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ACTIVE REACTIONS OF THE RABBIT EAR ARTERY TO DISTENSION

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SUMMARY

1. Changes in the external diameter of active arteries, excised from the rabbit ear, were recorded following jumps in pressure within the arteries. The arteries were either spontaneously active or were constricted with noradrenaline.

2. Active arteries dilated when the transmural pressure was jumped from 60 to 100 mmHg, but the dilatation was largely, sometimes completely, overcome by compensatory constriction within 1–2 min. Varying the constriction from 15 to 80 % of the maximal constriction had no effect on the ability of the arteries to counteract distension. An average of 90 ± 2 % of the distension was overcome in 2 min and this was achieved against increases in stress (force/wall cross-sectional area) on the muscle of not less than 74 %. Jumps in pressure rarely enhanced constriction and then only when constriction was slight (< 15 % of maximal).

3. Restoring the transmural pressure to 60 from 100 mmHg produced a transient constriction when the initial constriction was less than 50 % of the maximal constriction. The sequence of counteraction of distension and transient constriction on reversing the pressure jump was reproducible for many hours.

4. Increasing constriction of the arteries first decreased and then, at maximal constriction, suppressed all transient changes in diameter. Smaller jumps in pressure produced less dilatation which was more readily prevented by increasing constriction.

5. These results show that the wall of the ear artery possesses a pressure-sensitive, negative feed-back mechanism which minimized changes in diameter following jumps in pressure.

INTRODUCTION

The ability of vascular smooth muscle to respond to a stretching force with a contraction is called the myogenic or Bayliss response as it was first reported by Bayliss in 1902 (Bayliss, 1902). The contribution of the myogenic response to autoregulation of blood flow has not been easy to evaluate, and it has been even more difficult to study its mechanism which remains poorly understood (Bouskela & Wiederhelm, 1979; Johnson, 1980; Börgstrom, Grände & Mellander, 1982; Carlson, Burrows & Johnson, 1982; Morff & Granger, 1982). One major reason for the latter difficulty has been the inability to make use of the advantages of *in vitro* preparations because isolated segments of blood vessels have not responded reproducibly to a distending force (Bayliss, 1923; Davignon, Lorenz & Shepherd, 1965; Johnson, 1980).

More consistent reactions to stretch have been obtained with strips of the human umbilical artery (Sparks, 1964), the pig coronary artery (Peiper, Laven, Regnat & Schmidt, 1974) and rabbit basilar, coronary and renal arteries (Nakayama, 1982), but the physiological significance of these active tension responses is uncertain because of their long latency, slow development, small amplitude, their transiency and the need to have a 15–20 min interval between successive stretches to avoid deterioration of the preparations. The interpretation of these observations is complicated further by the destruction of the geometry of the blood vessel and by the assumptions involved in the conversion of active tension reactions of arterial strips to diameter changes in pressurized blood vessels. These limitations have been overcome in the present experiments. Isolated and pressurized segments of the rabbit ear artery reacted to distension by constricting, when active, and they could do so reproducibly every 4 min for many hours. A preliminary account of some of these experiments was given at the Second Australian and New Zealand Symposium on the Microcirculation (Speden, 1984).

METHODS

Central ear arteries were obtained from twenty-three semi-lop-eared rabbits of both sexes which were 3–11 months old. Nine of the arteries were perfused and their external diameters measured using methods which have been described in detail previously (Speden, 1973, 1975). These arteries were used to examine the effect of sympatholytic drugs on the distensibility of the arteries. The sympatholytics guanethidine (Ciba-Geigy), phentolamine hydrochloride (Ciba-Geigy) and bethanidine sulphate (Burroughs Wellcome) were added to the reservoir of Krebs solution. The remaining arteries were used in the pressure jump experiments. In these latter experiments, a 2–3 cm segment of the central ear artery was excised from an anaesthetized (urethane, $1{\cdot}75\ 10^{-3}$ kg/kg body weight I.V., with supplements as required) and heparinized (1000 u., I.V.) rabbit and immediately transferred to a Krebs-filled organ bath (Fig. 1). Each end of the artery was cannulated with a blunted hypodermic needle (19 gauge) which was attached to a three-way, miniature inert valve (Hamilton). One miniature valve was mounted on a three-way manipulator and the other on a two-way manipulator. Once cannulated, the arterial lumen was flushed out with and filled with Krebs solution through two of the ports of the valves. Both the flushing and filling pressures were kept below 60 mmHg. A Statham pressure transducer (P23Db) was connected to the third port of one valve and a horizontal 1 cm^3 reservoir to the remaining free port of the other valve. The small reservoir (the barrel of a 1 cm^3 hypodermic syringe) was needed to replace a slight leakage of liquid (usually $< 0{\cdot}1$ $cm^3\ h^{-1}$) from the lumen of the artery. The artery was left to equilibrate for 20–30 min before the intraluminal pressure was raised to 160 mmHg and the cannulae moved apart to remove all bowing of the artery. This artery length was not changed throughout the remainder of the experiment. The intraluminal pressure was varied by changing the gas pressure (95 % O_2, 5 % CO_2) on the reservoir liquid. The lumen of the artery was filled with this gas mixture in preliminary experiments, but the reaction of these arteries to distension was sluggish and small and the preparations deteriorated rapidly. Distension was produced by manually increasing the setting of the on-line Conoflow PH-10 pressure regulator or by using a pair of two-way solenoid valves to switch from one pressure line to another parallel pressure line set at a higher pressure with a second Conoflow PH-10 regulator. A 40 mmHg pressure jump was complete in 0·6–1·2 s.

The organ bath was a $47 \times 12 \times 9$ mm deep cavity cut into a 12·5 mm thick sheet of Perspex which was fixed to the stage of an Olympus ECEBi microscope (the binocular arm was removed). The contents of the bath (4·5 cm^3) were continuously replaced with fresh Krebs solution at a rate of one bath volume every 2 min. The bath temperature was kept at 308–310 K by circulating warm water through the Perspex sheet and a water jacket surrounding the inflow tubing using a Haake model E52 constant temperature circulator. A Sage model 355 syringe pump was used to infuse L-noradrenaline (Sigma) into the bath inlet at a rate of 0·1 $cm^3\ min^{-1}$. The L-noradrenaline and L-adrenaline (Sigma) were dissolved in 0·02 N-HCl and diluted with a 0·9 % w/v NaCl solution which

also contained EDTA (diaminoethanetetraacetic acid, disodium salt; 0·026 mM). The composition of the Krebs solution was (mM): NaCl, 118; KCl, 4·69; $NaHCO_3$, 25; KH_2PO_4, 1·08; $CaCl_2$, 2·52; $MgSO_4 . 7H_2O$, 1·05; dextrose, 5·55; EDTA, 0·026. The solution was bubbled with 95% O_2, 5% CO_2 to give a pH of 7·3–7·4.

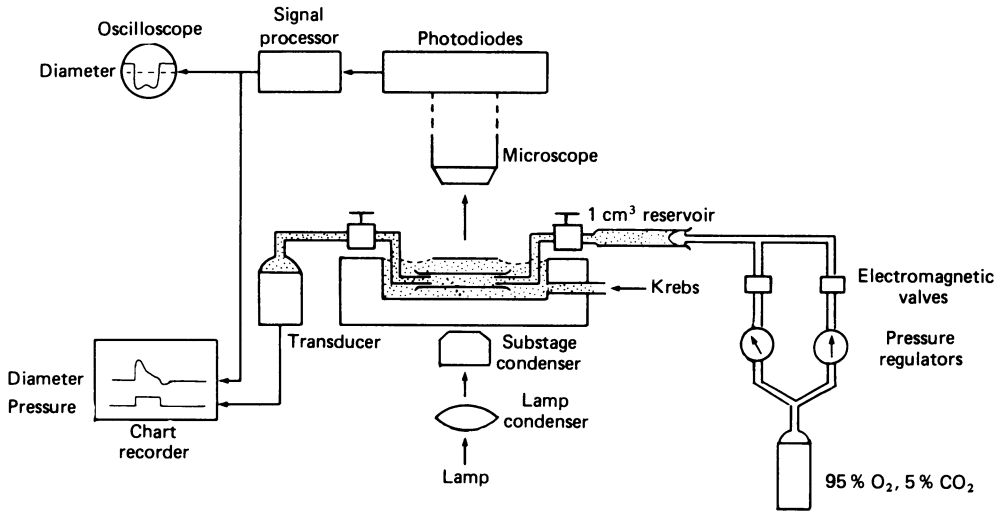

Fig. 1. Schematic illustration of the experimental apparatus. The Perspex organ bath is shown in longitudinal section with the artery being in the centre of the bath. Stippling has been used to show those parts of the apparatus which were filled with Krebs solution. The ties used to attach the artery to the cannulae are not shown.

Changes in external diameter were recorded at × 10 magnification using a linear array of self-scanning photodiodes (Reticon RL1024G) mounted at right angles to the long axis of the artery. A Wild M5 stereomicroscope was used with the photodiode array replacing the 35 mm film in the camera attachment. The 1024 photodiodes were scanned every 10 or 20 ms and the resulting video signal was processed using circuitry similar to that described by Sakaguchi, Ohhashi & Azuma (1979). Output of the signal processor was monitored on an oscilloscope and recorded, along with the pressure, on the chart of a Rikadenki B-24 pen recorder (pen response time of 0·5 s full scale). The voltage output of the signal processor was stable and linearly related to the external diameter. Resolving power of the image sensor is, in principle, 2·5 μm at × 10 magnification of the diameter as the 1024 diodes are on centres of 25 μm. The chart recordings of the diameter were read to the nearest 5 μm. The artery was illuminated from underneath the bath with an Olympus LSE illuminator and the meniscus of the bath solution was removed by placing a cover-slip over the top of the bath.

The wall cross-sectional area of the artery, which was needed to calculate the circumferential wall stresses, was obtained from measurements of the external diameters of the artery and a silicone cast of its lumen. Details of the method used are given elsewhere (Speden, 1975).

All values are given as means ± S.E. of means.

RESULTS

Active reactions to pressure jumps of different magnitude

The blood pressure in the ear artery of conscious rabbits was found to be 94/66 mmHg (mean systolic/mean diastolic) in earlier experiments with the upper limit for effective constriction of the isolated artery being 120 mmHg (Speden & Ryan, 1982). The base-line transmural pressure was therefore set at 60 mmHg and

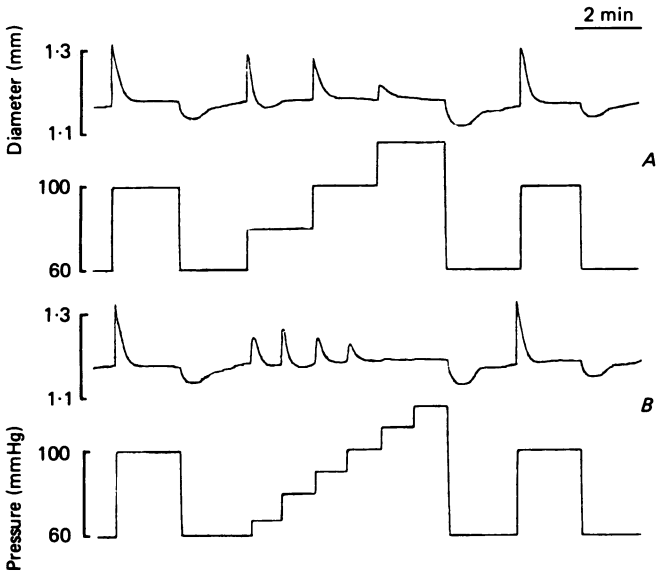

Fig. 2. Reactions of a spontaneously active ear artery to transmural pressure jumps of different magnitude. These recordings of external diameter were obtained 315–350 min after the artery was excised, with the time between *A* and *B* being 12 min. Other recordings from the same artery are presented in Fig. 3. The external diameter of the relaxed artery was 1·40 mm at 60 mmHg.

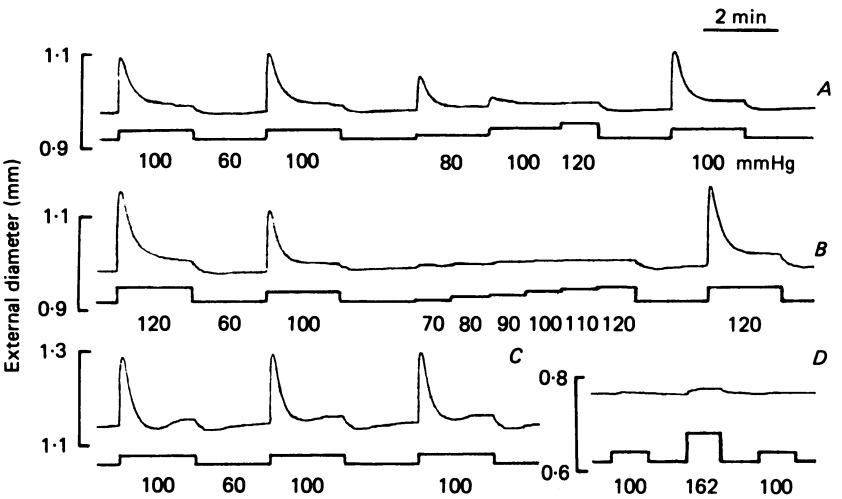

Fig. 3. Effect of constriction on active reactions to transmural pressure jumps of different magnitude. The lower recording in each panel is the transmural pressure and has been redrawn on a reduced scale from the actual pressure recordings (see Fig. 2) with the underlying numbers being the recorded pressure. The spontaneously active artery (Fig. 2) was constricted further using noradrenaline in bath concentrations of 118 nM (*A* and *B*), 59 nM (*C*) and 29·6 μM (*D*). By the time record *C* was obtained, spontaneous activity had declined and noradrenaline was used to reduce the external diameter from 1·32 mm to a diameter comparable to that recorded earlier (Fig. 2*A*). The time after excision of the artery, at the start of the recordings, was 473 min (*A*), 496 min (*B*), 620 min (*C*) and 636 min (*D*).

the maximum jump in pressure was restricted to 60 mmHg. The recordings shown in Figs. 2 and 3, which are from the same experiment, illustrate the major characteristics of the reaction to pressure jumps. Jumping the pressure from 60 to 100 mmHg dilated the constricted artery, but this dilatation was largely or completely overcome by compensatory constriction within 1–2 min (Fig. 2*A*). Restoring the pressure to 60 mmHg initiated a transient constriction which lasted 1–2 min. This sequence of transient diameter changes was reproducible. The transient dilatation was influenced by the size of the pressure jump, the pressure from which the jump was made and the degree of constriction of the artery. Jumps of 10 mmHg produced small transient dilatations which decreased with increasing pressure until no dilatation occurred (Fig. 2*B*). Larger jumps of 20 mmHg caused more dilatation which also decreased as the pressure was raised (Fig. 2*A*). All transient changes in external diameter were reduced and then abolished as the constriction was increased, with those initiated by the smallest pressure jumps being the most easily suppressed (Fig. 3). No transient diameter changes were seen when the arteries were maximally constricted even when the pressure was jumped from 60 to 160 mmHg (Fig. 3*D*). Such maximally constricted arteries were resistant to distension. These effects of constriction on the reaction to distension were reversible and repeatable when constriction was less than maximal. The reactions shown in Fig. 3*C* were obtained 305 min after those in Fig. 2*A*. The only changes were a slowing in the onset of the compensatory constriction which was less well maintained; there was some relaxation after the initial compensatory constriction.

Effect of vasoconstriction on pressure jumps of the same magnitude

A more detailed study of the effects of vasoconstriction was carried out using jumps of 40 mmHg from a pressure of 60 mmHg. Transient changes in external diameter following alterations in pressure were most marked when constriction was less than 50 % of maximal constriction (Figs. 2 and 4). Under these conditions, any transient over-compensation by the constriction elicited by distension was most pronounced as was the transient constriction produced by returning the pressure to 60 mmHg (Fig. 4*A*). Transient over-compensation was more clearly seen when the duration of the pressure jump and the interval between pressure jumps was doubled (Fig. 4*D*). With other arteries there was little or no transient over-compensation, especially at the start of an experiment (Figs. 2 and 3). The characteristics of these transient changes in diameter do not appear to depend upon the way the artery was activated. The constriction shown in Fig. 4*A* was spontaneous, whereas in Fig. 4*E* it was produced by noradrenaline as the spontaneous activity had disappeared at this late stage of the experiment. The similarity between these two recordings further demonstrates the long term reproducibility of the active reactions to pressure changes as the time between the two recordings was 386 min.

Increasing the constriction with noradrenaline suppressed both over-compensation in the reaction to distension and the subsequent transient constriction following reversal of the pressure jump (Fig. 4*B*) before reducing the distension produced by the pressure jump (Fig. 4*C*). Counteraction of the dilatation was least when this artery was moderately constricted (Fig. 4*B*), but this was not a consistent feature with all arteries (Fig. 5*A*). The reaction against distension was able to overcome not less than

68% of the dilatation in 2 min with the average being 90±2% for constrictions varying from 15 to 80% of the maximal constriction. The counteraction was sometimes 100% (Figs. 2*B* and 4*A*) or a little more (Figs. 4*D* and 5*A*). These observations may underestimate the full counteraction as the duration of the pressure jump was 2 min, apart from three instances when it was doubled. These latter experiments indicated that some slow additional constriction may occur after 2 min of raised pressure (Fig. 4*D*).

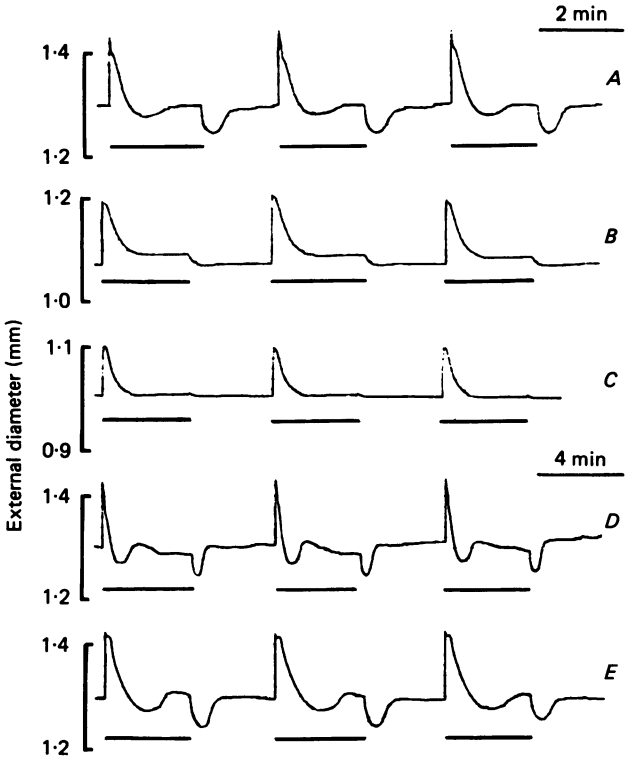

Fig. 4. Effect of constriction on active reactions to transmural pressure jumps of the same magnitude. The pressure was kept at 60 mmHg except where indicated by the underlining when the pressure was 100 mmHg. Constriction was either spontaneous (*A* and *D*), produced by 59 nM-noradrenaline (*E*) or was due to a combination of inherent activity and noradrenaline in bath concentrations of 59 nM (*B*) or 355 nM (*C*). The time after excision of the artery was, at the start of the recordings, 223 min (*A*), 247 min (*B*), 281 min (*C*), 318 min (*D*) and 609 min (*E*). The relaxed diameter of the artery was 1·485 mm which was reduced to 0·82 mm by 29·6 μM-noradrenaline. The constrictions, as a percentage of the maximal constriction, were 28% (*A*), 62% (*B*), 72% (*C*), 26% (*D*) and 29% (*E*).

An estimate of the contractile performance of the muscle during these active reactions to pressure changes can be obtained by subtracting the passive circumferential wall stress (force/wall cross-sectional area) from the total circumferential wall stress. The difference gives an indication of the force imposed upon the muscle (Speden, 1975; Speden & Ryan, 1982). These subtractions have been done for the active reactions shown in Figs. 4*A*, *C* and are presented in Fig. 6. The stress on the

muscle is influenced not only by the transmural pressure but also by the dimensions of the artery; it first increases and then decreases as the diameter decreases when the transmural pressure is constant. The maximum stress on the muscle occurred at 35 ± 4 and 19 ± 2% of the maximal constriction at 60 and 100 mmHg respectively. At 100 mmHg, the maximum stress on the muscle was 67 ± 1% of the maximum

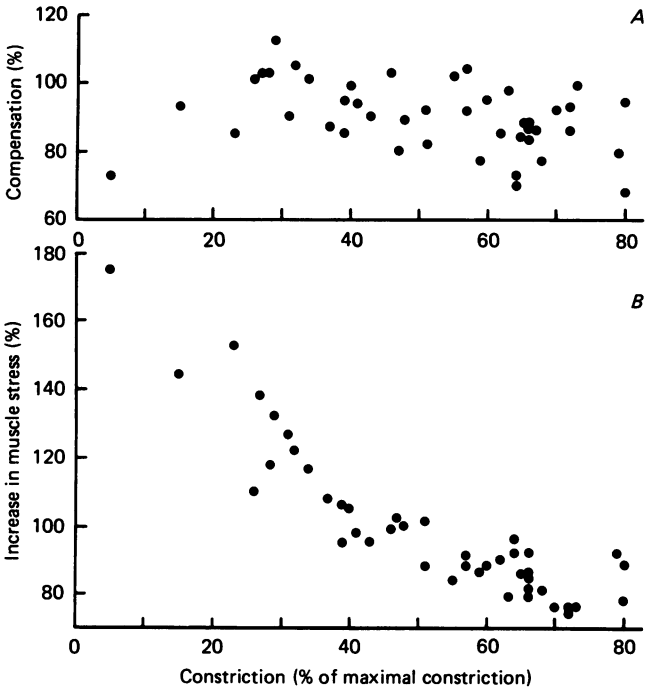

Fig. 5. Evaluation of the compensatory constriction against the distension produced by jumping the transmural pressure from 60 to 100 mmHg. Each point is the mean of not less than three compensatory constrictions (the average was five) recorded during the same activation of an artery. Constriction of the eight arteries against a pressure of 60 mmHg was varied by using different bath concentrations of noradrenaline and has been expressed as a percentage of the maximal constriction (29·6 μM-noradrenaline) at that pressure. Maximal constriction reduced the external diameter by 48 ± 2%. *A*, percentage of the dilatation overcome by the compensatory constriction. *B*, percentage increase in stress on muscle 2 min after raising the pressure. Details of the method used to calculate the stress (force/wall cross-sectional area) are given in the text, with the results of one set of calculations being shown in Fig. 6. For clarity of presentation, the three reactions which markedly enhanced constriction when constriction was less than 15% of maximal have been omitted.

circumferential wall stress at that diameter; at 60 mmHg it was 62 ± 1%. The sequence of arrows on the right (Fig. 6) shows the changes in stress on the muscle when the artery was least constricted (Fig. 4*A*). Jumping the pressure from 60 to 100 mmHg more than doubled the calculated stress on the muscle which was further increased by the subsequent compensatory constriction. The same jump in pressure also more than doubled the stress on the muscle when the artery was more constricted (Fig. 4*C*), but the stress was less and was further reduced by the compensatory

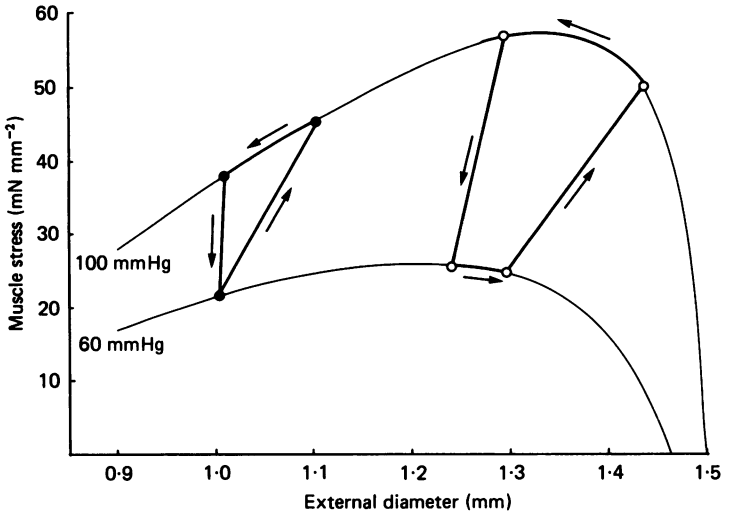

Fig. 6. Calculated changes in stress on the arterial muscle during the reactions to changes in pressure shown in Fig. 4*A* (○) and Fig. 4*C* (●). The stresses were highest when the artery was slightly constricted and increased during the compensatory constriction initiated by distension.

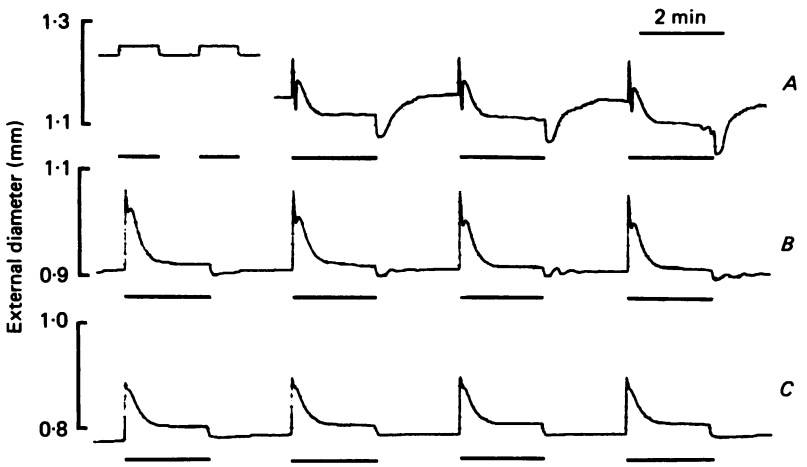

Fig. 7. Fast reactions to distension. The transmural pressure was jumped from 60 to 100 mmHg (underlined). This artery reacted to distension by rapidly constricting and then partially relaxing before constricting more slowly towards a steady diameter (*A*). Increasing the spontaneous constriction (*A*) with 30 nM (*B*) or 59 nM (*C*) noradrenaline reduced (*B*), and then, with more constriction (*C*), largely suppressed the fast reactions to distension. *A* shows one of the rare occasions where an increase in pressure enhanced constriction. No transient changes in diameter were seen when the artery was relaxed (upper left panel). The constrictions were 14·8% (*A*), 59% (*B*) and 80% (*C*) of the maximal constriction at 60 mmHg. The recordings were obtained 239–305 min after the artery was excised.

constriction (Fig. 6; sequence of arrows on the left). The percentage increase in stress on the muscle is summarized in Fig. 5*B*. The high compensation shown in Fig. 5*A* was achieved against increases in stress, 2 min after raising the pressure, which varied from not less than 74 % up to about 140 % when the arteries were least constricted. When compensation is complete, the active force must be equal to the stress on the muscle.

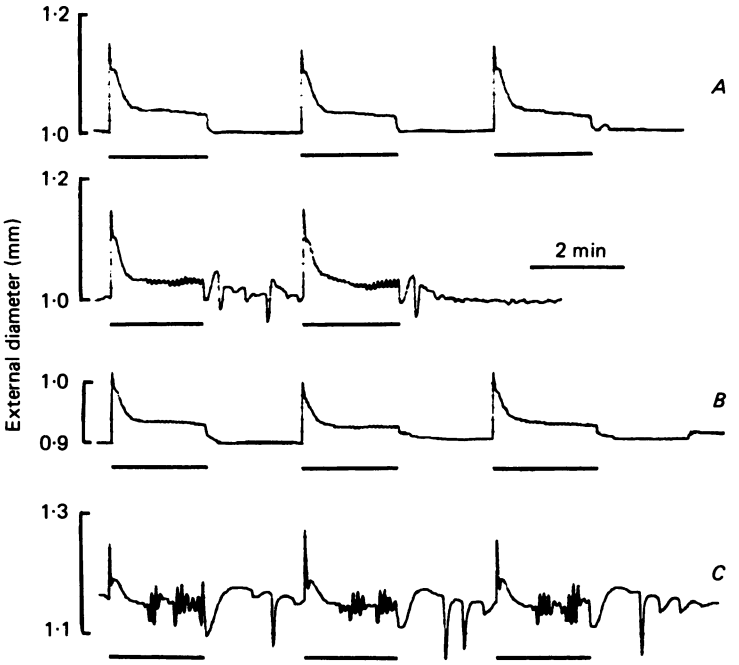

Fig. 8. Unstable constrictions. Repeated jumps in pressure from 60 to 100 mmHg (underlined) predisposed towards unstable constriction (*A*). Increasing constriction suppressed the instability (*B*) while decreasing constriction enhanced it (*C*). All constrictions were produced with noradrenaline in bath concentrations of 43 nM (*A*), 59 nM (*B*) and 7·4 nM (*C*). The constrictions were 47 % (*A*), 59 % (*B*) and 28 % (*C*) of the maximal constriction from a relaxed external diameter of 1·37 mm. The time after excision of the artery was, at the start of the recordings, 186 min (*A*), 308 min (*B*) and 382 min (*C*).

Other active reactions to pressure jumps

Most arteries (70 %) reacted to distension by rapidly constricting and then abruptly ceasing to do so (Fig. 4*A*) or dilating (Figs. 7*A* and *B*, and 8*C*) before completing the compensatory constriction more slowly. These rapid changes in diameter were suppressed by increasing the constriction of the arteries (Figs. 4, 7 and 8). Fig. 7*A* also shows one of the rare reactions where a jump in pressure markedly enhanced constriction. Such marked enhancement was seen only when constriction was slight (less than 15 % of maximal) and then only in three of five such slightly constricted arteries. No transient changes in diameter were observed when the arteries were relaxed (Fig. 7*A*, left panel).

Jumps in pressure from 60 to 100 mmHg also made the constriction become unstable in half of the preparations. A little instability can be seen in Fig. 7*B*

following reversal of the pressure jump. Fig. 8*A*, which is a continuous record, shows the development of more marked instability. No instability was seen during the first two jumps in pressure, but with the third there was a little instability when the pressure jump was ended. With the fourth and fifth pressure jumps, high frequency instability was present at 100 mmHg and there was marked low frequency instability at 60 mmHg which faded out when the pressure was kept at 60 mmHg. Increasing constriction of the artery suppressed the instability (Fig. 8*B*), whereas decreasing constriction enhanced it (Fig. 8*C*). Instability of the constriction did not affect the ability of the arteries to counteract distension (Fig. 8*C*). This artery at no time became spontaneously active.

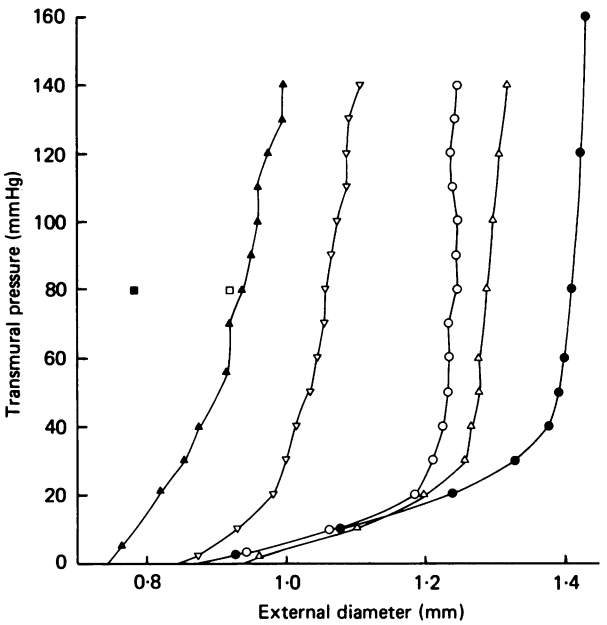

Fig. 9. Distensibility of a perfused ear artery before and during blockade of the sympathetic innervation. The passive curve (●), the distensibility of the artery in the presence of intraluminal adrenaline (○, 68 nM), and the constriction against a pressure of 80 mmHg produced by 4 Hz (□) and 16 Hz (■) electrical field stimulation (0·5 ms square pulses of maximal voltage for 75 s) were obtained before exposure to guanethidine (3·4 μM). This concentration of guanethidine both abolished the response to electrical field stimulation and made the artery constrict (△). Additional constriction of the guanethidine-treated artery was produced with adrenaline in perfusate concentrations of 5·5 nM (▽) and 11 nM (▲). The distensibility curves were obtained by dropping the presssure from 80 mmHg and then increasing it in steps of 10 or 20 mmHg. Sufficient time (2–3 min) was allowed for the diameter to reach a steady state before the pressure was further increased.

The role of the sympathetic innervation

Fig. 9 shows the distensibility of a perfused ear artery before and during exposure to guanethidine. The diameters are the steady-state diameters achieved after each increase in the transmural pressure. Guanethidine not only abolished the constriction to electrical field stimulation but also made the artery constrict. The resistance of the guanethidine-constricted artery to distension was high and similar to that of the

adrenaline-constricted artery (the second and third curves from the right). The guanethidine-treated artery was more distensible when constriction was increased with adrenaline, but it was still very resistant to distension between the pressures of 60 and 100 mmHg. Active, perfused ear arteries also showed a high resistance to distension after constriction by electrical field stimulation was abolished or greatly reduced (> 90 % reduction) by bethanidine (2 μM) or phentolamine (2 or 5 μM). This was so irrespective of whether the constriction was produced by adrenaline or noradrenaline. These observations made using a different method are consistent with the results of the pressure jump experiments. The perfused arteries treated with sympatholytic drugs did dilate transiently when the transmural pressure was raised, but the method used to detect diameter changes (microscopic observation) was not adequate for quantitative evaluation of the compensatory constriction. The small transient dilatations produced by the 10 mmHg increments in pressure, at pressures above 30 mmHg, lasted for less than 1 min.

DISCUSSION

The outstanding feature of the reaction of the active ear artery to changes in transmural pressure was its ability to minimize any resulting change in diameter. The steady-state diameter achieved is probably not dependent upon the sympathetic innervation as it was not affected by sympatholytic drugs. However, the effects of these drugs on the compensatory constriction initiated by distension has yet to be examined in detail, so that the possibility of a transient sympathetic nerve discharge still exists. The variations in the shape of the compensatory constriction indicate that a number of factors may have been contributing to the compensatory constriction. The fast spike-like response (Fig. 7) seen with most arteries could reflect transient activation of the sympathetic nerves. It could also arise non-neuronally from a burst of muscle action potentials like that seen when the rat portal vein was stretched (Johansson & Mellander 1975). However, muscle cells of the rabbit ear artery have high and stable membrane potentials (Speden, 1967), action potentials have not been observed and noradrenaline may contract the muscle with (Trapani, Matsuki, Abel & Hermsmeyer, 1981) or without sustained depolarization (Droogmans, Raeymaekers & Casteels, 1977). Instability of constriction need not necessarily arise from spontaneous fluctuations in membrane potential (Itoh, Kuriyama & Suzuki, 1983). Irrespective of the nature and number of contributing factors it is clear that a transmural pressure-sensitive mechanism which acted to minimize diameter changes had over-riding precedence.

There are undoubtedly many reasons why it has been difficult to demonstrate active reactions to distension using excised blood vessels. One of these reasons is the use of steady-state measurements of diameter instead of transient changes in diameter. There are a number of reports that excised and pressurized arteries (Hinke & Wilson, 1962; Speden, 1973, 1975, 1984) and arterioles (Duling, Gore, Dacey & Damon, 1981; Dacey & Duling, 1982) are very resistant to distension when submaximally activated. The recordings of transient changes in diameter provide strong support for the suggestion (Speden, 1973, 1975; Dacey & Duling, 1982) that this high resistance to distension is due to the presence of a stretch-sensitive myogenic

reaction. Another reason is that active reactions to stretch may be a property not simply of the vascular smooth muscle but of the wall of pressurized and longitudinally tethered blood vessels. Unlike strips of arteries (see Introduction), the reactions of the pressurized ear artery to stretch were prompt, sustained and reproducible at short time intervals. It may be essential to reproduce the *in vivo* loading conditions in order to obtain adequate reactions of the muscle to stretch. The contraction of the muscle cells in the wall of pressurized and tethered blood vessels is neither isometric nor isotonic (Fig. 6) and the wall is under both circumferential and axial stress. Transmission of force between contractile elements of minute cells embedded in a strained meshwork of connective tissue may play an important role in active reactions of vascular smooth muscle to stretch. A third reason is that maximal contracture of the muscle may need to be avoided as this impaired the active reactions to distension (Speden, 1984). It need not be necessary to perfuse the blood vessels as the steady-state reactions of perfused and unperfused ear arteries to distension were similar.

The steady-state distensibility characteristics of the active ear artery are very similar to those of active arterioles (12–112 μm in diameter) excised from a number of different vascular beds (Duling *et al.* 1981; Dacey & Duling, 1982). It is not clear why increases in transmural pressure rarely enhanced constriction of these isolated blood vessels in contrast to arterioles *in vivo* (Bouskela & Wiederhielm, 1979; Borgström, Grände & Lindbom, 1981; Burrows & Johnson, 1981; Morff & Granger, 1982). This difference between blood vessels *in vivo* and *in vitro* may, in part, reflect differences in activation of the muscle or in stress on the muscle. Increases in transmural pressure may enhance constriction of excised blood vessels, but only when both the activation (chemical or spontaneous) and the transmural pressure are low (Speden, 1973, 1975; Duling *et al.* 1981). Other possible explanations such as poorer control of the chemical environment of blood vessels *in vivo* (Johnson, 1980) or the presence of some essential blood component, not included in the physiological salt solutions, also need to be considered. While the reactions to change in transmural pressure seen with excised blood vessels may contribute to autoregulation of blood flow they cannot fully explain the phenomenon. Some additional local mechanism which enhances constriction of resistance vessels as the perfusion pressure rises appears to be operative *in vivo*.

The Bayliss phenomenon of enhanced constriction of blood vessels, following increases in transmural pressure, predisposes towards instability of the blood pressure – '...every rise in pressure would automatically cause a further rise, and every fall, from whatever cause, a further fall in blood pressure...' (Bayliss, 1902). Bayliss suggested that this inherent instability was kept under control by the regulatory centres of the central nervous system. The present observations indicate that the alterative of a transmural pressure-sensitive negative feed-back reaction, located in the blood vessel wall, should not be dismissed. Such a feed-back mechanism would be expected to place less demands on the central nervous system as it predisposes to stability by making blood vessel diameter relatively insensitive to fluctuations in blood pressure. The more restricted role of the sympathetic innervation would then be to help reset the blood vessel diameters to new but still transmural pressure-insensitive diameters.

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