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

Table 1 Effect of isoprenaline infusion (0.5 μg kg^{-1} min^{-1}) on systemic haemodynamics and regional vascular resistance in normotensive and hypertensive rabbits

	Normotensive		*Renal hypertensive*	
Haemodynamic variables	*Baseline* ($n = 22$)	*% Change by isoprenaline* ($n = 10$)	*Baseline†* ($n = 7$)	*% Change by isoprenaline* ($n = 7$)
Systemic haemodynamics				
Mean BP (mmHg)	87 ± 3	−4 ± 4	112 ± 4**	−16 ± 4*,**
Heart rate (beats/min)	263 ± 7	+27 ± 4*	229 ± 10**	+43 ± 7*
Cardiac output (ml.min^{-1} kg^{-1})	183 ± 9	+36 ± 6*	108 ± 10**	+38 ± 6*
Systemic vascular resistance (mmHg/ml min^{-1} kg^{-1})	0.49 ± 0.02	−27 ± 5*	1.16 ± 0.1**	−38 ± 3*
Regional vascular resistance (mmHg/ml min^{-1} 100 g^{-1})				
Heart	0.34 ± 0.02	−46 ± 5*	0.58 ± 0.09**	−49 ± 5*
Muscle	9.15 ± 0.48	−28 ± 8*	16.41 ± 2.17**	−30 ± 11*
Skin	9.57 ± 1.15	−49 ± 5*	21.09 ± 3.64**	−59 ± 4*
Fat	5.69 ± 0.85	−59 ± 4*	8.13 ± 2.75	−59 ± 7*
Gastrointestinal tract	1.46 ± 0.11	−8 ± 13	2.45 ± 0.50**	−23 ± 6*

Values are means ± s.e. mean. Renal hypertension was produced by unilateral nephrectomy and cellophane wrapping of the remaining kidney. The animals were studied 5–6 weeks later. †, $n = 16$ for systemic haemodynamics; *, significantly different ($P < 0.05$, two-tailed Mann-Whitney U-test) from corresponding changes induced by saline injection (values not shown in Table); **, significantly different ($P < 0.05$, two-tailed Mann-Whitney U-test) from corresponding values in the normotensive group.

in other regions did not change. The effects of isoprenaline in the hypertensive animals were comparable with those in the normotensives except that the decrease in the mean BP and vascular resistance in the gastrointestinal tract were more prominent.

In conclusion, the present results do not provide any evidence of sub-sensitivity to isoprenaline in the resistance vessels of renal hypertensive rabbits.

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Indomethacin and the hypotensive action of captopril in DOCA salt hypertensive rats

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The fall in blood pressure caused by the converting enzyme inhibitor captopril (CEI) is associated with a reduction in circulating angiotensin II (Ondetti, Cushman & Burin, 1977). CEI also inhibits the breakdown of bradykinin and this may contribute to its hypotensive effect (Wang, Talamo, Williams & Colman, 1975). As bradykinin may induce prostaglandin synthesis (Murthy, Waldron & Goldberg, 1978), we have studied the effect of prostaglandin synthetase inhibition on the action of CEI in hypertensive rats characterized by a suppressed renin angiotensin system.

Twenty four DOCA salt hypertensive (mean systolic pressure (MSP): 187.6 ± 5.6 mm Hg) male Wistar rats were randomly allocated to one of 4 groups. Captopril (1 mg/kg) was administered to groups I and III and a saline control to groups II and IV. Groups III and IV were pretreated with indomethacin (IND, 25 mg/kg). All doses were administered as an intraperitoneal bolus. Blood pressure fell significantly (mean maximum delta SBP: −23.4 ± 5.0 mm Hg; $P < 0.001$ vs baseline) in group I, reaching a minimum of 30 min after captopril. Pretreatment with IND in group III significantly attenuated this effect