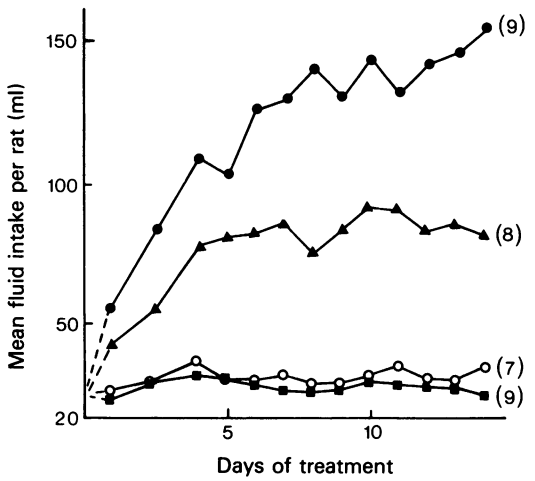

Figure 1 Daily fluid consumed by rats treated with (●) DOCA/salt, (▲) DOCA/salt and SQ 14225, (□) SQ 14225 alone and (○) control. Numbers of animals in parentheses.

averaged between days 6 to 14, was 139.2 ± 3.2 and 86.1 ± 1.7 ml for control and drug-treated rats respectively; these figures are significantly different ($P < 0.001$). A similar trend towards reduced fluid intake was seen when the drug was given to sham operated rats (Figure 1).

We think it unlikely that the effect on fluid intake of SQ 14225 results from peripheral actions since renin release has been reported to be 99% inhibited in DOCA/salt rats (Campbell & Pettinger, 1975). It is possible that SQ 14225 has some direct action on drinking unrelated to this inhibition of converting enzyme but it seems most likely that the effect of this compound on drinking is due either to inhibition of converting enzyme in the brain iso-renin system or to the potentiation of kinins.

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An inhibitory role for the adrenals in the cardiovascular effects of propranolol in the spontaneously hypertensive rat

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The anti-hypertensive effect of propranolol in different types of hypertension in man has been well documented (see Simpson, 1974). In rats with experimental hypertension however, the blood pressure lowering effect is less clear (Roba, Lambelin & De Schaepdryver, 1972; Fernandes, Onesti, Fiorentini, Gould, Kim & Swartz, 1977). We investigated the cardiovascular effects of (±)-propranolol in the unanesthetized spontaneously hypertensive rat (SHR). Blood pressure was recorded from a cannula in the caudal artery at the base of the tail in male rats 11–15 weeks of age. Heart rate was computed from the blood pressure recordings.

Different doses of propranolol (1 and 5 mg/kg subcutaneously) failed to decrease blood pressure during 2 h of measurement. At the highest dose heart rate decreased significantly (−50 ± 6 beats/min, $n = 6$) ($P < 0.01$). After central administration into a lateral ventricle (1.5 mg/kg), no cardiovascular changes were observed except a small hypertensive effect within the first 10 minutes. Peripheral administration of propranolol to animals which were subjected to bilateral adrenalectomy 4 h previously however, induced a profound decrease in blood pressure and heart rate. The effects were dose-dependent. Maximal effects were observed 15–30 min after the injection (−34 ± 6 mm Hg and −140 ± 8 beats/min respectively after 5 mg/kg, $n = 7$). Individual values for decreases in blood pressure and heart rate were not correlated ($r = 0.25$), indicating independent mechanisms for both parameters. In order to investigate whether the adrenal cortex or the adrenal medulla was responsible for the observed effects, rats were demedullated 2 days prior to the experiment. In these rats propranolol (5 mg/kg s.c.) caused no cardiovascular changes. After treatment of adrenalectomized animals with corticosterone (100 μg 100 g^{-1} h^{-1}) the decrease in blood pressure and heart rate due to propranolol were completely abolished. Substitution with 30 μg 100 g^{-1} h^{-1} corticosterone did not prevent the hypotensive action and bradycardia. Adrenal corticosteroids therefore seem to be responsible for the absence of

hypotension and bradycardia after propranolol in the SHR. Central injection of propranolol into a lateral brain ventricle of adrenalectomized rats (0.5–1.5 mg/kg) caused cardiovascular changes which were less pronounced as compared to peripheral injection of comparable doses. These results point to a peripheral site of action for propranolol under these conditions. Parasympathetic activation does not seem to be responsible for the bradycardia or hypotension since neither bilateral vagotomy nor pretreatment with atropine (5 mg/kg i.p.) prevented the cardiovascular effects of propranolol in adrenalectomized rats.

The inhibitory effects of propranolol are not restricted to the SHR, since similar effects were observed in the normotensive Wistar-Kyoto rat. However, in the adrenalectomized normotensive- or renal hypertensive Wistar rat no cardiovascular changes were observed with propranolol. This implies a strain dependent effect for propranolol.

In conclusion, in the Wistar-Kyoto strain adrenalcorticosteroids do prevent the lowering of blood pressure and heart rate after propranolol. Whether the inhibitory effects in the absence of these steroids are caused by an action on the heart or the peripheral vasculature remains to be determined.

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Changes in plasma renin levels of normotensive and spontaneously hypertensive rats with increasing age

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Renin levels in the plasma of spontaneously hypertensive rats (SHR) have been variously reported to increase, decrease or remain unchanged with age (for references see Shiono & Sokabe, 1976). The apparently equivocal nature of these results may have resulted from comparisons between rats which were based on small age difference.

The present study describes renin levels in the plasma of SHR (bred at Queen's Medical Centre) and control normotensive Wistar rats (NR) (obtained from Messrs. Bantin & Kingman Ltd.) aged between 11 and 235 days. Rats were divided into groups according to their age and allowed free access to food

Table 1 Mean systolic b.p. (± s.e. mean) and mean plasma renin concentration (PRC) (± s.e. mean) for groups of normotensive and spontaneously hypertensive rats at various ages from 11 to 235 days. (N = number of rats in each age group). Systolic blood pressure is expressed in mm Hg and PRC in ng angiotensin I generated ml^{-1} h^{-1}

	Normotensive Wistar rats			*Spontaneously hypertensive rats*		
Age (days)	*n*	*Systolic B.P.*	*PRC*	*n*	*Systolic B.P.*	*PRC*
11–13	6		16.3 ± 4.7	5		28.7 ± 2.8†
25–32	6		12.6 ± 3.1	3		18.2 ± 2.8*
44–46	6	133 ± 3	4.4 ± 1.7*	6	162 ± 7	7.8 ± 0.8*
60	6	135 ± 2	8.3 ± 2.9	6	198 ± 6	12.2 ± 2.0
92–96	6	140 ± 1	15.0 ± 5.0	6	217 ± 6	28.5 ± 2.8*†
158	6	141 ± 3	15.2 ± 2.7			
230–235	6	135 ± 3	19.9 ± 4.5	6	242 ± 8	27.5 ± 1.5

Notes: It was technically not possible to measure b.p. of rats less than about 40 days old. A group of SHR rats of 158 days old was not available. Differences between adjacent pairs of PRC's marked with an asterisk (*) were statistically significant ($P < 0.05$). Differences between corresponding pairs of PRC's for normotensive compared with hypertensive rats marked with (†) were statistically significant ($P < 0.05$).