Influence of Inhibitors of Prostaglandin Synthesis on Renal Vascular Resistance and on Renal Vascular Responses to Vasopressor and Vasodilator Agents in the Cat

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SUMMARY We determined the effects of indomethacin and meclofenamate, two inhibitors of prostaglandin synthesis, on renal vascular resistance and on renal responses to nerve stimulation, pressor and depressor hormones in the in situ feline kidney under conditions of controlled blood flow. Both inhibitors produced a gradual rise in renal vascular resistance which became maximal 15-20 minutes after administration. The increase in renal resistance after indomethacin was not attenuated during intrarenal infusion of either phenolamine or SQ 20881. Pretreatment with propranolol, in a dose sufficient to inhibit renin secretion, also did not attenuate the increase in renal resistance produced by indomethacin. However, infusion of [Sar1,Ala8]angiotensin II, an angiotensin II antagonist, did attenuate the indomethacin-induced increase in renal vascular resistance. After indomethacin, the vasocostrictor response to norepinephrine was enhanced, whereas responses to nerve stimulation and angiotensin were unaffected. Although meclofenamate enhanced renal vascular resistance, its effects on vasoconstrictor responses were inconsistent. After indomethacin, the renal dilator response to bradykinin was enhanced; however, dilator responses to nitroglycerin were unaltered. The present data indicate that the increase in renal vascular resistance after indomethacin does not depend on the adrenergic system but may be dependent on the renin-angiotensin system. The inconsistent effect of the inhibitors of synthesis on renal constrictor responses to nerve stimulation suggests that endogenous prostaglandins do not serve to modulate the effects of the sympathetic nervous system on the feline renal vascular bed. These results also indicate that renal dilator responses to bradykinin are not mediated by prostaglandins in the cat.

THE CAPACITY for prostaglandin synthesis in the renal medulla is exceeded only by that of the seminal vesicle. Prostaglandins are released continuously into renal venous blood in the dog. Since more prostaglandin can be released from an organ than can be extracted, and since these substances do not accumulate in any subcellular organelle, release is probably indicative of synthesis. Synthesis by and/or release of prostaglandins from the kidney is increased during renal nerve stimulation, infusion of pressor agents, or bradykinin administration. Prostaglandins, when infused into the renal artery, are capable of modulating responses to sympathetic nerve stimulation, norepinephrine, and angiotensin. It has been proposed recently that endogenous prostaglandins may be involved in the maintenance of resting renal blood flow and that these substances may act to modulate the effects of the sympathetic nervous system and pressor hormones on the renal vascular bed. In addition, bradykinin has been shown to increase the release of a prostaglandin E-like substance from the kidney and it has been suggested that prostaglandins may in part mediate the response of the renal vascular bed to the kinin. The demonstration that aspirin-like drugs inhibit synthesis of prostaglandins has provided an important means for evaluating the role of prostaglandin synthesis in a variety of physiological and pathophysiological processes. Studies with inhibitors of prostaglandin synthesis have implicated prostaglandins as modulators of responses to sympathetic nerve stimulation in the renal, cutaneous, skeletal muscle, and splenic vascular beds and in the maintenance of resting renal blood flow. However, there are conflicting reports on the effect of inhibition of prostaglandin synthesis on renal autoregulation. Furthermore, the effects of inhibitors of prostaglandin synthesis on renal vascular resistance, sympathetic neurotransmission, and responses to bradykinin have not been investigated before in the feline renal vascular bed.

In the present investigation two of these inhibitors, indomethacin and meclofenamate, which are chemically and structurally different, were used to study the influence of inhibition of prostaglandin synthesis on vascular resistance in the feline renal vascular bed under conditions of controlled blood flow. In addition, we determined effects of these inhibitors on renal vasocostrictor responses to norepinephrine, renal nerve stimulation, and angiotensin, and on renal vasodilator responses to bradykinin and nitroglycerin. We evaluated possible interactions of the prostaglandins with the major renal pressor systems, i.e., the autonomic nervous system and the renin-angiotensin...
system. Indomethacin was administered during infusion of phentolamine, an α-receptor blocking agent. In order to evaluate possible interactions of the prostaglandins with the autonomic nervous system. Possible interactions with the renin-angiotensin system were evaluated by administering indomethacin during infusion of either SQ 20881, the nonpeptide inhibitor of angiotensin I conversion to angiotensin II and of the breakdown of bradykinin,28,27 or [Sar'Ala8]angiotensin II, an analogue of angiotensin II which antagonizes the action of angiotensin II.28 In addition, since it has been shown that β-adrenergic blockade inhibits renin secretion,29,30 the influence of indomethacin on renal vascular resistance was determined after administration of propranolol.

Methods

Adult cats of either sex weighing 2.3-4.5 kg were anaesthetized with pentobarbital sodium (30 mg/kg, ip). The trachea was cannulated and a catheter was inserted into the external jugular vein for intravenous administration of drugs. The kidneys were perfused with homologous blood according to the following method.31 An extracorporeal circuit was established so that the kidneys could be perfused in situ under conditions of controlled blood flow. A midline abdominal incision was made and a section of the aorta superior to the renal axis was dissected free of surrounding connective tissue. After administration of heparin (1,000 U/kg, iv) a catheter was inserted into the carotid artery for withdrawal of blood from the thoracic aorta. The abdominal aorta was ligated below the renal axis and the distal end of the carotid catheter was inserted retrograde into the aorta and advanced to a position just below the origin of the renal arteries. The kidneys could then be perfused with blood withdrawn from the thoracic aorta. A Sigmamotor pump (model T8) was used to control blood flow in the perfusion circuit. After onset of pump perfusion the aorta was ligated above the renal arteries in order to isolate the kidneys from the systemic circulation. Thus, the entire blood flow to the kidney was contained within an aortic pouch. This technique allowed the circuit to be completed and the kidneys to be perfused at constant flow without the temporary interruption of blood flow which occurs when the renal arteries are cannulated. Systemic arterial pressure was measured either from a tap on the carotid artery catheter or from a catheter inserted into the brachial artery, and renal perfusion pressure was measured from a tap on the perfusion catheter between the pump and the renal arteries. Systemic arterial and renal arterial perfusion pressures were measured using Statham P23Ac transducers and recorded on a Grass polygraph (model 7C). Initially, the pumping rate was set so that perfusion pressure was 80-100 mm Hg and the flow rate was not changed during the experiment. The flow rate averaged 39 ± 1.3 ml/min or 1.6 ± 0.1 ml/min per g. The completeness of vascular isolation was assessed by stopping the pump at the end of the experiment and observing the residual pressure in the circuit. This pressure ranged between 10 and 20 mm Hg and since it approached small vein pressure was considered good evidence for vascular isolation. Resistance to flow in the perfusion circuit was low since pressure in the circuit itself ranged from 5 to 10 mm Hg over the range of flows employed.

The renal nerves were carefully isolated from both renal arteries and placed on shielded Palmer electrodes. The nerves were stimulated for a period of 30 seconds with rectangular pulses of 2-msec duration and supramaximal voltage at 3, 10, and 30 cycles/sec with either a Grass stimulator (model S48) or a Tektronix series 160 assembly. The stimulus was isolated from ground with a Grass (model SIU 5) isolation unit.

Norepinephrine (L-norepinephrine hydrochloride, Sigma, dose in terms of base), angiotensin II amide (Hyptensin, Ciba, dose in terms of the salt), and nitroglycerin (Lilly) were injected into the perfusion circuit close to the renal arteries in small volumes. 50-150 μl, Angiotensin I (Schwarz/Mann), arachidonic acid (Nu-Chek, 99%), prostaglandin E2 (Upjohn) and dl-propranolol hydrochloride (Ayerst) were injected intravenously. Bradykinin (Sigma) was injected both intravenously and intra-arterially in small volumes. Phentolamine hydrochloride (Regitine, Ciba) was infused directly into the perfusion circuit. SQ 20881 (Squibb) was infused into the jugular vein and [Sar'Ala8]angiotensin II was infused directly into the perfusion circuit with a Harvard infusion pump (model 600) at a rate of 0.2 ml/min. Solutions of arachidonic acid (10% ethanol, 100 mM sodium carbonate) were prepared daily. Prostaglandin E2 was dissolved in absolute ethanol and stored in a freezer. On the day of the experiment a sample of the stock solution was diluted with saline to the appropriate concentration. Indomethacin (Merck Sharp & Dohme) and meclofenamic acid (Parke, Davis) were solubilized by reacting the free acid with an equimolar amount of sodium carbonate and the resulting clear solution was injected intravenously.

All data were analyzed by the methods described by Steel and Torrie for paired analysis. All values are presented as mean ± se and a P value of less than 0.05 was considered significant.

Results

EFFECTS OF INDOMETHACIN AND MECLOFENAMATE ON RENAL VASCULAR RESISTANCE AND VASOCONSTRICTOR RESPONSES

The influence of the prostaglandin synthesis inhibitors, indomethacin and meclofenamate, on renal vascular resistance and on responses of the renal vascular bed to pressor stimuli was determined in four groups of cats. Since blood flow to the kidney was maintained constant with a pump, changes in renal perfusion pressure reflect changes in renal vascular resistance. Administration of either indomethacin, 2.5 and 5.0 mg/kg, iv, or meclofenamate, 2.5 mg/kg, iv, in three groups of cats resulted in a slow but steady increase in renal perfusion pressure (Fig. 1). The peak increase in resistance was attained 20-30 minutes after administration of the drugs and was 45% after indomethacin and 60% after meclofenamate. Mean arterial pressure was not affected by either synthesis inhibitor.

Norepinephrine, 0.3-3 μg, intra-arterially (ia), and renal nerve stimulation (3-30 cycles/sec) resulted in dose-
and frequency-related increases in renal perfusion pressure. Only one dose of angiotensin (1 fig) was used to avoid tachyphylaxis. These tests were made 30 minutes after administration of the synthesis inhibitors. The magnitude of vasoconstrictor responses was calculated without accounting for the rise in perfusion pressure caused by the synthetase inhibitor, since responses to vasoconstrictor stimuli do not depend on initial vascular resistance. After indomethacin. 2.5 mg/kg. iv. renal vasoconstrictor responses to all doses of norepinephrine were enhanced significantly, whereas responses to nerve stimulation and angiotensin were not significantly different from control values (Fig. 2). At a higher dose of indomethacin (5 mg/kg. iv) only the response to the 1-/*g dose of norepinephrine was enhanced significantly (Fig. 2). Although meclofenamate. 2.5 mg/kg. iv. appeared to increase renal vasoconstrictor responses to norepinephrine, nerve stimulation, and angiotensin. none of these enhanced responses was significantly greater than the preinjection control values (Fig. 2).

To evaluate the effects of indomethacin on prostaglandin synthesis, arachidonic acid, the precursor of the bieneic prostaglandins, was administered to five cats before and 30 minutes after indomethacin. Intravenous injection of arachidonic acid. 3 mg. and prostaglandin E2, 0.5 fig. as a bolus, produced a rapid and transient fall in mean arterial pressure. Arachidonic acid reduced mean arterial pressure by 56 ± 11 mm Hg and prostaglandin E2 by 25 ± 6 mm Hg. Thirty minutes after indomethacin. 2.5 mg/kg. iv. the fall in mean arterial pressure produced by arachidonic acid was markedly reduced to 14 ± 6 mm Hg (P < 0.05). While at the same time the effect of prostaglandin E2 on arterial pressure was enhanced and caused a decrease in mean arterial pressure of 39 ± 7 mm Hg (P < 0.05).

**INFLUENCE OF INDOMETHACIN ON RENAL VASCULAR RESISTANCE AFTER PHENTOLAMINE**

To determine the contribution of the sympathetic nervous system to the rise in resistance that followed indomethacin. infusion of phentolamine was begun prior to injection of this inhibitor of prostaglandin synthesis. Infusion of phentolamine at a rate of 10 fig/min markedly decreased renal vasoconstrictor responses to norepinephrine and nerve stimulation while the response to angiotensin was unaltered. This effect is illustrated in Figure 3 for the injection of 1 fig of norepinephrine. for nerve stimulation at 10 cycles/sec, and for angiotensin. Findings were similar for doses of 0.3 and 3 fig of norepinephrine and for nerve stimulation at 3 and 30 cycles/sec. Injection of indomethacin. 2.5 mg/kg. iv. 30 minutes after the onset of phentolamine infusion did not alter the vasoconstrictor responses obtained in the presence of phentolamine alone (Fig. 3). In these cats renal perfusion pressure was only slightly and transiently decreased during infusion of phentolamine. and aortic pressure was not affected (Fig. 4). However, when indomethacin was injected 30 minutes after the onset of phentolamine infusion a significant increase in renal vascular resistance was observed (Fig. 4).
The increase in renal resistance in response to indomethacin during phenolamine infusion, shown in Figure 4, appeared to be greater than that seen in experiments in which indomethacin alone was given (Fig. 1). Aortic pressure was not affected either by renal artery infusion of phenolamine alone or after administration of indomethacin (Fig. 4).

EFFECT OF INDOMETHACIN ON RENAL VASCULAR RESISTANCE AFTER CONVERSION ENZYME INHIBITION

To determine the contribution of the renin-angiotensin system to the rise in resistance resulting from indomethacin, infusion of SQ 20881 was begun prior to injection of indomethacin in another group of cats. During infusion of SQ 20881, 50 μg/kg per min. iv, the aortic pressor response (68 ± 18 mm Hg) to angiotensin I, 3 μg, iv, was abolished, while at the same time the systemic depressor response to bradykinin, 1 μg, iv, was markedly enhanced from −9 ± 2 mm Hg to −64 ± 10 mm Hg (P < 0.05). Aortic pressure and renal perfusion pressure were not affected during infusion of SQ 20881 alone (Fig. 4). Injection of indomethacin, 2.5 mg/kg, iv, 30 minutes after the onset of SQ 20881 infusion resulted in a gradual but steady increase in renal vascular resistance (Fig. 4) which was similar to that produced by indomethacin alone (Fig. 1). Ten minutes after injection of indomethacin renal vascular resistance had increased by 27% and 30 minutes after injection of indomethacin renal resistance had increased by 57%.

INFLUENCE OF INDOMETHACIN ON RENAL VASCULAR RESISTANCE AFTER PROPRANOLOL

To further evaluate the contribution of the renin-angiotensin system to the rise in resistance after indomethacin, a separate group of cats was pretreated with propranolol in a dose sufficient to inhibit renin secretion. Propranolol (10 mg/kg, iv) was infused into the jugular vein over a 15-minute period. During infusion aortic pressure decreased markedly while at the same time renal perfusion pressure was not altered (Fig. 5). Although aortic pressure tended to return toward the control level after termination of propranolol infusion, it was still slightly, but significantly, reduced 20 minutes after administration of this agent. At 10–15 minutes after termination of the propranolol infusion the renal vasodilator response to isoproterenol was reversed while at the same time the response to norepinephrine was unchanged (Fig. 5). This indicated β-receptor blockade. Administration of indomethacin, 2.5 mg/kg, iv, 20 minutes after propranolol resulted in a gradual increase in renal vascular resistance (Fig. 5). Under these conditions the increase in resistance in response to indomethacin appeared to be greater than that observed in experiments in which indomethacin was given alone (Fig. 1). Aortic pressure was not affected after indomethacin in this group of cats (Fig. 5).

EFFECT OF INDOMETHACIN ON RENAL VASCULAR RESISTANCE AFTER ANGIOTENSIN RECEPTOR BLOCKADE

The influence of indomethacin on renal vascular resistance was determined during infusion of [Sar1,Ala8]angiotensin II, an analogue of angiotensin II that antagonizes the pressor action of angiotensin. Infusion of [Sar1,Ala8]angiotensin II directly into the perfusion circuit at a rate of 0.5 μg/min markedly reduced the renal vasoconstrictor response to angiotensin while at the same time the renal pressor response to norepinephrine was not al-

![Figure 3](http://circres.ahajournals.org/content/14/12/351/F3.large.jpg)

**Figure 3** Effect of infusion of phenolamine (10 μg/min, ia) directly into the renal perfusion circuit on renal vasoconstrictor responses to norepinephrine, renal nerve stimulation, and angiotensin. Vasoconstrictor responses were obtained prior to phenolamine infusion (all doses and frequencies), after the onset of infusion (norepinephrine, 1 μg; nerve stimulation, 10 cycles/sec; angiotensin, 1 μg), and after the injection of indomethacin (all doses and frequencies). Once begun, phenolamine infusion was maintained for the remainder of the experimental period. n = number of cats. *P < 0.05 indicates significantly different from preinfusion control.

![Figure 4](http://circres.ahajournals.org/content/14/12/351/F4.large.jpg)

**Figure 4** Top: effect of injection of indomethacin (2.5 mg/kg, iv) 30 minutes after onset of infusion of SQ 20881 (50 μg/kg per min, iv) on renal perfusion pressure and mean aortic pressure. Bottom: effect of injection of indomethacin (2.5 mg/kg, iv) 30 minutes after onset of infusion of phenolamine (10 μg/min, ia) directly into the renal perfusion circuit. Once begun, infusion of SQ 20881 and phenolamine was maintained throughout the experimental period. n = number of cats. *P < 0.05 indicates significantly different from control, 30 minutes after onset of infusion.
Renal perfusion pressure and systemic arterial pressure were not altered during infusion of the angiotensin analogue. Administration of indomethacin, 2.5 mg/kg, iv, 15 minutes after the onset of [Sar¹,Ala⁶]-angiotensin II infusion resulted in a very slowly developing, moderate increase in renal vascular resistance but had no effect on aortic pressure (Fig. 5). The increase in renal resistance was less than that observed after indomethacin alone (Fig. 1).

**EFFECT OF INDOMETHACIN ON RENAL VASODILATOR RESPONSES TO BRADYKININ AND NITROGLYCERIN**

We studied the effect of indomethacin, 2.5 mg/kg, iv, on renal vasodilator responses to bradykinin and nitroglycerin in a separate group of cats. Twenty minutes after injection of indomethacin, the vasodilator responses elicited by all doses of bradykinin (1, 3 and 10 µg, ia) and by nitroglycerin (10 µg, ia) were significantly greater than the control (Table 1). However, when these data were expressed as percent decrease in pressure, in order to take into account the increase in perfusion pressure produced by indomethacin, only dilator responses to bradykinin were enhanced (Fig. 6).

Saline was infused directly into the renal perfusion circuit in order to control for the effects of time and the saline vehicle. Neither renal vascular resistance nor aortic pressure was affected during the entire period of saline infusion (Fig. 1).

**Discussion**

Results of the present investigation show that renal arterial perfusion pressure is increased in the cat after administration of indomethacin or meclofenamate, two inhibitors of prostaglandin synthesis that differ structurally. Since blood flow was maintained constant, the increase in pressure reflects an increase in renal vascular resistance. The increase in renal resistance was progressive and is consistent with results of studies on the anesthetized dog although the magnitude of the increase in resistance was smaller in the cat. In the conscious animal, however,

<table>
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<th>Table 1 Effect of Indomethacin (2.5 mg/kg, iv) on Vasodilator Responses to Bradykinin and Nitroglycerin</th>
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<tr>
<td><strong>Bradykinin</strong></td>
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<tr>
<td><strong>1 µg (ia)</strong></td>
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<tr>
<td>(-13 ± 1.3)</td>
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<td>(n = 7)</td>
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<tr>
<td><strong>3 µg (ia)</strong></td>
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<td>(-14 ± 3.1)</td>
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<td>(n = 7)</td>
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<td><strong>10 µg (ia)</strong></td>
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<td>-13 ± 2.6</td>
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All values are expressed as mm Hg ± SEM; n = number of cats.

* Significantly different from control (P < 0.05).
it has been reported that indomethacin has essentially no effect on either basal renal blood flow or renal resistance.12-13 The reasons for this are unclear. The present data can be interpreted to support the hypothesis that the maintenance of renal flow may be dependent on prostaglandin synthesis in the anesthetized animal.4 These studies extend the findings of previous investigations by showing that the rise in renal vascular resistance after indomethacin is not modified by phentolamine, an a-adrenergic blocking agent. It was also found that neither the angiotensin-converting enzyme inhibitor, SQ 20881, nor propranolol in a dose sufficient to block renin secretion, altered the increase in renal vascular resistance after indomethacin. However, [Sar',Ala']angiotensin II, an antagonist of angiotensin, reduced the increase in renal resistance after indomethacin. If endogenous prostaglandins serve to maintain the renal bed in a dilated state by opposing the effects of either of the two major renal pressor systems, i.e., adrenergic or renin-angiotensin systems, then inhibition of either pressor system should have led to the attenuation of the increase in renal resistance in response to indomethacin. However, in the present experiments, when responses to sympathetic nerve stimulation and norepinephrine were reduced markedly by phentolamine, the increase in renal resistance in response to indomethacin was not attenuated but in fact may have been enhanced. These data indicate that if the increase in renal resistance after indomethacin is the result of inhibition of prostaglandin synthesis, then endogenous prostaglandins do not maintain the kidney in a dilated state by opposing the effect of the adrenergic system. In addition, SQ 20881, a converting enzyme and kininase inhibitor, although enhancing responses to bradykinin, had no effect on the increase in renal resistance in response to indomethacin. Furthermore, pretreatment of cats with propranolol also had no effect on the indomethacin-induced increase in renal resistance. These data do not support the hypothesis that endogenous prostaglandins maintain the kidney in a dilated state by opposing the renin-angiotensin system. In contrast, however, infusion of the angiotensin antagonist, [Sar'Ala']angiotensin II, did reduce the rise in renal vascular resistance in response to indomethacin. In addition, it has been reported that the intrarenal infusion of [Sar',Ala']angiotensin II reduced the increase in renal resistance caused by meclofenamate in the dog kidney during renal artery occlusion.44 Since inhibition of angiotensin I conversion and propranolol, in a dose sufficient to block renin secretion, had no effect on the rise in renal resistance after indomethacin, the reduction of the renal response to indomethacin during infusion of [Sar',Ala']angiotensin II may indicate a greater blockade of the effects of angiotensin or may represent some non-specific effect of the angiotensin antagonist. Therefore, the hypothesis that the renal prostaglandins may maintain the kidney in a dilated state by opposing the effects of angiotensin cannot be completely ruled out.

Prostaglandins are released by the kidney during stimulation of the sympathetic nerves or infusion of vasoconstrictor hormones.38-41 Prostaglandin E2, the major renal prostaglandin, possesses the ability to attenuate renal vasoconstrictor responses to nerve stimulation and pressor hormones.16 These findings led to the hypothesis that endogenous prostaglandins may serve to modulate the effects of the sympathetic nervous system and pressor hormones on the renal vascular bed.19 If endogenous prostaglandin E2 modulates the effects of pressor stimuli on the renal bed, then inhibition of prostaglandin synthesis should enhance renal vasoconstrictor responses to nerve stimulation and pressor hormones. In the present study, indomethacin and meclofenamate in doses that inhibit the biotransformation of arachidonic acid to prostaglandins in renal tissue had no significant effect on the responses to nerve stimulation or angiotensin in the feline kidney perfused in situ. Responses to norepinephrine were enhanced after indomethacin but were not modified by meclofenamate. The failure of the synthesis inhibitors to enhance responses to nerve stimulation or angiotensin in addition to inconsistent effects on responses to norepinephrine, suggest that endogenous prostaglandins do not serve to modulate the response of the feline kidney to sympathetic stimulation or vasoconstrictor hormones. The effects of indomethacin on responses to angiotensin appear to be different in the feline and canine kidney. In the dog, indomethacin enhances the response to infused angiotensin, whereas in our present study with cats we observed no effect on the response to angiotensin injection either in terms of peak response or T_{\text{max}} of the response. Inhibition of prostaglandin synthesis has been reported to enhance responses to sympathetic stimulation in the rabbit heart, spleen, kidney, and portal vein and in the canine cutaneous vascular bed.7 The reason for differences in effects of synthesis inhibitors is unknown although organ, species, and level of prostaglandin synthesis may be important factors.7

It has been reported that bradykinin releases a prostaglandin E-like substance from the canine kidney whereas edeotoxin in equilator doses does not increase the concentration of prostaglandins in renal venous blood.7 It has,
therefore, been proposed that a prostaglandin E-like substance participates in the renal vasodilator and the diuretic responses to bradykinin. If the renal vasodilator response to bradykinin is dependent in part on synthesis of a prostaglandin, then inhibition of the synthesis should attenuate the response of the renal vascular bed to the peptide. However, in the present investigation, the response to bradykinin was not blocked after indomethacin. In fact, vasodilator responses to the kinin were enhanced after indomethacin. These data indicate that in the feline renal vascular bed the effects of bradykinin are probably not dependent on release of a dilator prostaglandin.

In summary, results of the present investigation indicate that, in the anesthetized cat, the slowly developing increase in renal vascular resistance produced by indomethacin is not mediated by the adrenergic nervous system, while the role of the renin-angiotensin system cannot be completely ruled out. The failure of indomethacin and meclofenamate to modify the vasoconstrictor response to renal nerve stimulation suggests that locally formed prostaglandins, in contrast to exogenous prostaglandins, do not modulate the effects of the sympathetic nervous system in the feline kidney. Since responses to bradykinin were enhanced after indomethacin, it does not appear that endogenous prostaglandins mediate the renal dilator response to bradykinin in the feline kidney. It is possible that effects of indomethacin and meclofenamate on the renal vascular bed may be due to actions of these agents which are unrelated to inhibition of prostaglandin synthesis.

References

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