*J. Physiol.* (1976), **262**, *pp.* 659–677
*With 7 text-figures*
*Printed in Great Britain*



# RESPONSES OF ABDOMINAL VASCULAR CAPACITANCE IN THE ANAESTHETIZED DOG TO CHANGES IN CAROTID SINUS PRESSURE

BY R. HAINSWORTH AND F. KARIM

*From the Departments of Cardiovascular Studies and Physiology, University of Leeds, Leeds LS2 9JT*

(*Received 21 April 1976*)

SUMMARY

1. The abdominal circulation of anaesthetized dogs was vascularly isolated without opening the abdomen, by cutting or tying all structures immediately above the diaphragm and tying the proximal ends of the hind limbs. The region was perfused at constant flow through the aorta and drained at constant pressure from the inferior vena cava.

2. Vascular resistance responses were expressed as the changes in perfusion pressure and capacitance responses were determined by integrating changes in vena caval outflow.

3. Decreasing the pressure in the isolated carotid sinuses over the whole baroreceptor sensitivity range increased mean perfusion pressure from 91 to 149 mmHg (a 67 % increase in resistance) and decreased mean capacitance by 111 ml. (5 ml. $kg^{-1}$).

4. The range of carotid sinus pressures over which capacitance responses occurred was at a significantly higher level than the corresponding range for resistance responses.

5. Comparison of the reflex responses with the responses to direct stimulation of efferent sympathetic nerves shows that quantitatively similar responses of resistance and capacitance to those induced by a large step decrease in carotid pressure could be produced by stimulating maximally the efferent sympathetic nerves at 5 Hz. These results also suggest that at all levels of carotid sinus pressure there is no difference in the impulse traffic to resistance and capacitance vessels.

## INTRODUCTION

The importance of vascular resistance responses in many regions of the body in the baroreceptor reflex has long been established (see Heymans & Neil, 1958). However, the role of the capacitance vessels is less clear.

Some earlier workers (Alexander, 1954; Bartelstone, 1960; Salzman, 1957; Zinger & Grodins, 1964) claim that venous or capacitance responses do occur as a result of decreasing carotid sinus pressure. More recent reports, describing the results of experiments with more carefully controlled preparations, indicate that active constriction of some capacitance vessels in response to carotid hypotension either does not occur or responses are very small (Browse, Donald & Shepherd, 1966; Epstein, Beisser, Stampfer & Braunwald, 1969; Hainsworth, Karim & Stoker, 1975). However, it is likely that the differing reports can be explained in terms of regional variations, since Brender & Webb-Peploe (1969) and Iizuka, Mark, Wendling, Schmid & Eckstein (1970) described constriction in some abdominal veins but no responses in limb veins. One aim of the present experiments was to determine the capacitance responses in a preparation of the entire abdominal circulation. This is a large region containing about 25 % of the blood volume and it has been shown that a large proportion of this volume is expelled in response to direct stimulation of the sympathetic nerves (Karim & Hainsworth, 1976). The preparation which we devised (Hainsworth & Karim, 1974; Karim & Hainsworth, 1976) enables us to determine active resistance and capacitance responses in the abdominal circulation without opening the abdominal cavity.

Earlier work (Mellander, 1960; Karim & Hainsworth, 1976) has shown that when efferent sympathetic nerves were stimulated electrically at high frequencies (10–20 Hz), capacitance responses were only a little greater than the responses at 2 Hz. Resistance responses, however, increased progressively with increasing stimulus frequency. A further aim of the present work, therefore, was to determine whether there was a similar differential effect in response to reflex activation of sympathetic nerves. The reflex responses were compared, in the same animals, with the responses to direct stimulation to estimate the impulse traffic in nerves to resistance and capacitance vessels at different carotid pressures.

## METHODS

Dogs (18–29 kg) were anaesthetized using chloralose (0·1 g. $kg^{-1}$, Etablissement Kuhlman, Paris) infused through a catheter inserted into the inferior vena cava through a saphenous vein. Further doses of chloralose (about 10 mg. $kg^{-1}$ every 15 min) were given to maintain a state of light surgical anaesthesia. The neck was opened in the mid line, the trachea cannulated and the dogs were ventilated with positive pressure by means of a Starling 'Ideal' pump using 40 % oxygen in nitrogen humidified at room temperature. The rate of the pump was 18 strokes/min and the stroke volume was approximately 17 ml. $kg^{-1}$. When the pleura was opened a resistance to expiration was inserted equivalent to 3 cm $H_2O$.

Both carotid sinuses were vascularly isolated. The internal carotid artery was tied about 1 cm distal to the sinus and the external carotid artery was tied just distal to the lingual artery. The occipital and ascending pharyngeal arteries were tied near

their origins from the external carotid artery and any small branches arising from the carotid bifurcation were also tied. Polyethylene cannulae were tied in the lingual arteries to permit drainage of blood from the isolated sinuses. Both vagus nerves were cut in the neck.

All structures immediately above the diaphragm, except the sympathetic nerves, were cut or tied. The thoracic wall was divided by cutting through the sternum and the eighth to thirteenth ribs on both sides. The dorsal spinal muscles were cut transversely and a strong nylon cord round the spine and the anterior muscles was tightened mechanically using a lever and ratchet system. Circulation through the spinal canal was prevented by packing the canal tightly with surgical gauze through a hole drilled in the first lumbar vertebra. The oesophagus, the attachments of the pericardium to the diaphragm and the phrenic and vagus nerves were tied and cut. The lowest four pairs of intercostal arteries were cut between ties close to the aorta.

Temporary by-passes were connected between the proximal ends of a carotid and a femoral artery and an external jugular and a femoral vein to allow some circulation to the abdomen during the cannulation procedures. The animal was given suxamethonium chloride (0·5 mg $kg^{-1}$ every 15 min) and heparin (500 i.u. $kg^{-1}$ followed by 50 i.u. $kg^{-1}$ every 30 min). The circuit (Fig. 1) was filled with dextran solution (Dextraven 150, Fisons Pharmaceuticals Ltd) or a mixture of dextran and blood obtained from a second dog. After the aortic cannulae were inserted the abdomen was perfused for about 5 min then the perfusion was stopped and the inferior vena cava was cannulated. The time of each cannulation was less than 3 min during which time abdominal aortic pressure remained above 40 mmHg. Blood from the abdomen was drained through a cannula (11 mm internal diameter), from the inferior vena cava into a reservoir, from which it was pumped into an external jugular vein. Strong nylon cords were tightened mechanically at the proximal ends of the hind limbs, leaving the area investigated to extend from the diaphragm down to the limb ties. The abdomen was not opened.

The by-passes were clamped and the arterial perfusion pump was set at the start of the experiment so that abdominal aortic pressure was approximately the same as systemic arterial pressure; it was left unchanged for the rest of the experiment. The level of the venous reservoir was set so that pressure in the inferior vena cava was approximately the same as it was before cannulation. The pressure in the arteries other than those in the abdomen was maintained using an arterial reservoir which had a constant pressure of air above the blood. The reservoir enabled large changes in abdominal vascular volume to occur with little change in systemic arterial blood pressure. The volume of blood in the circuit was about 200 ml. plus the variable volume in the reservoirs (up to one l.).

Blood pressures were recorded using Statham (P 23 Gb) transducers connected to cannulae in the carotid arteries, the abdominal aorta (passed through a femoral artery), the inferior vena cava (passed through a femoral vein) and a brachial artery (systemic arterial pressure). The pressure signals were amplified and mean pressures were obtained using R.C. networks with time constants of 2 sec incorporated in the amplifiers (S.E. Laboratories, Feltham, Middlesex). Blood flows were recorded using a Biotronex flow-meter with cannulating transducers in the aortic inflow and vena caval outflow. Zero flows were recorded at intervals during the experiment and the flowmeters were calibrated using the animals' blood at the end of the experiment. Pressures and flows were recorded on photographic paper using a direct-writing ultraviolet light recorder (S.E. Laboratories).

Arterial blood gases and pH were measured frequently during each experiment using standard glass electrode systems. Since the dogs were ventilated with 40% oxygen, $P_{O_2}$ was always greater than 150 mmHg. Arterial $P_{CO_2}$ and pH were

maintained at 35–40 mmHg and 7·30–7·40 respectively by adjusting the stroke of the respiratory pump and intravenous infusion of molar sodium bicarbonate.

*Experimental procedure.* No experiments were done until blood gas and pH values were adjusted to the values specified above and all pressure and flow records had become stable.

Carotid sinus pressure (non-pulsatile) was raised to a level sufficient to maximally excite all baroreceptors (186–314 mmHg). This was confirmed in each dog by noting

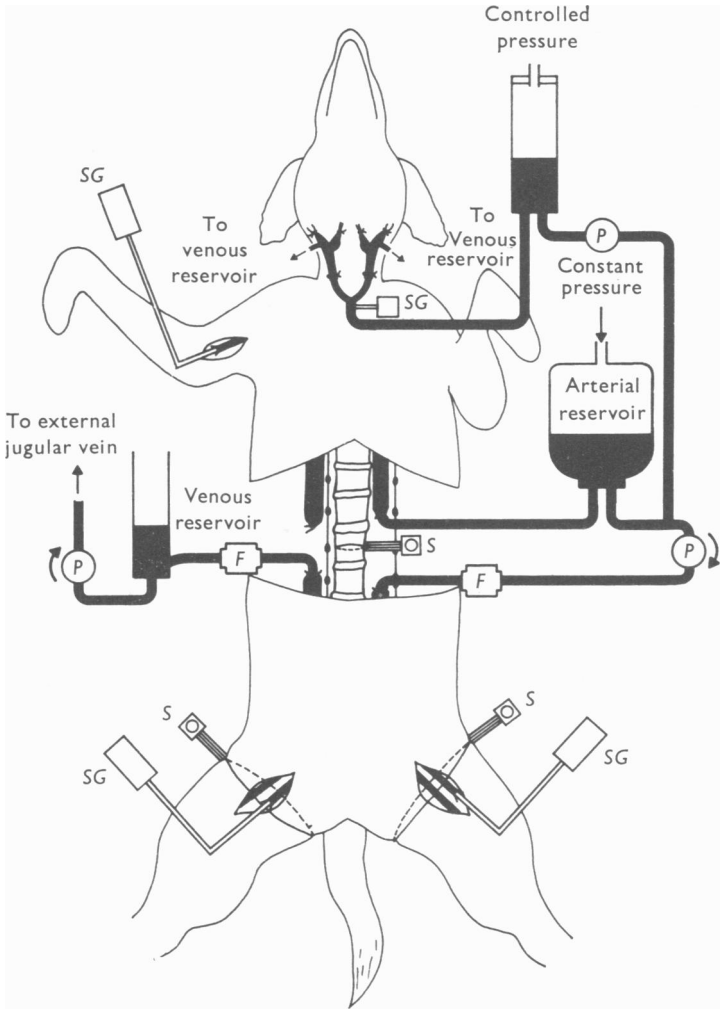


Fig. 1. Diagram of experimental preparation. Abdomen vascularly isolated from rest of circulation. Blood from thoracic aorta passes into reservoir maintained at constant pressure and pumped at constant flow into abdominal aorta. Blood drains from abdomen through inferior vena cava into venous reservoir. *SG*, strain guage; *P*, roller pump; *F*, electromagnetic flowmeter transducer; *S*, snare tightened by lever and ratchet.

the absence of further responses of any of the measured variables when the carotid pressure was raised by a further small step. After 1–2 min when all records had become stable, carotid pressure was reduced in a single step to a level below the threshold for any reflex changes (34–84 mmHg). The minimum carotid pressure was confirmed by the absence of any further responses to another step decrease. Records were taken during the step decrease and for 1–2 min until all variables were stable.

Resistance responses were calculated as the percentage changes in perfusion pressure (flow constant) when the records had become stable. Capacitance responses were calculated by integrating the *changes* in vena caval outflow following the carotid pressure changes. This was done by drawing a horizontal line from the outflow trace before a change in carotid pressure until the trace had returned to the original level and become stable. The area enclosed by this line and the outflow trace was determined using a planimeter, taking the mean of at least five planimeter estimations. Capacitance changes in responses to increasing carotid pressure were not usually analysed because the flow changed more gradually and estimations were less accurate. However, the responses to increasing carotid pressure were approximately the same as the responses to decreases.

*Accuracy of estimates of capacitance changes.* The accuracy of method of estimating capacitance changes by integration of the changes in the outflow was assessed by use of an extracorporeal circuit which pumped saline through a flowmeter transducer at 1200 ml. $min^{-1}$ and injecting and withdrawing 50 or 100 ml. at different rates proximal to the flowmeter. The method was shown to slightly underestimate the volume changes: injections of saline (equivalent to decreases in vascular capacitance) were underestimated by 9 % and withdrawals by 4 %. The random errors of a series of twelve injections and twelve withdrawals of 100 ml. were both only $\pm 2{\cdot}5$ % (two standard deviations).

In eleven of the dogs, responses were also obtained to a series of smaller decrements of carotid sinus pressure. Steps were about 25 mmHg with about 1 min between each step to allow steady states to be obtained.

In seven dogs, the splanchnic sympathetic nerves (splanchnic nerves + sympathetic trunks) on both sides immediately above the diaphragm were crushed and their distal ends stimulated using a Grass Model S4 stimulator with pulses of 10–15 V, 2 msec duration and frequencies between 1 and 10 Hz.

In four dogs, electrical resistance in the outflow blood to a 4000 Hz current was measured to assess haematocrit changes (Okada & Schwan, 1960; Devonshire, Nashat & Palmer, 1971).

## RESULTS

All values reported are means $\pm$ one standard error of mean except where otherwise indicated.

In thirty dogs the mean value of abdominal aortic inflow was $1201 \pm 72{\cdot}5$ ml. $min^{-1}$, vena caval outflow, $1186 \pm 66{\cdot}2$ ml. $min^{-1}$ and inferior vena caval pressure, $9{\cdot}4 \pm 0{\cdot}85$ cm $H_2O$.

### *Responses from large step decreases in carotid sinus pressure*

At high carotid sinus pressures ($262 \pm 8{\cdot}1$ mmHg), aortic perfusion pressure was $94{\cdot}3 \pm 8{\cdot}8$ mmHg, mean systemic arterial pressure, $116 \pm 6{\cdot}5$ mmHg and heart rate, $153 \pm 5{\cdot}4$ beats $min^{-1}$.

When carotid pressure was decreased in a single step to $59 \pm 2{\cdot}6$ mmHg

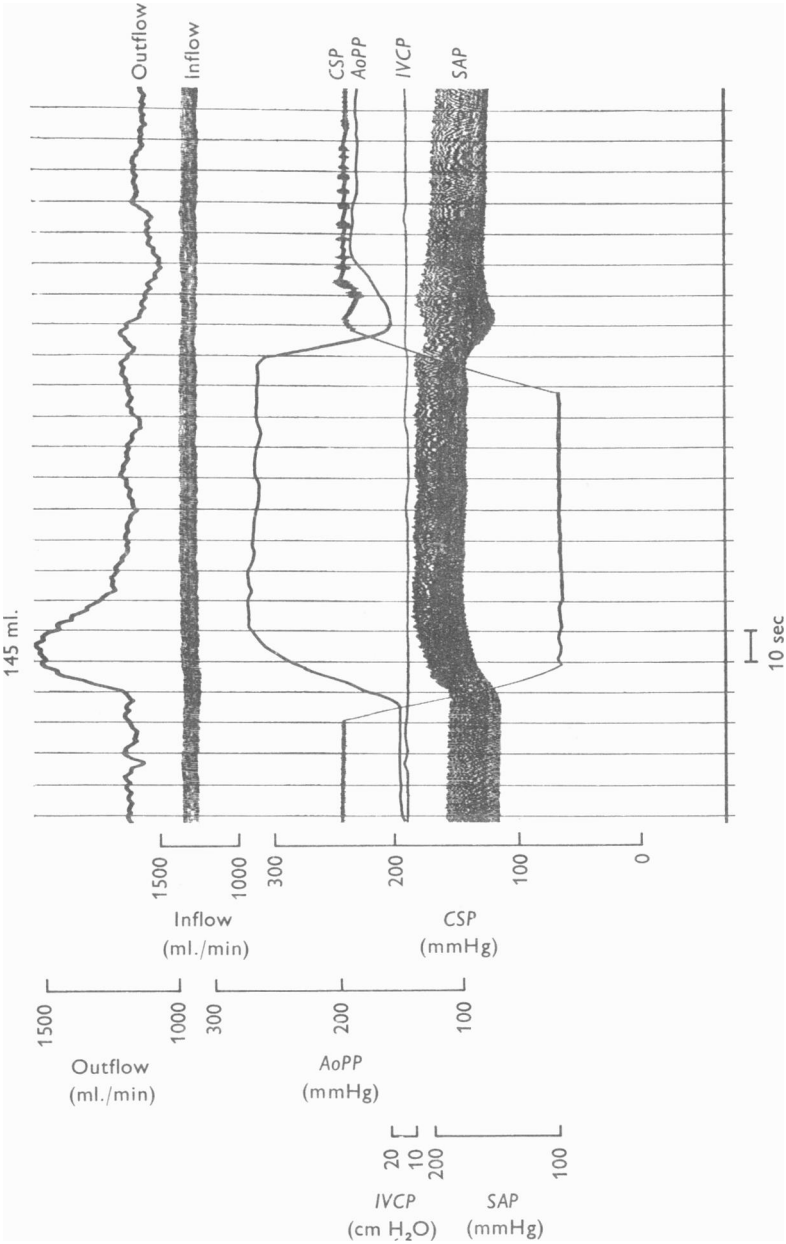


Fig. 2. Response to a large step decrease in carotid sinus pressure. Abbreviations: outflow, flow from inferior vena cava; inflow, flow into abdominal aorta; *AoPP*, abdominal aortic perfusion pressure; *IVCP*; inferior vena cava pressure; *SAP*, systemic arterial blood pressure; *CSP*, carotid sinus pressure. Decreasing carotid pressure caused a transient increase in outflow resulting in the expulsion of 145 ml. from the abdominal circulation, an increase in perfusion pressure in the abdominal aorta and an increase in systemic arterial blood pressure. Abdominal aortic inflow and inferior vena cava pressure remained constant. Note that the changes were reversed when carotid pressure increased but that the change in outflow was slower.

there was a transient increase in vena caval outflow (e.g. Fig. 2) which, since inflow was constant and inferior vena caval pressure was constant, signified a reduction in vascular capacitance in the abdomen. The average capacitance response was calculated to be $111 \pm 12$ ml. or

TABLE 1. Responses to changing carolid sinus pressure

| Dog no. | Wt. (kg) | Carotid sinus pressure (mmHg) A | Carotid sinus pressure (mmHg) B | Aortic perfusion pressure (mmHg) A | Aortic perfusion pressure (mmHg) B | Aortic perfusion pressure (mmHg) Change | Change in resistance (%) | Change in capacitance (ml.) |
|---|---|---|---|---|---|---|---|---|
| 1 | 23 | 260 | 41 | 172 | 230 | 58 | 34 | 115 |
| 2 | 25 | 186 | 34 | 56 | 110 | 54 | 96 | 179 |
| 3 | 24 | 224 | 46 | 42 | 92 | 50 | 119 | 198 |
| 4 | 21 | 226 | 64 | 154 | 228 | 74 | 48 | 41 |
| 5 | 27 | 256 | 64 | 94 | 118 | 24 | 26 | 70 |
| 6 | 25 | 234 | 50 | 52 | 112 | 60 | 115 | 63 |
| 7 | 23 | 224 | 62 | 74 | 100 | 26 | 35 | 49 |
| 8 | 18 | 206 | 60 | 84 | 104 | 20 | 24 | 58 |
| 9 | 21 | 245 | 62 | 165 | 204 | 39 | 17 | 57 |
| 10 | 22 | 228 | 54 | 54 | 108 | 54 | 100 | 78 |
| 11 | 20 | 264 | 66 | 69 | 129 | 60 | 87 | 65 |
| 12 | 24 | 250 | 50 | 143 | 251 | 108 | 75 | 145 |
| 13 | 22 | 258 | 66 | 145 | 274 | 129 | 90 | 53 |
| 14 | 22 | 296 | 60 | 71 | 140 | 69 | 97 | 261 |
| 15 | 24 | 276 | 74 | 120 | 262 | 142 | 118 | 152 |
| 16 | 29 | 314 | 68 | 79 | 138 | 59 | 75 | 79 |
| 17 | 20 | 314 | 66 | 116 | 168 | 52 | 45 | 137 |
| 18 | 21 | 300 | 70 | 124 | 176 | 52 | 47 | 46 |
| 19 | 20 | 294 | 84 | 88 | 106 | 18 | 21 | 72 |
| 20 | 28 | 307 | 43 | 40 | 63 | 23 | 59 | 302 |
| 21 | 22 | 297 | 44 | 75 | 149 | 74 | 91 | 177 |
| 22 | 24 | 312 | 58 | 55 | 86 | 31 | 56 | 123 |
| 23 | 31 | 230 | 66 | 64 | 108 | 44 | 69 | 95 |
| 24 | 33 | 209 | 64 | 80 | 172 | 92 | 115 | 118 |
| 25 | 24 | 210 | 54 | 68 | 118 | 50 | 94 | 77 |
| 26 | 22 | 212 | 52 | 78 | 150 | 72 | 108 | 179 |
| 27 | 28 | 211 | 55 | 129 | 182 | 13 | 41 | 105 |
| 28 | 27 | 272 | 73 | 105 | 161 | 56 | 53 | 178 |
| 29 | 25 | 191 | 50 | 54 | 118 | 64 | 119 | 103 |
| 30 | 28 | 207 | 55 | 84 | 122 | 38 | 44 | 56 |
| Mean | 24·1 | 253 | 59 | 91 | 149 | 58 | 71 | 111 |
| S.E. of mean | 0·64 | 7·3 | 2·0 | 6·9 | 10·5 | 5·4 | 6·0 | 12·0 |

Results are given of the average responses obtained from each dog. Carotid sinus pressure was decreased from the values listed under *A* to those listed under *B*. The corresponding values of aortic perfusion pressure are also listed under *A* and *B*. The responses of resistances are expressed as the percentage increases and the responses of capacitance are given in ml.

$4{\cdot}96 \pm 0{\cdot}64$ ml. $kg^{-1}$. The time for the outflow trace to return to its control level was $62 \pm 4{\cdot}3$ sec.

The large decrease in carotid pressure also resulted in a change in abdominal aortic perfusion pressure from $91 \pm 6{\cdot}9$ to $149 \pm 10{\cdot}5$ mmHg, an increase in resistance of $71 \pm 6{\cdot}0$ %. The capacitance and resistance responses from each dog are listed in Table 1. Other responses were an increase in heart rate from $153 \pm 5{\cdot}4$ to $188 \pm 6{\cdot}3$ beats/$min^{-1}$ (vagus nerves were cut) and an increase in mean systemic blood pressure from $116 \pm 6{\cdot}5$ to $153 \pm 5{\cdot}4$ mmHg. Systemic arterial pressure changes were limited by the arterial reservoir which served as a 'windkessel'.

*Responses from series of small step changes in carotid sinus pressure*

Over a range of carotid sinus pressures each step decrease of carotid pressure resulted in an increase in aortic perfusion pressure and an increase in outflow from the inferior vena cava. At the upper end of the range the first step decrease in carotid pressure usually resulted in outflow responses only with no change in perfusion pressure, although in eight out of sixteen dogs perfusion pressures increased transiently then returned to its initial level before the end of 1 min (e.g. Fig. 3). Measurements of pressure changes were made in the steady state only. At the lower end of the carotid pressure range a step of carotid pressure was usually obtained which produced an increase in perfusion pressure without any further change in outflow. An example of the resistance and capacitance responses obtained from one dog when carotid pressure was reduced in small steps is shown in Fig. 3. The first step of carotid pressure caused no responses. The next two steps caused small capacitance responses and only transient changes in aortic perfusion pressure. The next two steps caused both capacitance and resistance responses and the last step illustrated caused no capacitance change but a large increase in perfusion pressure.

The responses of resistance and capacitance were analysed by expressing the changes obtained from each dog when carotid pressure was decreased over the entire baroreceptor sensitivity range at 100 % and expressing the responses at each carotid pressure tested as a percentage of the maximum (e.g. Fig. 4). From each of these plots, values of carotid pressure corresponding to 5 %, 50 % and 95 % of the responses were read to describe the operating ranges of carotid sinus pressure for resistance and capacitance responses. These results, listed in Table 2, show that the range of carotid pressures over which capacitance responses occurred was at a significantly higher level than the range for resistance responses. Also when resistance and capacitance changes at each carotid pressure were expressed as percentages of the maximum responses (e.g. Fig. 4), at most carotid pressures, the relative capacitance responses were significantly greater than the

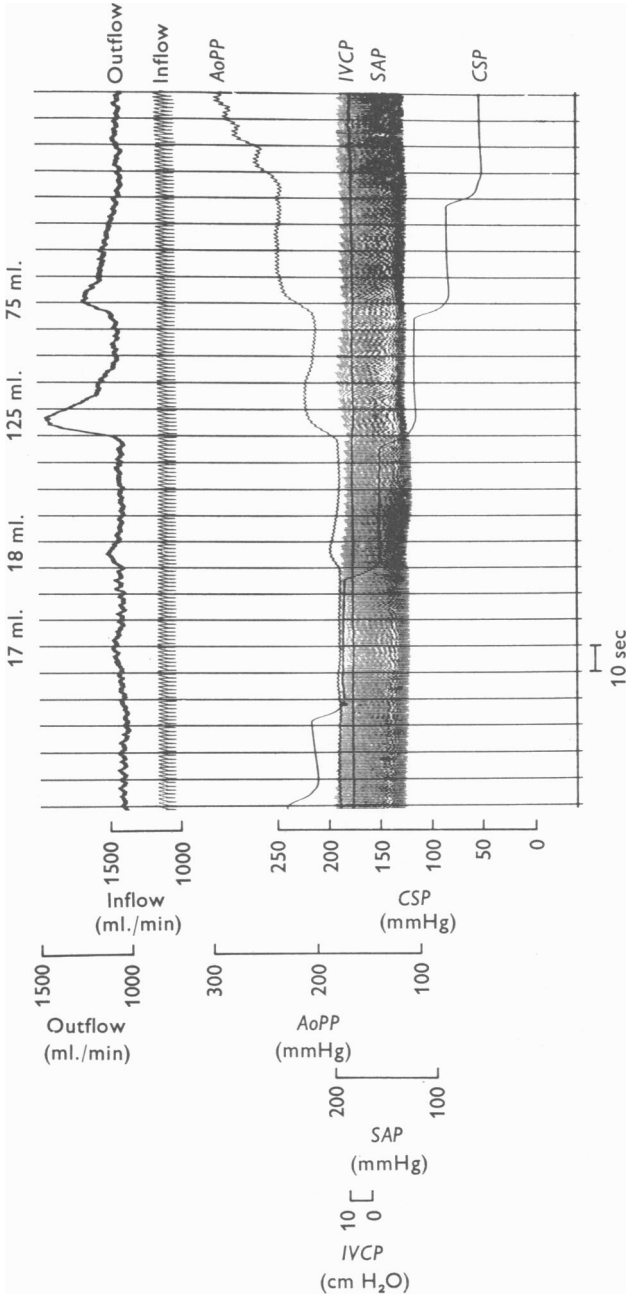


Fig. 3. Responses to a series of small steps in carotid sinus pressure. Abbreviations as in Fig. 2. Note that changing carotid pressure down to about 140 mmHg caused small capacitance responses but no changes in aortic perfusion pressure apart from small transient changes. The lowest step in carotid pressure shown (to 50 mmHg) caused a large increase in aortic perfusion pressure but no change in outflow.

corresponding resistance responses. The average responses from all dogs are shown in Fig. 5. This Figure does not show clearly the difference in carotid pressures for capacitance and resistance responses (Fig. 4, Table 2) because averaging a large number of experiments with different carotid pressure ranges has the effect of rounding the upper and low ends of the curves.

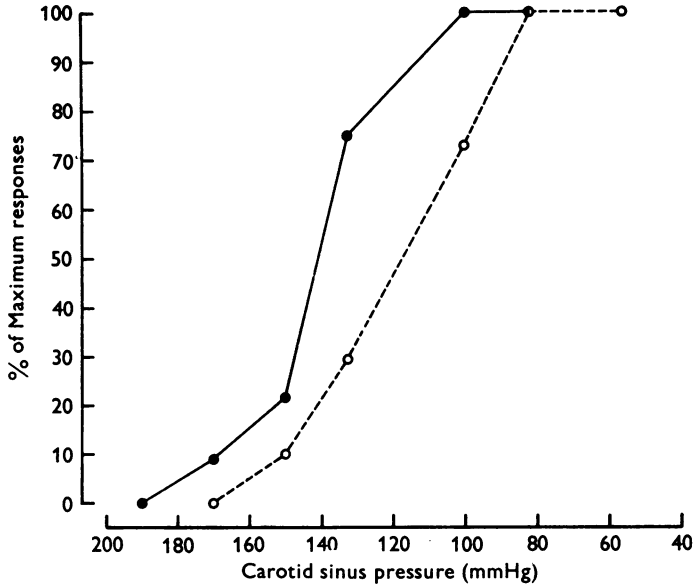


Fig. 4. Responses of resistance and capacitance obtained from one dog. The maximum changes obtained over the entire ranges of carotid pressures have been expressed at 100%. Note that the range of carotid pressures for capacitance responses (●—●) is higher than the range for resistance responses (○- - -○) and at mid-range carotid pressures the capacitance responses were nearer their maximum values than were the resistance responses.

*Effects on haematocrit*

In four dogs electrical resistance in the blood flowing from the abdominal was measured and was found to change by a peak corresponding to a change in haematocrit of +2·2% (range +1·7 to +2·9) following a large step decrease in carotid pressure. The peak haematocrit response coincided with the peak outflow response and in 39 sec (range 20–55 sec) it returned to its initial level despite the large change in total vascular resistance (average change +57% in those dogs).

*Effects of crushing abdominal sympathetic nerves*

Since the vagi were cut and the spinal cord tightly packed, the only nerves supplying the abdomen were in the sympathetic trunk and splanch-

nic nerves immediately above the diaphragm. In ten dogs all these nerves were crushed. Before crushing, the average resistance responses to a large step decrease in carotid pressure was an increase of $77 \pm 16{\cdot}5\,\%$ and the capacitance response was a change of $98 \pm 23$ ml. After crushing the nerves the average resistance and capacitance responses were $2{\cdot}1 \pm 2{\cdot}5\%$ and $0{\cdot}4 \pm 0{\cdot}4$ ml.

TABLE 2. Carotid sinus pressures for abdominal vascular responses

| | 5 % | | 50 % | | 95 % | |
|---|---|---|---|---|---|---|
| Dog no. | Resis-tance | Capaci-tance | Resis-tance | Capaci-tance | Resis-tance | Capaci-tance |
| 1 | 160 | 178 | 117 | 141 | 85 | 107 |
| 2 | 166 | 180 | 123 | 126 | 91 | 96 |
| 3 | 140 | 162 | 102 | 146 | 68 | 108 |
| 4 | 183 | 192 | 140 | 135 | 88 | 109 |
| 6 | 165 | 216 | 128 | 146 | 87 | 115 |
| 7 | 136 | 156 | 92 | 95 | 62 | 70 |
| 10 | 199 | 232 | 130 | 178 | 62 | 122 |
| 12 | 236 | 238 | 161 | 181 | 129 | 130 |
| 14 | 207 | 220 | 128 | 160 | 94 | 124 |
| 15 | 252 | 250 | 209 | 186 | 120 | 140 |
| 17 | 212 | 260 | 160 | 190 | 102 | 139 |
| 23 | 155 | 191 | 115 | 157 | 90 | 116 |
| 24 | 194 | 203 | 131 | 140 | 89 | 110 |
| 25 | 139 | 171 | 97 | 126 | 65 | 84 |
| 28 | 160 | 201 | 162 | 132 | 85 | 91 |
| 29 | 131 | 152 | 102 | 115 | 72 | 77 |
| Mean | 177 | 200 | 129 | 147 | 87 | 109 |
| S.E. of mean | 9·1 | 8·4 | 7·3 | 6·7 | 4·8 | 5·2 |
| *P* | < 0·001 | | < 0·005 | | < 0·001 | |

Results are given of the average responses obtained from each dog. Responses of resistance and capacitance to small step changes in carotid pressure were drawn for each dog by expressing the maximum changes as 100 % (e.g. Fig. 4). Values of carotid pressure corresponding to 5 %, 50 % and 95 % of the responses were read from these plots and are listed here. The carotid pressures corresponding to all three levels of the responses were at significantly higher levels for capacitance responses than for resistance responses. The levels of significance for paired observations are given.

In five dogs the effects were recorded of crushing the sympathetic nerves with carotid pressure held high (mean pressure, 311 mmHg). The average change in resistance following crushing was 2·2 % (range 0 to − 7·30) and there were no measurable capacitance changes.

In five dogs the sympathetic nerves were crushed with a constant low carotid pressure (mean pressure, 61 mmHg). This resulted in an average

decrease in resistance of 35% (range 22–55%) and an increase in capacitance of 55 ml. (range, 41–73 ml.). These changes were similar to the reflex responses obtained in the same dogs before sympathetic crushing: raising carotid pressure to 261 mmHg decreased resistance by 29% (range, 19–48) and increased capacitance by 49 ml. (range, 24–67 ml.).

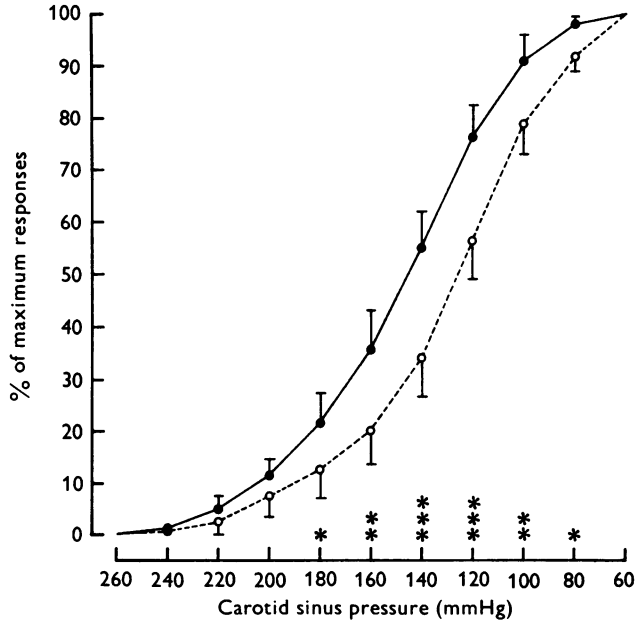


Fig. 5. Responses of resistance and capacitance at different carotid pressures. Results of means ± 1 S.E. of mean from ten dogs: ●—● capacitance; ○- - -○, resistance. Values were read at intervals of 20 mmHg from individual plots (e.g. Fig. 4). Note that this averaging results in more rounded curves than those obtained for single experiments. The significance of differences between resistance and capacitance responses at the various carotid pressures is given by the asterisks: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.005$ (paired $t$ tests).

*Responses to stimulation of distal ends of crushed sympathetic nerves*

Responses of resistance and capacitance to stimulation at frequencies between 1 and 10 Hz were similar to those reported elsewhere (Karim & Hainsworth, 1976). The average resistance and capacitance responses obtained at 10 Hz were $132 \pm 15.6$% and $169 \pm 17.7$ ml. Capacitance changes in one dog at different stimulus frequencies are shown in Fig. 6.

*Comparison of capacitance and resistance responses induced reflexly with responses to direct stimulation of efferent sympathetic nerves*

Since, when carotid pressure was held high, crushing the sympathetic nerves did not induce any changes in resistance or capacitance, it can be assumed that at high carotid pressures the efferent discharge in these

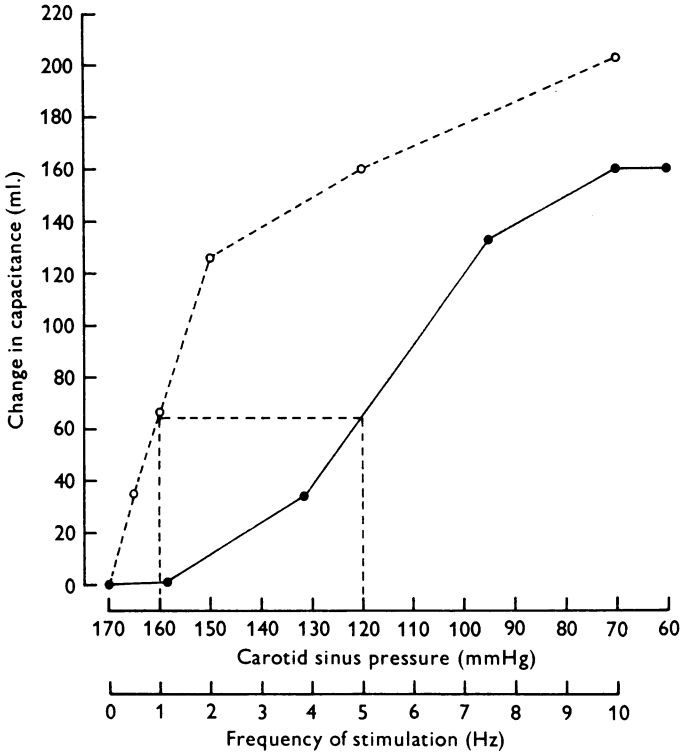


Fig. 6. Capacitance responses induced in one dog by changes in carotid pressure (●—●) and by direct stimulation (○- - -○) of both efferent sympathetic nerves at 10 V, 2 msec and different frequencies. From these plots it was possible to estimate the stimulus frequencies required to produce responses equal to those obtained reflexly. For example, at 120 mmHg carotid pressure 65 ml. would be expelled from the abdominal circulation. This response could also be obtained by direct stimulation at 1 Hz. The same response as the maximum response obtained reflexly could also be obtained by direct stimulation at 5 Hz.

nerves was near zero. Therefore, by determining the responses to electrically stimulating the efferent nerves at different frequencies it is possible to estimate the frequency of direct stimulation required to produce responses of resistance and capacitance vessels similar to those obtained at each carotid pressure.

For each dog, the capacitance responses obtained by reflex and direct stimulation were plotted on the same graph (e.g. Fig. 6). Similar plots were drawn for resistance responses. From each plot, the responses induced reflexly were read at intervals of 20 mmHg and the stimulus frequency which resulted in the same responses were read from the plot of

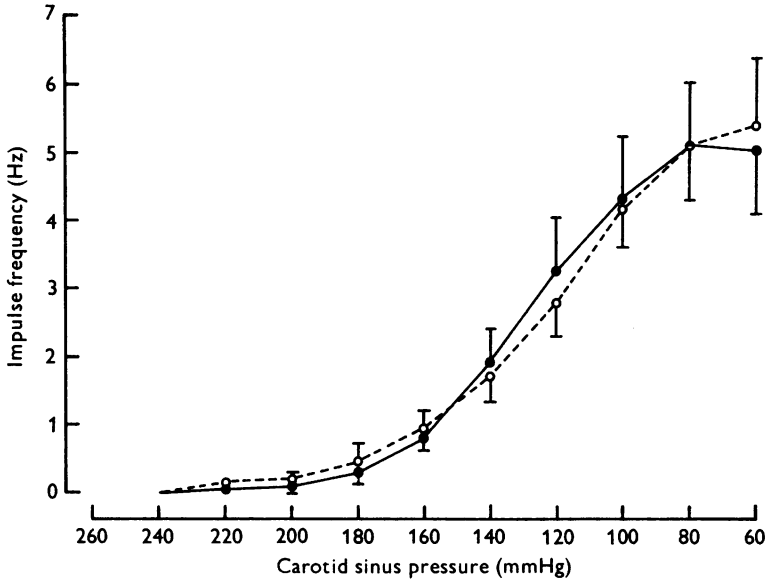


Fig. 7. Comparison of impulse frequencies of direct stimulation of sympathetic nerves with carotid sinus pressures which produced same responses reflexly. Results of means and standard errors from ten dogs. Points calculated from plots of capacitance (●—●) and resistance (○- - -○) responses at intervals of carotid pressure of 20 mmHg. The procedure used to calculate each point is shown in Fig. 6. These results show that the impulse frequencies to resistance and capacitance vessels are identical at each carotid sinus pressure.

responses to direct stimulation. This procedure is illustrated in Fig. 6. We thus obtained, for both resistance and capacitance responses, a series of stimulus frequencies corresponding to a series of carotid pressures. These values have been compared in Fig. 7. This Figure reveals that, corresponding to each level of carotid pressure, the stimulus frequency required to induce the resistance response was the same as that required to induce the capacitance response.

## DISCUSSION

For active capacitance responses in a region to be measured quantitatively several criteria must be satisfied: (1) the region studied must be vascularly isolated from the rest of the body; (2) the pressure distending

the capacitance vessels must remain constant; (3) responses must not be modified by changing concentrations of vasoactive metabolites; and (4) there must be no change in vascular volume due to tissue fluid absorption or transudation. These criteria can be met only by vascularly isolating the region, perfusing it at a constant flow and holding the pressure in the veins constant. The preparation used in the present study was specifically designed to meet these criteria (Hainsworth & Karim, 1975; Karim & Hainsworth, 1976). The area studied was vascularly isolated from the rest of the body. The technique of constant flow perfusion with a constant venous pressure should maintain a constant pressure to the capacitance vessels (predominantly veins) and prevent changes in concentration of metabolites. The almost complete absence of changes in capillary/tissue-fluid exchange was shown by the almost steady haematocrit level. The slight rise in haematocrit during the phase of rapid expulsion was due either to a transient washing out of red cells, e.g. from the spleen, or to a slight transient increase in filtration to the tissues which might occur if the capillary pressure increased slightly as blood was expelled from veins. In any case the changes observed were very small and can be regarded as negligible.

The responses of resistance and capacitance to decreases in carotid pressure were probably due predominantly to the direct effects of the sympathetic nerves rather than to changes in concentration of circulating catecholamines because responses occurred rapidly (e.g. Fig. 2) and, due to the large circuit volume, any catecholamines released from the adrenal glands would be diluted and there would be a delay before recirculation to the abdomen.

The method used here may slightly underestimate the responses since only sympathetic nerves which left the spinal cord above the level of the diaphragm were intact. The lower sympathetic ganglia which supply nerves to some of the pelvic viscera (Miller, Christensen & Evans, 1964) would not receive their full innervation.

The results show that, in the dog, large reflex changes do occur in the vascular capacitance of the abdominal circulation when carotid sinus pressure is changed. The total volume of blood in the splanchnic circulation of a dog weighing 24 kg is about 410 ml. (Chien, 1963; Horvath, Kelly, Folk & Hutt, 1957; Johnstone, 1956). The average change in volume when carotid sinus pressure was changed over the entire range (111 ml.) represents, therefore, about 25% of the abdominal blood volume. The large volume of blood mobilized from the abdomen contrasts with the small venous constriction which occurs in the hind-limb circulation (Brender & Webb-Peploe, 1969; Hainsworth *et al.* 1975). In our earlier investigation (Hainsworth *et al.* 1975) we estimated that the change in

capacitance in a superficial vein in the hind limb was about 6% of the volume of the vein. If this response occurred in all the veins of a 24 kg dog except those in the abdomen the capacitance change would be 67 ml. (24 kg dog has blood volume of about 2 l.; about 1·6 l. is contained outside the abdomen and 70% of this is in the veins (Green, 1950)). If we add to this volume 111 ml. from the abdomen, the total, 178 ml., is very close to that calculated for a 24 kg dog from the results of Shoukas & Sagawa (1973) (180 ml.). Thus, although these calculations are only approximate, they do show agreement between the results of the present investigation and our earlier investigation with the results of Shoukas & Sagawa. They also imply that the capacitance responses in the abdominal circulation comprise the major part of the total body capacitance response.

We did not attempt in these experiments to determine the relative contributions of the different organs within the abdomen to the over-all responses. However, it is likely that the spleen makes a major contribution since after clamping the splenic pedicle the capacitance response to direct stimulation was reduced by about 40% (Karim & Hainsworth, 1976).

Shoukas & Sagawa (1973) determined the 'gains' of resistance and capacitance of the whole animal at different carotid pressures (gain = change in resistance or capacitance/change in carotid pressure) and found that the carotid pressures for peak gains of resistance and capacitance responses were identical. We did not measure gains because we found that the plots of responses against carotid pressure were approximately linear over a wide range of carotid pressures (e.g. Fig. 4). Instead we measured the carotid pressures corresponding to 5%, 50% and 95% of the total responses. These were easy measurements to make and were much more accurate that assessments of carotid pressures at which the slopes of the curves were greatest. Using our methods we found that the carotid pressures for 5%, 50% and 95% of the maximum capacitance responses were about 20 mmHg higher than the corresponding pressures for resistance responses and that the differences were statistically significant. This does not necessarily disagree with the conclusions of Shoukas & Sagawa, that the carotid pressures for maximum 'gains' were the same. However, a careful comparison of the left hand sides of their Figs. 4 and 8 does show that resistance responses were relatively larger than capacitance responses at low carotid pressures.

We observed that the range of carotid pressures over which capacitance responses were obtained was significantly higher than the range for resistance responses. There are two possible explanations for this difference: the activity in sympathetic efferent nerves to capacitance vessels differs from that to resistance vessels; or capacitance vessels are relatively nearer

their maximum construction at low impulse frequencies. The greater sensitivity of capacitance vessels to low frequencies of simulation has been shown for hind quarters of the cat (Mellander, 1960) and for the isolated abdominal circulation of the dog (Karim & Hainsworth, 1976). In the present investigation a quantitative comparison was made of responses to reflex stimulation with responses to direct stimulation to estimate the frequencies in efferent sympathetic nerves to resistance and capacitance vessels at different carotid pressures. This comparison is made on the assumptions that the fibres stimulated electrically are identical with those excited reflexly and that regular stimulation of all efferent sympathetic fibres has the same effect as the more physiological asynchronous discharge. We know that all the fibres excited reflexly were stimulated electrically because a supramaximal stimulus was used and no other anatomical pathways were left intact. However, the possibility that electrical stimulation may excite some fibres which are not excited reflexly cannot be excluded. Although supramaximal electrical stimulation excites all fibres with a regular pulse whereas the natural stimulus is asynchronous, the synchronous nature of the stimulus is not likely to affect the interpretation of the results since the fibres innervating both resistance and capacitance vessels would be stimulated in the same way. We found no difference in the estimated impulse fequencies to resistance and capacitance vessels at all carotid pressures. Similar responses of both resistance and capacitance to those induced reflexly were obtained by changing the stimulus frequency between zero and 5 Hz. These results contrast with results obtained using a perfused hind-limb preparation (Hainsworth *et al.* 1975) in which there was undoubtedly evidence of differential activation of the nerves supplying the artery and the vein; a very much higher stimulus frequency was required to produce resistance responses similar to those obtained reflexly than the frequency required to produce the corresponding venous responses.

The present results indicate that the difference in the ranges of carotid pressure for resistance and capacitance responses is due to the greater sensitivity of the capacitance vessels to sympathetic nerve activity. The relative responses of resistance and capacitance to changes in carotid pressure depend on the initial position on the stimulus–response wave. For example, in Fig. 4, changes in carotid pressure above 140 mmHg would result in predominantly capacitance responses. Between 140 and 100 mm Hg large responses of both capacitance and resistance would occur and below 100 mmHg responses would be predominantly of resistance. In the intact animal, however, it is likely that the ranges of carotid pressure which produce the reflex responses would be lower than reported here because the stimulus would be a pulsatile pressure (Ead, Green & Neil, 1952). Also,

direct recordings from sympathetic efferent fibres have shown that in the relatively intact animal the impulse frequency is only about 1–2 Hz (see Koizumi & Brooks, 1972). This implies that the response to an increase in blood pressure would be predominantly a dilation of capacitance vessels. If blood pressure falls, initially capacitance responses would predominate, thereby enabling the maintenance of blood pressure with little reduction in flow. More severe hypotension would result in pronounced resistance responses which, although limiting the fall in blood pressure, does so at the expense of reducing flow.

This work was supported by grants from the British Heart Foundation, the Medical Research Council and the Wellcome Trust.

The authors are grateful to Mrs M. Lindley and Mr B. Griffiths for technical assistance.

## REFERENCES

ALEXANDER, R. S. (1954). The participation of the venomotor system in pressor reflexes. *Circulation Res.* **2**, 405–409.

BARTELSTONE, H. J. (1960). Role of the veins in venous return. *Circulation Res.* **8**, 1059–1076.

BRENDER, D. & WEBB-PEPLOE, M. M. (1969). Influence of carotid baroreceptors on different components of the vascular system. *J. Physiol.* **205**, 257–274.

BROWSE, N. L., DONALD, D. E. & SHEPHERD, J. T. (1966). Role of the veins in the carotid sinus reflex. *Am. J. Physiol.* **210**, 1424–1434.

CHIEN, S. (1963). Cell volume, plasma volume and cell percentage in splanchnic circulation of splenectomized dogs. *Circulation Res.* **12**, 22–28.

DEVONSHIRE, R. E., NASHAT, F. S. & PALMER, J. F. (1971). The effects of sudden changes in pressure on the haematocrit of venous effluent from isolated perfused kidneys of dogs. *J. Physiol.* **216**, 72–74*P*.

EAD, H. W., GREEN, J. H. & NEIL, E. (1952). A comparison of the effects of pulsatile and non-pulsatile blood flow through the carotid sinus on the reflexogenic activity of the sinus baroreceptors in the cat. *J. Physiol.* **118**, 509–519.

EPSTEIN, S. E., BEISSER, G. G., STAMPFER, M. & BRAUNWALD, E. (1969). Role of venous system in baroreceptor-mediated reflexes in man. *J. clin. Invest.* **47**, 139–152.

HAINSWORTH, R. & KARIM, F. (1974). A method for measurement of changes in abdominal vascular capacitance. *J. Physiol.* **238**, 13–14*P*.

HAINSWORTH, R., KARIM, F. & STOKER, J. B. (1975). The influence of aortic baroreceptors on venous tone in the perfused hind limb of the dog. *J. Physiol.* **244**, 337–351.

HEYMANS, C. & NEIL, E. (1958). *Reflexogenic Areas of the Cardiovascular System*, pp. 56–66. London: Churchill.

HORVATH, S. M., KELLY, T., FOLK, G. E. & HUTT, B. K. (1957). Measurement of blood volumes in the splanchnic bed of the dog. *Am. J. Physiol.* **189**, 573–575.

IIZUKA, I., MARK, A. L., WENDLING, M. G., SCHMID, P. G. & ECKSTEIN, J. W. (1970). Differences in responses of mesenteric veins to reflex stimuli. *Am. J. Physiol.* **219**, 1066–1070.

JOHNSTONE, F. R. C. (1956). Measurement of splanchnic blood volume in dogs. *Am. J. Physiol.* **185**, 450–452.

KARIM, F. & HAINSWORTH, R. (1976). Responses of abdominal vascular capacitance from stimulation of splanchnic nerves. *Am. J. Physiol.* **231**, 434–440.

KOIZUMI, K. & BROOKS, McC. C. (1972). The integration of autonomic system reactions. *Ergebn. Physiol.* **67**, 1–68.

MELLANDER, S. (1960). Comparative studies on the adrenergic neuro-hormonal control of resistance and capacitance blood vessels in the cat. *Acta physiol. scand.* suppl. 176, 1–86.

MILLER, M. R., CHRISTENSEN. G. C. & EVANS, H. E. (1964). *The Anatomy of the Dog*, pp. 638–641. London: Saunders.

OKADA, R. H. & SCHWAN, H. P. (1960). An electrical method to determine haematocrits. *IEEE Trans. med. Electron.* **7**, 188–192.

SALZMAN, E. W. (1957). Reflex peripheral venoconstriction induced by carotid occlusion. *Circulation Res.* **5**, 149–152.

SHOUKAS, A. A. & SAGAWA, K. (1973). Control of total systemic vascular capacity by the carotid sinus baroreceptor reflex. *Circulation Res.* **33**, 22–33.

ZINGER, D. & GRODINS, F. S. (1964). Effect of carotid baroreceptor stimulation upon the forelimb vascular bed of the dog. *Circulation Res.* **14**, 392–399.