinary TxB$_2$ excretion in response to sodium loading.

The changes in PRA, urinary aldosterone, and urinary kallikrein with sodium depletion and sodium loading are shown in table 3. Sodium depletion increased PRA, urinary aldosterone, and urinary kallikrein significantly in both normotensive and hypertensive subjects. The increase in urinary kallikrein excretion was only slight in hypertensive patients. The increases in PRA and urinary aldosterone excretion were greater in normotensive subjects than hypertensive patients, possibly a reflection of the fact that hypertensive patients, and there was no evidence for an interaction of race or renin status on urinary PGE$_2$ excretion.

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Urinary excretion of PGE$_2$ did not differ significantly in normotensive vs hypertensive subjects during the baseline phase of the sodium depletion protocol. In hypertensive patients, however, it was significantly higher ($p < 0.05$) during the baseline phase of the sodium loading protocol.
Hypertensive subjects

Florinef plus low renin hypertension. The 200 mEq/day sodium
accompanied by any significant changes in PGE₂, PGF₂α, or TxB₂.

pertensive patients frequently did not achieve metabolic balance after 6 days of 10 mEq sodium diet whereas 14/15 normotensive subjects did (table 3). After sodium depletion nine of 14 hypertensive patients had 10 to 33 mEq Na⁺/24 hr. and six of nine of these patients had low renin hypertension. The 200 mEq/day sodium diet plus Florinef significantly reduced PRA and urinary aldosterone excretion and increased urinary kallikrein excretion in both normal subjects and hypertensive patients (table 3). These changes were not accompanied by any significant changes in PGE₂, PGF₂α, or TxB₂.

**Discussion**

Lee et al.¹ suggested that a deficiency of the known vasodilating and natriuretic effects of prostaglandins might be of importance in causing essential hypertension, either by diminished release of renal prostaglandins into the systemic circulation or by defective natriuresis, thus leading to sodium-mediated hypertension. Determinations of urinary PGE₂ and PGF₂α have been utilized to investigate this hypothesis, since urinary PGE₂ and PGF₂α appear to be derived from de novo renal synthesis in women, though striking variations in urinary prostaglandin excretion may

**Table 2. Effect of Sodium Status on Urinary Prostaglandin Excretion in Normotensive and Hypertensive Subjects**

<table>
<thead>
<tr>
<th>No.</th>
<th>Subj.*</th>
<th>120 mEq sodium</th>
<th>10 mEq sodium</th>
<th>200 mEq sodium</th>
<th>Florinef plus 200 mEq sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PGE₂ (ng/24 hr)</td>
<td>PGF₂α (ng/24 hr)</td>
<td>TxB₂ (ml)</td>
<td>PGE₂ (ng/24 hr)</td>
<td>PGF₂α (ng/24 hr)</td>
</tr>
<tr>
<td>Normotensives</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6</td>
<td>272 ± 546</td>
<td>73 ↑</td>
<td>330 ± 980</td>
<td>118</td>
</tr>
<tr>
<td>Black</td>
<td>6</td>
<td>389 ± 458</td>
<td>129</td>
<td>559 ± 1464</td>
<td>331</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>330 ± 502</td>
<td>99 ↑</td>
<td>444 ± 1222</td>
<td>216</td>
</tr>
</tbody>
</table>

| Hypertensives | | | | | | | | | |
| White | 7 | 324 ± 749 | 129 | 273 ± 721 | 148 | 7 | 299 ± 750 | 125 | 354 ± 639 | 139 |
| Black | 7 | 189 ± 683 | 83 | 250 ± 980 | 118 | 6 | 205 ± 579 | 74 | 190 ± 510 | 97 |
| Normal renin | 6 | 281 ± 649 | 118 | 252 ± 1038 | 143 | 6 | 219 ± 546 | 98 | 288 ± 486 | 167 |
| Low renin | 8 | 238 ± 767 | 113 | 240 ± 710 | 125 | 7 | 321 ± 816 | 105 | 268 ± 688 | 122 |
| Total | 14 | 256 ± 716 | 106 | 2618 ± 8508 | 132 | 13 | 255 ± 671 | 1018 | 278 ± 580 | 146 |

Vol = 24 hr urine volume.

**Table 3. Effect of Sodium Status on Plasma Renin Activity and Urinary Aldosterone and Kallikrein Excretion in Normotensive and Hypertensive Subjects**

<table>
<thead>
<tr>
<th>Dietary Na⁺ mEq/24 hr</th>
<th>Normotensives (urinary excretion/24 hr)</th>
<th>Hypertensives (urinary excretion/24 hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Subj.</td>
<td>PRA (ng/ml/hr)</td>
<td>Aldo (µg)</td>
</tr>
<tr>
<td>120</td>
<td>12</td>
<td>6.1 ± 1.5</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>17.9 ± 3.7</td>
</tr>
<tr>
<td>200</td>
<td>10</td>
<td>2.1 ± 0.7</td>
</tr>
<tr>
<td>200 plus</td>
<td>10</td>
<td>0.2 ± 0.2</td>
</tr>
</tbody>
</table>

Data are presented as means ± SEM; PRA = plasma renin activity, ng/ml/hr; Aldo = aldosterone; Kal = kallikrein; EU = esterase units; Vol = 24 hr urine volume.

* p < 0.05; † p < 0.01 compared to 120 mEq sodium diet.

**p < 0.05, $p < 0.01 compared to 200 mEq sodium diet.**
result in men from entry of seminal prostaglandins into the urine. Thus, changes in urinary prostaglandin excretion in essential hypertension are most clearly assessed in women. Furthermore, changes in urinary prostaglandin excretion during sodium loading are of interest in evaluating the possible role of prostaglandins as natriuretic substances. In addition, stimulation of renal prostaglandin synthesis in response to furosemide administration has been utilized to evaluate renal reserve for prostaglandin synthesis.

Considerable controversy about urinary prostaglandin excretion in essential hypertension has developed. Part of this controversy may result from differences in assay methodology and specificity, in study protocols, particularly with respect to the use of male patients, and in fluid consumption by the patients during the time of study. Abe et al. noted decreased urinary prostaglandin E excretion in response to acute furosemide administration, though about two-thirds of the study population were men, and the basal levels of PGE excretion were about threefold the usual values for normal women. Tan et al. also noted decreased urinary PGE excretion in essential hypertension, particularly in low-renin hypertension. These patients were studied while consuming their usual outpatient diet without attention to sodium or fluid content.

In contrast, we did not find decreased urinary PGE, PGF2α, and TxB2 excretion in hypertensive patients vs normal subjects consuming 120 or 200 mEq sodium diets. Furthermore, low-renin hypertensives did not have lower values than normal-renin hypertensives, and there were no differences between black vs white normal subjects and hypertensive patients. Weber and coworkers noted decreased urinary PGF2α excretion after acute furosemide administration, though an increase with sodium depletion was suggested. We also found no consistent difference between urinary TxB2 excretion between normal subjects and hypertensive patients. Alternatively, the lesser PRA increases in hypertensive patients during sodium depletion may have resulted, at least in part, from a failure in renal prostaglandin production. Further studies are required to explore this possibility.

Other factors that might have contributed to the rise in urinary prostaglandins during sodium depletion were the increases in urinary aldosterone and kallikrein excretions, since both of these have been implicated in stimulation of prostaglandin synthesis. However, since the high-sodium-FHC protocol stimulated urinary kallikrein excretion by pharmacological mineralocorticoid administration in both normal subjects and hypertensive patients but had no effect on PGE2, PGF2α, and TxB2 excretion, it appears that neither mineralocorticoids nor kallikrein stimulate renal PGE2, PGF2α, or thromboxane A2 synthesis. Similar dissociations between urinary kallikrein and prostaglandin excretion during mineralocorticoid administration have been noted in normotensive man. Thus, the reason for stimulation of renal prostaglandin synthesis by sodium depletion remains unresolved at present, but enhanced renin release may play a prominent role.

Since about 4% of circulating TxB2 (a metabolite of TXA2) is filtered unchanged into the urine, urinary TxB2 reflects a combination of that produced by the kidney and that excreted unchanged. This factor limits evaluation of our data about urinary TxB2 to some extent. Nonetheless, we found no significant alterations in TxB2 with alterations in sodium status, though an increase with sodium depletion was suggested (fig. 1). We also found no consistent difference between urinary TxB2 excretion between normal subjects and hypertensive patients. Our data thus agree with recent reports of normal generation of TxB2 by platelets from hypertensive patients.

Renal prostaglandins have been postulated to be involved in natriuresis and their deficiency to be important in the genesis of essential hypertension. Conflicting changes in urinary excretion of PGE2 and PGF2α in experimental animals with changes in dietary sodium have been reported, however, and a review of these data suggests that evidence for a natriuretic role for these prostaglandins is not convincing. Our studies represent the most extensive evaluation of changes in urinary PGE2, PGF2α, and TxB2 excretion with changes in sodium status. Renal prostaglandins other than those we have determined could be involved in natriu-
resis, however, and studies of renal production of prostacyclin and prostaglandin D₂ will be of particular interest. Nonetheless, we found little evidence for a natriuretic role of PGE₂, PGF₂α, and TxB₂ in humans. Except during sodium depletion, we found no evidence for diminished urinary excretion of PGE₂, PGF₂α, and TxB₂ in patients with essential hypertension. This diminished excretion may have resulted from lesser renin stimulation in hypertensive patients with sodium depletion or, alternatively, a defect in renal prostaglandin production uncovered by the stimulus of sodium depletion may have led to the lesser renin stimulation. Further studies are necessary to evaluate the role of renal prostaglandins in essential hypertension.

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