

DIRECT OBSERVATIONS OF EFFECTS OF BARORECEPTOR STIMULATION ON MESENTERIC CIRCULATION OF THE RAT

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SUMMARY

1. In anaesthetized rats, supramaximal baroreceptor stimulation by carotid sinus inflation evoked a reflex fall in systemic arterial pressure and an increase in gross mesenteric vascular conductance, but no significant change in gross mesenteric blood flow.

2. Principal arteries (80–350 μm internal diameter (i.d.)) which supply the intestine and mesentery, small arteries (30–40 μm) and some terminal arterioles (18–30 μm) of the mesentery showed a diameter increase beginning with the fall in arterial pressure, but remaining terminal arterioles and precapillary arterioles (10–18 μm) showed a diameter increase beginning when arterial pressure neared its lowest level.

3. Application of phentolamine to the mesentery abolished diameter increases that began with the reflex fall in arterial pressure. Thereafter, 50% of small arteries and terminal and precapillary arterioles showed diameter increases that began when the fall in arterial pressure neared its zenith.

4. It is proposed that the proximal arterial vessels, which are known to be sympathetically innervated, predominantly showed dilatation mediated by reflex inhibition of sympathetic tone, while more distal arterioles showed myogenic dilatation secondary to the fall in systemic arterial pressure.

5. Small veins (30–50 μm) of the mesentery and principal veins (100–560 μm) that drain mesentery and intestine also showed a diameter increase beginning with the reflex fall in systemic arterial pressure. Since they are known to have a sympathetic noradrenergic supply, and in the absence of changes in mesenteric blood flow likely to cause passive changes in venous diameter, they apparently showed dilatation due to inhibition of sympathetic tone.

6. The above responses are all compatible with, and so suggest underlying mechanisms for, changes in blood flow, regional blood volume, and capillary filtration evoked by baroreceptor stimulation in studies of whole mesenteric circulation, i.e. intestine as well as mesentery.

INTRODUCTION

In previous studies on the influence of the carotid baroreceptor reflex on the mesenteric circulation, the behaviour of the consecutive sections of the micro-circulation has been deduced by indirect means, that is, changes in vascular

resistance have been used to indicate the behaviour of the arterioles and changes in vascular capacity and the behaviour of venous vessels. The results of these studies have been inconclusive. Thus, Resnicoff, Harris, Hempsey & Schwartz (1969) found that during electrical stimulation of the carotid sinus nerve, which in fact may activate chemoreceptor as well as baroreceptor afferent fibres, blood flow in naturally perfused mesenteric circulation fell in parallel with the evoked reflex decrease in arterial pressure, leading to the suggestion that the mesenteric arteriolar resistance vessels responded passively to the change in perfusion pressure rather than to the reflex decrease in sympathetic tone. By contrast, others found that blood flow in naturally perfused mesenteric circulation remained virtually constant during sinus nerve stimulation, for the decrease in mesenteric vascular resistance matched the evoked fall in systemic arterial pressure (Vatner, Franklin, Van Citters & Braunwald, 1971). As Kircheim (1976) pointed out, the latter findings could be ascribed either to an active myogenic response of the arterioles to the change in perfusion pressure which allows perfect autoregulation of blood flow, or to a reflex change in sympathetic tone just sufficient to prevent blood flow from changing with systemic arterial pressure. On the other hand, in experiments in which mesenteric circulation was perfused at constant pressure, baroreceptor stimulation by inflation of the carotid sinus induced a fall in mesenteric vascular resistance and an increase in blood flow, while baroreceptor unloading produced the opposite effects (Oberg, 1964; Brooksby & Donald, 1971), indicating that at least under these circumstances mesenteric arterioles do respond actively to baroreceptor-induced changes in sympathetic activity. Moreover, under these last experimental conditions the capillary filtration coefficient (CFC) increased during baroreceptor stimulation and fell during baroreceptor unloading, which was taken to mean that the distal arterioles that give rise to the capillaries and determine the capillary surface area available for filtration also respond actively to the reflex changes in sympathetic tone (Oberg, 1964).

As far as the behaviour of mesenteric venous vessels is concerned, there is more unanimity. Under conditions of constant-pressure perfusion, carotid sinus inflation produced a substantial increase in mesenteric vascular capacity which was attributed mainly to dilatation of venous vessels caused by inhibition of sympathetic tone, but partly also to their passive relaxation secondary to the rise in intravascular pressure caused by the concomitant arteriolar dilatation (Oberg, 1964). The conclusion that mesenteric venous vessels take an active part in the baroreceptor reflex also accords with the results of Hainsworth & Karim (1976), who found that carotid sinus inflation produced an increase in the vascular capacity of the abdominal circulation, even when the distending pressure in the vessels was kept virtually constant by perfusing the circulation at constant flow. However, even if it is accepted that changes in vascular capacity indicate the behaviour of venous vessels, it is not clear whether the venous vessels concerned are those of the microcirculation within the intestine, or the larger veins which drain the intestine and which cross the tissue of the mesentery.

We have sought to clarify some of the issues raised by the studies discussed above by making direct observations on individual vessels of the mesentery of the small intestine during carotid baroreceptor stimulation. Since a detailed study of the

distribution of the sympathetic noradrenergic nerve supply to the mesenteric circulation has already been made (Furness & Marshall, 1974), we have been able to interpret our findings in this context. Some of our results have been published in brief (Hébert & Marshall, 1984; Marshall & Hébert, 1986).

METHODS

Experiments were performed on Sprague-Dawley rats (225–375 g body weight). Anaesthesia was induced with ether and maintained with sodium pentobarbitone (50 mg kg i.m.); supplementary doses (5–10 mg kg⁻¹) were given via a cannula placed in the jugular vein. After tracheal cannulation, a femoral artery was cannulated to allow arterial pressure to be recorded via a pressure transducer (Bell & Howell); heart rate was derived from the pressure recording via an instantaneous rate-meter (Ormed). In three experiments blood flow was recorded from the anterior mesenteric artery by means of a cuff-type electromagnetic transducer and meter (Carolina Medical Electronics). Zero flow was obtained at intervals during the experiment by occluding the artery distal to the transducer with a pair of small forceps, the tips of which were covered with soft vinyl to avoid damage to the tissue. The transducer was calibrated *in vitro* by constant-flow perfusion. Mesenteric vascular conductance was computed on-line via an electronic divider which divided mesenteric blood flow by arterial pressure.

In all experiments the bifurcation of the right common carotid artery was exposed, and all branches of the internal and external carotid arteries and the internal carotid itself as it entered the skull were ligated (cf. Nosaka & Wang, 1972) whilst viewing under a Zeiss Operating Microscope. A saline-filled cannula was then inserted retrogradely through the lingual artery into the external carotid artery so that its tip lay at the bifurcation. In order to temporarily occlude the carotid artery and so make the carotid sinus 'blind', a cotton thread was looped around the carotid artery below the bifurcation and the two ends were pushed through a 2–3 cm length of soft vinyl tubing; the vinyl tubing could be gently pushed along the threads to the artery and held in position by a clip applied to the distal ends of the thread. The carotid sinus could then be inflated by opening the cannula in the external carotid artery towards a pressure reservoir which had been raised to the desired pressure with O₂, to avoid stimulating carotid chemoreceptors. A pressure transducer connected to a side arm of the pressure system served to register the pressure and acted as a stimulus marker.

With the animal lying on its left side a loop of small intestine was drawn out and arranged for *in vivo* microscopy using techniques and equipment described previously (Hébert & Marshall, 1985). Briefly, the mesentery was arranged over a transparent plate set into the modified stage of a bench microscope. The circulation was viewed via the eyepiece and via a television camera and monitor. The camera was connected to a video recorder which enabled measurements of vessel diameter to be made or checked off-line as well as on-line. Continuous recordings of the diameters of individual vessels were made using a photo-electric device similar to that described by Cardinal & Higgs (1980) which was placed on the television monitor across the relevant vessel, at right angles to its longitudinal axis. The photo-electric device was calibrated for each vessel as described previously (Hébert & Marshall, 1985). The accuracy of these diameter measurements was regularly assessed by playing back video recordings and making direct measurements on the TV monitor whilst the recorder was in the 'freeze frame' mode. The output of the photo-electric cell, together with the other recorded variables was displayed on a pen recorder (Devices M8).

In order to investigate the effects of α -adrenoreceptor blockade on the responses to carotid sinus inflation, the Krebs solution bathing the mesenteric tissue was replaced with one containing phentolamine (10⁻⁶ g ml⁻¹).

RESULTS

Arterial pressure, mesenteric blood flow and vascular conductance

Inflation of the carotid sinus for 15–20 s to 240–250 mmHg evoked the expected reflex fall in arterial pressure; such pressures were found to be supramaximal stimuli. The fall in arterial pressure began within 3–4 s of inflating the sinus and reached its

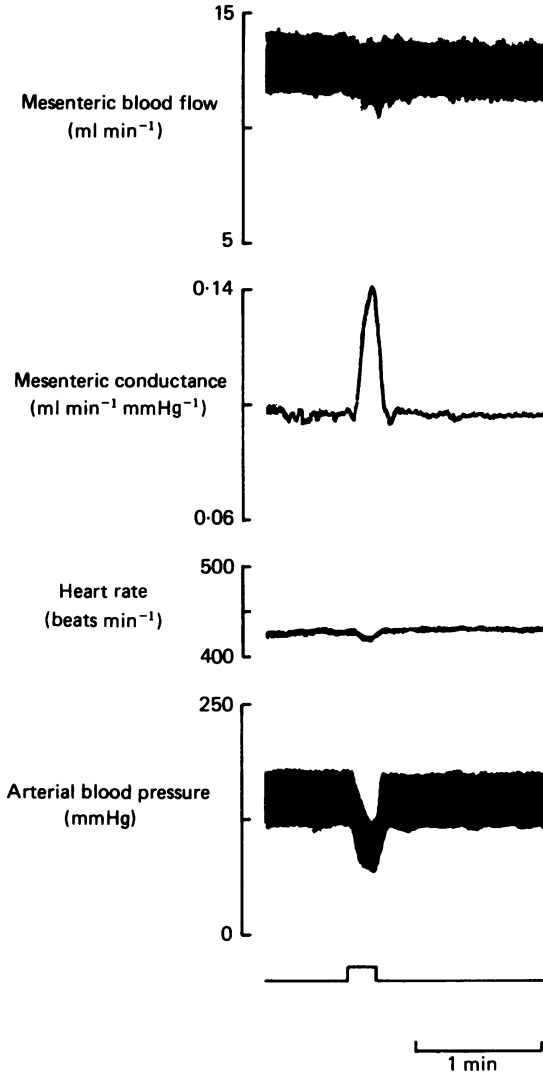


Fig. 1. Gross changes in mesenteric blood flow and vascular conductance produced by carotid baroreceptor stimulation. Traces from above down: blood flow in cranial mesenteric artery, mesenteric vascular conductance, heart rate and arterial pressure. Stimulus marker indicates period of carotid sinus inflation.

lowest level, such that mean arterial pressure was 40–60 mmHg below the control level of 80–120 mmHg, within 10–18 s. There was then a gradual return to the control level so that the whole change was generally completed within 45–60 s. Heart rate usually fell by 10–20 beats min⁻¹. Simultaneously with the fall in arterial pressure, mesenteric vascular conductance increased to reach a peak 20–40% above control levels, while mesenteric blood flow remained more or less constant; any change in flow was always less than 10% of control levels (Fig. 1).

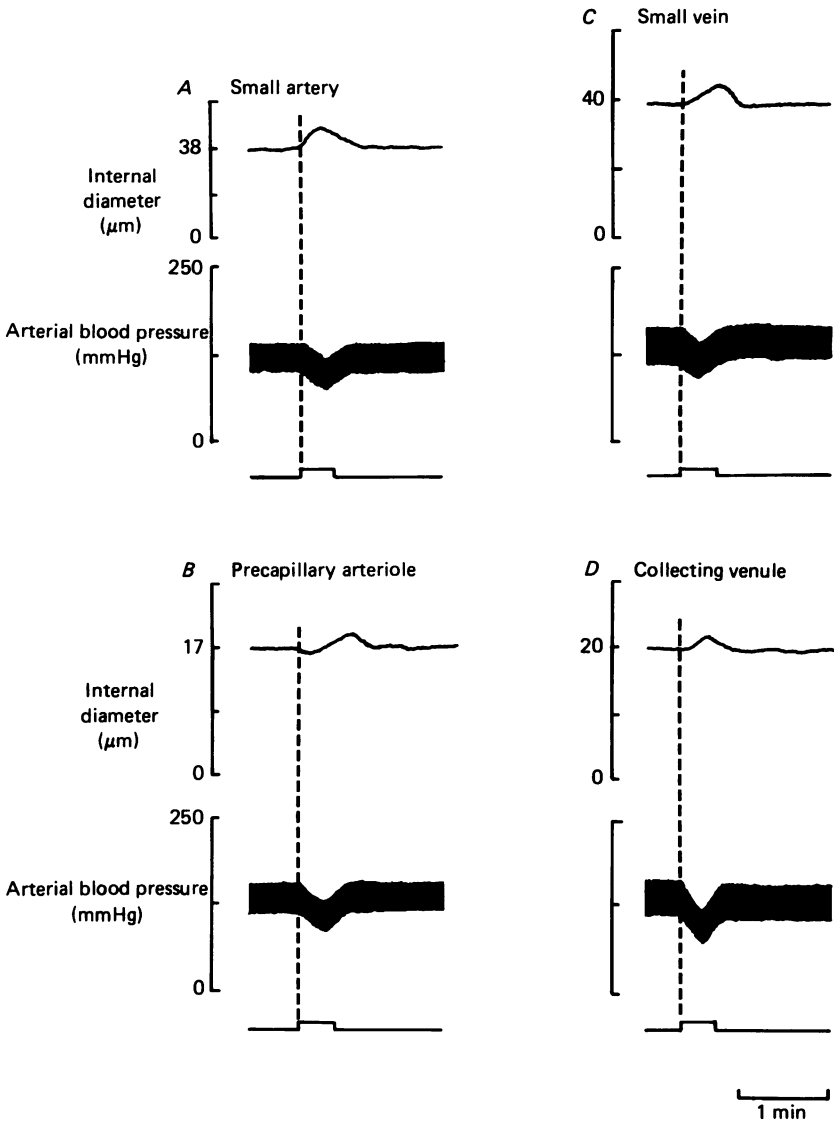


Fig. 2. Representative traces from different animals showing the effects of baroreceptor stimulation upon individual vessels of mesentery. Traces in A-D are vessel diameter, above, and arterial pressure, below. Stimulus markers indicate period of carotid sinus inflation. Vertical lines mark the onset of the fall in arterial pressure.

Responses of individual mesenteric blood vessels

The vessels of the mesentery were classified according to their diameters and relative positions as described previously (Furness & Marshall, 1974; Hébert & Marshall, 1985). Briefly, arteries and veins which cross the mesentery to supply and drain the intestine are referred to as principal arteries (80–350 μm , i.d.) and principal veins (100–560 μm) respectively. The branches of these, which supply the mesentery, are referred to as small arteries (30–40 μm). These branch to form terminal arterioles

TABLE 1. Diameter changes recorded in individual vessels of mesentery in response to carotid baroreceptor stimulation vessel type

Vessel type	<i>N</i>	Control i. d. (μm)	'Early' increase (% change)	<i>n</i>	'Early' decrease (% change)	<i>n</i> ₁	'Late' increase (% change)	<i>n</i> ₂
PA	15	139.8 ± 6.6	7.8 ± 1.8	8	—	—	—	—
SA	29	32.2 ± 5.2	12.03 ± 2.7	19	—	—	—	—
TA	48	21.8 ± 3.1	9.02 ± 1.7	12	8.8 ± 1.8	4	11.6 ± 2.4	10
PCA	48	13.8 ± 2.7	—	—	8.9	2	13.9 ± 2.9	20
CV	33	22.93 ± 4.7	—	—	—	—	13.1 ± 3.3	8
SV	24	37.5 ± 6.3	13.0 ± 3.3	9	8.3	2	16	2
PV	14	200 ± 15.5	7.8 ± 2.4	6	—	—	—	—

Vessel type: PA, principal artery; SA, small artery; TA, terminal arteriole; PCA, precapillary arteriole; CV, collecting venule; SV, small vein; PV, principal vein. *N* indicates total number of each vessel type studied; *n*, *n*₁, *n*₂ indicate number of vessels showing 'early' increase, 'early' decrease and 'late' increase in diameter, respectively. 'Early', beginning simultaneously with the reflex fall in arterial pressure; 'late', beginning as arterial pressure reached its lowest level. All values are mean ± s.e.m., except where *n*₁, *n*₂ = 2 when the mean only is given.

(18–30 μm) which continue into precapillary arterioles (7–18 μm); capillaries arise from both of these sections. Capillaries drain into collecting venules (12–30 μm) which after receiving several convergent branches drain into small veins (30–50 μm) and then into the principal veins.

In describing the responses in individual vessels we have related the time course of the change in vessel diameter to the time course of the change in arterial pressure, principally because we reasoned that this might indicate whether the diameter change was contributory to, or secondary to, the change in arterial pressure. Accordingly, vertical dashed lines have been drawn on Figs 2, 3 and 4 to indicate the start of the fall in arterial pressure. Approximately 50% of the principal arteries and 65% of the small arteries showed a change in diameter in response to baroreceptor stimulation and they all responded in a similar manner; they showed an increase in diameter that began as arterial pressure began to fall and reached a peak as arterial pressure reached its lowest level (Fig. 2*A*). The magnitude of the increase in diameter was, on average, larger in the small arteries (Table 1). In general, principal and small arteries returned to control diameter concomitant with the return of arterial pressure towards control level, but in about 20% of the small arteries the diameter increase was longer lasting and outlasted the depressor response by 15–25 s (Fig. 4).

Approximately 50% of the terminal arterioles that responded to baroreceptor stimulation also showed an increase in diameter which began when arterial pressure began to fall. However, the remaining 50% showed a 'late' increase in diameter which did not begin until arterial pressure neared its lowest level, i.e. 6–15 s after arterial pressure began to fall; in some of these vessels this increase in diameter was preceded by a decrease which began as arterial pressure was falling (cf. Fig. 2*B*, Table 1). The 40% of precapillary arterioles that showed a change in diameter all responded like the latter group of terminal arterioles (Fig. 2*B*, Table 1).

In some experiments the duration of the carotid sinus inflation was increased to 45 s in an attempt to examine more closely the relationship between the return of vessel diameter to control level and the return of arterial pressure to control level. As

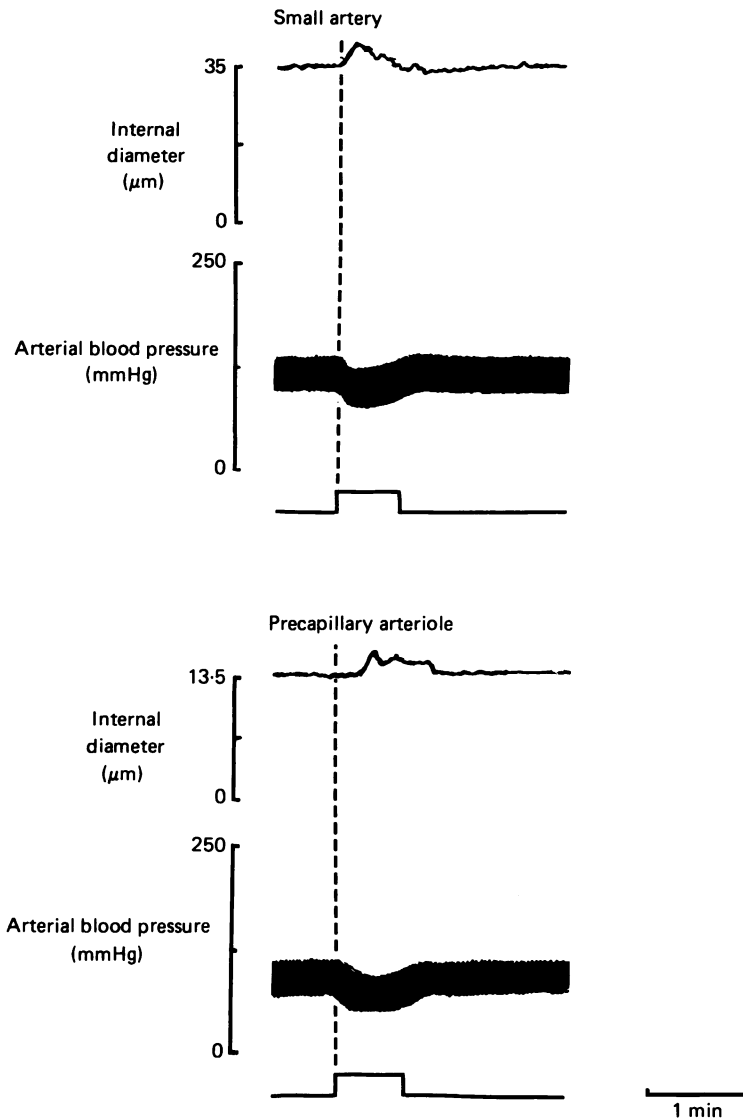


Fig. 3. Representative traces from different animals showing the effect of prolongation of the period of carotid sinus inflation to 45 s. Traces as in Fig. 2. Note that vessel diameter returned to control level simultaneously with or after, but not before, arterial pressure returned to control level.

can be seen from Fig. 3, both the proximal and distal arterioles generally returned to control diameter concomitantly with the return of arterial pressure; there was no tendency for them to return to control *before* arterial pressure (see Discussion).

On the venous side of the circulation, only about 25% of the collecting venules showed any change in diameter and these all showed a late increase that began 6–10 s after arterial pressure began to fall (Fig. 2D). About 50% of the small veins and principal veins showed diameter changes and of these the great majority showed

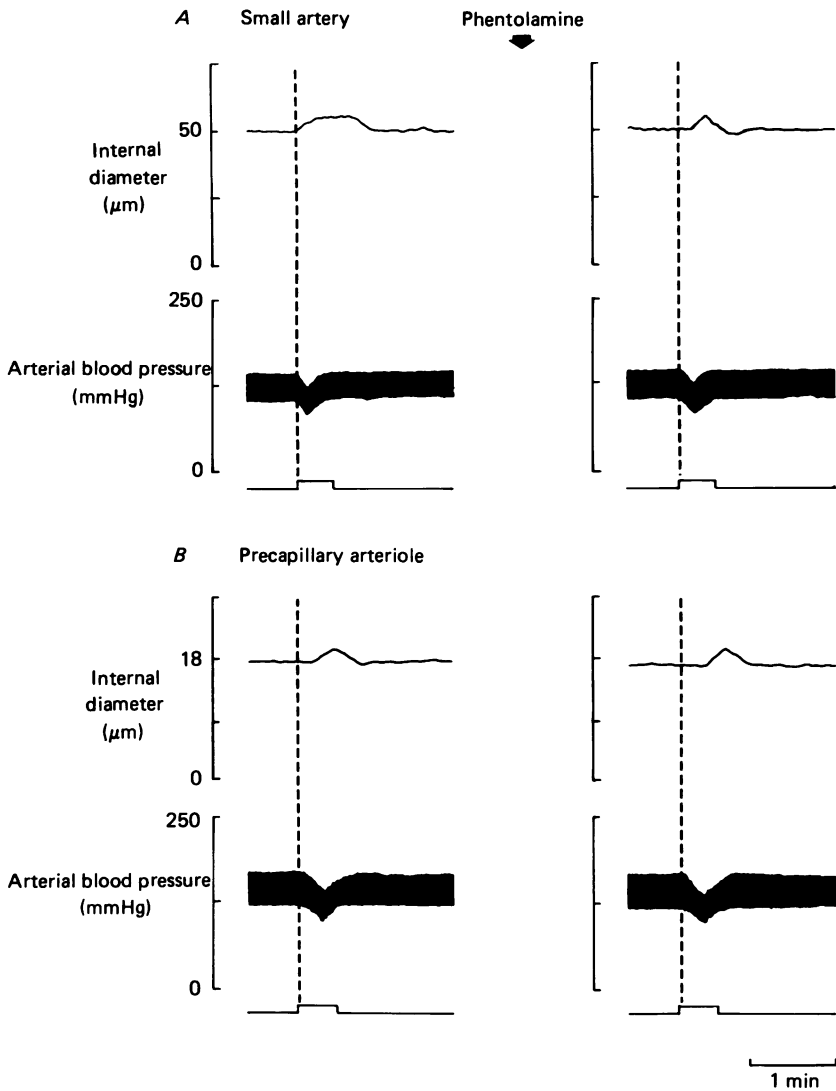


Fig. 4. Representative traces from two different animals showing the effect of local application of phentolamine to the mesentery upon responses induced by baroreceptor stimulation. The small artery is an example of a vessel whose increase in diameter outlasted the reflex fall in arterial pressure. Note that the diameter increase of the small artery which began simultaneously with the fall in arterial pressure was converted by phentolamine to a response which began when arterial pressure neared its lowest level (*A*), whereas the onset of the diameter increase in the precapillary arteriole was unchanged (*B*).

an increase which began as arterial pressure began to fall, but reached a peak some 12–15 s later than arterial pressure reached its lowest level (Fig. 2*C*). The exceptions were two small veins in which the diameter increase was preceded by a decrease (Table 1). The diameter increases shown by the venous vessels were comparable in magnitude with those seen in arterial vessels (Table 1).

Effects of local application of phentolamine

In experiments in which phentolamine was added to the Krebs solution bathing the mesentery, 15–20 min were allowed to elapse before the vessels were examined again. Only those vessels which had returned to their original control diameter were tested. We first verified that constrictor responses evoked by topical application of noradrenaline 10^{-6} g ml⁻¹ had been abolished (cf. Hébert & Marshall, 1985).

Phentolamine applied in this way had no detectable effect on the fall in arterial pressure evoked by baroreceptor stimulation, indicating that there was no significant escape of the drug into the general circulation. A total of thirty-five arterial vessels were studied: three principal arteries, nine small arteries, eleven terminal arterioles and twelve precapillary arterioles, all of which had responded to baroreceptor stimulation before phentolamine in a manner which was representative of their type as described above. After phentolamine, no changes in diameter were seen during baroreceptor stimulation in any of the principal arteries, five small arteries, eight terminal arterioles nor in one of the precapillary arterioles. The remaining eighteen vessels (i.e. 50% of the total) all showed 'late' increases in diameter which began when arterial pressure neared its lowest level (Fig. 4), i.e. there were no increases in diameter beginning simultaneously with the fall in arterial pressure. The increases in diameter observed after phentolamine ranged from 7 to 11% of control diameter.

After phentolamine, the nine small veins examined showed no change in diameter during baroreceptor stimulation, although six of them had shown an increase concomitant with the fall in arterial pressure before phentolamine. However, eight of the thirteen collecting venules showed an increase in diameter, averaging 12% from control, which began as arterial pressure reached its lowest level, as had occurred in these vessels before phentolamine.

DISCUSSION

In the present experiments on anaesthetized rats, stimulation of carotid baroreceptors evoked the expected reflex fall in arterial pressure and a concomitant increase in mesenteric vascular conductance, but little or no change in mesenteric blood flow. This is compatible with findings of others who have investigated the effects of sinus nerve stimulation on naturally perfused mesenteric vasculature in conscious or anaesthetized dogs (Vatner *et al.* 1970). As indicated in the Introduction such results could be interpreted either as a myogenic dilatation to the fall in arterial pressure which results in perfect autoregulation of blood flow, or as a sympathetically mediated dilatation which matches the fall in arterial pressure. However, we believe that our direct observations on individual vessels of the mesenteric circulation allow us to make a more complete interpretation.

First, it must be stated that approximately 50% of the mesenteric vessels we studied showed no change in diameter during baroreceptor stimulation. Obviously we have no way of knowing whether they would have shown a change in diameter *in situ*, i.e. whether the trauma of the experimental preparation prevented them from doing so. However, it seems reasonable to assume that for these vessels the neurally mediated and local influences upon them, as discussed below, opposed one another

and effectively cancelled out so that the diameter remained unchanged, or at least was not measurably changed. We have estimated that the smallest diameter change we can record with our recording system amounts to 1–2% of the control diameter (cf. Hébert & Marshall, 1985).

Arterial vessels

It has previously been demonstrated that the principal and small arteries of the mesentery are supplied with a dense network of sympathetic noradrenergic fibres, one or two fibres run alongside the terminal arterioles but no fibres follow the precapillary arterioles. Correspondingly, sympathetic stimulation constricted all of the innervated arterial vessels but not the precapillary arterioles (Furness & Marshall, 1974). Since baroreceptor stimulation evoked an increase in the diameter of principal and small arteries and of many terminal arterioles, which occurred more or less simultaneously with the reflex fall in arterial pressure, it seems most likely that these responses were induced by the reflex decrease in sympathetic vasoconstrictor activity and that they contributed to the fall in arterial pressure and, indeed, to the rise in mesenteric vascular conductance. On the other hand, the most obvious explanation for the 'late' increases in diameter that began in some terminal arterioles and in precapillary arterioles when arterial pressure neared its lowest level is that they were myogenic responses, initiated by a fall in intravascular pressure transmitted to them from the systemic arteries. The initial decrease in diameter that occurred in some of them would then be seen as a passive response to that fall in pressure, attributable to the fall in wall tension and acting as the stimulus for the myogenic response as described by Burrows & Johnson (1981). The other possibility, namely that these 'late' increases in diameter were induced by accumulation of vasodilator metabolites, can be discounted for several reasons. Firstly, blood flow through the mesenteric circulation as a whole hardly changed during baroreceptor stimulation and, even if there was redistribution away from the mesentery towards the intestine, it is unlikely that sufficient vasodilator metabolites would have accumulated within 5–10 s, in a tissue with a metabolic rate as low as the mesentery, to cause significant vasodilatation. Secondly, the detailed analysis of diameter changes in mesenteric arterioles following experimentally induced changes in arterial perfusion pressure or venous outflow pressure indicated that they were far more likely to be pressure dependent than flow dependent (Burrows & Johnson, 1983). Thirdly, when tissue P_{O_2} was maintained at a high level with the aim of preventing the build-up of vasodilator metabolites, this had no effect on dilator responses induced in mesenteric arterioles by a fall in arterial perfusion pressure (Lang & Johnson, 1986).

The fact that the diameter increases in principal and small arteries and in terminal arterioles which were simultaneous with the reflex fall in arterial pressure were abolished by local blockade of α -adrenoreceptors supports the view that they were neurally mediated. Once sympathetic vasoconstrictor tone had been abolished, the few principal arteries investigated apparently behaved like conduit vessels, showing no change in diameter in response to the fall in pressure that must have occurred within them during the reflex fall in systemic arterial pressure. However, some of the small arteries showed dilator responses that began after arterial pressure began to

fall. They were therefore comparable in time course with those that the terminal and precapillary arterioles showed both before and after phentolamine, as would be consistent with their being myogenic responses. It has been reported previously that arterioles of denervated cat mesentery, comparable in diameter to those we designate small arteries, dilate in response to reductions in intravascular pressure in a manner which is consistent with myogenic behaviour (Lang & Johnson, 1986).

Thus, our results lead us to propose that the ability of naturally perfused mesenteric circulation, i.e. gastrointestinal tract plus its attached mesentery, to maintain constant blood flow during baroreceptor stimulation can be ascribed both to neurally mediated and to myogenic dilatation, but the former occurs predominantly in the proximal arterial vessels and the latter predominantly in the distal arterioles. This seems reasonable, for the principal arteries supply the intestine as well as the mesentery. Moreover, evidence that arterial vessels of the intestine behave like those of the mesentery is provided by the work of Bohlen & Gore (1977) who measured the diameters of individual vessels of the rat intestinal wall when arterial pressure was changed by bleeding and reinfusion over a range that would certainly have, respectively, decreased and increased baroreceptor activity. When arterial pressure was increased in that study, all arteries and arterioles that supply the mucosal villi and the smooth muscle showed constriction which was abolished by denervation of the vasculature. However, after denervation, distal arterioles showed a decrease in diameter when arterial pressure was raised, compatible, in this case, with a myogenic constrictor response to the rise in intravascular pressure that was measured within them. Further evidence that the arterioles of the intestine behave in a myogenic fashion in response to changes in arterial perfusion pressure is provided by measurements of total vascular resistance in preparations of denervated intestine (Johnson, 1960).

Our results are also compatible with the effects of baroreceptor stimulation on preparations of small intestine plus mesentery perfused at constant pressure (Oberg, 1964). For the increase in blood flow and decrease in total mesenteric vascular resistance could be ascribed to reflex dilatation of the arteries and arterioles, while the accompanying increase in CFC could be explained by reflex dilatation of all those distal arterioles, comparable to the terminal arterioles of the mesentery, which give rise to the capillaries. Under the conditions of our experiments dilatation of the non-innervated precapillary arterioles might also contribute to the increase in the capillary surface area available for filtration, since they too give rise to capillaries. However, if we are correct in our suggestion that these vessels respond myogenically, then during constant-pressure perfusion (cf. Oberg, 1964) such distal arterioles would be expected to constrict myogenically in response to the rise in intravascular pressure caused by dilatation of proximal arterioles, therefore tending to limit the increase in CFC.

Oberg (1964) emphasized that even though the increase in CFC persisted throughout baroreceptor stimulation the initial increase in blood flow and decrease in vascular resistance waned, so that steady levels nearer to control were maintained until the stimulus ceased. This was exactly the opposite of the pattern of flow and resistance change that he recorded during the reflex increase in sympathetic activity induced by baroreceptor unloading (Oberg, 1964) and that many others have

recorded in whole mesenteric circulation during direct stimulation of the sympathetic supply or infusion of noradrenaline and which has been termed 'autoregulatory escape' or 'escape' (Folkow, Lewis, Lundgren, Mellander & Wallentin, 1964; Hébert & Marshall, 1985, for further references). We have previously reported that distal arterioles of the mesentery show maintained constriction during sympathetic stimulation and noradrenaline infusion, while the principal and small arteries showed a secondary relaxation from their initial constriction, which would account for the escape phenomenon (Hébert & Marshall, 1985; Marshall & Hébert, 1986). However, we failed to obtain evidence of the opposite pattern of behaviour in the present study: all arterial vessels returned to control diameter either concomitant with, or after, the return of arterial pressure. It may simply be that the decrease in sympathetic activity did not last long enough in the present experiments for us to see such behaviour. Thus, Oberg (1964) was able to produce a sustained decrease in sympathetic activity during baroreceptor stimulation lasting up to 3 min, judging from the sustained fall in systemic arterial pressure shown in the illustrations to that paper, whereas when we prolonged the period of carotid sinus inflation, even to 45 s, arterial pressure returned towards the control level during the stimulus, presumably due to a secondary increase in sympathetic activity initiated by the contralateral carotid baroreceptors and the aortic baroreceptors. We preferred to allow this to occur rather than subject the animal to the additional surgery and trauma required to denervate these receptors. Nevertheless, the fact that the dilatation of the distal arterioles, i.e. terminal and precapillary arterioles, did persist in our experiments for as long as the reflex fall in arterial pressure is of significance for it contrasts strongly both with our finding that dilatation of the distal arterioles of skeletal muscle was transient and reversed to constriction even during a 20 s period of baroreceptor stimulation (Hébert & Marshall, 1988) and with the report that CFC in skeletal muscle was decreased during baroreceptor stimulation, rather than increased as in mesenteric circulation (Oberg, 1964). It seems that the factors involved in controlling the diameters of distal arterioles are different in mesenteric and muscle arterioles (see Hébert & Marshall, 1988).

Venous vessels

A dense network of noradrenergic nerve fibres supplies principal and small veins of the mesentery, but no nerve fibres follow the collecting venules. Correspondingly, the principal and small veins were actively constricted by sympathetic stimulation, whereas the collecting venules were not (Furness & Marshall, 1974). If the collecting venules cannot show active neurally mediated responses and if they do not show active myogenic responses, as is generally assumed for venous vessels, then it seems reasonable to suppose that the late increases in diameter that we observed in about 25% of collecting venules, beginning as arterial pressure neared its lowest level, were passive responses to a rise in intravascular pressure. The dilatation of the arteries and arterioles that supplied these few venules may have been sufficient to overcome the fall in systemic arterial pressure and cause an increase in intravascular pressure to be transmitted across the capillary bed. The fact that such responses still occurred after phentolamine would suggest that the arterial dilatations which persisted under those conditions (see above) were able to produce a similar effect. That this could

occur is supported by the results of Burrows & Johnson (1981) for they found that over 25% of mesenteric arterioles 'over-regulated' in response to a fall in perfusion pressure in that the dilation they showed was so great as to increase volume flow through them, rather than allowing it to remain constant; an increase in flow reaching the venous vessels from such arterioles would be expected to cause passive distension.

The two small veins which showed a transient decrease in diameter as arterial pressure began to fall, followed by an increase in diameter, presumably collapsed initially to a fall in intravascular pressure concomitant with the fall in systemic arterial pressure. The issue then is whether the increases in diameter in those vessels and the increases that occurred in other small veins and principal veins, which generally began as arterial pressure began to fall and reached a maximum rather later than arterial pressure reached its lowest point, were passive distensions, neurally mediated dilatations or a combination of the two. The effect of local application of phentolamine upon responses in venous vessels is of little help in elucidating their underlying mechanisms, since this procedure would not only block neurally mediated responses in venous vessels, but by blocking neurally mediated responses in arterial vessels may affect the changes in intravascular pressure that produce passive effects in the venous vessels. Accordingly, the fact that phentolamine abolished the diameter increases in small veins is inconclusive, though it is of interest because it suggests that the fall in systemic arterial pressure that still occurred during baroreceptor stimulation after local sympathetic blockade was dissipated by the myogenic dilatation of arterioles and the passive behaviour of venules discussed above. Of more significance is our observation that blood flow through the entire mesenteric vascular bed remained more or less constant during baroreceptor stimulation, for this suggests that the pressure distending the venous vessels, particularly the principal veins that drain the intestine as well as the mesentery, must also have remained virtually constant, so precluding passive effects. We therefore propose that the increases in diameter induced in small and principal veins by baroreceptor stimulation under the conditions of our experiments were predominantly, if not entirely, active dilatations mediated by reflex inhibition of sympathetic activity. The fact that these venous responses were somewhat later to begin and to reach a peak than the responses we judged to be neurally mediated in arterial vessels is consistent with previous comparisons of reflex responses induced in venous and arterial vessels by baroreceptor stimulation (Rothe, 1983).

The magnitudes of the diameter increases in the venous vessels ranged from a mean of 8% of control in principal veins to 13% in small veins and collecting venules. Assuming that the pressure within the venous vessels was high enough for them to be circular in transverse section rather than elliptical, then the blood content of each one would be roughly proportional to the square of its radius. Thus, by simple calculation, if the venous vessels of the whole mesenteric circulation behaved like those of the mesentery, a supramaximal stimulus to the baroreceptors, such as we used, would be expected to cause an increase in regional blood volume of between 17 and 28%. This compares favourably with the report of Hainsworth & Karim (1975) that in abdominal circulation, which was perfused at constant flow so as to minimize passive changes in venous capacity, changes in carotid sinus pressure over the full

baroreceptor sensitivity range (60–250 mmHg) caused an increase in abdominal vascular capacity of 25%. Similarly, Oberg (1964) found that a 25–30% increase in blood volume could be produced in preparations of the intestine plus mesentery, which were perfused at constant pressure, by varying baroreceptor activity over the full range. He acknowledged that under such experimental conditions which allowed blood flow to increase with arteriolar dilatation a proportion of the total volume change was attributable to passive venous distension (Oberg, 1964), and showed subsequently (Oberg, 1967) that this proportion was greatest at low venous pressures and negligible when venous pressure was > 15 mmHg.

Thus, we propose that the active component of the increase in volume evoked by baroreceptor stimulation in whole mesenteric circulation is due to active dilatation of the principal veins which drain the gastrointestinal tract and the mesentery, of small veins of the mesentery proper and probably of comparable vessels of the intestinal wall. Our own findings indicate that passive responses can occur in the collecting venules of the mesentery during baroreceptor stimulation. Moreover, measurements of the diameter of small venules and veins that drain the intestinal wall, after their denervation indicate that they respond passively to changes in pressure within them (Bohlen & Gore, 1977), while measurements of compliance in larger venules and veins of the mesentery indicate that they are highly distensible over the pressure range 0–30 mmHg (Gaehtgens & Uekermann, 1971). Therefore, it seems likely that all venous vessels of the mesenteric circulation have the potential to contribute passively to changes in vascular capacity during baroreceptor stimulation; whether any particular venule or vein does so will depend upon the prevailing intravascular pressure and any change in that pressure produced by responses of vessels up-stream and down-stream.

Functional implications

It has already been proposed by others that the mesenteric circulation as a whole has such a large vascular capacity, over 45% of it being in venules and small veins (Rothe, 1983), that active dilatation of those vessels, possibly augmented by their passive distension, can play a major role in the reflex response to baroreceptor stimulation by allowing accumulation of blood in a functional blood reservoir, thereby limiting venous return to the heart (e.g. Oberg, 1964; Karim & Hainsworth, 1975). Our observations provide direct evidence for that view. It has also been suggested that this venous dilatation performs a second important function: the maintenance of a constant capillary hydrostatic pressure (Oberg, 1964). Thus, in preparations of intestine plus mesentery perfused at constant pressure, baroreceptor stimulation induced no net outward filtration of fluid from the vasculature into the tissue space, indicating that the decrease in precapillary resistance attributable to arteriolar dilatation was exactly balanced by a decrease in postcapillary resistance caused by venous dilatation (Oberg, 1964). Indeed, it has been proposed that the ability to maintain a constant capillary hydrostatic pressure is particularly important for the intestine since it has an enormous capillary surface area available for filtration and would be functionally impaired by accumulation of fluid in the tissue space (Folkow *et al.* 1964). Although we made no measurements of capillary hydrostatic pressure or fluid flux, it is reasonable to assume that any increase in

hydrostatic pressure in capillaries of the mesentery due to arteriolar dilatation would be offset to some extent by concurrent venous dilatation. Moreover, if we are correct in our suggestion that the distal arterioles behave in a myogenic fashion during baroreceptor stimulation then this too would be expected to limit any change in capillary pressure. Since measurements of capillary hydrostatic pressure indicate that at normal levels of arterial pressure there is already net *outward* filtration of fluid across capillaries of mesentery, but net *inward* filtration across mucosal capillaries (Gore, 1982), it seems that the factors that help to maintain a constant hydrostatic pressure in capillaries of the mesentery during baroreceptor stimulation may be particularly important in preventing excessive loss of fluid into the peritoneal cavity. Further, given that myogenic behaviour tends to maintain blood flow as well as capillary hydrostatic pressure and that the entire mesenteric circulation, intestine as well as mesentery, has a well-developed ability to maintain blood flow in the face of changes in perfusion pressure (Johnson, 1960; Burrows & Johnson, 1981), it is perhaps not surprising that naturally perfused mesenteric circulation appears to show autoregulation rather than strong baroreceptor-mediated reflex responses to changes in systemic arterial pressure. Indeed, if myogenic behaviour can predominate over neurally mediated effects on arterioles, this would tend to limit the role that changes in mesenteric vascular resistance can make to reflex regulation of arterial pressure.

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