Constriction–distension relationships of resistance vessels in normo- and hyper-tension

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Summary
A haemodynamic analysis of resistance vessel behaviour in normo- and hyper-tension has been performed, relating vessel design, degree of contraction, wall distensibility and transmural pressure to each other in a way which allows a semiquantitative prediction of their respective influences in various situations.

Key words: haemodynamics, resistance vessels.

Abbreviations: SH, spontaneously hypertensive; WK, Wistar–Kyoto strain.

Introduction
The behaviour of resistance vessels as a haemodynamic entity depends on four major factors, which are all variable:

(1) Structural design, which is best characterized by average wall/internal radius ($w/r_i$) and resistance during full relaxation and normal distension;

(2) Smooth muscle activity, as averaged for consecutive resistance sections; its haemodynamic impact is greatly dependent on (1);

(3) Wall distensibility, as averaged for consecutive resistance sections; it is strongly influenced by both (1) and (2);

(4) Transmural pressure, which is gradually reduced along the resistance sections to an extent which depends on (1), (2) and (3).

Full insight into resistance control in normo- and hyper-tension demands precise knowledge of all these four variables, although commonly only (2) is considered. The present study attempts to determine the relationships between (1), (2), (3) and (4), comparing normotensive resistance vessels with hypertensive ones, since all of them are more or less altered in hypertension.

Methods
Pair-perfused hindquarters from 10 pairs of 3–4 months old spontaneously hypertensive (SH) rats and Wistar–Kyoto (WK) normotensive rats were studied, starting from maximal vasodilatation. 6% Dextrane/Tyrode solution, containing 0.3% of horse serum proteins at body temperature was used as perfusate, having a viscosity slightly above that for normal blood in vivo at maximal flow rates (Bäckström, Folkow, Kendrick, Löfving & Öberg, 1971). Increasing levels of stable vasostrictions, up to the maximum, were induced by noradrenaline infusions during constant-flow conditions ($10 \text{ ml min}^{-1} \text{ 100 g}^{-1}$). Complete constant-flow 'resistance curves' were thus obtained for both SH and WK rats, from which relative differences between them concerning structural design of the resistance vessels could be deduced (cf. Folkow, 1978).

At each well-defined level of smooth muscle activity, reached during these constant-flow conditions in SH and WK rats, sudden stepwise changes in flow were induced, which over a wide range shifted inflow pressures so rapidly that prevailing smooth muscle activity had no time to readjust. This was verified by largely unaltered resistance values at rapid return to control. In this way pressure-induced passive resistance shifts were determined over a wide range of distending pressures and at exactly comparable levels of smooth muscle activity in SH and WK rats. A
series of characteristic 'resistance lines' were thus obtained, each representing the correlation between transmural pressure and wall distension at the prevailing degree of smooth muscle contraction. From the mean values for all 10 experiments, with altogether about 600 measurements, a diagram could be constructed reflecting the precise relationships between factors (2), (3) and (4) in SH and WK rats, thereby providing information also about the average differences in $r_i$ and $w/r_i$. Such precise relationships cannot be achieved by comparing resistance vessels of SH and WK rats in ordinary constant-pressure perfusions, since prevailing differences in (1) and (3) would then cause differences also in flow, supply of noradrenaline and local metabolite concentrations. This would leave (2) poorly defined, thereby disturbing estimations of (3) as well.

Results

Fig. 1(a) summarizes the experimentally deduced relationships between factors (2), (3) and (4) for resistance vessels of both SH and WK rats. The constant-flow 'resistance curves' for the rats are also replotted into this diagram. The slope of each 'resistance line' for a given smooth muscle activity in Fig. 1(a) reflects average wall distensibility, as expressed by its most relevant consequence, i.e. for resistance to flow by way of average passive shifts of $r_i$.

SH rat resistance vessels have clearly stiffer walls, which is particularly obvious by the fact that the 'resistance lines' for SH and WK rats cross each other wherever resistances are similar. This can here only be explained by a thicker media in SH rats because the resistance to stretch during constriction is essentially offered by the contracted media. Had SH and WK rat resistance vessels differed only in functional characteristics, their resistance lines should at these points by definition have been parallel (cf. Hallbäck, Lundgren & Weiss, 1974). Fig. 1 also shows how smooth muscle contractions 'yield' to overwhelmingly high distending pressures, where vessels of SH rats exhibit some 40% greater strength, again reflecting a thicker media. Conversely, at low pressures, increasing tendencies of 'critical closing' occur, particularly obvious in SH rat vessels at intense constrictions.

Thus, over a wide range of pressures and smooth muscle activations, this diagram reflects the resis-

![Fig. 1. (a) Relationships between distending pressure (MAP) and flow resistance (PRU) over the complete range of smooth muscle activities in hindquarter vessels of SH rats and WK rats. Their 'constant-flow resistance curves' in response to noradrenaline are also plotted into the diagram. (b) Shape of 'constant-pressure resistance curves' for SH and WK rats in response to noradrenaline, as deduced from (a) for the respective MAP values in vivo (166 and 115 mmHg).]
stances which are maintained by vessels of SH and WK rats at any given level of smooth muscle activity and distending pressure. By drawing vertical lines from the 115 to 166 mmHg abscissa levels in Fig. 1(a), the complete resistance response characteristics can be derived, also for the 'normal' constant-pressure condition present in most situations in vivo, and then at exactly comparable levels of media activation and noradrenaline concentration for SH and WK rats (Fig. 1b). Fig. 1(b) shows how resistance vessels of SH rats are markedly hyper-reactive in relation to WK rat vessels, when both are compared at 166 mmHg. Further, even at this higher distending pressure, vessels of SH rats remain considerably hyper-reactive when compared with WK rat vessels at 115 mmHg. When exposed to this lower pressure SH rat vessels become so hyper-reactive compared with WK rat vessels that partial 'critical closing' occurs, presumably at 'sphincter' levels and particularly at more intense smooth muscle activations. During ordinary blood perfusion the ranges of resistance increases would in fact be some 30–50% greater in both SH and WK rats, since blood viscosity in vivo increases to this extent, from maximal flow rates at full relaxation to intense constrictions, while Newtonian perfusates maintain a constant viscosity (Bäckström et al., 1971).

Discussion

These results provide a semiquantitative multifactorial analysis of average resistance vessel behaviour in both normotension and hypertension. Apart from their relevance for normal resistance vessel regulation, some haemodynamically important conclusions concerning chronic hypertension may be drawn from these results. Because of wider lumina, with thinner and more distensible walls, normotensive resistance vessels must at hypertensive pressures display considerably accentuated smooth muscle activations to match what hypertensive vessels then achieve by modest active adjustments. Conversely, if hypertensive resistance vessels are exposed to rapid normalization of pressure by, e.g., intense therapy, considerable vascular hyper-reactivity is bound to ensue from the reduced distension, until vessel design readapts towards normotensive levels. Thus, primary hypertension is certainly not a mere reflection of accentuated smooth muscle activity in systemic resistance vessels, but represents a fundamental shift in their design and physical characteristics.

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References


FOLKOW, B. (1978) Cardiovascular structural adaptation; its role in the initiation and maintenance of primary hypertension. Clinical Science and Molecular Medicine, 55 (Suppl. 4), 3s–22s.