Table 1 Comparison of the vasodilator potencies of some prostaglandins in the anaesthetized dog

	Equipotent dose to cause 30% decrease in vascular resistance		
Prostaglandin	*Common carotid vascular bed*	*Femoral vascular bed*	*Mesenteric vascular bed*
E_1	1	1	1
E_2	1.3	0.7	1.2
	(0.6–2.9)	(0.3–1.3)	(1.1–1.3)
11deoxy E_0	9.4	8.9	3.6
	(3.4–26)	(5.3–15)	(1.4–9.1)
A_1	16	8.9	5.5
	(7.4–36)	(2.7–30)	(3.6–8.5)
A_2	20	21	15
	(6.0–64)	(4.5–101)	(5.5–41)
I_2	52	74	1.1*
	(36–76)	(50–110)	(0.7–1.6)
B_1	276	266	113
	(145–521)	(79–896)	(63–203)
B_2	357	287	165
	(128–997)	(78–1059)	(62–444)

Each value is the mean of 4–10 determinations (95% confidence limits).
* Significantly different from corresponding value obtained in femoral and carotid vascular beds at $P = 0.01$.

being 0.7 (0.5–0.9, $n = 24$), 0.3 (0.2–0.4, $n = 20$) and 1.0 (0.8–1.3, $n = 8$) ng/kg on the common carotid, femoral and superior mesenteric arterial beds respectively. With the exception of PGI_2, the order of agonist potency on all three vascular beds (PGE > deoxy E_0 = A > B; 1- and 2-series equipotent) is very similar to that previously described on cat isolated trachea (Apperley, Coleman, Kennedy & Levy, 1979). The same receptor may therefore mediate relaxation of the trachea and vasodilatation in dog. PGI_2 was 50–70 times less active than PGE_1 on the carotid and femoral beds and on the trachea. However, PGI_2 and PGE_1 were equipotent on the mesenteric bed. The mesenteric bed may therefore contain an additional PGI_2-sensitive receptor which also mediates vasodilatation.

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Cardiovascular effects of α-adrenoceptor antagonists in the conscious rabbit

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α-Adrenoceptors, like β-adrenoceptors, have been divided on the basis of agonist and antagonist potencies into two categories: α_1 or classical postsynaptic receptors and α_2, which appear to be presynaptically located, at least in some peripheral tissues and inhibit neurotransmitter release from sympathetic nerve terminals (Berthelsen & Pettinger, 1977).

We examined three α-adrenoceptor antagonists, prazosin, phentolamine and yohimbine, which have differing affinities for α_1- and α_2-receptors (Drew, 1976; Doxey, Smith & Walker, 1977). All drugs were administered intravenously to conscious male New Zealand white rabbits. Blood pressure (MAP) and heart rate (HR) were measured directly from a catheter in the central artery of the ear and arterial plasma noradrenaline (NA) assayed radiometrically.

Twenty minutes after administration of prazosin (0.1 mg/kg) MAP was significantly lower while plasma NA was unchanged. Administration of phen-

tolamine (1.0 mg/kg) produced a similar shift in the dose response curve to intravenous phenylephrine but did not alter either MAP or plasma NA. Yohimbine (1 mg/kg) did not influence phenylephrine responses but caused both MAP and plasma NA to rise.

When a wide range of concentrations of prazosin (0.05–2.0 mg/kg) and phentolamine (0.5–20 mg/kg) were examined a significant and similar increase in plasma NA was observed at higher doses of both drugs. The rise in plasma NA correlated significantly with the fall in BP ($P < 0.01$); the slopes of the lines were −0.2621 for prazosin and −0.1324 for phentolamine and were not significantly different. Over the dose range examined the degree of postsynaptic blockade produced by phentolamine and prazosin was similar and resulted in similar falls in BP for both drugs. The relationship between changes in MAP and NA found for these α-adrenoceptor antagonists was similar to that obtained after giving the vasodilators sodium nitroprusside (2.5–20 μg kg^{-1} min^{-1}) and hydrallazine (1–10 mg/kg).

Baroreceptor reflexes will modify efferent sympathetic outflow in response to changes in pressure, and in individual rabbits, there was a negative correlation ($r = 0.8699$; $P < 0.01$) between MAP fall and plasma NA increase in rabbits treated with prazosin (0.1 mg/kg). In order to exclude baroreflex effects, studies were repeated in groups of rabbits 3 to 6 weeks after bilateral sino-aortic denervation (SAD) (Chalmers & Wurtman, 1971). The reduction in blood pressure after prazosin (0.1 mg/kg) and phentolamine (1.0 mg/kg) was significantly greater after SAD. Plasma NA and HR were not altered compared to vehicle treated controls and were inappropriately low for the fall in MAP obtained, confirming that an important component of the changes in HR and NA is mediated via the baroreflex arc. The increase in blood pressure and plasma noradrenaline caused by yohimbine was not altered by SAD. Although the changes observed after yohimbine are consistent with blockade of presynaptic α_2-receptors in the periphery, the present experiments do not exclude a central site of action of yohimbine as the rabbits were hyperactive and restless after receiving this agent.

It was not possible, in these studies, to detect any differences in the fall in MAP or in the release of NA produced by a relatively selective α_1-adrenoceptor antagonist prazosin and the mixed α_1- and α_2-adrenoceptor antagonist phentolamine. However, these studies highlight the importance of the baroreflex arc in maintaining homeostasis and in the difficulties in investigating drug actions on α-adrenoceptors in conscious animals with intact circulatory reflexes.

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Regional haemodynamic changes evoked by isoprenaline in conscious normotensive and renal hypertensive rabbits

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It is generally agreed that the vascular resistance is increased in hypertensive disease, however, the mechanisms responsible for this change are poorly understood. Reduced aortic relaxation to vasodilating agents such as isoprenaline, has been proposed as one of the contributing factors in hypertension (Cohen & Berkowitz, 1976). Since there is considerable heterogeneity in the regional vascular responsiveness, we have used the microsphere technique and electromagnetic flow probe implantation in conscious rabbits (Saxena, van Boom, van Doorn & Cairo-Rawlins, 1979) to study the effects of a 10 min infusion of isoprenaline hydrochloride (0.5 μg kg^{-1} min^{-1} i.v.) or 0.9% NaCl on regional vascular resistance in normotensive and 1-kidney renal hypertensive animals.

The results presented in Table 1 show that arterial BP and vascular resistances were higher, but the heart rate (HR) and cardiac output (CO) lower, in the hypertensive rabbits than in the normotensive controls. In the normotensive animals, isoprenaline evoked increases in HR and CO and decreases in peripheral vascular resistance, particularly in the heart, muscle, skin and fat. The vascular resistance