Short communications

Escape from tension induced by noradrenaline or electrical stimulation in isolated mesenteric arteries

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Isolated mesenteric arteries, studied under 25–30 mg resting tension, responded to prolonged noradrenaline or electrical stimulation with a 50–500 mg increase in tension from which they subsequently escaped towards resting tension levels.

The mesenteric vascular bed has the ability to escape from vasoconstriction induced by continued sympathetic nerve stimulation or catecholamine infusion. Several mechanisms have been proposed for this so-called 'autoregulatory escape' (Folkow, Lewis, Lundgren, Mellander & Wallentin, 1964a). These include a parallel-circuit blood flow redistribution at the mucosal-submucosal level (Folkow *et al.* 1964a; Folkow, Lewis, Lundgren, Mellander & Wallentin, 1964b), a series-coupled vasoconstriction and vasodilatation (Richardson & Johnson, 1969), metabolic and intestinal motility effects (Baker & Mendel, 1967), and other alternatives (Shanbour & Jacobson, 1971). Additionally, and of particular interest, is the hypothesis of Richardson & Johnson (1969) and Ross (1971) that the escape may be an inherent property of specific vascular elements which initially constrict and then relax. To further investigate this possibility, in this study the contractor responses of mesenteric arteries to noradrenaline and electrical stimulation were studied.

Methods.—Sections of arteries, 2–3 mm long, were removed from nine anaesthetized cats and placed in a Krebs-bicarbonate solution (Su & Bevan, 1970) which contained 0·2 mg/ml ascorbic acid and was equilibrated with 95% O_2 and 5% CO_2. Vessels studied included the superior mesenteric artery and its distribution arteries (1–2 mm outside diameter), intestinal arcuate arteries (0·6–1 mm outside diameter), and several femoral arteries (1–1·5 mm outside diameter). A vessel ring was mounted between a stationary stainless steel rod and a Statham Model UC 2 isometric strain gauge (Su & Bevan, 1970) with tension changes recorded on a Grass Model 7 polygraph. The mounted vessel was superfused with the Krebs-bicarbonate solution maintained at 38°C. The solution dripped at a constant rate of 10 ml/minute. Noradrenaline (Levophed, Winthrop Laboratories) was administered in Krebs solution. For electrical stimulation, platinum wire electrodes, 2 mm long, were positioned longitudinally along either side of the vessel ring, leaving a narrow gap between the tissue and the electrode. This gap remained filled with Krebs superfusate to provide electrical conductivity.

Results. — Mesenteric and femoral vessels, mounted with a 25–300 mg resting tension, developed a 50–500 mg increase in tension when noradrenaline was added to the superfusate (Fig. 1). The degree of tension development was directly related to the initial resting tension placed on the vessel (in the range 25–300 mg), and to the concentration of noradrenaline in the superfusate (0·01–1·0 μg/ml); 0·5 μg/ml noradrenaline gave a substantial and consistent tension increase at 25–300 mg resting tension and was used as the test stimulus for most vessels.

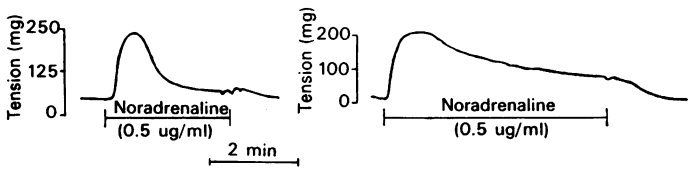

FIG. 1. Response of two cat mesenteric arcuate artery segments when 0·5 μg/ml noradrenaline was added to the Krebs superfusate. Both vessels were 2 mm in length, 650 μm outside diameter, and were taken from the same animal. Artery at left was mounted under 65 mg resting tension; artery at right under 25 mg tension.

The latency of the response was 5–10 s, and, after reaching a maximum, tension in mesenteric, but not femoral, arteries decreased during continued noradrenaline superfusion, often returning to the control tension within 2–3 minutes. None of the femoral artery segments relaxed; however, all mesenteric vessels demonstrated varying degrees of relaxation (Fig. 1). This variability did not appear to be related to vessel diameter or to the initial or developed tension over the range studied. Additionally, the relaxation phase of the tension response was often accompanied by rhythmical oscillations in tension at 1–3/min, ±25–300 mg tension. When noradrenaline was removed from the Krebs superfusate, tension returned to the control level.

Transmural electrical stimulation of mesenteric arteries, with unipolar square-wave pulses at 5–16 Hz:0·04 ms:10–30 V, produced a rapid increase in tension of 50–500 mg, which was directly related to the intensity of stimulation. Given a train of pulses at 5 Hz:0·04 ms:20 V, vessels developed 25–50 mg tension, whereas stimulation at 15 Hz:0·04 ms:30 V increased tension 200–350 mg. The latency of the response was 1–3 s, and after a maximum increase was reached, tension declined during continued electrical stimulation, although the degree and rate of decline was never as great nor as rapid as that observed with noradrenaline superfusion.

Oscillations in tension were observed only in mesenteric artery segments, and only when vessel tension was increased by noradrenaline superfusion, not during electrical stimulation, nor when an equivalent amount of tension was put on the vessels by passive stretching.

Discussion. — Since the observations described were made in isolated vessels, it must be concluded that the inability of mensenteric vessels to remain contracted under the influence of noradrenaline or electrical stimulation depends on local events.

A similar inability to remain contracted occurs in individual, but not isolated, vessels (Duling, Berne & Born, 1968; Richardson & Johnson, 1970), and vascular readjustments during mesenteric escape occur in small resistance vessels of the precapillary section (Folkow *et al.*, 1964a; Johnson, 1968; Johnson & Hanson, 1962; Johnson & Wayland, 1967). Whilst the present work does not eliminate the possibility that blood flow redistributions accompany, or may in part be responsible for loss of tension in the intact animal, there seems to be no need to postulate a redistribution mechanism at the precapillary level to account for the escape from the response. Although small resistance vessels could not be studied, because of a vessel size limitation of 500 μm with this technique, it is significant that the larger mesenteric vessels responded to noradrenaline and electrical stimulation with an escape pattern which closely mimicks that reported in the intact animal (Folkow *et al.*, 1964a; Ross, 1971). The relative contribution of these large vessels as opposed to smaller resistance vessels in the escape mechanism is unknown.

While the loss of tension in the isolated mesenteric vessels was qualitatively consistent, the pattern was quite variable quantitatively, and no loss of tension was demonstrated in femoral arteries. This variability may be due to peculiarities of the site and level of the arterial tree from which vessels were taken, or to surgical trauma to the vessel upon dissection; it may also reflect an inherent characteristic of the vascular smooth muscle itself. Tension changes and contraction in vascular smooth muscle involve the movement of calcium ions to and from the contractor mechanism (Somlyo & Somlyo, 1968). Thus the escape from induced tension as well as its variability may be related to the availability of calcium to the contractile proteins. Also, the oscillations in tension appear to involve a noradrenaline-induced movement of calcium, for no oscillations were observed when vessel tension was comparably increased by stretch or by electrical stimulation.

Undoubtedly, in the intact animal there are numerous neuronal and humoral controls which influence mesenteric vascular escape, but it seems that the phenomenon involves a mechanism inherent in the vascular smooth muscle itself.

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REFERENCES

BAKER, R. & MENDEL, D. (1967). Some observations on autoregulatory escape in cat intestine. *J. Physiol., Lond.*, **190**, 229–240.

DULING, B. R., BERNE, R. M. & BORN, G. V. R. (1968). Microiontophoretic application of vasoactive agents to the microcirculation of the hamster cheek pouch. *Microvasc. Res.*, **1**, 158–173.

FOLKOW, B., LEWIS, D. H., LUNDGREN, O., MELLANDER, S. & WALLENTIN, I. (1964a). The effect of graded vasconstrictor fibre stimulation on the intestinal resistance and capacitance vessels. *Acta physiol. scand.*, **61**, 445–457.

FOLKOW, B., LEWIS, D. H., LUNDGREN, O., MELLANDER, S. & WALLENTIN, I. (1964b). The effect of the sympathetic vasoconstrictor fibres on the distribution of capillary blood flow in the intestine. *Acta physiol. scand.*, **61**, 458–466.

JOHNSON, P. C. (1968). Autoregulatory responses of cat mesenteric arterioles measured *in vivo*. *Circulation Res.*, **22**, 199–212.

JOHNSON, P. C. & HANSON, K. M. (1962). Effect of arterial pressure on arterial and venous resistance of intestine. *J. appl. Physiol.*, **17**, 503–508.

JOHNSON, P. C. & WAYLAND, H. (1967). Regulation of blood flow in single capillaries. *Am. J. Physiol.*, **212**, 1405–1415.

RICHARDSON, D. R. & JOHNSON, P. C. (1969). Comparison of autoregulatory escape and autoregulation in the intestinal vascular bed. *Am. J. Physiol.*, **217**, 586–590.

RICHARDSON, D. R. & JOHNSON, P. C. (1970). Changes in mesenteric capillary flow during norepinephrine infusion. *Am. J. Physiol.*, **219**, 1317–1323.

ROSS, G. (1971). The escape of mesenteric vessels from adrenergic and non-adrenergic vasoconstriction. *Am. J. Physiol.*, in the Press.

SHANBOUR, L. L. & JACOBSON, E. D. (1971). Autoregulatory escape in the gut. *Gastroenterology*, **60**, 145–148.

SOMLYO, A. P. & SOMLYO, A. V. (1968). Vascular smooth muscle. Normal structure, pathology, biochemistry and biophysics. *Pharmac. Rev.*, **20**, 197–272.

SU, C. & BEVAN, J. (1970). The release of H^3-norepinephrine in arterial strips studied by the technique of superfusion and transmural stimulation. *J. Pharmac. exp. Ther.*, **172**, 62–68.

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