J. Physiol. (1970), **209**, *pp.* 257–293
With 15 *text-figures*
Printed in Great Britain

COMPARISON OF THE REFLEX VASOMOTOR RESPONSES TO SEPARATE AND COMBINED STIMULATION OF THE CAROTID SINUS AND AORTIC ARCH BARORECEPTORS BY PULSATILE AND NON-PULSATILE PRESSURES IN THE DOG

BY JENNIFER E. ANGELL JAMES AND M. DE BURGH DALY
From the Department of Physiology, St Bartholomew's Hospital Medical College, London, E.C.1

(*Received 14 July 1969*)

SUMMARY

1. In the anaesthetized dog the carotid sinuses and aortic arch were isolated from the circulation and separately perfused with blood by a method which enabled the mean pressure, pulse pressure and pulse frequency to be varied independently in each vasosensory area. The systemic circulation was perfused at constant blood flow by means of a pump and the systemic venous blood was oxygenated by an extracorporeal isolated pump-perfused donor lung preparation.

2. When the vasosensory areas were perfused at non-pulsatile pressures within the normal physiological range of mean pressures, the reflex reduction in systemic vascular resistance produced by a given rise in mean carotid sinus pressure was significantly greater than that resulting from the same rise of aortic arch pressure.

3. On the other hand, when the vasosensory areas were perfused at normal pulsatile pressures and within the normal physiological range of mean pressures, there was no difference in the size of the reflex vascular responses elicited by the same rise in mean pressure in the carotid sinuses and in the aortic arch.

4. Whereas the vasomotor responses elicited reflexly by changes in mean carotid sinus pressure are modified by alterations in pulse pressure, those evoked by the aortic arch baroreceptors through changes of mean pressure are only weakly affected by modifications in pulse pressure. Evidence for this was obtained from single stepwise changes of mean pressure in each vasosensory area during pulsatile and non-pulsatile perfusion, and from curves relating the mean pressure in the carotid sinuses or aortic arch and systemic arterial perfusion pressure.

5. The vasomotor response elicited by combined stimulation of the

carotid sinus and aortic arch baroreceptors was greater than either response resulting from their separate stimulation.

6. When the mean perfusion pressures in the two vasosensory areas are changed together, the curve relating mean pressure to systemic arterial pressure during pulsatile perfusion of the areas is considerably flatter than that for non-pulsatile perfusion.

7. Increasing the pulse pressure in the carotid sinuses or aortic arch caused a decrease in systemic vascular resistance, the response elicited from the carotid sinuses being the larger.

8. Altering the phase angle between the pulse pressure waves in the carotid sinuses and aortic arch had no effect on systemic vascular resistance.

9. In both vasosensory areas, increasing the pulse frequency caused a reduction in systemic vascular resistance.

INTRODUCTION

It is well known that stimulation of the baroreceptors in the carotid sinuses causes reflexly bradycardia and a reduction in systemic vascular resistance (for references, see Heymans & Neil, 1958). Although baroreceptor reflexes from the aortic arch have received less attention it has been shown that distension of the region causes slowing of the heart and that this response is dependent on the integrity of the vagus nerves (Eyster & Hooker, 1908; Anrep & Segall, 1926; I. de B. Daly & Verney, 1927; Levy, Ng & Zieske, 1966; Carswell, Hainsworth & Ledsome, 1968). Anrep & Starling (1925) were the first to obtain unequivocal evidence that receptors in the cardio-aortic area reflexly controlled vasomotor tone, and showed that a rise in pressure in the heart and aorta caused vasodilatation in the isolated perfused head of the animal, provided the vagus nerves were intact. Localizing the stimulus still further Daly & Daly (1959) showed that a rise in pressure in the isolated perfused aortic arch caused a reflex reduction in total systemic vascular resistance, a finding which was confirmed by Daly, Hazzledine & Howe (1965).

It has not yet been established whether there are any differences in the control of the heart and circulation exerted reflexly by the carotid sinus and aortic arch vasosensory areas. Carswell *et al.* (1968) compared the cardiac and vasomotor responses to changing the pressure in the carotid arteries, and therefore in the carotid circulation, with those elicited from the isolated perfused aortic arch. By means of a cross-perfused head preparation, Glick & Covell (1968) compared the responses to altering the pressure in the carotid arteries with those to altering the arterial pressure in the trunk of the recipient animal, so that reflexes from the heart and pulmonary circulation may have contributed to those from the aortic

arch. Irisawa & Ninomiya (1967), recording averaged afferent nerve activity in the carotid sinus and aortic nerves of the cat and rabbit, concluded that the carotid sinus baroreceptors were more sensitive to a unit change of arterial blood pressure than the aortic baroreceptors.

This paper describes experiments in which a quantitative comparison was made of the reflex vasomotor responses elicited by stimulation of the baroreceptors in the carotid sinuses and aortic arch. For this purpose a preparation was devised in which the carotid sinuses and aortic arch were isolated from the circulation and separately perfused with blood. The importance of pulse pressure (McCrea & Wiggers, 1933; Ead, Green & Neil, 1952) and of pulse frequency (Gero & Gerová, 1962; Scher & Young, 1963) in the control of heart rate and blood pressure by the carotid sinus baroreceptors has been stressed previously, but no similar studies appear to have been made in respect to the control by the aortic arch baroreceptors. To compare the reflex effects from each vasosensory area of changes in mean pressure, pulse pressure and pulse frequency, provision was made in the present experiments to control independently each of these parameters in the carotid sinuses and aortic arch.

METHODS

The preparation used in this study was a modification of that described previously by Daly & Ungar (1966), and therefore only the essential details of the technique and the subsequent modifications will be given here.

Two dogs were used for each experiment and after premedication with morphine hydrochloride (2 mg/kg subcutaneously) were anaesthetized by intravenous injection of 2·75 ml./kg of a mixture of α-chloralose (0·055 g/kg) and urethane (0·55 g/kg) dissolved in a solution containing 85 parts sodium chloride solution (0·9 g/100 ml.) and 15 parts polyethylene glycol ('Carbowax', Union Carbide Ltd.). The recipient (test) dogs varied in weight from 11·6 to 16·2 kg. Four independent perfusion systems were established: (1) perfusion of both carotid sinus regions; (2) perfusion of the aortic arch and portions of its major branches which were isolated from the circulation; (3) perfusion of the remainder of the circulation; and (4) perfusion of the isolated lungs of the donor animal by means of which the systemic venous blood of the recipient animal was oxygenated. The details of the perfusion systems are shown in Fig. 1.

Perfusion of the isolated carotid sinuses and aortic arch. Both carotid sinuses were isolated from the circulation and perfused by the method of Moissejeff (1927) as modified by Daly (1955). A blind sac of each carotid sinus area was made by ligating the internal carotid artery and also the external carotid artery and its branches. Cannulae were inserted into the common carotid arteries, pointing towards the sinuses, and connected to a special type of blood reservoir by means of which the mean pressure, pulse pressure and pulse frequency in the sinuses could be varied independently (Daly, 1955). A steady pressure was applied to the heparinized blood in the reservoir by means of an air compressor and could be varied by an adjustable air-leak by-pass system (Fig. 1). In this way variations in mean pressure in the carotid sinuses were brought about. The bottom of the reservoir consisted of a rubber diaphragm which separated the blood from a chamber filled with water and attached

to a Dale–Schuster pump. Rhythmic movements of the rubber diaphragm produced by the pump imparted an oscillatory pressure to the blood in the reservoir and hence in the carotid sinuses. The size of the pulsations was varied by altering the stroke of the pump. The frequency of the pulsations was varied by altering the gear ratio between the motor and pump.

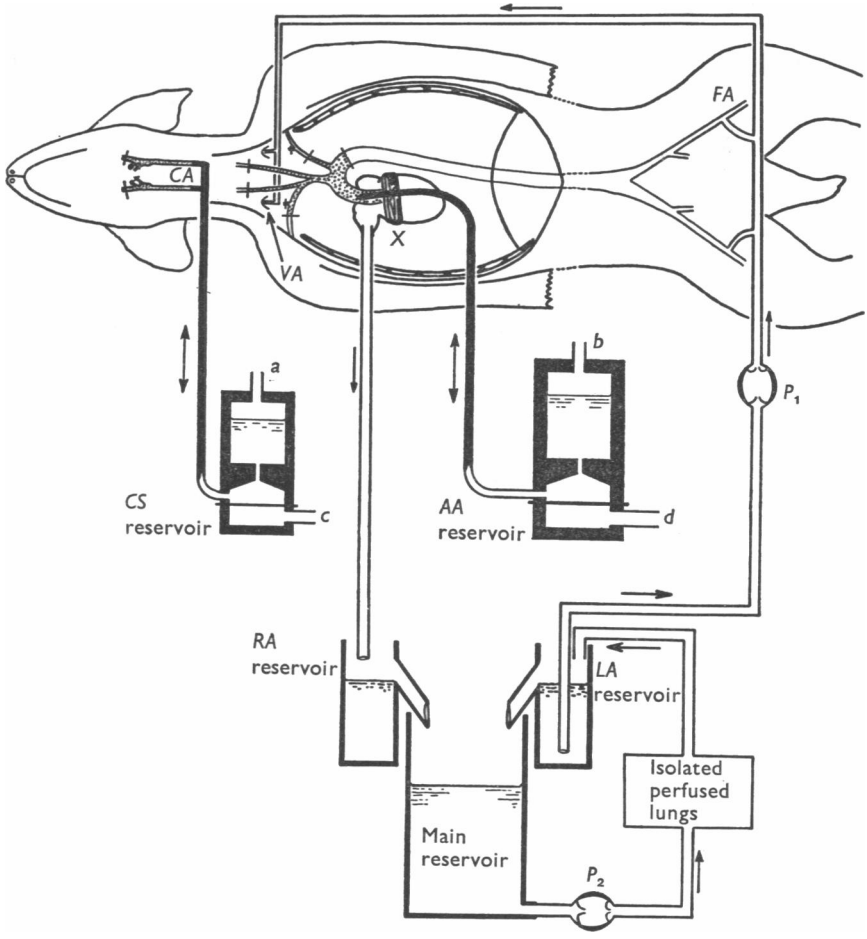

Fig. 1. For legend see facing page.

The aortic arch was isolated from the circulation as described by Daly *et al.* (1965). The following arteries were tied: both common carotid, vertebral, subclavian, and internal mammary arteries, the right omocervical, costocervical and inferior thoracic arteries, and the aorta distal to the origin of the left subclavian artery at the point it is crossed by the left pulmonary artery. In this way a blind sac was made of the aortic arch. A metal cannula (bore 7 mm) was inserted through the wall of the left ventricle into the ascending aorta and held in place with the tape tied round the ventricles just below the atrio-ventricular groove. The cannula was connected to a

second blood reservoir (Daly, 1955) and Dale–Schuster pump for controlling independently the mean and pulse pressures and pulse frequency in the aortic arch (Fig. 1).

The two Dale–Schuster pumps providing the oscillatory pressures were connected mechanically in such a way that the geared electric motor driving the shaft of one of the pumps was directly linked to the shaft of the second pump. When a pulsatile pressure was applied to the carotid sinuses and aortic arch simultaneously, the two pumps were in phase. The form of the pulse pressure waves is shown in Fig. 2. In some experiments the phase angle of the pulsatile pressures applied to the two vasosensory areas was altered to determine the effect on systemic vascular resistance, as described by Angell James (1969).

The blood reservoirs serving the carotid sinuses and the aortic arch were immersed in water which was circulated from a thermostatically controlled water-tank maintained at a temperature of 38° C. The temperature of the blood in the carotid sinuses and in the aortic arch was measured by copper-constantan thermocouples using a galvanometer (Cambridge Instrument Co. Ltd.). The thermocouples lay in the common carotid artery within 5 mm of the carotid sinus and in the tip of the aortic cannula respectively and were calibrated before and after each experiment. The temperatures ranged from 34 to 37° C in all experiments, and the difference in temperature between the carotid sinuses and aortic arch was always less than 2° C.

Perfusion of the systemic circulation. The systemic circulation was perfused at constant-volume blood flow by means of a Dale–Schuster pump, through cannulae inserted into the cranial ends of the vertebral arteries and through T-cannulae

---

Fig. 1. Diagram showing the methods of separate perfusions of the isolated carotid sinuses, the isolated aortic arch, the systemic circulation and the isolated perfused lungs of a donor animal. The *filled tubes* are the perfusion circuits for the isolated carotid sinuses and aortic arch; the *open tubes*, the perfusion circuits for the systemic circulation and isolated lungs. The *stippled* blood vessels are those included in the carotid sinus and aortic arch perfusions. By means of the reservoirs *CS* and *AA* which contain blood, the mean pressure, pulse pressure and pulse frequency are controlled independently in the carotid sinuses and aortic arch (Daly, 1955).

The systemic circulation is perfused by pump P_1 with blood from the left atrial reservoir. Blood from the systemic circulation drains through a cannula in the right atrium into the right atrial reservoir and thence into the main reservoir. The lungs (not shown) of the recipient animal are not perfused but the left atrium is cannulated to drain broncho-pulmonary blood into the main reservoir.

The isolated lungs of a donor dog are perfused through the pulmonary artery by pump P_2 with blood from the main reservoir; blood from the left atrium drains into the left atrial reservoir. For a description of the position of the catheters for measuring vascular pressures and of other details, see text. *a*, *b*, connexions to compressed air air-leak by-pass systems for controlling mean pressures in the two reservoirs; *c*, *d*, connexions to spaces above diaphragms of Dale–Schuster pumps (water-filled systems) for controlling pulse pressure and pulse frequency in the reservoirs. *AA*, aortic arch; *CA*, carotid arteries; *CS*, carotid sinus; *FA*, femoral arteries; *LA*, left atrium; *RA*, right atrium; *VA*, vertebral arteries; *X*, tape tied round ventricles below atrio-ventricular groove and embracing the aortic arch cannula.

inserted into the femoral arteries. The systemic venous blood returning to the heart drained from the right atrium into the right atrial and main reservoirs (Fig. 1) and was then oxygenated in the isolated perfused lungs of the second dog, before being returned to the systemic circulation of the recipient animal. There was therefore no blood flowing through the pulmonary circulation of the recipient dog, but the blood supply to its lungs was maintained by the bronchial circulation. The lungs of the recipient were artificially ventilated so as to maintain the normal rhythmic dis-

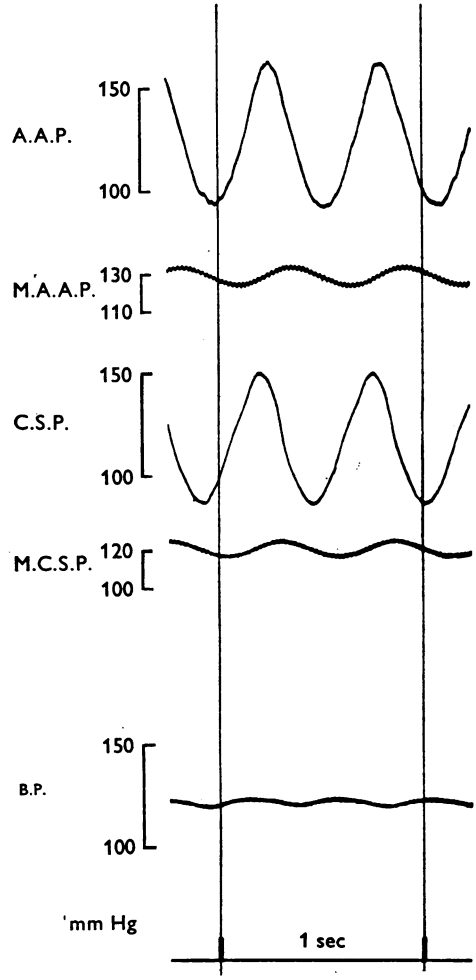

Fig. 2. Records showing the form of the pulse wave in the isolated perfused carotid sinuses and isolated perfused aortic arch. Pulse frequency 110 c/min. Time marker, 1 sec. Dog, male, 11·6 kg. Separate perfusion of the systemic circulation. In this and in subsequent figures: A.A.P., aortic arch pressure; M.A.A.P., mean aortic arch pressure; C.S.P., carotid sinus pressure; M.C.S.P., mean carotid sinus pressure; B.P., mean systemic arterial perfusion blood pressure.

charge from the lungs of impulses which affect the cardiovascular system (Anrep, Pascual & Rössler, 1936; Daly, Hazzledine & Ungar, 1967; Daly & Robinson, 1968).

In all experiments coagulation of the blood was prevented by heparin ('Pularin', Evans Medical Ltd., 2000 i.u./kg). To correct the metabolic acidosis which develops during the course of perfusion experiments, sodium bicarbonate, 75 m-equiv, was added to the blood in the main reservoir at the beginning of perfusion and then infused at a rate of 7·7–13 m-equiv/hr.

Perfusion of isolated lungs. The isolated perfused lungs of the donor animal were prepared from greyhound dogs, varying in weight from 22·0 to 33·3 kg, and were ventilated artificially by a Starling 'Ideal' pump at 20 c/min, the tidal volume being 400 ml. As the lungs were over-ventilated in relation to their blood flow carbon dioxide was added to the inspired gas (60 % O_2 in N_2) through a rotameter at a rate sufficient to raise the end-tidal P_{CO_2} to 35–40 mm Hg, measured by an infra-red CO_2 analyser (type URAS 4, Hartmann & Braun).

Measurement of pressures. The mean systemic arterial perfusion pressure was measured from a no. II (Luer) serum needle inserted into a femoral artery. The carotid sinus pressure was measured by way of a flexible nylon catheter (Portex, Portland Plastics Ltd.; length 20 cm, bore 1·5 mm) inserted through a common carotid or lingual artery; the tip of the catheter lay within 1 cm of the carotid sinus. For measurement of the aortic arch pressure a flexible nylon catheter (length 20 cm, bore 1·5 mm) was inserted in a retrograde direction through the left common carotid artery so that the tip lay in the brachiocephalic artery or aortic arch. Each pressure was measured by means of a Statham strain-gauge (model P23Gb) and after amplification by a carrier amplifier (S.E. Laboratories Ltd., Feltham, Middlesex) the pressure was recorded on a direct-writing ultra-violet light recorder (S.E. Laboratories Ltd.). The frequency response of the catheter-manometer systems was determined using the method of Frank (1903). The undamped natural frequency response of all systems was greater than 130 c/s, the degree of damping being 0·2. This gave an estimated amplitude distortion of less than 5 % up to about 40 c/s. Mean pressure in each system was obtained electrically by passing the amplifier output through a simple R-C network with a time constant of 1 sec and was recorded by a separate galvanometer. The manometers were calibrated before and after each experiment using a mercury manometer. Zero reference pressures were obtained post mortem and taken as those recorded when the tips of the needles or catheters were exposed to air.

Systemic vascular resistance. At constant systemic blood flow a change in vascular resistance can be taken as being proportional to the change in the pressure difference across the systemic vascular bed, i.e. mean arterial perfusion pressure minus the mean right atrial pressure. The right atrial pressure was maintained constant at approximately zero pressure, and the change in vascular resistance could be expressed therefore as a percentage change in arterial perfusion pressure.

Reflex changes in systemic arterial perfusion pressure were elicited by altering the mean pressure, pulse pressure and pulse frequency in the carotid sinuses and aortic arch. In the comparisons that were made between responses, the tests were performed immediately following each other to eliminate factors due to spontaneous changes in the potency of the reflexes which sometimes occur with time. For this reason, direct comparisons between sets of data should not be made unless specified.

Blood gas analysis. Samples of arterial blood withdrawn anaerobically from a systemic artery were transferred to electrode systems for measuring P_{O_2}, P_{CO_2} and pH as described by Daly & Ungar (1966).

RESULTS

The initial control values for the systemic arterial perfusion pressure, the pressure in the carotid sinuses and aortic arch, and the P_{O_2}, P_{CO_2} and pH of the blood perfusing these areas are shown for sixteen consecutive experiments in Table 1. The values for the arterial perfusion pressure are those

TABLE 1. Initial control values for the mean systemic arterial perfusion pressure, mean carotid sinus and aortic arch perfusion pressures (non-pulsatile), and for the composition of the blood perfusing the systemic circulation and the isolated carotid sinuses and aortic arch. Sixteen experiments

Dog, wt. (kg)	13·51 ± 0·40 (11·1–16·2)
Systemic arterial perfusion pressure (mm Hg)	130·7 ± 3·9 (102–160)
Carotid sinus perfusion pressure (mm Hg)	114·4 ± 2·8 (100–136)
Aortic arch perfusion pressure (mm Hg)	115·8 ± 2·8 (99–135)
Blood perfusate	
P_{O_2} (mm Hg)	189·5 ± 23·0 (86–330)
P_{CO_2} (mm Hg)	38·2 ± 1·3 (34–50)
pH	7·39 ± 0·017 (7·30–7·46)

The open values are the means ± S.E. of mean, those in parentheses the range.

TABLE 2. Non-pulsatile pressure perfusion of the vasosensory areas. The effects on systemic vascular resistance of separate stimulation of the carotid sinus and aortic arch baroreceptors by raising the mean perfusion pressure. Unpaired observations

Expt. no.	Carotid sinus pressure (mm Hg)		Aortic arch pressure (mm Hg)		Systemic arterial perfusion pressure (mm Hg)		Systemic vascular resistance (% decrease)
	Control	Increase	Control	Increase	Control	Decrease	
			A. Carotid sinuses				
1	138	10	113		125	47	38
2	125	21	105		120	52	43
4	140	24	124		184	104	57
5*a*	126	15	124		146	42	29
5*b*	129	20	129		134	45	34
6*a*	133	15	126		122	42	34
6*b*	100	20	99		144	49	34
7*a*	130	10	126		142	48	34
7*b*	130	20	136		140	63	45
8*a*	117	11	135		147	25	17
8*b*	114	23	135		154	57	37
8*c*	118	20	135		145	53	37
8*d*	136	23	104		154	59	38

TABLE 2 (*cont.*)

Expt. no.	Carotid sinus pressure (mm Hg)		Aortic arch pressure (mm Hg)		Systemic arterial perfusion pressure (mm Hg)		Systemic vascular resistance (% decrease)
	Control	Increase	Control	Increase	Control	Decrease	
			A. Carotid sinuses				
8*e*	120	21	125		150	57	38
8*f*	124	11	128		150	50	33
9	131	9	135		146	46	32
10*a*	109	11	117		134	37	28
10*b*	110	19	119		132	40	30
10*c*	106	10	114		120	35	29
11	110	10	115		130	30	23
12	120	10	114		142	58	41
$n = 21$							
Mean	122·2	15·9	121·8		141·0	49·5	34·8
S.E. of mean	±2·4	±1·2	±2·4		±3·2	±3·5	±1·8
Range	100–140	9–24	99–136		120–184	25–104	17–57
			B. Aortic arch				
4*a*	136		130	22	120	20	17
4*b*	133		122	21	138	25	18
4*c*	139		126	23	160	43	26
4*d*	122		119	10	155	29	19
4*e*	118		130	22	160	44	28
5*a*	127		125	24	145	25	17
5*b*	129		129	23	140	26	19
6*a*	118		122	20	140	44	32
6*b*	106		102	20	140	45	32
7*a*	136		140	19	130	10	8
7*b*	138		147	20	132	22	17
7*c*	129		135	22	138	29	21
8*a*	120		118	17	158	48	30
8*b*	119		121	12	157	29	18
8*c*	127		120	20	156	44	28
8*d*	120		126	21	143	40	28
8*e*	124		127	11	151	31	21
9	129		133	12	140	5	4
10*a*	104		111	10	128	14	11
10*b*	108		118	11	118	17	14
10*c*	107		117	23	130	35	27
11	108		114	12	132	34	26
12	120		115	11	156	18	12
$n = 23$							
Mean	122·5		123·8	17·7	142·0	29·4	20·6
S.E. of mean	±2·2		±2·0	±1·1	±2·6	±2·5	±1·6
Range	104–139		102–147	10–24	118–160	5–48	4–32

observed while the carotid sinuses and aortic arch were perfused at a non-pulsatile pressure.

In subsequent sections of this paper we describe the peak response of the systemic arterial perfusion pressure to altering the mean pressure, pulse pressure and pulse frequency in the perfused carotid sinuses and in the separately perfused aortic arch. The reflex nature of these responses was determined by repeating the tests after cutting the carotid sinus nerves and cervical vagosympathetic nerves. In all cases these procedures abolished the responses elicited from the carotid sinuses and aortic arch respectively.

Stimulation of arterial baroreceptors by raising the mean perfusion pressure

Non-pulsatile perfusion of the vasosensory areas

The carotid sinuses and aortic arch were subjected to non-pulsatile pressures and the control mean pressures in the two areas were set at approximately the same values within the normal range of arterial pressure for the dog. Stimulation of the baroreceptors in one area was carried out by raising in a single step the mean perfusion pressure while the mean pressure in the other area was maintained constant. The effects on the systemic arterial perfusion pressure were observed.

Carotid sinus baroreceptors. The effects of stimulation of the carotid sinus baroreceptors in this way were studied in eleven experiments and are summarized in Table 2*A*. In twenty-one tests the mean carotid sinus pressure (non-pulsatile) was increased by 9–24 mm Hg (mean $15{\cdot}9 \pm 1{\cdot}2$) and this resulted in a peak fall of systemic arterial perfusion pressure of 25–104 mm Hg (mean $49{\cdot}5 \pm 3{\cdot}5$). Since the systemic blood flow was maintained constant this fall of pressure represents a reduction in systemic vascular resistance of 17–57 % (mean $34{\cdot}8 \pm 1{\cdot}8$).

Aortic arch baroreceptors. The effects of stimulation of the aortic arch baroreceptors were studied in nine experiments. The results of twenty-three tests in which the mean aortic arch pressure (non-pulsatile) was raised 10–24 mm Hg (mean $17{\cdot}7 \pm 1{\cdot}1$) are summarized in Table 2*B*. A fall in systemic arterial perfusion pressure occurred of 5–48 mm Hg (mean $29{\cdot}4 \pm 2{\cdot}5$), representing a reduction in systemic vascular resistance of $20{\cdot}6 \pm 1{\cdot}6$ % (range 4–32).

Comparison of the carotid sinus and aortic arch baroreceptors. A group analysis of the data in Table 2 indicates that a rise in mean perfusion pressure in the carotid sinuses results in a significantly larger reflex reduction in systemic vascular resistance than a similar rise of aortic arch pressure ($P < 0{\cdot}001$). This finding was confirmed by an analysis of paired observations from experiments in which the systemic vascular responses

elicited in the same animal by equal rises in pressure in the carotid sinuses and aortic arch were compared. The control levels of mean pressure in each vasosensory area and the mean systemic arterial perfusion pressure were approximately the same for each paired test. The results are summarized in Table 3, from which it may be seen that in fourteen paired tests the systemic vascular resistance fell by $37{\cdot}6 \pm 2{\cdot}5$ and $23{\cdot}5 \pm 3{\cdot}0\%$ in response to raising the carotid sinus pressure and aortic arch pressure respectively ($P < 0{\cdot}001$).

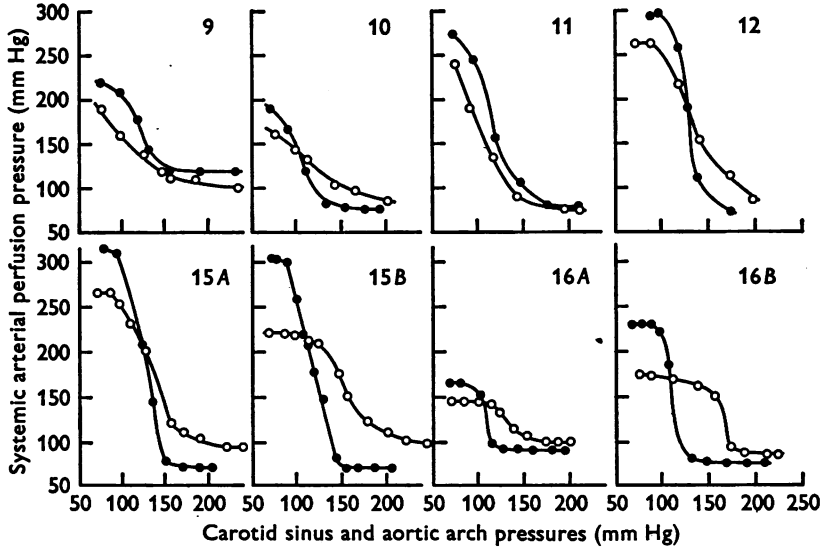

Fig. 3. Comparison of the relationship between the mean pressure in the carotid sinuses or aortic arch and the mean systemic arterial perfusion pressure during non-pulsatile perfusion of the vasosensory areas in six experiments (nos. 9, 10, 11, 12, 15*A*, *B* and 16*A*, *B*) under steady-state conditions. ●—●, carotid sinuses; ○—○, aortic arch. In each experiment the mean pressure (non-pulsatile) in the vasosensory area not under test was maintained constant.

Koch (1931) related mean carotid sinus pressure, over a wide range of pressure, to arterial blood pressure and obtained a curve which was sigmoid in shape. His results imply that an incremental rise of carotid sinus pressure produces a reflex blood pressure response the size of which is dependent on the initial level of the sinus pressure. Thus our finding that when the vasosensory areas are perfused with a non-pulsatile pressure the systemic vascular responses evoked by a change in pressure in the carotid sinuses is about twice that produced by the same rise in pressure in the aortic arch, applies only to one level of pressure in these areas,

TABLE 3. Non-pulsatile pressure perfusion of the vasosensory areas. The effects on systemic vascular resistance of separate stimulation of the carotid sinus (*CS*) and aortic arch (*AA*) baroreceptors by raising the mean perfusion pressure. Paired observations

Expt. no.		Carotid sinus pressure (mm Hg)		Aortic arch pressure (mm Hg)		Systemic arterial perfusion pressure (mm Hg)		Systemic vascular resistance	
		Control	Increase	Control	Increase	Control	Decrease	Decrease (%)	Difference
2	*CS*	105	35	107	.	110	56	51	.
	AA	105	.	120	40	125	61	49	2
3	*CS*	119	29	118	.	99	43	43	.
	AA	120	.	119	31	102	32	31	12
4	*CS*	140	24	124	.	184	104	57	.
	AA	139	.	126	23	160	43	26	31
5*a*	*CS*	110	38	124	.	138	39	28	.
	AA	110	.	126	39	126	40	32	−4
5*b*	*CS*	129	20	129	.	134	45	34	.
	AA	129	.	129	23	140	26	19	15
6	*CS*	100	20	99	.	144	49	34	.
	AA	105	.	102	20	140	45	32	2
7	*CS*	130	20	136	.	140	63	45	.
	AA	129	.	135	22	138	29	21	24
8*a*	*CS*	120	21	125	.	150	57	38	.
	AA	120	.	126	21	143	40	28	10
8*b*	*CS*	124	11	128	.	150	50	33	.
	AA	124	.	127	11	151	31	21	12
9	*CS*	131	9	135	.	146	46	32	.
	AA	129	.	133	12	140	5	4	28

TABLE 3 (*cont.*)

Expt. no.		Carotid sinus pressure (mm Hg)		Aortic arch pressure (mm Hg)		Systemic arterial perfusion pressure (mm Hg)		Systemic vascular resistance	
		Control	Increase	Control	Increase	Control	Decrease	Decrease (%)	Difference
10	*CS*	106	10	114	.	120	35	29	.
	AA	104	.	111	10	128	14	11	18
11	*CS*	110	10	115	.	130	30	23	.
	AA	108	.	114	12	132	34	26	−3
12*a*	*CS*	120	10	114	.	142	58	41	.
	AA	120	.	115	11	156	18	12	29
12*b*	*CS*	126	10	125	.	174	68	39	.
	AA	128	.	128	12	186	31	17	22
$n = 14$									
(*a*) Mean		119·3	19·1	120·9	.	140·1	53·1	37·6	.
S.E. of mean		± 3·1	± 2·6	± 2·8	.	± 6·0	± 4·8	± 2·5	.
(*b*) Mean		119·3	.	122·2	20·5	140·5	32·1	23·5	14·1
S.E. of mean		± 3·0	.	± 2·5	± 2·7	± 5·2	± 3·8	± 3·0	± 3·2
									$P < 0{\cdot}001$

namely that which falls within the normal range of mean arterial pressure for the dog. But our results indicate that within this range of pressure the slope of the curve relating carotid sinus pressure to systemic arterial perfusion pressure is steeper than that relating aortic arch pressure to systemic arterial perfusion pressure.

Further experiments were therefore performed to determine the relationship between the carotid sinus or aortic arch pressure and systemic arterial perfusion pressure over a wide range of pressures in the vasosensory areas under steady-state conditions. The mean pressures were initially set at the same level and that in the vasosensory area not under test was maintained constant.

In five of six such experiments shown in Fig. 3 (expt. nos. 9, 10, 12, 15*A*, *B* and 16*A*, *B*) the curve for the aortic arch (open circles) is flatter than that for the carotid sinuses (closed circles), particularly in the range of sinus and aortic pressures of 100–140 mm Hg. At the lower end of the range of pressures in the vasosensory areas, the systemic arterial perfusion pressure is higher at a carotid sinus pressure of, for instance, 80 mm Hg than at the same aortic arch pressure. These differences are less obvious in the sixth experiment (no. 11). In all six experiments the curves tend towards a plateau at high carotid sinus and aortic arch pressures. It is apparent from these curves that the size of the reflex response to a given rise of mean pressure in each vasosensory area will depend on the control level of carotid sinus or aortic arch pressure.

Pulsatile perfusion of the vasosensory areas

In this series of experiments the carotid sinuses and aortic arch were each subjected to a pulsatile pressure of the same size at a pulse frequency of 110 c/min. Stimulation of the baroreceptors in one area was carried out by raising in a single step the mean perfusion pressure while the mean and pulse pressures in the other area were maintained constant.

The results of nine paired tests of stimulation of the carotid sinus and aortic arch baroreceptors in six experiments are summarized in Table 4. A rise of mean carotid sinus pressure of 10–26 mm Hg (mean $14{\cdot}2 \pm 2{\cdot}0$) caused a fall in systemic arterial perfusion pressure of 10–49 mm Hg (mean $22{\cdot}1 \pm 3{\cdot}9$) from a mean control value of $127{\cdot}8 \pm 3{\cdot}5$ mm Hg. This represents a reduction in systemic vascular resistance of $16{\cdot}9 \pm 2{\cdot}5\%$ (range 9–34).

When the mean aortic arch pressure was raised in each paired test by the same amount (mean increase $15{\cdot}4 \pm 1{\cdot}8$ mm Hg; range 10–25), a fall in systemic arterial pressure of $21{\cdot}0 \pm 3{\cdot}9$ mm Hg occurred from an initial control value of $131{\cdot}6 \pm 3{\cdot}8$ mm Hg. This fall of pressure represents a reduction in systemic vascular resistance of $15{\cdot}8 \pm 2{\cdot}9\%$ (range 8–33). A paired analysis of this data indicates that the differences in the reflex

TABLE 4. Pulsatile perfusion of the vasosensory areas. The effects on systemic vascular resistance of separate stimulation of the carotid sinus (*CS*) and aortic arch (*AA*) baroreceptors by raising the mean perfusion pressure. Paired observations

Expt. no.		Carotid sinus pressure (mm Hg)			Aortic arch pressure (mm Hg)			Systemic arterial perfusion pressure (mm Hg)		Systemic vascular resistance	
		Pulse pressure	Mean control	Mean increase	Pulse pressure	Mean control	Mean increase	Control	Decrease	Decrease (%)	Difference
8	*CS*	60	127	21	60	104	.	143	49	34	.
	AA	60	132	.	60	118	22	144	48	33	1
9	*CS*	62	130	10	60	126	.	132	21	16	.
	AA	62	120	.	60	136	14	142	12	8	8
10	*CS*	68	105	11	62	110	.	106	10	9	.
	AA	68	112	.	62	126	14	114	11	10	−1
11	*CS*	62	115	11	64	120	.	126	12	10	.
	AA	62	116	.	64	114	12	130	28	22	−12
12*a*	*CS*	58	111	11	56	124	.	132	18	14	.
	AA	58	122	.	56	130	10	138	16	12	2
12*b*	*CS*	58	112	10	56	122	.	138	22	16	.
	AA	58	120	.	56	126	12	144	20	14	2
12*c*	*CS*	58	120	10	56	132	.	124	24	19	.
	AA	58	126	.	56	132	10	132	22	17	2
14*a*	*CS*	60	110	26	62	110	.	125	28	22	.
	AA	60	115	.	62	110	25	120	20	17	5
14*b*	*CS*	62	114	18	62	106	.	125	15	12	.
	AA	62	108	.	62	110	20	120	12	10	2
$n = 9$											
(*CS*) mean		±1·1	±2·5	±2·0	±1·0	±3·3	.	±3·5	±3·9	±2·5	.
S.E. of mean		60·9	115·4	14·2	59·8	117·1	.	127·8	22·1	16·9	.
(*AA*) mean		60·9	118·3	.	59·8	122·4	15·4	131·6	21·0	15·8	1·0
S.E. of mean		±1·1	±2·7	.	±1·0	±3·2	±1·8	±3·8	±3·9	±2·9	±1·8
											$P > 0·5$

changes in systemic vascular resistance elicited from the two vasosensory areas are not significant ($P > 0{\cdot}5$). This is in contrast to the responses elicited by changes in mean carotid sinus and aortic arch pressure during non-pulsatile perfusion.

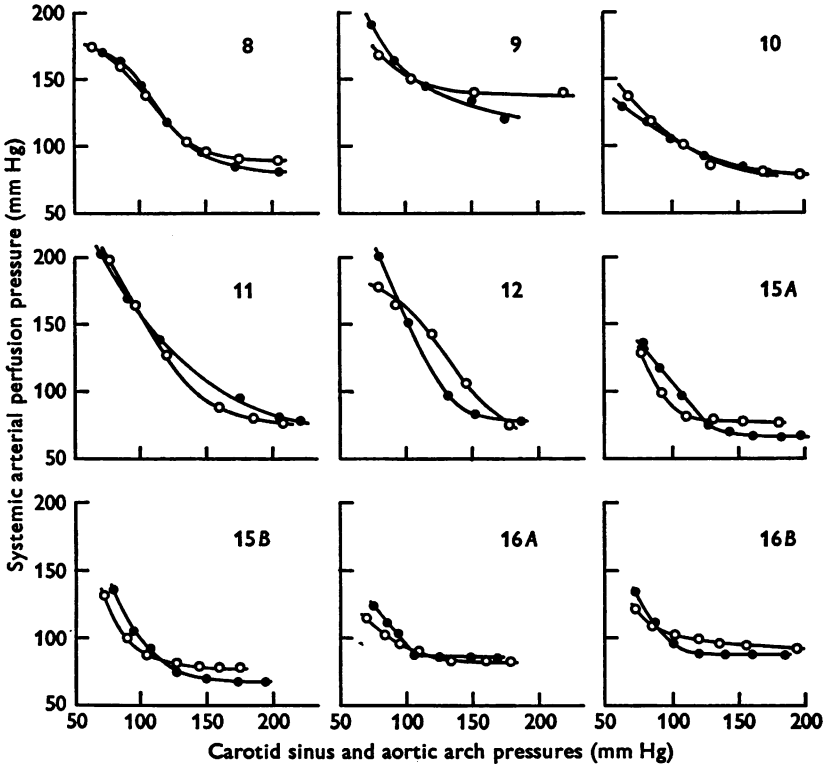

Fig. 4. Comparison of the relationship between the mean pressure in the carotid sinuses or aortic arch and the mean systemic arterial perfusion pressure during pulsatile perfusion of the vasosensory areas in seven experiments (nos. 8–12, 15*A*, *B* and 16*A*, *B*) under steady-state conditions. Pulse frequency, 110 c/min. ●—●, carotid sinuses; ○—○, aortic arch. In each experiment the mean pressure, pulse pressure and pulse frequency in the vasosensory area not under test were maintained constant.

These results suggest that during pulsatile perfusion of the vasosensory areas the slope of the curves relating mean sinus or aortic pressure and systemic arterial perfusion pressure are the same, at least over this limited pressure range.

The curves relating the mean pressure in the carotid sinuses or aortic arch and systemic arterial perfusion pressure are shown in Fig. 4. The

differences between the curves for the carotid sinuses and aortic arch are considerably less than under conditions of non-pulsatile perfusion of the two vasosensory areas (Fig. 3).

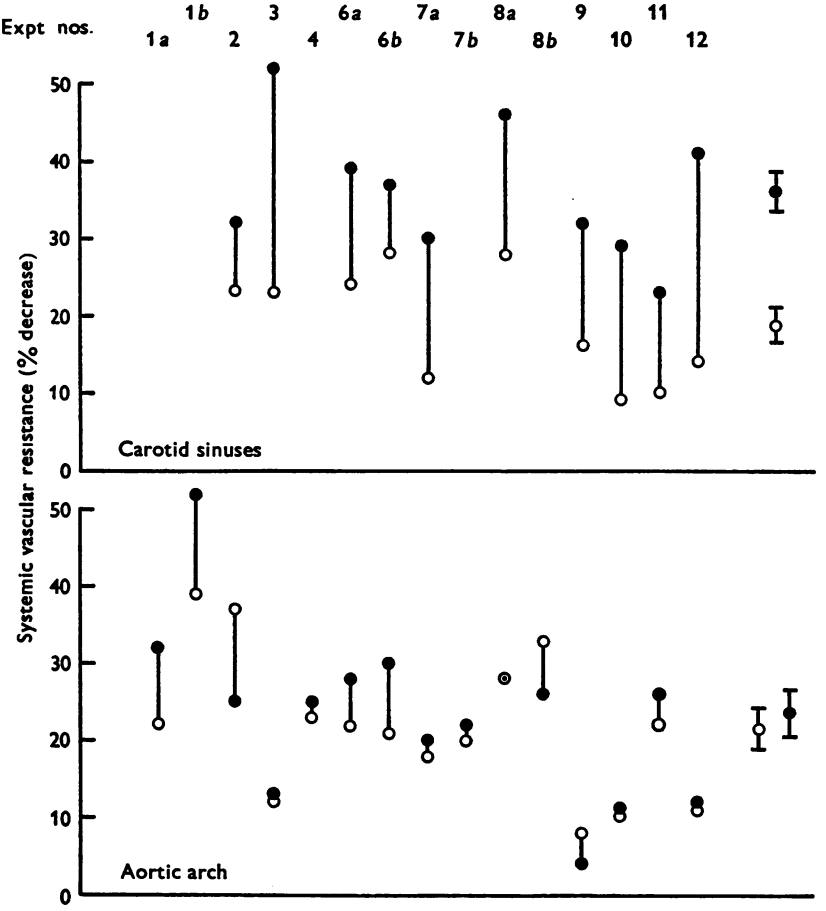

Fig. 5. The effects on systemic vascular resistance of stimulation of the arterial baroreceptors by raising the mean perfusion pressure: comparison of non-pulsatile and pulsatile perfusion of the carotid sinuses and aortic arch. In each experiment the mean pressures in the carotid sinuses or aortic arch were raised by the same amount during non-pulsatile perfusion (●) and during pulsatile perfusion (○); the bars connecting the open and closed circles indicate the differences in the responses. Pulse frequency, 110 c/min. Mean changes in systemic vascular resistance and S.E. of mean are given for the carotid sinuses (ten observations in nine experiments) and for the aortic arch (fifteen observations in eleven experiments).

Stimulation of arterial baroreceptors by raising the mean pressure: comparison of pulsatile and non-pulsatile pressures in each vasosensory area

The finding that the difference in potency between the carotid sinus and aortic arch vasomotor reflexes depends on whether or not the pressure is pulsatile suggests that the reflex effects of pulsatile pressure are different in the two vasosensory areas. In an attempt to gain further information on this point a comparison was made in each area of the effects of stimulation of the baroreceptors by raising the mean pressure during non-pulsatile and during pulsatile perfusion, the initial control value being the same. The pressure in the vasosensory area not under test was non-pulsatile and was maintained constant.

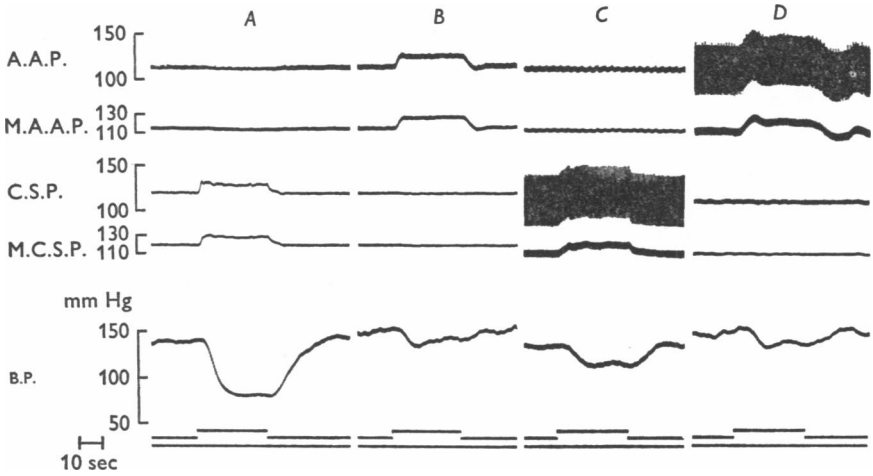

Fig. 6. The effects of stimulation of the arterial baroreceptors by raising the mean pressure in the carotid sinuses and aortic arch during non-pulsatile and pulsatile perfusion. *A* and *C*, mean carotid sinus pressure increased by 10 mm Hg during non-pulsatile and pulsatile perfusion respectively. *B* and *D*, mean aortic arch pressure increased by 12 mm Hg during pulsatile and non-pulsatile perfusion respectively. Pulse frequency, 110 c/min. Time calibration, 10 sec. Dog, male, 15·3 kg. Separate perfusion of the isolated carotid sinuses and aortic arch, and of the systemic circulation.

Carotid sinus baroreceptors. The results of ten paired observations in nine experiments are summarized in Fig. 5 and the typical response is shown in Fig. 6*A*, *C*. In all tests the reduction in systemic vascular resistance was greater when the rise in mean carotid sinus pressure was produced during non-pulsatile than during pulsatile perfusion.

During non-pulsatile perfusion of the carotid sinuses a rise in mean

pressure of 14·0 ± 1·7 mm Hg (range 9–21) caused a fall in systemic arterial perfusion pressure of 50·2 ± 4·6 mm Hg (range 30–74), the initial control value being 138·1 ± 4·0 mm Hg (range 120–160). This corresponds to a reduction in systemic vascular resistance of 36·1 ± 2·7 % (range 23–52).

By contrast are the results obtained during pulsatile perfusion of the carotid sinuses, the average pulse pressure in different experiments being 52·7 ± 3·0 mm Hg (range 40–68). It was found that the same rise of mean carotid sinus pressure of 13·6 ± 1·2 mm Hg (range 10–18) caused a fall in systemic arterial perfusion of 24·3 ± 3·2 mm Hg (range 10–38) from its initial control level of 128·6 ± 2·7 mm Hg (range 106–137). This represents a reduction in systemic vascular resistance of 18·7 ± 2·3 % (range 9–28); that is, about one half the value obtained during non-pulsatile perfusion. A paired analysis of the data indicates that these differences are statistically highly significant ($P < 0·001$).

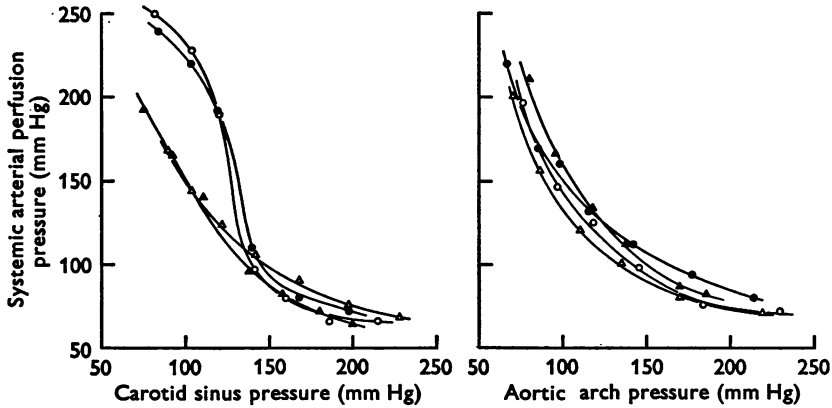

Fig. 7. Left: carotid sinuses. The effects of pulsatile pressure on the relationship between the mean carotid sinus pressure and systemic arterial perfusion pressure at constant aortic arch mean pressure (pulse pressure 62 mm Hg). Right: aortic arch. The effects of pulsatile pressure on the relationship between mean aortic arch pressure and systemic arterial perfusion pressure at constant carotid sinus mean pressure (pulse pressure 60 mm Hg). Steady-state conditions. ●, ○, non-pulsatile perfusion of the vasosensory area; ▲, △, pulsatile perfusion of the vasosensory area (pulse pressure 60 mm Hg).

These findings are supported by the results of experiments in which the relationship was determined between the mean carotid sinus pressure and systemic arterial perfusion pressure during pulsatile and non-pulsatile perfusion of the carotid sinuses. The mean pressure and pulse pressure in the aortic arch were maintained constant. Four curves obtained in one of four experiments are shown in Fig. 7 (left). The two curves for pulsatile

perfusion are appreciably lower than those for non-pulsatile perfusion between a mean carotid sinus pressure of 80 and about 140 mm Hg. Similar results were obtained in the three other experiments.

Aortic arch baroreceptors. The results of fifteen paired observations in eleven experiments during pulsatile and non-pulsatile pressure perfusion are shown in Fig. 5 and the typical response is illustrated by Fig. 6*B*, *D*. Taking all observations into account it was found that during non-pulsatile perfusion a rise in mean aortic arch pressure of 20·2 ± 1·7 mm Hg (range 10–33) resulted in a fall in systemic arterial perfusion pressure of 31·9 ± 3·7 mm Hg (range 5–68), the initial control value being 137 ± 2·2 mm Hg (range 122–156). This represents a reduction in vascular resistance of 23·6 ± 2·9 % (range 4–52). On the other hand, during pulsatile perfusion, the average pulse pressure being 56·7 ± 1·5 mm Hg (range 41–64), the same rise in mean aortic arch pressure of 20·9 ± 1·7 mm Hg (range 10–33) caused a fall in systemic arterial perfusion pressure of 29·1 ± 3·6 mm Hg (range 11–58) from an initial control value of 133·0 ± 3·0 mm Hg (range 114–150), or a reduction in vascular resistance of 21·7 ± 2·4 % (range 8–37). A paired comparison of this data indicates that the differences are not statistically significant ($P > 0·2$).

The curves relating mean aortic arch pressure and systemic arterial perfusion pressure, under conditions of constant mean and pulse pressures in the carotid sinuses, were obtained in four experiments and the typical results from one of them are shown in Fig. 7 (right). It may be noted that by comparison with the data obtained from the carotid sinuses in the same animal, there is no difference between the curves obtained during pulsatile and non-pulsatile perfusion of the aortic arch.

Effects of substituting pulsatile for non-pulsatile pressure

The effects on systemic vascular resistance of substituting a pulsatile for a non-pulsatile pressure without change of mean pressure in the carotid sinuses and aortic arch were studied. The mean pressure in the vasosensory area not under test was maintained constant at the same level as in the test area and was non-pulsatile. Fifteen paired observations were made in ten experiments in which the size of the applied pulse pressure was the same in each vasosensory area, the pulse frequency being 110 c/min.

Carotid sinus baroreceptors. The average control carotid sinus pressure (non-pulsatile) was 124·3 ± 2·4 mm Hg (range 105–140) and the systemic arterial perfusion pressure was 143·4 ± 4·1 mm Hg (range 118–180). When the carotid sinus pressure was made pulsatile, without change in the mean pressure, the pulse pressure varying in different experiments from 24 to 66 mm Hg (mean 51·7 ± 3·3), a fall in systemic arterial perfusion pressure of 29–89 mm Hg (mean 41·3 ± 3·7) occurred, corresponding to a reduction

in vascular resistance of 28·4 ± 1·8 % (range 20–49). Re-establishing a non-pulsatile pressure reversed the response.

Aortic arch baroreceptors. A similar, though smaller, effect was observed when a pulsatile pressure was substituted for a non-pulsatile pressure in the aortic arch. It was found that the application of a pulse pressure of 26–63 mm Hg (mean 51·1 ± 3·3), the mean aortic arch pressure being 125·8 ± 2·5 mm Hg (range 107–140), caused a reduction in systemic arterial

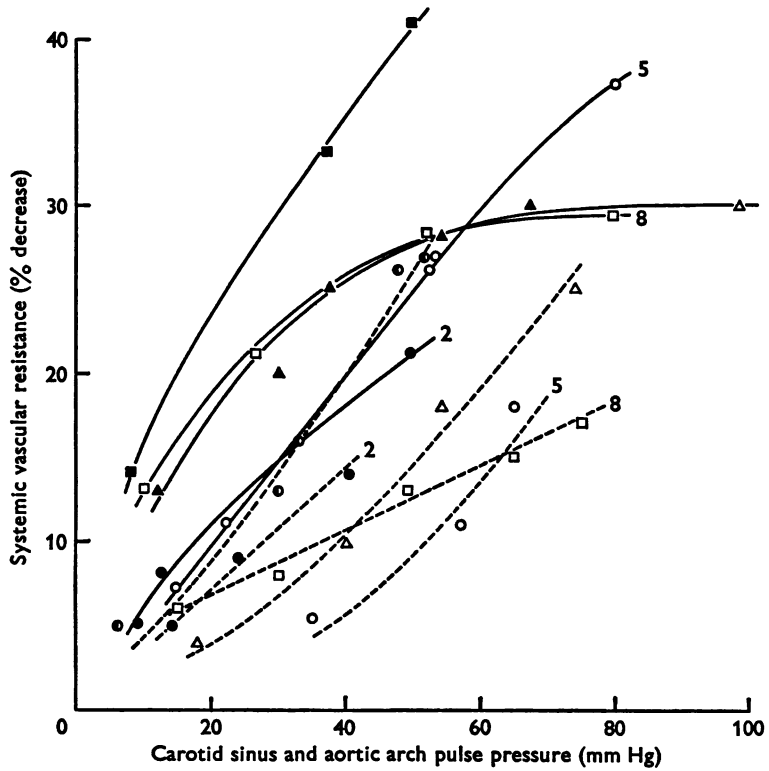

Fig. 8. The effects on systemic vascular resistance of substituting a pulsatile pressure at different pulse pressures for a non-pulsatile pressure without change of mean pressure in the carotid sinuses (continuous lines) and aortic arch (interrupted lines). Each symbol represents an experiment. In expt. nos. 2, 5 and 8, observations were made on both the carotid sinuses and aortic arch.

perfusion pressure of 3–66 mm Hg (mean 24·3 ± 4·7) from a control value of 143·0 ± 4·1 mm Hg (range 124–185). This fall in pressure represents a reduction in systemic vascular resistance of 16·4 ± 2·8 % (range 2–44). Statistical analysis of the fifteen paired observations indicates that the difference between the vasomotor responses to the change from non-

pulsatile to pulsatile pressure in the carotid sinuses and in the aortic arch is highly significant ($P < 0{\cdot}001$).

Effects of altering the pulse pressure

It was found that when a pulsatile pressure was substituted for a non-pulsatile pressure at constant mean pressure and pulse frequency (110 c/min) in the carotid sinuses and aortic arch, the larger the pulse pressure the greater the reduction in systemic vascular resistance. This conclusion is based on forty-six observations in five experiments and all the results are summarized graphically in Fig. 8. In Fig. 8 it may be noted that not only is there a close relationship between pulse pressure in each vasosensory area and the reduction in systemic vascular resistance but that, in general, the larger vascular responses for any given change in pulse pressure are elicited from stimulation of the carotid sinus baroreceptors. This is also apparent in the three experiments in which observations were made on both the carotid sinuses and the aortic arch (Fig. 8; expt. nos. 2 (●), 5 (○) and 8 (□)).

In these experiments the range of pulse pressures applied to the carotid sinuses was 8–100 mm Hg and these resulted in falls in systemic arterial perfusion pressure of 7–65 mm Hg corresponding to reductions in systemic vascular resistance of 5–41 %. In the aortic arch, pulse pressures varying from 6 to 75 mm Hg caused falls in systemic arterial perfusion pressure of 5–42 mm Hg corresponding to reductions in systemic vascular resistance of 5–27 %.

The effects of changes in the phase relationship between the pulse pressure waves in the carotid sinuses and aortic arch

In all experiments described so far, the two Dale–Schuster pumps providing the pulsatile pressures in the carotid sinuses and aortic arch were in phase, so that the peak systolic pressure in each vasosensory area occurred simultaneously. The effects on systemic vascular resistance of altering the phase angle between the pulse pressure waves in the two areas was studied in two types of experiment.

In the first a pulsatile pressure at a frequency of 110 c/min was substituted for a non-pulsatile pressure in the carotid sinuses and aortic arch simultaneously with the two pumps connected in such a way that the pulses were in phase. This resulted in a fall in systemic arterial pressure as described in the preceding section. The test was then repeated with the pumps either 90 or 180° out of phase. In a total of seven such comparisons in three experiments there was no appreciable difference in the size of the fall in systemic arterial perfusion pressure and hence in the reduction in vascular resistance.

In the second type of experiment both vasosensory areas were perfused with a pulsatile pressure, the pulse pressure waves being in phase with each other. Then the pulse pressure waves were made 180° out of phase without stopping the pumps. Finally, ½–2 min later, the pulse pressure waves were set in phase again. The pulse frequencies in each vasosensory area were either 72 or 110 c/min. This procedure was carried out in eight tests in three experiments and in none was any change in systemic arterial perfusion pressure observed.

In all these experiments it was established that substitution of a pulsatile pressure for a non-pulsatile pressure in the carotid sinuses and aortic arch separately caused a reduction in systemic arterial perfusion pressure.

The effects of altering the pulse frequency

The effects of altering the pulse frequency in each vasosensory area were studied under conditions in which the mean pressure and the pulse pressure were maintained constant. The pressure (non-pulsatile) in the area not under test was also maintained constant. In practice a pulsatile pressure varying from 32 to 60 mm Hg in different experiments was substituted for a non-pulsatile pressure at pulse frequencies of 28, 54, 72, 110, 166 or 216 c/min, and the effects on systemic arterial perfusion pressure were observed.

The results of eight experiments on the carotid sinuses and aortic arch are shown in Fig. 9. In confirmation of the results reported above, the systemic vascular responses to the application of the pulse pressures *per se* were with the exception of one experiment (no. 11), larger for the carotid sinuses than the aortic arch. In both vasosensory areas, however, increasing the pulse frequency caused, in general, increasing reductions in systemic vascular resistance. It will be noted in Fig. 9 that in the majority of experiments the larger proportion of the maximum observed response occurred at the lower frequencies of 28–72 c/min, and that increasing the frequency above these values had only a small additional effect on systemic vascular resistance.

The effects of combined stimulation of the carotid sinus and aortic arch baroreceptors

Evidence is presented from two types of experiment that the response to combined stimulation of the carotid sinus and aortic arch baroreceptors is greater than either of their responses when stimulated separately. In each case the initial control mean pressures were the same and within the normal physiological range.

Changes in mean pressure. In seven experiments the mean pressure during

non-pulsatile perfusion of the vasosensory areas was temporarily raised first in the carotid sinuses, then the aortic arch and finally in both regions simultaneously. The rise in pressure was the same in both regions and varied from 9 to 20 mm Hg in different experiments. The results are shown in Fig. 10, from which it may be seen that the largest response in each

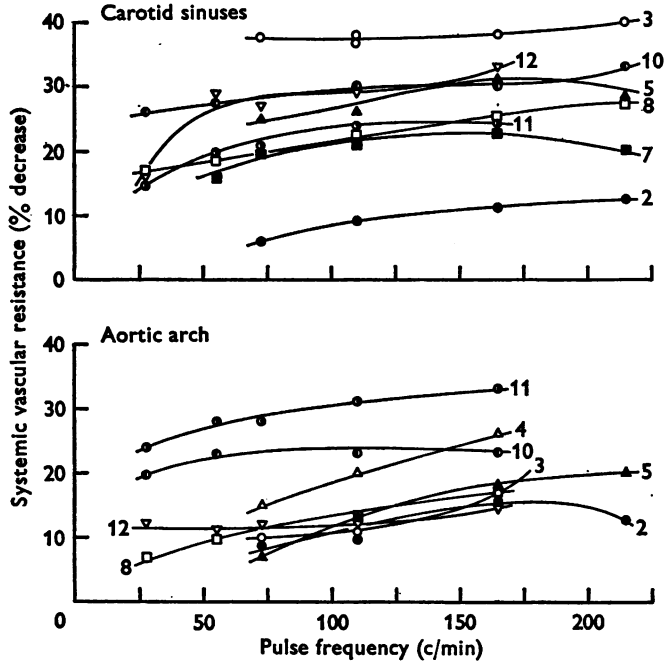

Fig. 9. The effects on systemic vascular resistance of substituting a pulsatile pressure at different pulse frequencies for a non-pulsatile pressure in the carotid sinuses and aortic arch in eight experiments. The curves are numbered according to the experiment number. The mean pressure (non-pulsatile) in the vasosensory area not under test was maintained constant. In experiment nos. 3, 5, 8, 11 and 12, the size of the applied pulse pressure was the same in the carotid sinuses as in the aortic arch. Symbols: expt. no. 2 (●), 3 (○), 5 (▲), 7 (■), 8 (□), 10 (◐), 11 (◑), 12 (△).

experiment occurred when the pressure in both areas was raised simultaneously.

Changes in pulse pressure. The effects of substituting a given pulsatile pressure for a non-pulsatile pressure in the carotid sinuses, aortic arch and simultaneously in the two vasosensory areas were observed in seven experiments. In four of these the combined response was greater than either of their separate effects. In the remaining three the aortic arch response

was small and the size of the combined effect was equal to that of the carotid sinuses alone.

In the seven experiments the average reduction in systemic vascular resistance on substituting a pulsatile for a non-pulsatile pressure in both vasosensory areas simultaneously was $36{\cdot}7 \pm 2{\cdot}6\,\%$ (range 28–46). The typical response is illustrated by Fig. 11*b*. When perfusion of the vasosensory areas was converted from a pulsatile to a non-pulsatile state without changing the mean pressure, the opposite effects were observed (Fig. 11*a*).

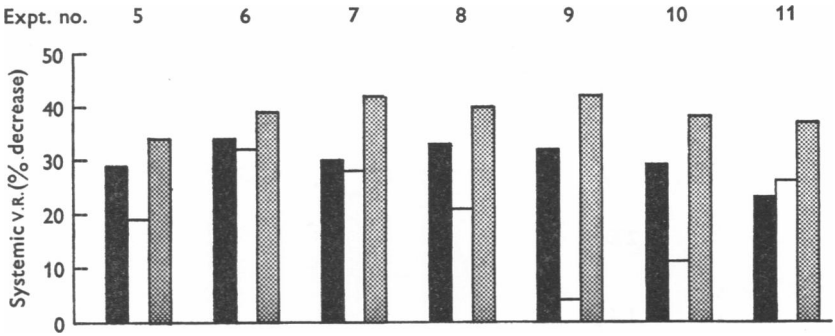

Fig. 10. The effects of separate and combined stimulation of the baroreceptors in the carotid sinuses and aortic arch on systemic vascular resistance (V.R.). Non-pulsatile perfusion of the vasosensory areas. In each experiment the mean perfusion pressure was raised by an equal amount in the carotid sinuses (closed blocks), the aortic arch (open blocks) and in the carotid sinuses and aortic arch simultaneously (stippled blocks).

Comparison of pulsatile and non-pulsatile perfusion

Evidence has been presented that the two vasosensory areas differ in the way in which the reflex vascular responses to changes in mean pressure are modified by the pulse pressure in that area. The question now arises as to whether or not the vascular responses elicited by raising the mean pressure in the carotid sinuses and aortic arch *simultaneously* differ according to the pulse pressure in the two regions.

The results of three experiments are shown in Fig. 12. The systemic vascular responses produced by raising the mean carotid sinus and aortic arch pressures during non-pulsatile perfusion of the two areas were diminished when the tests were repeated during pulsatile perfusion by an average of 59 %.

Fig. 13 shows the relationship between the mean carotid sinus and aortic arch pressure (the pressure in both areas being varied together) and systemic arterial perfusion pressure in two experiments during non-

pulsatile perfusion (■) and at a pulse pressure of 60 mm Hg (□). It may be noted that the curves obtained during pulsatile perfusion fall below those for non-pulsatile perfusion.

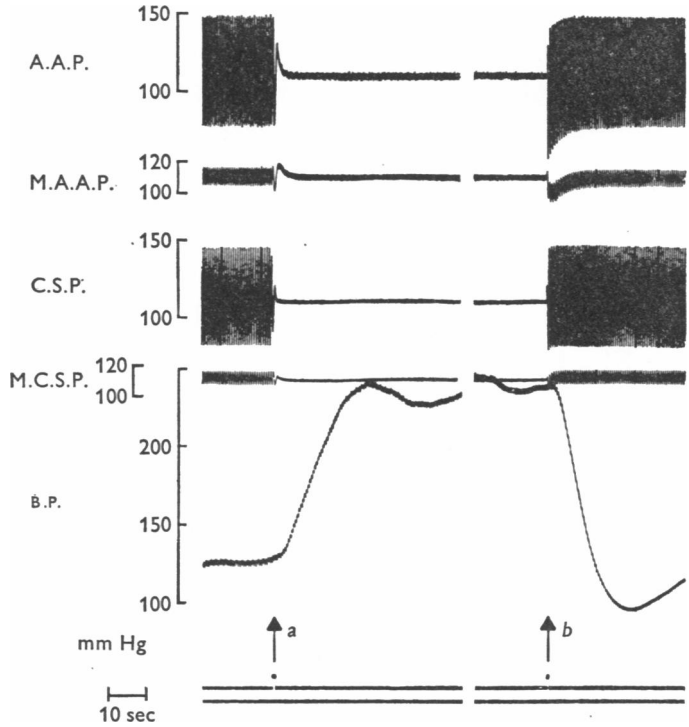

Fig. 11. The effect on the systemic arterial perfusion pressure of reducing the pulse pressures to zero in the carotid sinuses and aortic arch simultaneously at (*a*) and restoring them to their original values at (*b*). The break in the record lasted 1 min. Dog, female, 14·4 kg. Separate perfusion of the isolated carotid sinuses and aortic arch, and of the systemic circulation.

Interaction between carotid sinus and aortic arch baroreceptor reflexes

The effect of altering the mean pressure in the carotid arteries on the aortic-arch baroreceptor reflex has been demonstrated by Carswell *et al.* (1968). In the present experiments it was shown that substituting a pulsatile for a non-pulsatile pressure in the carotid sinuses at a constant mean pressure modified the relationship between the mean aortic arch pressure and systemic arterial perfusion pressure. This is evident from Fig. 14, which shows that curve 2 obtained during pulsatile perfusion of the carotid sinuses is appreciably lower than the two control curves (1 and 3) determined during non-pulsatile perfusion of the sinuses.

DISCUSSION

Our results have shown that there are quantitative differences between the reflex vasomotor responses elicited from baroreceptors situated in the carotid sinus and aortic arch regions. It is unlikely that these differences

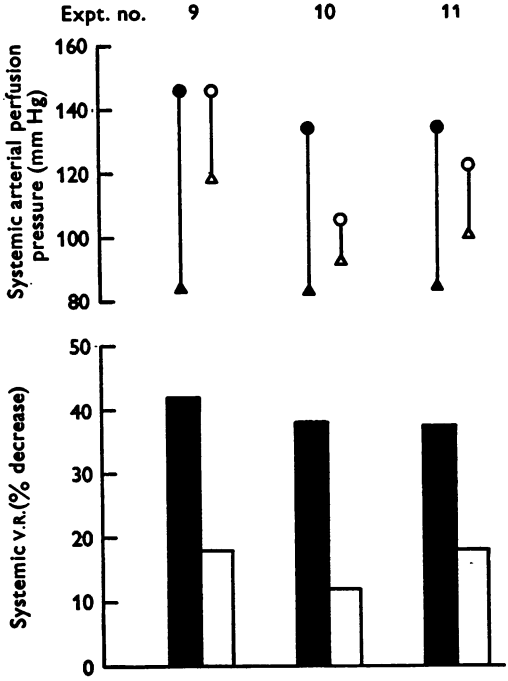

Fig. 12. The effects on systemic arterial perfusion pressure and systemic vascular resistance (V.R.) of combined stimulation of the carotid sinus and aortic arch baroreceptors by raising the mean carotid sinus and aortic arch pressures: comparison of non-pulsatile and pulsatile perfusion. The mean pressures in the carotid sinuses and aortic arch were raised simultaneously by the same amount, 10, 12 and 15 mm Hg respectively in the three experiments, during non-pulsatile perfusion (closed blocks and symbols) and during pulsatile perfusion (open blocks and symbols). (●, ○) control systemic arterial perfusion pressure during non-pulsatile and pulsatile perfusion respectively; (▲, △) systemic arterial perfusion pressure values during raised mean carotid sinus and aortic arch pressures. The carotid sinus and aortic arch pulse pressures were 62, 62 and 66 mm Hg in three experiments respectively. Pulse frequency, 110 c/min.

are due to surgical interference with the vasosensory areas themselves. The small branches of the external carotid arteries were ligated individually well away from the sinus region and no mass ligature techniques were used. Again in the case of the aortic arch, all its major branches were tied some

distance from the known baroreceptor area, and we deliberately excluded the use of any type of cannula which might alter the longitudinal tension on the aorta as this is known to affect the physiological characteristics of the baroreceptors (Angell James, 1969).

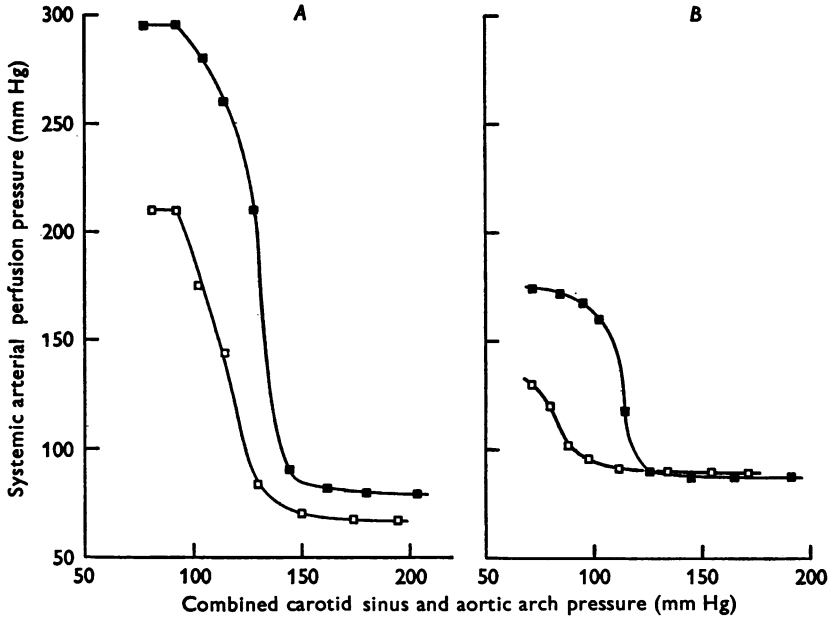

Fig. 13. Combined perfusion of the carotid sinuses and aortic arch. The effects of pulsatile pressure on the relationship between mean carotid sinus and aortic arch pressure and systemic arterial perfusion pressure in two experiments (*A* and *B*). ■, non-pulsatile perfusion; □, pulsatile perfusion (pulse pressure 60 mm Hg; pulse frequency 110 c/min).

The vascular area isolated and perfused included not only the aortic arch itself but also the region of the bifurcation of the innominate artery. This latter region has also been shown to contain baroreceptors (Nonidez, 1935) and reflex changes in blood pressure have been elicited from the perfused region (Nakayama, 1954; Neil, 1956; Ueda, Uchida, Yasuda & Takeda, 1966). However, Nakayama (1954) found in the dog that a rise in pressure of 200–300 mm Hg in the perfused right subclavian area was required to produce reflex falls of arterial pressure of only 7–18 mm Hg. Furthermore, we have shown that the vasomotor responses elicited by raising the pressure in the aortic arch and subclavian areas together are not appreciably different to those produced by raising the pressure in the aortic arch alone by occluding the brachiocephalic artery (unpublished observations). It is concluded therefore that the responses observed by us are due pre-

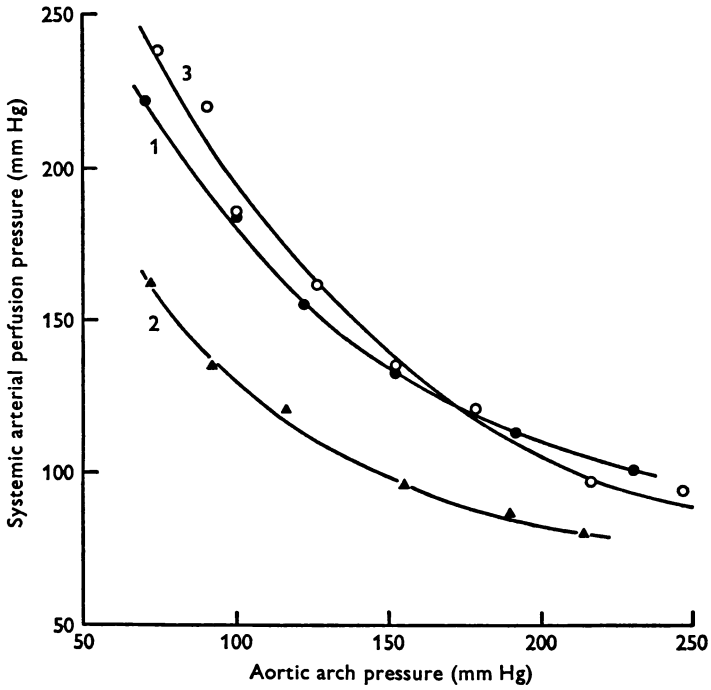

Fig. 14. The effects of pulsatile pressure in the carotid sinuses on the relationship between aortic arch pressure (non-pulsatile) and systemic arterial perfusion pressure under steady-state conditions. Curves 1 (●) and 3 (○) during non-pulsatile perfusion of the carotid sinuses at a constant pressure of 122 mm Hg. Curve 2 (▲) during pulsatile perfusion of the carotid sinuses (pulse pressure, 70 mm Hg) at constant mean pressure of 122 mm Hg. Curves 1, 2 and 3 were obtained in that order. Dog, male, 11·8 kg.

dominantly to an alteration in the discharge of impulses from the aortic arch baroreceptors.

Responses to changes in mean carotid sinus and aortic arch pressures

The systemic circulation in our experiments was perfused at constant blood flow and a change in systemic arterial perfusion pressure indicates therefore a similar directional change in systemic vascular resistance which must be due to a predominance of vasoconstriction or vasodilatation.

Carotid sinuses

Evidence is presented that the size of the vasomotor response to a given rise of mean carotid sinus perfusion pressure is greater during non-pulsatile perfusion than during pulsatile perfusion of the vasosensory area.

This only applies over the normal range of arterial pressure but suggests that the slope of the curve relating mean carotid sinus pressure and systemic arterial perfusion pressure during non-pulsatile perfusion is steeper than that during pulsatile perfusion. Evidence confirming that this is so was obtained by studying the relationship between carotid sinus pressure and systemic arterial perfusion pressure (Fig. 7, left). Thus, at any given mean carotid sinus pressure below about 140 mm Hg the systemic arterial perfusion pressure, and hence the vascular resistance, is lower during pulsatile than during non-pulsatile pressure perfusion. At high mean carotid sinus pressure (> about 200 mm Hg) when the systemic vascular resistance is lower, there is no difference between pulsatile and non-pulsatile perfusion, as found by Ead *et al.* (1952).

The finding that a given rise in mean carotid sinus pressure during pulsatile perfusion causes a significantly smaller systemic arterial depressor response than when the pressure is non-pulsatile may therefore be explained on the basis of the different position and shape of the two curves relating carotid sinus pressure and systemic arterial perfusion pressure. Another factor is that the 'background' vasomotor tone is less during pulsatile perfusion so that there is proportionately less tone that can be reflexly inhibited.

Our findings are supported by the observations of Spickler, Kezdi & Geller (1967), who found that as the mean sinus pressure increased the averaged impulse discharge in the renal and splanchnic sympathetic nerves decreased. The curve was sigmoid in shape and that for pulsatile perfusion of the carotid sinuses fell to the left of that for non-pulsatile perfusion, so that at a given mean carotid sinus pressure the activity in the sympathetic nerves was less during pulsatile perfusion.

A number of workers have studied the relationship between arterial blood pressure (or heart rate) and the pressure in the carotid sinuses (Koch, 1931; Heymans, Bouckaert & Dautrebande, 1931) or aortic arch (Levy *et al.* 1966; Carswell *et al.* 1968). The relationship is a curve which is sigmoid in shape, but with the exception of the experiments of Heymans *et al.* (1931) it appears that non-pulsatile pressures have been used exclusively to perfuse the vasosensory areas. During non-pulsatile pressure perfusion of the carotid sinuses the curve reaches a plateau at pressures below about 50 mm Hg (Koch, 1931), when the impulse discharge in most baroreceptor fibres ceases, at least in the cat (Bronk & Stella, 1935; Landgren, 1952). During pulsatile perfusion, however, some fibres show a phasic discharge even although the mean pressure may be below the threshold pressure for a steady discharge (Ead *et al.* 1952; Landgren, 1952). Trank & Visscher (1962) and Spickler & Kezdi (1967) found that for the same mean pressure the averaged discharge frequency in the carotid sinus nerve was

greater during pulsatile than non-pulsatile pressure perfusion. It might be anticipated therefore that at low sinus pressures the curve for pulsatile pressure perfusion would reach a plateau at a lower level of systemic arterial pressure than that for non-pulsatile pressure.

Ead *et al.* (1952) demonstrated that the 'threshold for the sinus reflex' (Koch, 1931) was lower for pulsatile perfusion of the carotid sinuses than for non-pulsatile perfusion. We have not been able to determine the extent of the curves at low carotid sinus and aortic arch pressures (< 80 mm Hg) or the threshold pressure values for these reflexes because of the concomitant excitation of the arterial chemoreceptors as indicated by increased rhythmic movements of the diaphragm and ribs. This is presumably the result of local stagnant hypoxia engendered by a reduced blood flow through the glomus tissue (Landgren & Neil, 1951; Lee, Mayou & Torrance, 1964; Daly *et al.* 1965). Thus the possibility cannot be excluded that at carotid sinus and aortic arch mean pressures below about 80 mm Hg the reflex increase in systemic vascular resistance may be due in part to excitation of arterial chemoreceptors (Daly & Ungar, 1966).

Aortic arch

By contrast with the responses elicited from the carotid sinuses, it was found that at normal levels of mean pressure there were no appreciable differences between the size of the vascular responses produced by a given rise of aortic arch pressure during pulsatile and non-pulsatile pressure perfusion of the vasosensory area. This finding is supported by the curves relating mean aortic arch pressure and systemic arterial perfusion pressure under the two conditions (Fig. 7, right).

When a comparison is made of the reflex vasomotor responses to a given rise in mean pressure in each of the two vasosensory areas, the size of the response depends on whether or not the perfusing pressure is pulsatile. When the pressure is non-pulsatile the carotid sinuses elicit the larger vasomotor response, as demonstrated by Carswell *et al.* (1968). During pulsatile perfusion, on the other hand, there is no significant difference between the size of responses from the two areas at least at a level of pulse pressure of 60 mm Hg. On the basis of the curves shown in Fig. 7, it is suggested that the relative potency of the reflexes from the two areas in response to an incremental rise of mean pressure will depend on the initial level of mean pressure and also on the size of the pulse pressure.

It is evident from these experiments and from those in which the pulse pressure alone was altered that the reflex control of systemic vascular resistance by the carotid sinus baroreceptors is determined by both the local mean pressure and pulse pressure; by contrast, the control exerted by the aortic arch baroreceptors is determined largely by the local mean

pressure, changes in pulse pressure being relatively less effective. The reason for the different reflex characteristics of the baroreceptors in the two areas, in particular the responses to pulse pressure, is uncertain. A central phenomenon could be responsible or it could be related to differences either in the distensibility of the two areas (Remington, Hamilton & Dow, 1945; Landgren, 1952; Rushmer, 1955), in the wall structure (De Castro, 1928; Pease & Paule, 1960; Rees, 1968), or in the distribution of the nerve endings within the walls of the carotid sinus and aortic arch (see Abraham, 1969; also Rees, 1967).

Combined stimulation of the carotid sinus and aortic arch baroreceptors

Although a greater response was produced by combined stimulation of the carotid and aortic baroreceptors than by each group separately, nevertheless it was always less than the algebraic sum of the individual responses. This occurred whether the mean pressure or the pulse pressure was increased. A similar effect had been observed previously in a comparison of the arterial blood pressure reflex responses elicited by changing the pressure in the separately perfused left and right carotid sinus regions (Wang & Borison, 1947; Sagawa & Watanabe, 1965). Although in the present experiments the control carotid sinus and aortic arch mean pressures were the same and within the normal range for the dog, the result of combined stimulation will depend on the exact part of the curves relating carotid sinus or aortic arch pressure and systemic arterial perfusion pressure on which the tests are carried out, and also on the size of the stimulus. Further quantitative information on this point is required.

Although there are quantitative differences between the vascular responses elicited by pulsatile pressures in the carotid sinuses and aortic arch separately, pulse pressure is nevertheless an important factor determining the response to altering the mean pressure in both areas simultaneously.

Responses to changes in pulse frequency

The effects of altering the pulse frequency in the vasosensory areas was studied over a frequency range of 28–216 c/min which covers the lower and middle range of heart rates found in the dog. With both the carotid sinus and aortic arch baroreceptors the relationship between the size of the vasodilator response and pulse frequency was non-linear in that only a small increase in the size of the response occurred above a frequency of about 72 c/min. These findings are consistent with those of other workers who found that an increase of carotid sinus pulse frequency caused a fall in blood pressure (Scher & Young, 1963; Levison, Barnett & Jackson, 1966; Stegemann & Tibes, 1969) and a reduction in the discharge of impulses in renal and splanchnic sympathetic nerves (Spickler *et al.* 1967).

On the afferent side of the reflex arc it has been shown that an increase in carotid sinus pulse frequency is associated with an increase in the ratio of the amplitude of the averaged nerve action potentials to the carotid sinus pressure ('relative gain') (Spickler & Kezdi, 1967). This is due to recruitment of fibres and to a small increase in the number of impulses per unit time in single units (Angell James, 1968, 1969).

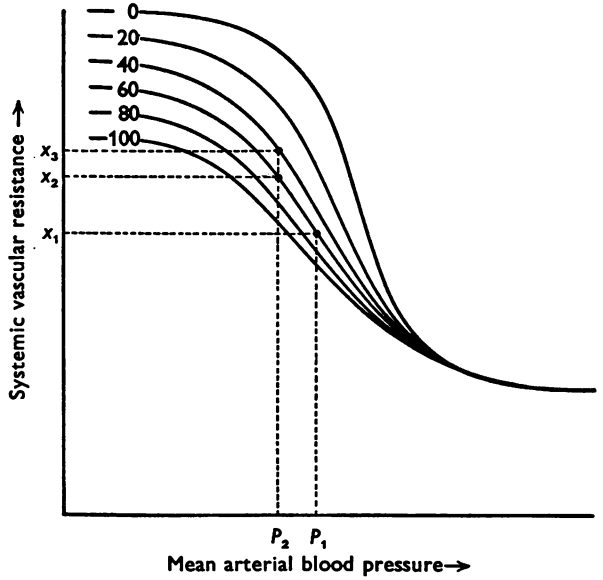

Fig. 15. Diagram showing the 'family' of curves relating the mean arterial (carotid sinus and aortic arch) pressure and systemic vascular resistance at pulse pressures of 20, 40, 60, 80 and 100 mm Hg. For details, see text.

Interrelation of mean pressure, pulse pressure and pulse frequency

Although during combined stimulation of the carotid sinus and aortic baroreceptors the curves relating mean pressure in the vasosensory areas and systemic arterial pressure have only been determined at two levels of pulse pressure, zero and at about 60 mm Hg, there exists a 'family' of curves for different pulse pressures (Angell James & Daly, 1970). Such curves, shown diagrammatically in Fig. 15, have certain implications in the control of vascular resistance, and the events occurring during haemorrhage may be taken as an example: the control mean arterial pressure (carotid sinus and aortic arch pressure) is P_1 mm Hg (Fig. 15) corresponding to a systemic vascular resistance of X_1 P.R.U. (peripheral resistance units) at an arterial pulse pressure of 60 mm Hg. If the mean arterial pressure falls during haemorrhage to P_2 mm Hg, the

pulse pressure remaining the same, the systemic vascular resistance will increase reflexly to X_2 P.R.U. The pulse pressure, however, also decreases, e.g. to 40 mm Hg, and, at the same mean arterial pressure of P_2 mm Hg, this further reduction in pulse pressure contributes to the reflex increase in systemic vascular resistance brought about by the arterial baroreceptors.

Consideration must be given to another contributory factor that affects the arterial baroreceptor activity during haemorrhage, namely acceleration of the heart. By a reflex mechanism this would tend to off-set the changes in systemic vascular resistance produced by the reduction in mean arterial and pulse pressures. However, over the physiological range of heart rate in the dog, the role of pulse frequency changes in the reflex control of vascular resistance is probably small (Fig. 9).

Fig. 15 demonstrates another point of practical importance in whole body perfusions. Alterations of arterial pulse pressure at constant mean arterial pressure cause inverse changes in systemic vascular resistance, as demonstrated experimentally. This emphasizes the need of ensuring that in whole body perfusions the systemic circulation is perfused in such a way that the pulse pressure, as well as the mean pressure, is maintained within normal limits. A diminished pulse pressure due to the characteristics of the perfusion pump or to the use of arterial cannulae with too small a bore will cause reflex systemic vasoconstriction through the arterial baroreceptors and result in a reduced systemic blood flow (pump output) at the same mean pressure.

Response of the vasomotor centre

Douglas, Ritchie & Schaumann (1956) showed that within wide limits the vasomotor response to electrical stimulation of all the fibres of the aortic nerve depends mainly on the number of shocks applied in a given time and hardly at all on the pattern in which they are applied. They attributed the greater effectiveness of pulsatile pressure largely to recruitment of fibres. In support of this view we found that changing the phase angle between the pulse pressure waves in the carotid sinuses and aortic arch had no effect on systemic vascular resistance. Under these conditions of constant mean pressure, pulse pressure and pulse frequency in each area, the pattern of the bursts of impulses reaching the vasomotor centre would be altered while maintaining the total number of impulses per unit time the same. On the assumption that the vasomotor centre responds to the total number of impulses it receives per unit time, its inhibition by substituting in the carotid sinuses a pulsatile pressure for a non-pulsatile pressure at the same mean pressure must result from an increased discharge. Evidence from averaged whole nerve recordings from the carotid sinus nerve indicates that this is so (Trank & Visscher, 1962; Spickler &

Kezdi, 1967; Koushanpour & McGee, 1969). This increased total nerve activity is not the result of an alteration in the number of impulses per cycle in individual baroreceptor units firing throughout the cycle (Ead *et al.* 1952) but is presumably due to recruitment of additional fibres. Recruitment occurs as a result of the phasic pressure rising above the levels of threshold pressure for a steady discharge of other receptors, and because the increased rate of change of pressure caused the discharge of receptors at levels of pressure below their threshold pressure for a steady discharge (Landgren, 1952). In the case of the aortic arch baroreceptors, it has been found that although recruitment occurs because the phasic pressure rises to threshold levels of other receptors, there is little or no additional recruitment of receptors resulting solely from the alteration in the rate of change of pressure (Angell James, 1968, 1969).

We wish to express our thanks to Mr D. R. Bacon for expert technical assistance. This work was generously supported by grants from the Medical Research Council and St Bartholomew's Hospital Endowment Fund.

REFERENCES

ABRAHAM, A. (1969). *Microscopic Innervation of the Heart and Blood Vessels in Vertebrates Including Man.* Oxford: Pergamon.

ANGELL JAMES, J. E. (1968). Studies of the impulse activity in baroreceptor fibres from an isolated aortic arch preparation of the rabbit. *J. Physiol.* **198**, 51–52*P*.

ANGELL JAMES, J. E. (1969). Studies of baroreceptor discharge and vasomotor reflexes elicited from an isolated perfused aortic arch preparation. Ph.D. Thesis. University of London.

ANGELL JAMES, J. E. & DALY, M. DE B. (1970). Reflex vasomotor responses elicited from the carotid sinus and aortic arch baroreceptors: comparison of pulsatile and non-pulsatile pressures. *J. Physiol.* **209**, 22*P*.

ANREP, G. V., PASCUAL, W. & RÖSSLER, R. (1936). Respiratory variations of the heart rate. I. The reflex mechanism of the respiratory arrhythmia. *Proc. R. Soc.* B **119**, 191–217.

ANREP, G. V. & SEGALL, H. N. (1926). The central and reflex regulation of the heart rate. *J. Physiol.* **61**, 215–231.

ANREP, G. V. & STARLING, E. H. (1925). Central and reflex regulation of the circulation. *Proc. R. Soc.* B **97**, 463–487.

BRONK, D. W. & STELLA, G. (1935). The response to steady pressures of single end organs in the isolated carotid sinus. *Am. J. Physiol.* **110**, 708–714.

CARSWELL, F., HAINSWORTH, R. & LEDSOME, J. R. (1968). The effects of varying pressures in the aortic arch on limb resistance and heart rate. *J. Physiol.* **196**, 38–39*P*.

DALY, I. DE B. & DALY, M. DE B. (1959). The effects of stimulation of the carotid sinus baroreceptors on the pulmonary vascular bed in the dog. *J. Physiol.* **148**, 220–226.

DALY, I. DE B. & VERNEY, E. B. (1927). The localisation of receptors involved in the reflex regulation of the heart rate. *J. Physiol.* **62**, 330–340.

DALY, M. DE B. (1955). A method for eliciting baroreceptor reflexes from the isolated carotid sinus. *J. Physiol.* **128**, 33–35*P*.

DALY, M. DE B., HAZZLEDINE, J. L. & HOWE, A. (1965). Reflex respiratory and peripheral vascular responses to stimulation of the isolated perfused aortic arch chemoreceptors of the dog. *J. Physiol.* **177**, 300–322.

DALY, M. DE B., HAZZLEDINE, J. L. & UNGAR, A. (1967). The reflex effects of alterations in lung volume on systemic vascular resistance in the dog. *J. Physiol.* **188**, 331–351.

DALY, M. DE B. & ROBINSON, B. H. (1968). An analysis of the reflex systemic vasodilator response elicited by lung inflation in the dog. *J. Physiol.* **195**, 387–406.

DALY, M. DE B. & UNGAR, A. (1966). Comparison of the reflex responses elicited by stimulation of the separately perfused carotid and aortic body chemoreceptors in the dog. *J. Physiol.* **182**, 379–403.

DE CASTRO, F. (1928). Sur la structure et l'innervation du sinus carotidien de l'homme et des mammifères. Nouveaux faits sur l'innervation et la fonction du glomus caroticum. Etudes anatomiques et physiologiques. *Trab. Lab. Invest. biol. Univ. Madr.* **25**, 331–380.

DOUGLAS, W. W., RITCHIE, J. M. & SCHAUMANN, W. (1956). A study of the effect of the pattern of electrical stimulation of the aortic nerve on the reflex depressor responses. *J. Physiol.* **133**, 232–242.

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.

EYSTER, J. A. E. & HOOKER, D. R. (1908). Direct and reflex responses of the cardio-inhibitory centre to increased blood pressure. *Am. J. Physiol.* **21**, 373–399.

FRANK, O. (1903). Kritik der elastischen Manometer. *Z. Biol.* **44**, 445–613.

GERO, J. & GEROVÁ, M. (1962). The role of parameters of pulsating pressure in the stimulation of intracarotid receptors. *Archs int. Pharmacodyn. Thér.* **140**, 35–44.

GLICK, G. & COVELL, J. W. (1968). Relative importance of the carotid and aortic baroreceptors in the reflex control of heart rate. *Am. J. Physiol.* **214**, 955–961.

HEYMANS, C., BOUCKAERT, J. J. & DAUTREBANDE, L. (1931). Sur la régulation réflexe de la circulation par les nerfs vasosensibles du sinus carotidien. *Archs int. Pharmacodyn. Thér.* **40**, 292–343.

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

IRISAWA, H. & NINOMIYA, I. (1967). Comparison of the averaged nervous activities of aortic and carotid sinus nerves. *Am. J. Physiol.* **213**, 504–510.

KOCH, E. (1931). *Die reflektorische Selbststeuerung des Kreislaufes.* Leipzig: Steinkopf.

KOUSHANPOUR, E. & MCGEE, J. P. (1969). Effect of mean pressure on carotid sinus baroreceptor response to pulsatile pressure. *Am. J. Physiol.* **216**, 599–603.

LANDGREN, S. (1952). On the excitation mechanism of the carotid baroreceptors. *Acta physiol. scand.* **26**, 1–34.

LANDGREN, S. & NEIL, E. (1951). Chemoreceptor impulse activity following haemorrhage. *Acta physiol. scand.* **23**, 158–167.

LEE, K. D., MAYOU, R. A. & TORRANCE, R. W. (1964). The effect of blood pressure upon chemoreceptor discharge to hypoxia, and the modification of this effect by the sympathetic–adrenal system. *Q. Jl exp. Physiol.* **49**, 171–183.

LEVISON, W. H., BARNETT, G. O. & JACKSON, W. D. (1966). Nonlinear analysis of the baroreceptor reflex system. *Circulation Res.* **18**, 673–682.

LEVY, M. N., NG, M. L. & ZIESKE, H. (1966). Cardiac and respiratory effects of aortic arch baroreceptor stimulation. *Circulation Res.* **19**, 930–939.

MCCREA, F. D. & WIGGERS, C. J. (1933). Rhythmic arterial expansion as a factor in the control of heart rate. *Am. J. Physiol.* **103**, 417–431.

MOISSEJEFF, E. (1927). Zur Kenntnis des Carotissinusreflexes. *Z. ges. exp. Med.* **53**, 696–704.

NAKAYAMA, S. (1954). The circulatory and respiratory reflexes from the brachiocephalic artery. *Yonago Acta med.* **1**, 110–114.

NEIL, E. (1956). Reflex responses elicited in the cat by perfusion of the root of the right subclavian artery. *Archs int. Pharmacodyn. Thér.* **105**, 468–476.

NONIDEZ, J. F. (1935). The aortic (depressor) nerve and its associated epithelioid body, the glomus aorticum. *Am. J. Anat.* **57**, 259–301.

PEASE, D. C. & PAULE, W. J. (1960). Electron microscopy of elastic arteries; the thoracic aorta of the rat. *J. Ultrastruct. Res.* **3**, 469–483.

REES, P. M. (1967). Observations on the fine structure and distribution of presumptive baroreceptor nerves at the carotid sinus. *J. comp. Neurol.* **131**, 517–548.

REES, P. M. (1968). Electron microscopical observations on the architecture of the carotid arterial walls, with special reference to the sinus portion. *J. Anat.* **103**, 35–47.

REMINGTON, J. W., HAMILTON, W. F. & DOW, P. (1945). Some difficulties involved in the prediction of the stroke volume from the pulse wave velocity. *Am. J. Physiol.* **144**, 536–545.

RUSHMER, R. F. (1955). Pressure–circumference relations in the aorta. *Am. J. Physiol.* **183**, 543–549.

SAGAWA, K. & WATANABE, K. (1965). Summation of bilateral carotid sinus signals in the barostatic reflex. *Am. J. Physiol.* **209**, 1278–1286.

SCHER, A. M. & YOUNG, A. C. (1963). Servoanalysis of carotid sinus reflex effects on peripheral resistance. *Circulation Res.* **12**, 152–162.

SPICKLER, J. W. & KEZDI, P. (1967). Dynamic response characteristics of carotid sinus baroreceptors. *Am. J. Physiol.* **212**, 472–476.

SPICKLER, J. W., KEZDI, P. & GELLER, E. (1967). Transfer characteristics of the carotid sinus control system. In *Baroreceptors and Hypertension*, pp. 31–39, ed. KEZDI, P. Oxford: Pergamon.

STEGEMANN, J. & TIBES, U. (1969). Der Einfluss von Amplitude, Frequenz und mittelwert Sinus förmiger Reizdrucke an den Pressoreceptoren auf den arteriellen Mitteldruck des Hundes. *Pflügers Arch. ges. Physiol.* **305**, 219–228.

TRANK, J. W. & VISSCHER, M. B. (1962). Carotid sinus baroreceptor modifications associated with endotoxin shock. *Am. J. Physiol.* **202**, 971–977.

UEDA, H., UCHIDA, Y., YASUDA, H. & TAKEDA, T. (1966). Reflex control of blood pressure by the right subclavian baroreceptor in experimental renal hypertension of rabbit. *Jap. Heart J.* **7**, 543–555.

WANG, S. C. & BORISON, H. L. (1947). Decussation of the pathways in the carotid sinus cardiovascular reflex: an example of the principle of convergence. *Am. J. Physiol.* **150**, 722–728.