Assessment of autonomic and non-autonomic components of resting hindlimb vascular resistance and reactivity to pressor substances in renal hypertensive rabbits

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Summary
1. Hindlimb vascular resistance (HVR) was measured before and after pharmacological autonomic blockade in unanaesthetized renal cellophan-wrap hypertensive or normotensive rabbits with previously implanted Doppler ultrasonic flowmeters.
2. When the blood pressure was restored to resting values after autonomic block, the elevated resting HVR in the hypertensive rabbits was entirely accounted for by an increased non-autonomic component (i.e. HVR after block). If the pressure was not restored after block the autonomic component (i.e. resting HVR minus non-autonomic HVR) was overestimated and the non-autonomic component was underestimated.
3. During maximum vasodilatation the minimum HVR was significantly higher in the hypertensive rabbits than in the normotensive group, probably due to structural differences of resistance vessels.
4. Reactivity of the hindlimb bed to noradrenaline, angiotensin II and vasopressin injections was approximately twice as great in the hypertensive rabbits as in the sham-operated group, probably as a consequence of the structural changes.

Key words: autonomic nervous system, renal hypertension, smooth muscle tone, vascular reactivity, vascular resistance.

Introduction
In previous studies in hypertensive man and animals the rise in vascular resistance has been reported to be due to changes in non-autonomic factors and increased autonomic constrictor tone (Mendlowitz & Touroff, 1952; Conway, 1963; Cohn, Liptak & Freis, 1963; Korner, Shaw, Uther, West, McRitchie & Richards, 1973). However, in all these studies measurements after block have been made at a lower blood pressure than before block (Cohn et al., 1963; Korner et al., 1973; Tarazi & Dustan, 1973). This will alter transmural pressure, local chemical substances controlling vascular resistance and possibly circulating hormones. Therefore if these factors contributing to the non-autonomic component of vascular resistance change after autonomic block the magnitude of both non-autonomic and autonomic components of the resting vascular resistance will be inaccurately assessed. We have determined the effects of changes in blood pressure on this assessment in rabbits with cellophan-wrap renal hypertension. Further, we have estimated any structural changes in hypertensive rabbits by comparing vascular resistance at maximum vasodilatation. We also compared the reactivity of the hindlimb vascular bed to noradrenaline, angiotensin II and vasopressin in rabbits in which the autonomic reflex pathways had been interrupted.

Methods
At a preliminary operation under halothane anaesthesia a Doppler ultrasonic flow transducer (4 mm internal diameter) was implanted around the lower abdominal aorta. At the same operation both kidneys were wrapped in cellophan to produce perinephritic hypertension or were left undisturbed (sham operation). Four weeks later, on the day of the experiment mean ear artery pressure, lower aortic blood flow assumed to be hindlimb blood flow, and hindlimb vascular resistance were measured in unanaesthetized rabbits. In series A (eleven
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sham, seven hypertensive rabbits) measurements were made for a 30 min control period before producing total autonomic blockade with injections of guanethidine, atropine, propranolol and phentolamine as described previously (West, Angus & Korner, 1975). 90–120 min after starting the autonomic blockade further measurements were made to assess the non-autonomic HVR.\(^{11}\) In series B (seven sham-operated and nine hypertensive rabbits) the same protocol was followed except the blood pressure was restored to initial resting levels after the guanethidine injection by infusing 20–30 ml of 6% dextran. The minimum vascular resistance of the hindlimbs was assessed in seven sham-operated and eight hypertensive rabbits after giving increasing doses of papaverine hydrochloride or glyceryl trinitrate.

In 'open-loop' areflexic unanaesthetized rabbits subjected to presynaptic sympathetic constrictor block with guanethidine plus block with atropine and propranolol we assessed the reactivity of the hindlimb vessels to different bolus doses of noradrenaline, angiotensin II and vasopressin (L-8 Vasopressin, Sandoz) whilst not under the influence of baroreceptor reflexes. Regression equations relating change in HVR to log dose of vasoconstrictor drug were calculated for sham-operated and hypertensive rabbits.

**Results**

Resting mean arterial pressure (MAP) and hindlimb vascular resistance (HVR) were higher in both series of hypertensive rabbits than in sham-operated animals, and hindlimb blood flow (HBF) was lower (Fig. 1). In series A, where the blood pressure was not restored to resting levels after autonomic block, MAP was 15–20 mmHg below pre-block values in both the hypertensive and normotensive animals. HVR fell from 77.7 units to 49.4 units after autonomic block (difference 28.3, SE 5.0, units) in the hypertensive rabbits and 33.7 units to 22.3 (difference 11.4, SE 1.9) in sham-operated animals, i.e. significantly less than the hypertensive rabbits.

In series B where mean arterial pressure was restored after block to the resting value by giving dextran, in hypertensive rabbits resting HVR was 68.0 units falling to 62.5 units after autonomic block (difference 5.5, SE 3.9, units) and in the sham-operated group it fell from 24.7 units to 20.0 units (difference 4.7, SE 2.7). In series B the non-autonomic component thus accounted for the entire elevation of initial resting HVR in the hypertensive rabbits.

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**Fig. 1.** Average values of mean arterial pressure (MAP), hindlimb bloodflow (HBF) and hindlimb vascular resistance (HVR) from sham-operated normotensive rabbits (eleven from series A and seven from series B) and renal cellophan-wrap hypertensive rabbits (seven from series A and nine from series B). Measurements were made before (open columns) autonomic block, and 90–120 min after (cross-hatched columns) induction of block. The heights of the columns are mean values; bars indicate ± SE difference within animal between adjoining means.

During maximum vasodilatation of the hindlimb bed the minimum HVR was significantly higher in hypertensive rabbits (13·6, SEM 2·6, units) than in normotensive rabbits (5·8, SEM 1·9, units). Reactivity of the hindlimb resistance vessels to noradrenaline, angiotensin II, and vasopressin were similar whether mean arterial pressure after block was restored to resting in series B or whether it was 15–20 mmHg below as in series A. Average ratios of slopes of dose–response curves in hypertensive/normotensive animals were 1·9/1 for noradrenaline, 1·9/1 for angiotensin II and 2·0/1 for vasopressin.

**Discussion**

Restoring the blood pressure after autonomic blockade influences the estimation of the magnitude of

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\[^{11}\text{Abbreviations: HVR, hindlimb vascular resistance.}\]
of the autonomic and non-autonomic components in hypertension. When the blood pressure was not restored, as in series A, the elevated resting vascular resistance in renal hypertension was considered to be due to elevation of both autonomic and non-autonomic components. However, the results of series B strongly suggest that under these conditions the non-autonomic component was underestimated and the autonomic component overestimated. They suggested that the elevated resistance was entirely due to non-autonomic factors and that the autonomic component was not significantly different from that in normotensive animals. The results from the vasodilator experiments suggest that the raised non-autonomic component probably was due to structural changes in the hindlimb bed, since abolishing vessel tone results in a significantly higher resistance value in the hypertensive than normotensive rabbits. Further, increase in reactivity of the hindlimb resistance vessels of hypertensive rabbits was probably non-specific and also a consequence of the structural changes, including medial hypertrophy producing encroachment on the vascular lumen (Folkow, Hallbäck, Lundgren, Sivertsson & Weiss, 1973) and/or diminished vascularity (Guyton & Coleman, 1967).

References


