Aortic intubated hypertensive rats: responses to drugs and diurnal variations in arterial blood pressure

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Hypertensive rats are more sensitive to the blood pressure lowering actions of hypotensive agents than are normotensive. However, not all experimental models of hypertension, using rats, are equally sensitive to clinically effective drugs (Sturtevant, 1958; Stanton & Cooper, 1966; Stanton & White, 1965). For these reasons the effects of potential antihypertensive agents are best examined using rats made hypertensive by at least two different methods.

Arterial blood pressures were recorded from unanaesthetized animals using the aortic intubation method of either Weeks & Jones (1960) or Popovic & Popovic (1960). A cannula placed in the aorta during a brief period of halothane anaesthesia 3 days previously, when connected to a pressure transducer, permitted simultaneous determination of systolic and diastolic blood pressures, together with heart and respiratory rates.

Metacorticoid hypertension was produced in groups of rats weighing 90–120 g by removing one kidney and giving four subcutaneous injections of DOCA (100 mg/kg) at weekly intervals while substituting the drinking water for 0·9% saline. The mean blood pressure rose from approximately 120 mm Hg to approximately 190 mm Hg within 3 weeks. Concomitantly bradycardia, probably of reflex origin, also developed, the mean heart rate falling from 452 to 428 beats/min. In a second group, of similar weight range, "renal" hypertension was caused by constriction of a renal artery with a silver clip 0·25 mm in diameter and contralateral nephrectomy. This developed more slowly, the arterial blood pressure rising to 190 mm Hg within 5 weeks.

TABLE 1. *Variation of blood pressure and heart rate of metacorticoid hypertensive and normotensive rats with time*

(1) Metacorticoid hypertensive rats (group size 13)

Mean/Period h	9–10	11–12	13–14	15–16	17–18	19–20	21–22	23–24
Mean b.p. (mm Hg)	190	191	183	178	170	170	173	176
Systolic b.p. (mm Hg)	211	217	210	204	198	200	204	206
Diastolic b.p. (mm Hg)	168	167	157	142	142	141	142	150
Heart rate (beats/min)	429	430	435	427	424	420	417	425

(2) Normotensive rats (group size 10)

Mean/Period h	9–10	11–12	13–14	15–16	17–18	19–20	21–22	23–24
Mean b.p. (mm Hg)	116	119	119	117	113	114	117	117
Systolic b.p. (mm Hg)	134	139	136	137	135	137	141	141
Diastolic b.p. (mm Hg)	98	99	99	96	93	92	94	93
Heart rate (beats/min)	452	458	458	454	455	467	471	456

Using these techniques it was found that the mean arterial blood pressures of rats made metacorticoid hypertensive were significantly higher in the morning than during the afternoon or evening (Table 1). This was mainly, but not entirely, due to a change in diastolic pressure. In contrast normotensive and renal hypertensive animals did not show this variation.

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The effect of adrenergic neurone blockade on responses of the cat heart to sympathetic nerve stimulation

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Stimulation of the right cardiac nerve, in the cat anaesthetized with chloralose, causes both positive inotropic and chronotropic effects on the myocardium, whereas during stimulation of the left cardiac nerve only an inotropic response is usually seen. This difference is analogous to that recently reported to occur in the dog (Furnival, Linden & Snow, 1968) and may be related to differences between the anatomical distributions of the two sympathetic postganglionic nerves within the heart.

TABLE 1. *Mean intravenous doses of bethanidine sulphate required for complete suppression, within one hour, of responses of the heart and nictitating membrane to indirect stimulation* (0·3–30 *Hz*)

Nerve	No. of expts.	Dose (mg/kg)	Range
Right cardiac nerve	4	0·5 } *	0·4–0·8
Left cardiac nerve	2	0·6 } *	0·4–0·8
Postganglionic superior cervical	4	3·2 *	

* Significance of difference between means $P<0·001$.

Preliminary results indicate that both nerves are blocked equally readily by bethanidine and confirm their relatively high sensitivity (Boura & Green, 1963). Table 1 summarizes findings which show that the mean intravenous threshold dose of bethanidine necessary to abolish cardiac responses to indirect stimulation was approximately one-sixth of that required to block contractions of the nictitating membrane elicited by postganglionic superior cervical nerve stimulation.

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