Enhanced Renal Prostaglandin Production in the Dog

I. EFFECTS ON RENAL FUNCTION

By Jerome Tannenbaum, Jacek A. Splawinski, John A. Oates, and Alan S. Nies

ABSTRACT

The changes in renal function produced by endogenous synthesis of prostaglandins by the kidney were evaluated by infusing sodium arachidonate, the precursor of the prostaglandins, into one renal artery of the dog. These changes were compared with those produced by similar infusions of preformed prostaglandin (PG) E₂ and F₂α, given at 0.01–0.3 μg/kg min⁻¹, produced dose-related increases in urine flow, sodium and potassium excretion, free water clearance, and renal blood flow. The glomerular filtration rate increased only at the lowest dose and the calculated filtration fraction fell. Arachidonic acid at 1.0–30.0 μg/kg min⁻¹ similarly produced dose-related increases in electrolyte excretion, but the increase in renal blood flow was much less than that produced by PGE₂ and there were no changes in glomerular filtration rate, filtration fraction, or free water clearances. PGF₂α had essentially no effects at infusion rates of 0.03–1.0 μg/kg min⁻¹. All renal effects of arachidonic acid were inhibited by simultaneous infusions of an inhibitor of prostaglandin synthetase, 5, 8, 11, 14-eicosatetraynoic acid (20:4). None of the effects produced by PGE₂ were inhibited by 20:4. These results indicate that enhanced endogenous renal prostaglandin synthesis, which can be produced by arachidonate infusion, results in significant alterations of renal function. This finding strengthens the hypothesis that renal prostaglandins formed in vivo have physiological importance as regulators of renal function.

KEY WORDS: arachidonic acid prostaglandin synthetase inhibitor renal hemodynamics prostaglandin E₂ renal medulla prostaglandin F₂α renal electrolyte excretion

The ability of prostaglandins to affect renal function has allowed speculation about the possible functions of endogenously formed prostaglandins. Early experiments showed that infusion of some prostaglandins into the renal artery produced large changes in renal blood flow and urinary sodium excretion (1–3). Prostaglandin (PG) E₂ and PGA₁, have been investigated most intensively, whereas the prostaglandins of renal origin, PGE₂ and PGF₂α, have received little attention. Nonetheless, no route of administration of any kind of exogenous prostaglandins can mimic the situation which exists for prostaglandins produced at the sites of synthesis, primarily the renal medulla. Also, since other vasodilators infused into one kidney can produce effects similar in many respects to those of prostaglandins, the effects of infused prostaglandins may be nonspecific (4, 5). Thus, the physiological significance of data obtained by administration of prostaglandins is open to question.

We approached the possible role of endogenously synthesized prostaglandins by attempting to increase their production at the sites of prostaglandin synthetase in the kidney. This increase was accomplished by administering the precursor of the renal prostaglandins, arachidonic acid, into the renal artery of dogs. It is known that in vitro the renal medulla of a variety of species can convert arachidonic acid to PGE₂ and PGF₂α and that the availability of the precursor acid appears to be rate limiting (6–9). Thus, those renal effects produced by an infusion of arachidonic acid which can be blocked by an inhibitor of prostaglandin synthetase should indicate the functional significance of increased amounts of the renal prostaglandins formed at their sites of synthesis in the renal medulla. We compared the effects of enhanced endogenously formed renal prostaglandins with those of exogenous PGE₂ and PGF₂α administered into the renal artery.

Methods

A total of 41 experiments were performed in mongrel dogs of either sex weighing 10–23 kg. The dogs were
allowed water ad libitum. On the day of the experiment, the dogs were anesthetized with intravenously administered sodium thiopental which was prepared as a 0.1% solution in 0.9% saline and allowed to drip at a rate that maintained the dog in a light plane of surgical anesthesia. The trachea was intubated, and the dogs were ventilated with a Harvard respiration pump.

A midline incision was made which permitted the retrograde placement of bilateral ureteral polyethylene catheters, the placement of a 23-gauge needle into one of the renal arteries, and in some dogs the placement of electromagnetic flow probes around both renal arteries. In 11 dogs a polyethylene catheter was inserted into the vein of the kidney receiving an intra-arterial infusion. In these instances renal blood flow was measured with para-aminohippuric acid (PAH). Polyethylene catheters were also inserted into the femoral artery and vein; the arterial catheter was used for arterial blood pressure measurements and blood sampling and the venous catheter for infusions of dextrone, saline, and anesthetic. After completion of the surgical procedure, which required approximately 60 minutes, an intravenous infusion of creatinine (0.7 mg/min) and, in some cases, PAH (0.23 mg/min) in 0.9% saline was begun at 1 ml/min. A bolus of 500-800 ml of 2.5% dextrose in water was also given through the femoral vein over a 45-minute period and continued at an infusion rate of approximately 5 ml/min throughout the course of the experiment. Saline (0.9%) was infused at a rate of less than 0.2 ml/min through the renal arterial needle with a Harvard Apparatus infusion pump. The experiment was begun after three 5-minute urine volumes were stable within 0.5 ml from each kidney.

Five groups of experiments were performed. Sodium arachidonate was administered through the renal artery to 12 dogs in doses of 1.0, 3.0, 10.0, and 30.0 μg/kg min^-1. The second group of 12 dogs received intrarenal arterial infusions of PGE₂ in doses of 0.01, 0.03, 0.1, and 0.3 μg/kg min^-1. A third group of 5 dogs received infusions of PGF₂α into the renal artery at rates of 0.03, 0.1, 0.3, and 1.0 μg/kg min^-1. A fourth group of 7 dogs received sodium arachidonate through the renal artery throughout the dose range described for the first group of dogs together with a simultaneous infusion of 0.3 μg/kg min^-1 of an inhibitor of prostaglandin synthesis, 5, 8, 11, 14-eicosatetraynoic acid (20:4) (10, 11). The fifth group of 5 dogs similarly received 20:4 concomitantly with PGE₂ after the dose-response relationship to PGE₂ had been determined.

Two 5-minute urine collections with blood samples drawn at the midpoint of each period were taken as controls while the renal artery was being infused with saline. The experimental agent was then infused into the renal artery for two 5-minute periods at each of the four doses on the cumulative dose schedule. Different concentrations were prepared to avoid changing the infusion pump speed during the experiment, and less than 10 seconds was required to change the dose at the end of 10 minutes of infusion. When 20:4 was given simultaneously with arachidonate or PGE₂, two syringe pumps were used, one for each agent; the drugs were infused into the renal artery through a common renal artery needle.

Systemic arterial blood pressure was monitored with Hewlett-Packard 1280 transducers and recorded on a Hewlett-Packard 1788 direct-writing recorder. PAH, creatinine, sodium, potassium, and osmolality were measured by standard methods. Renal blood flow was measured with a Statham SP2202 electromagnetic flowmeter. Zero flow was determined mechanically prior to and at the end of each experiment to verify the accuracy of the electronic zero, which was used during the experiment so that renal function and hemodynamics were not disturbed. Only cases in which mechanical and electronic zeroes agreed within 5% full-scale deflection were used for data analysis. In cases in which a direct electromagnetic flow measurement was not available, renal plasma flow was calculated as the clearance of PAH divided by the renal extraction of PAH, and renal blood flow was calculated as renal plasma flow divided by (1 - hematocrit). The glomerular filtration rate was calculated as creatinine clearance, the tubular rejection fraction of sodium as the clearance of sodium divided by the glomerular filtration rate, and the filtration fraction as glomerular filtration rate divided by renal plasma flow.

**Preparation of Drugs**

Prostaglandin E₂ was stored in 100% ethanol under nitrogen until the day of the experiment. Only the amount required each day was titrated with sodium carbonate to pH 7.0 to obtain a sodium salt. Arachidonic acid was stored as 99% pure arachidonic acid in airtight ampuls from the supplier (Nu Check Prep Inc.) until the day of the experiment. The ampul was opened in a nitrogen atmosphere, and the drug was dissolved in 100% ethanol with phenolphthalein indicator and converted to the sodium salt with 0.1N sodium hydroxide titration to pH 7.0. A nitrogen atmosphere was maintained constantly in the arachidonic acid vessel to prevent autoxidation to substances in the prostaglandin series in vitro, and the lack of such conversion was confirmed by mass spectroscopy as described previously (12). After conversion to the sodium salt, the ethanolic solution of either agent was evaporated to dryness with nitrogen and then immediately redissolved in normal saline. Any excess agent was discarded at the end of the experiment. Until the day of its use, 20:4 was stored in an ethanolic solution. The necessary quantity was suspended in saline by sonication after first evaporating the ethanol with nitrogen. PGF₂α was obtained as the tromethamine salt.

**Assay of Renal Venous Blood**

In six experiments a 25-ml sample of renal venous blood was collected in a plastic tube containing ethylenediaminetetraacetic acid (EDTA) and indomethacin (1 mg) prior to and during the infusion of sodium arachidonate into the ipsilateral renal artery. Ten ml of the platelet-poor plasma was shaken with an equal volume of 100% ethanol and centrifuged. The supernatant fluid was decanted and washed once with 15 ml of petroleum ether, which was discarded. The aqueous phase was acidified with 92% formic acid to pH 3-3.5, and prostag-
landinlike substances were extracted with two volumes of chloroform. The aqueous phase was extracted again with one volume of chloroform, and the chloroform fractions were combined and evaporated to a volume of less than 2 ml under vacuum at 35°C. This volume was quantitatively transferred with an additional 2 ml of chloroform. The aqueous phase was extracted again (Table 2), or sodium arachidonate (Table 3) into the odor of formic acid was no longer detectable, and then redissolved in 0.5 ml of ethanol for bioassay on the rat stomach strip as previously described (12). PGE$_2$, fractions were combined and evaporated to a volume of 0.1 ml to extraction, and a 0.1-ml sample of the final solution in ethanol was counted in dioxane with a liquid scintillation counter (Nuclear Chicago) to correct for losses during extraction.

Results

The infusion of either PGE$_2$ (Table 1), PGF$_2$-a (Table 2), or sodium arachidonate (Table 3) into one renal artery resulted in changes of renal function seen only in that kidney; no significant change in any variable was observed in the contralateral kidney. The results are presented as means ± se, and statistics were calculated from the net change (infused minus contralateral) produced by any given infusion rate using Student's t-test for paired observations.

### TABLE 1

<table>
<thead>
<tr>
<th>Dose (µg/kg min$^{-1}$)</th>
<th>N</th>
<th>Kidney</th>
<th>Urine flow (ml/min)</th>
<th>Sodium excretion (µEq/min)</th>
<th>Potassium excretion (µEq/min)</th>
<th>TRF (Na) × 1000</th>
<th>CH$_2$O (ml/min)</th>
<th>GFR (ml/min)</th>
<th>RBF (ml/min)</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>12</td>
<td>I</td>
<td>0.70 ± 0.20</td>
<td>20 ± 9.3</td>
<td>9 ± 1.5</td>
<td>4.3 ± 1.7</td>
<td>-0.07 ± 0.17</td>
<td>29 ± 3.7</td>
<td>143 ± 35</td>
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<tr>
<td>C</td>
<td>0.77 ± 0.20</td>
<td>18 ± 6.3</td>
<td>10 ± 2.0</td>
<td>3.9 ± 1.3</td>
<td>-0.07 ± 0.18</td>
<td>31 ± 3.6</td>
<td>136 ± 19</td>
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<td></td>
</tr>
<tr>
<td>0.01</td>
<td>9</td>
<td>I</td>
<td>1.38 ± 0.37</td>
<td>66 ± 31</td>
<td>15 ± 2.7</td>
<td>10.9 ± 3.9</td>
<td>0.19 ± 0.34</td>
<td>43 ± 7.9</td>
<td>151 ± 51</td>
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<tr>
<td>C</td>
<td>0.72 ± 0.26</td>
<td>19 ± 7.4</td>
<td>8 ± 1.9</td>
<td>4.4 ± 1.5</td>
<td>-0.03 ± 0.19</td>
<td>30 ± 4.6</td>
<td>126 ± 27</td>
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<tr>
<td>Δ(1 − C)</td>
<td>0.60 ± 0.15</td>
<td>43 ± 19</td>
<td>7 ± 1.7</td>
<td>5.8 ± 2.2</td>
<td>0.16 ± 0.11</td>
<td>11 ± 3.9</td>
<td>38 ± 38</td>
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<td>P</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>NS</td>
<td>&lt;0.05</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.03</td>
<td>11</td>
<td>I</td>
<td>1.65 ± 0.51</td>
<td>74 ± 30</td>
<td>16 ± 2.4</td>
<td>15.1 ± 5.5</td>
<td>0.30 ± 0.36</td>
<td>42 ± 8.3</td>
<td>193 ± 42</td>
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<td>C</td>
<td>0.68 ± 0.22</td>
<td>15 ± 4.6</td>
<td>9 ± 1.8</td>
<td>5.3 ± 1.0</td>
<td>0.20 ± 0.19</td>
<td>32 ± 3.8</td>
<td>136 ± 21</td>
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<td></td>
</tr>
<tr>
<td>Δ(1 − C)</td>
<td>0.93 ± 0.28</td>
<td>57 ± 22</td>
<td>8 ± 1.6</td>
<td>11.3 ± 4.1</td>
<td>0.43 ± 0.16</td>
<td>11 ± 5.0</td>
<td>50 ± 12</td>
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<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>NS</td>
<td>&lt;0.01</td>
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<tr>
<td>0.1</td>
<td>12</td>
<td>I</td>
<td>2.12 ± 0.51</td>
<td>86 ± 26</td>
<td>19 ± 3.0</td>
<td>18.3 ± 5.3</td>
<td>0.69 ± 0.37</td>
<td>40 ± 8.3</td>
<td>217 ± 43</td>
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<td>C</td>
<td>0.80 ± 0.21</td>
<td>13 ± 3.3</td>
<td>10 ± 1.4</td>
<td>3.4 ± 0.8</td>
<td>0.02 ± 0.26</td>
<td>30 ± 3.1</td>
<td>144 ± 25</td>
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<td></td>
</tr>
<tr>
<td>Δ(1 − C)</td>
<td>1.39 ± 0.36</td>
<td>71 ± 22</td>
<td>10 ± 2.5</td>
<td>14.5 ± 4.4</td>
<td>0.66 ± 0.18</td>
<td>11 ± 6.5</td>
<td>62 ± 10</td>
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<td>P</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>NS</td>
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</tr>
<tr>
<td>0.3</td>
<td>9</td>
<td>I</td>
<td>1.75 ± 0.50</td>
<td>65 ± 25</td>
<td>19 ± 3.8</td>
<td>17.0 ± 7.5</td>
<td>0.49 ± 0.37</td>
<td>36 ± 6.2</td>
<td>213 ± 42</td>
</tr>
<tr>
<td>C</td>
<td>0.66 ± 0.12</td>
<td>13 ± 3.3</td>
<td>10 ± 1.5</td>
<td>2.7 ± 0.7</td>
<td>-0.23 ± 0.15</td>
<td>34 ± 4.4</td>
<td>137 ± 24</td>
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</tr>
<tr>
<td>Δ(1 − C)</td>
<td>1.32 ± 0.54</td>
<td>57 ± 25</td>
<td>11 ± 3.2</td>
<td>14.9 ± 7.2</td>
<td>0.82 ± 0.36</td>
<td>5 ± 3.9</td>
<td>63 ± 11</td>
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<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I = infused kidney, C = contralateral kidney, Δ(1 − C) = net change on infused side, TRF (Na) = tubular rejection fraction of sodium, CH$_2$O = free water clearance - urine flow = osmolar clearance, GFR = creatinine clearance, and RBF = renal blood flow. NS = not significant.

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Effects of Intra-Arterially Administered Sodium Arachidonate on Renal Function

At no infusion rate were the changes in renal blood flow produced by sodium arachidonate as large as those produced by the smallest infusion rate of PGE₂. The calculated filtration fraction fell with PGE₂, but it remained unchanged during sodium arachidonate infusion. Free water clearance increased significantly only with PGE₂ infusion.

The only significant change produced by PGF₂α was a modest increase in urine flow at infusion rates of 0.1 and 0.3 μg/kg min⁻¹ (Table 2).

In none of the dogs reported on in the present paper were changes in heart rate or aortic pressure

### Table 2

Effects of Intra-Arterially Administered Prostaglandin F₂α on Renal Function

<table>
<thead>
<tr>
<th>Dose (μg/kg min⁻¹)</th>
<th>N</th>
<th>Kidney</th>
<th>Urine flow (ml/min)</th>
<th>Sodium excretion (μEq/min)</th>
<th>Potassium excretion (μEq/min)</th>
<th>TRF (Na) x 1000 (ml/min)</th>
<th>CH₅₀ (ml/min)</th>
<th>GFR (ml/min)</th>
<th>RBF (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>I</td>
<td>0.93 ± 0.26</td>
<td>36 ± 8.8</td>
<td>18 ± 3.1</td>
<td>4 ± 1.9</td>
<td>13 ± 4.3</td>
<td>31 ± 3.2</td>
<td>158 ± 31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C</td>
<td>0.65 ± 0.27</td>
<td>34 ± 8.7</td>
<td>12 ± 3.2</td>
<td>4 ± 1.9</td>
<td>13 ± 4.3</td>
<td>31 ± 3.2</td>
<td>158 ± 31</td>
</tr>
<tr>
<td>0.03</td>
<td>5</td>
<td>I</td>
<td>1.0 ± 0.38</td>
<td>61 ± 14.6</td>
<td>14 ± 3.5</td>
<td>4 ± 1.9</td>
<td>13 ± 4.3</td>
<td>31 ± 3.2</td>
<td>158 ± 31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C</td>
<td>0.65 ± 0.27</td>
<td>34 ± 10.4</td>
<td>12 ± 2.7</td>
<td>7 ± 1.5</td>
<td>13 ± 4.3</td>
<td>31 ± 3.2</td>
<td>158 ± 31</td>
</tr>
<tr>
<td>Δ(I - C)</td>
<td></td>
<td>P</td>
<td>0.06 ± 0.09</td>
<td>1 ± 2</td>
<td>1 ± 0.7</td>
<td>0.01 ± 0.11</td>
<td>-5 ± 4.8</td>
<td>-6 ± 6</td>
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</tr>
</tbody>
</table>

### Table 3

Effects of Intra-Arterially Administered Sodium Arachidonate on Renal Function

<table>
<thead>
<tr>
<th>Dose (μg/kg min⁻¹)</th>
<th>N</th>
<th>Kidney</th>
<th>Urine flow (ml/min)</th>
<th>Sodium excretion (μEq/min)</th>
<th>Potassium excretion (μEq/min)</th>
<th>TRF (Na) x 1000 (ml/min)</th>
<th>CH₅₀ (ml/min)</th>
<th>GFR (ml/min)</th>
<th>RBF (ml/min)</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>12</td>
<td>I</td>
<td>0.93 ± 0.29</td>
<td>34 ± 8.8</td>
<td>18 ± 3.1</td>
<td>4 ± 1.9</td>
<td>13 ± 4.3</td>
<td>31 ± 3.2</td>
<td>158 ± 31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C</td>
<td>0.78 ± 0.25</td>
<td>21 ± 7.0</td>
<td>11 ± 2.2</td>
<td>3.6 ± 1.1</td>
<td>13 ± 4.3</td>
<td>31 ± 3.2</td>
<td>158 ± 31</td>
</tr>
<tr>
<td>Δ(I - C)</td>
<td></td>
<td>P</td>
<td>0.16 ± 0.09</td>
<td>7 ± 3.1</td>
<td>2 ± 0.7</td>
<td>0.9 ± 0.3</td>
<td>3 ± 3</td>
<td>6 ± 3</td>
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</tr>
</tbody>
</table>

### Abbreviations

Abbreviations are the same as they are in Table 1.
seen. However, in six dogs excluded from data analysis, infusion of either PGE₂ or sodium arachidonate in the doses described produced significant \((P < 0.05)\) systemic hemodynamic changes including a decrease in arterial blood pressure associated with a bilateral decrease in urine flow and free water clearance. These six dogs which were more sensitive to the systemic hypotensive effects, all had an initially high free water clearance \((> 2.0 \text{ ml/min})\). The systemic and renal effects were similar to those reported following intravenous prostaglandin infusions that result in antidiuresis and systemic hemodynamic changes \((13)\).

In seven dogs sodium arachidonate was infused simultaneously with 20:4, and in five dogs PGE₂ was infused with 20:4. The results in Figures 1 and 2 show that the effects of sodium arachidonate were inhibited whereas those of PGE₂ were not altered. In addition to the parameters presented in these figures, the effect of sodium arachidonate on potassium excretion was also inhibited by 20:4.

In six experiments renal venous blood was bioassayed for prostaglandinlike material. The results in Figure 3 indicate a significant increase in this material during infusion of sodium arachidonate at 10 \(\mu\)g/kg min\(^{-1}\). We have also seen two- to
threefold increases in ipsilateral urinary PGE$_2$ and PGF$_{2\alpha}$ during sodium arachidonate infusion (10 \(\mu\)g/kg min$^{-1}$ into one renal artery (unpublished observations).

Discussion

A variety of physiological and pharmacological stimuli which affect renal blood flow will increase renal prostaglandin output (14-19). However, the physiological significance of the prostaglandin so formed is still open to question. The administration of pure prostaglandins cannot directly demonstrate the functional implications of increased prostaglandin production by an organ. The present experiments show that renal prostaglandin production in vivo can be stimulated by infusing sodium arachidonate; such infusions result in detectable prostaglandin in renal venous blood and changes in renal function which can be reversed by an inhibitor of prostaglandin synthesis. Similar conclusions have been reached by others from observations on systemic arterial blood pressure in rabbits (20) and rats (21) or renal blood flow in rabbits (22).

Our data showed that in the dog the enhanced endogenous prostaglandin output produces a natriuresis, a kaliuresis, an increased urine flow, and a modest change in renal blood flow. These effects differ from those produced by infusions of PGE$_2$ or PGF$_{2\alpha}$ into the renal artery primarily with respect to the changes in renal hemodynamics. PGE$_2$ produces much larger changes in renal blood flow than does sodium arachidonate, whereas PGF$_{2\alpha}$ has essentially no effect.

The reasons for the differences between the effects of PGE$_2$ and sodium arachidonate are probably related to differences in access to sites of action. Prostaglandins infused into the renal artery have direct access to the pre- and postglomerular resistance vessels and peritubular capillaries of all nephrons. However, prostaglandins produced within the kidney from sodium arachidonate are known to be synthesized within the renal medulla, although the exact site of prostaglandin formation in the medulla is not clear (6-8, 23-27). To have an effect on glomerular resistance vessels, prostaglandin produced in the medulla must be transported to the renal cortex. Since prostaglandins formed in the kidney appear in renal venous blood and in the urine, transport from the medulla to the cortex could occur either by the vascular route or possibly in the tubular fluid as suggested by Frolich et al. (28). Because of the medullary site of prostaglandin synthesis, the nephrons most likely to be affected by endogenous renal prostaglandins are those in the juxtamedullary region whose tubules and vascular supply reach into the medulla. Thus, the effects on total renal hemodynamics and function produced by sodium arachidonate infusion would be expected to be less than those produced by PGE$_2$ infusion, which would affect all nephrons not just the juxtamedullary ones. Indeed, arachidonate infusions in the dog (29) and the rabbit (22) do preferentially affect the vascular resistance of the juxtamedullary nephrons.

The renal functional changes induced by arachidonate could be direct effects of the endogenous prostaglandins on renal tubular function, or they could be related to the altered renal hemodynamics (30). However, the renal hemodynamic effects of endogenously produced prostaglandins differed from those of infused vasodilators in that there was little change in total renal blood flow, at least at the lower infusion rates of arachidonate, and no change in filtration fraction. Other vasodilators caused alterations of renal function associated with a large increase in renal blood flow and a decrease in filtration fraction, allowing physical factors to account for the natriuresis so produced (1-5). Because of these differences, there is the distinct possibility that the prostaglandin formed in the medulla may have direct tubular effects. This view is consistent with micropuncture studies which show that prostaglandins impair only distal tubular sodium reabsorption (31).

Regardless of the relationship between renal function and renal hemodynamics, it is clear from the evidence presented that increased endogenous renal prostaglandins will increase renal sodium and potassium excretion with a small increase in renal blood flow. There is also strong support for the hypothesis that prostaglandin production in
vivo has physiological importance as a regulator of renal function.

Acknowledgment

We thank Mr. Bob Rush and Mr. Jerry Strother for excellent technical assistance.

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