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THE EFFECTS OF ALTERING MEAN PRESSURE, PULSE PRESSURE AND PULSE FREQUENCY ON THE IMPULSE ACTIVITY IN BARORECEPTOR FIBRES FROM THE AORTIC ARCH AND RIGHT SUBCLAVIAN ARTERY IN THE RABBIT

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SUMMARY

1. A method is described for perfusing an isolated preparation of the rabbit aortic arch with independently controlled mean pressure, pulse pressure and pulse frequency.

2. Recordings made from single or few-fibre preparations from the aortic arch and right subclavian baroreceptor regions show that the number of impulses per second or per cycle in a single fibre is the same during pulsatile perfusion as during non-pulsatile perfusion if the pressure is above the threshold pressure to non-pulsatile perfusion during all phases of the pressure cycle.

3. In multi-fibre recordings the total number of impulses is greater during pulsatile perfusion than during non-pulsatile perfusion due largely to recruitment of fibres during systole.

4. The relationship between instantaneous impulse frequency and aortic arch pressure during one pressure cycle forms an elliptiform curve.

5. Increasing the pulse pressure increases the ellipse and causes additional recruitment of other fibres during systole, thus augmenting the total impulse activity.

6. Increasing the pulse frequency reduces the number of impulses per cycle for single fibres but produces a small increase in the total impulse frequency in one second period due to recruitment.

7. Increasing the rate of change of pressure by increasing the pulse pressure or pulse frequency produced a small reduction or no change of the threshold pressure. Similarly the 'cut off' pressure was elevated in some fibres.

8. At low initial mean pressures, an increment of pressure, at constant pulse pressure and pulse frequency, increases the total impulse activity

by increasing the frequency of impulses in single fibres already active during systole and diastole and by additional recruitment of other fibres. At higher mean pressures there is little increase in impulse activity as the maximum frequency of fibres is attained or superseded and there is little recruitment.

INTRODUCTION

The importance of the arterial pulse pressure, as distinct from the mean pressure, in the reflex control of heart rate, systemic and pulmonary arterial blood pressure and systemic vascular resistance by baroreceptors in the carotid sinuses has been stressed by numerous workers (McCrea & Wiggers, 1933; Ead, Green & Neil, 1952; Agostoni, Chinnock & Daly, 1957; Gero & Gerová, 1962; Angell James & Daly, 1970*a*, *b*). At a given mean arterial pressure a pulsatile pressure results in a greater cardiac vagal tone and a diminished vasomotor tone compared with a non-pulsatile pressure, the magnitude of the response depending on the pulse pressure. Compared with the carotid sinuses, however, the reflex vasomotor responses from the aortic arch baroreceptors are relatively less affected by pulse pressure (Angell James & Daly, 1970*a*, *b*). The difference in the reflex responses to changes of pulse pressure in the two vasosensory areas may be a central phenomenon or it may be related in part to differences in the physiological characteristics of the two groups of baroreceptors. In this connexion electroneurographic studies of impulse activity in baroreceptor fibres in the carotid sinus nerve were studied by Ead *et al.* (1952) during pulsatile and non-pulsatile perfusion of the area but similar studies on the aortic arch baroreceptors have not previously been reported.

The experiments described in this paper were undertaken to study the effects of altering the mean pressure, pulse pressure and pulse frequency on the impulse activity in single or few-fibre preparations of the aortic nerves in the isolated perfused aortic arch. Some of the results have been reported briefly elsewhere (Angell James, 1968).

METHODS

New Zealand white rabbits weighing between 2·4 and 2·7 kg were used. Each animal was anaesthetized with 25% urethane (British Drug Houses, Ltd) made up in dionized water and given intravenously in a dose of 1·5–2·1 g/kg at a temperature of 38° C. A tracheostomy was performed and the animal was artificially ventilated with a respiratory pump (C. F. Palmer, Ltd) at 30 c/min. A mid line thoracotomy was performed and the internal mammary vessels were ligated.

Isolation and perfusion of the aortic arch and right subclavian areas

The aortic arch and right subclavian areas were isolated from the circulation by ligating the right and left subclavian arteries, the left common carotid artery and

any other anomalous branches arising from the area (Angell James, 1969). The descending thoracic aorta was ligated at the level of the left pulmonary artery and the right common carotid was cannulated for drainage of the effluent perfusion fluid.

The area was perfused with Krebs–Henseleit solution through a cannula tied in the wall of the left ventricle with its tip lying in the aortic arch (Angell James, 1968, 1969, 1971). The mean temperature of the perfusate was 38·2° C (range 37·5–38·5° C).

Perfusion of the aortic arch

Perfusion of the aortic arch was carried out by means of a special reservoir (Daly, 1955) connected to a Dale–Schuster pump. Mean aortic arch pressure was controlled by a compressed air by-pass leak system and the pulse pressure and pulse frequency were varied by changing the stroke and gear ratio of the pump. The whole reservoir was immersed in a heated water-jacket at 39° C.

A Bell & Howell transducer (Type 4–326–L. 212) excited at 10 V d.c. was used to record aortic mean and full pressure. The signals were recorded, after suitable amplification, on a multi-channel ultra-violet recording oscillograph (Type S.E. 2005; S.E. Laboratories, Ltd) using Kodak 1843 Linagraph paper. At the same time they were displayed on a large screen oscilloscope (Airmec Type 279 with time base 370). The pressures were transmitted to the transducer by a saline-filled Sterivac polyethylene cannulae (length 30 cm, 1·5 mm bore with 0·5 mm wall thickness). The signals were amplified by a system containing Fenlow AD 2000 operational amplifiers one of which was arranged as a fixed gain differential amplifier with a switched high frequency loss giving a flat (−3 db) frequency response from d.c. to 200, 100, 50, 10 c/s or a mean position. The second amplifier was arranged as a variable gain inverting amplifier. Full range output was standardized at 2·5 V d.c. which allowed the B. 450 galvanometer in the recorder to deflect 5 cm at full range.

The frequency response of the catheter-manometer system was determined by the method of Frank (1903). The undamped natural frequency response of the system was greater than 70 c/s, the degree of damping being 0·35. This gave an estimated amplitude distortion of less than 5 % up to about 25 c/s (Fry, 1960).

Action potential recordings

Action potentials were recorded, with saline-wick silver–silver chloride electrodes, from single or few-fibre preparations of the aortic nerves prepared with the aid of a × 10 operating microscope (Beck.) They were recorded on ultra-violet light sensitive paper using a A 3300 galvanometer (S.E. Laboratories; flat frequency response to 2000 c/s) after amplification with a Tektronic 122 preamplifier used in conjunction with a system containing differential operational amplifiers with an AD 2002 unity gain booster. The output was also passed to a loudspeaker via an A.F. amplifier (Newmarket p.c. 5) for audible monitoring and to the large screen oscilloscope.

During pulsatile perfusion of the aortic arch the maximum and minimum peak impulse frequencies were calculated during systole and diastole by measuring the distance between two adjacent impulses. The number of impulses during a 1 sec period and per cycle were also counted for every fibre. The *total* number of impulses in a few fibre preparations was also counted. In the experiments in which the pulse frequency was varied the total number of impulses for a fibre was counted over a number of complete cycles and the average discharge per second was calculated. The pulse frequency measurements were accurate to within 5 %.

RESULTS

The effect of substituting a pulsatile for a non-pulsatile pressure in the aortic arch

In a previous study (Angell James, 1968, 1969, 1971) no systematic differences were found between the physiological characteristics of the baroreceptors in the aortic arch and right subclavian areas as indicated by electroneurographic studies. This was confirmed by the present experiments and so the results obtained on the left and right aortic nerve will be considered together.

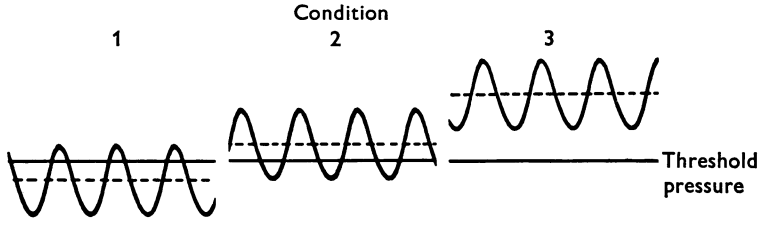

Fig. 1. Diagram showing three conditions (1, 2 and 3) under which the effects on impulse activity of substituting a pulsatile pressure for a non-pulsatile pressure are discussed. For details, see text. *Interrupted lines*, mean pressure; *continuous straight line*, threshold pressure; *sinusoidal continuous line*, pulse pressure wave.

In six experiments tests were carried out on single or few-fibre preparations of the left and right aortic nerves to study the effects on impulse activity of substituting a pulsatile for a non-pulsatile pressure at the same mean pressure. As expected, the impulse activity occurred at a steady rate during non-pulsatile perfusion and during pulsatile perfusion became phasic synchronous with the pulse wave. A quantitative analysis of the discharge in single fibres, however, indicated that its characteristics depended, at least in part, on the relationship of the mean pressure, systolic pressure, and diastolic pressure to the threshold pressure of the receptor determined by using a non-pulsatile pressure (Angell James, 1968, 1969, 1971). Three different conditions will be considered which are depicted in Fig. 1.

Condition 1. During pulsatile perfusion the mean and the diastolic pressure are below the threshold pressure for steady (non-pulsatile) pressure and only the systolic pressure rises above the threshold pressure (Fig. 1). This is illustrated by experiments from which Figs. 2 and 3 are taken. It can be seen that the large action potentials only appear during systole when the pressure exceeds the threshold pressure to a steady pres-

sure (Fig. 2*D*). During non-pulsatile perfusion (Figs. 2*B*, 3*A*) at the same mean pressure there is no discharge of these larger action potentials. The threshold pressure was only 2 mm Hg lower during pulsatile perfusion (pulse pressure 12 mm Hg; pulse frequency 210 c/min) than during non-pulsatile perfusion in the fibre depicted in Fig. 2. The number of impulses increased from 0 to 26 impulses in a 1 sec period with a maximum peak

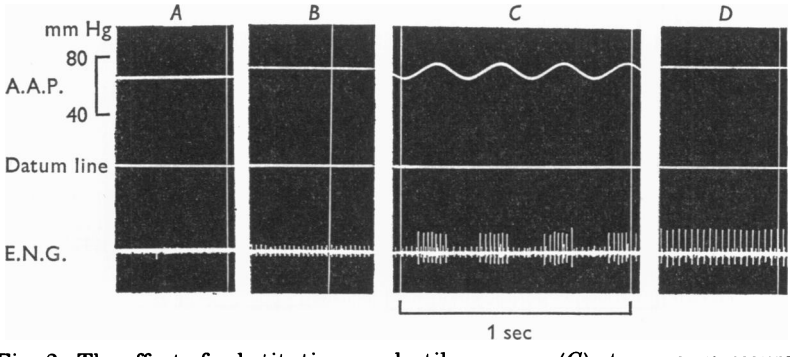

Fig. 2. The effect of substituting a pulsatile pressure (*C*) at a mean pressure equal to a non-pulsatile pressure (*B*) which is below the threshold pressure (*D*) for the larger action potential. Nerve fibre slip from the left aortic nerve in an isolated perfused aortic arch preparation. The mean pressure of 63 mm Hg (*A*) was below the threshold pressure (*B*) of the smaller potential. A.A.P., aortic arch perfusion pressure; E.N.G., electroneurogram

	Aortic arch pressure (mm Hg)			Impulse frequency (impulses/sec)		
	mean	pulse pressure	Potential	Max.	Min.	Impulses total/sec
A	63	0	Large	—	—	—
			Small	—	—	—
B	71	0	Large	—	—	—
			Small	49	49	49
C	71	12	Large	59	0	26
			Small	59	35·6	42
D	73	0	Large	36	36	36
			Small	46	46	46

frequency of 59 impulses/sec during pulsatile perfusion. In this condition the number of impulses in a 1 sec period is increased when the perfusion is pulsatile.

Condition 2. The systolic and mean pressure are above and the diastolic pressure below the threshold pressure (Fig. 1). The typical response is shown in Fig. 4*A*, *C* and *D*. In *A*, the non-pulsatile pressure is above threshold, but in *C* and *D* the diastolic pressure during pulsatile perfusion falls below the threshold pressure, and firing ceases. The number of

impulses per 1 sec period was less during pulsatile than during non-pulsatile perfusion.

Condition 3. The pressure during all phases of the pressure cycle remains above the threshold pressure to a steady pressure. Substitution of a pul-

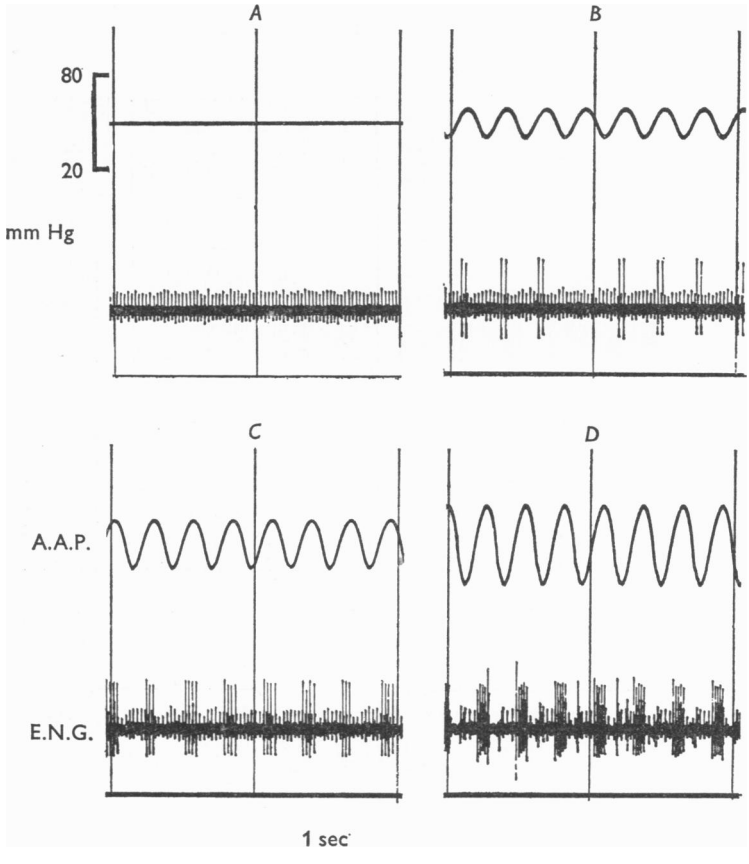

Fig. 3. Recordings of impulse activity in a multi-fibre preparation of the left aortic nerve. The isolated aortic arch preparation was perfused with Krebs–Henseleit solution at different pulse pressures. Constant mean pressure (46 mm Hg) and pulse frequency (210 c/min). R, recruitment of other fibres; A.A.P., aortic arch pressure (mm Hg); E.N.G., electroneurogram.

	Aortic arch pulse pressure (mm Hg)	No. of impulses	
		Total/cycle	Total/sec
A	0	11	38
B	19	11+2	38+6
C	31	11+4	38+14
D	53	11+5+R	38+24+R

satile for a non-pulsatile pressure resulted in the frequency increasing during the systolic phase of the cycle and decreasing during the diastolic phase (Fig. 4*A*, *B*).

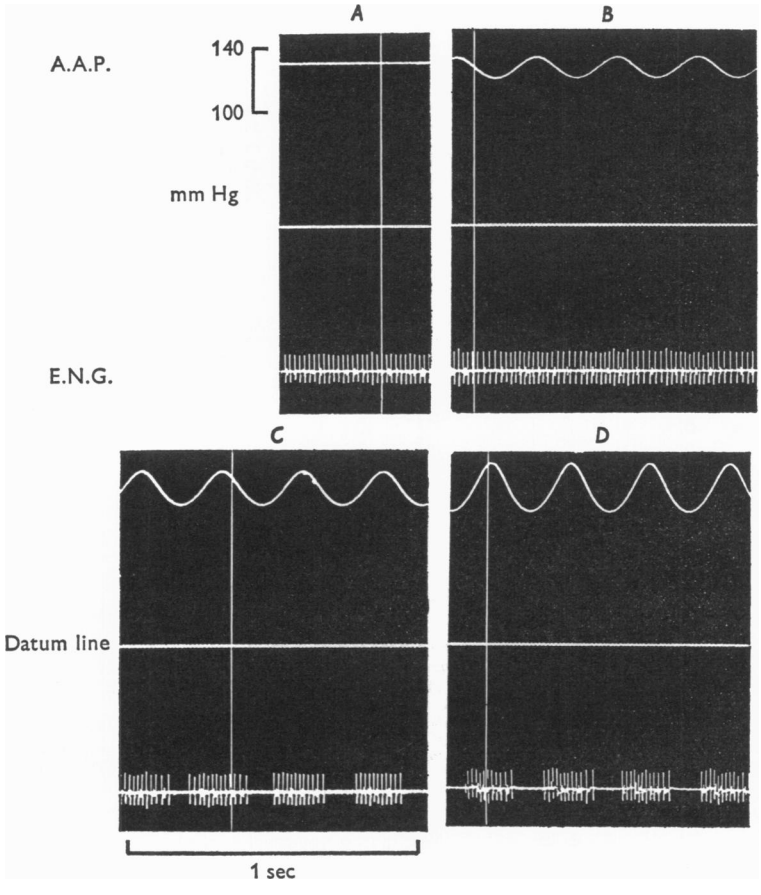

Fig. 4. Recordings of a single baroreceptor fibre from the left aortic nerve. Rabbit wt. 2·5 kg. Non-pulsatile and pulsatile perfusion of an isolated aortic arch perfused with Krebs–Henseleit solution at a mean pressure of 125 mm Hg. Pulse frequency 210 c/min. Perfusion temperature, 37° C. A.A.P., aortic arch pressure (mm Hg); E.N.G., electroneurogram

	Pulse pressure (mm Hg)	Impulse frequency (impulses/sec) Max.	Min.	Impulses/ cycle time
A	0	59	59	18–17
B	16	62·5	50	17
C	22	67	0	12
D	32	83	0	12

TABLE 1. The effects on aortic baroreceptor activity in single fibres of substituting a pulsatile for a non-pulsatile pressure in the aortic arch at pulse frequencies of 160 and 210 c/min

		Aortic perfusion				
	Non-pulsatile	Pulsatile 160 c/min	Difference	Non-pulsatile	Pulsatile 210 c/min	Difference
Mean aortic pressure (mm Hg)	70·9 ± 5·5 (51–90)	70·3 ± 5·5 (51–87)	−0·9 ± 0·6 (−3 to +2) $P > 0·2$	68·7 ± 4·8 (32–143)	67·2 ± 4 3 (31–135)	−1·7 ± 0·6 (0–9) $P > 0·4$
Pulse pressure (mm Hg)	0	30·6 ± 4·6 (10–45)	—	0	25·3 ± 1·9 (10–53)	—
Systolic pressure (mm Hg)	—	85·7 ± 6·7 (66–110)	—	—	80·1 ± 4·4 (44–143)	—
Diastolic pressure (mm Hg)	—	55·1 ± 5·3 (34–72)	—	—	56·5 ± 4·7 (13–127)	—
Impulse frequency (impulses/sec)						
Maximum	—	58·8 ± 6·4 (34·5–59)	—	—	61·9 ± 3·6 (22–100)	—
Minimum	—	30·2 ± 5·4 (29–43·5)	—	—	35·9 ± 2·4 (6–59)	—
No. of impulses (impulses/cycle time)	20·4 ± 1·5 (14–27)	20·3 ± 1·5 (14–27)	0·1 ± 0·14 (0–1) $P > 0·4$	13·0 ± 0·7 (4–18)	13·0 ± 0·8 (4–18)	0·13 ± 0·1 (−1 to +2) $P > 0·4$
No. of tests	—	—	7	—	—	30
No. of fibres	—	—	3	—	—	12
No. of experiments	—	—	3	—	—	5

The values are the means ± S.E. of mean; those in parentheses are the ranges.

The results of thirty-seven tests on fifteen fibres in five experiments are summarized in Table 1. In different tests the pulse pressure varied from 10 to 53 mm Hg at pulse frequencies of 160 and 210 c/min. It will be noted that although the discharge is phasic during pulsatile perfusion, the number of impulses per cycle time remains the same as during non-pulsatile perfusion at the same mean pressure. This is independent of the pulse frequency (Table 1). Further analysis showed that the number of impulses per 1 sec period was also the same during pulsatile as during non-pulsatile perfusion. Similar observations in other experiments were made at pulse frequencies varying from 110 to 450 c/min.

Analysis of the phasic changes in impulse activity indicates that the larger number of impulses and higher peak frequency of impulses occurring during systole are compensated by a smaller number and reduced peak frequency during diastole. At higher rates of change of pressure the minimum frequency may reach zero despite the pressure remaining above the threshold to steady pressure and there is a compensatory diastolic pause. This is illustrated by another experiment in Fig. 5 in which the instantaneous impulse frequency was plotted against the aortic arch pressure at various phase sof the pressure cycle (*open circles*). The threshold pressure for a steady pressure and the impulse frequency at various non-pulsatile aortic pressures are also plotted for the same fibre (*filled circles*). The number of impulses during a 1 sec period during pulsatile perfusion is indicated by the larger circle and it will be seen that it falls on the curve for non-pulsatile perfusion. At any given mean pressure the impulse activity during the systolic phase of the pressure cycle is higher than during the diastolic phase, and the peak frequency does not coincide with the peak pressure but precedes it. In the case illustrated the maximum peak frequency was 143 impulses/sec during systole but fell to zero during diastole despite the fact that the pressure did not fall below the threshold pressure for a steady pressure.

In conclusion these experiments demonstrate that the effect on baroreceptor impulse activity in single fibres of substituting a pulsatile for a non-pulsatile perfusion pressure depends on the relationship of the mean systolic and diastolic pressures to the threshold pressure for a steady pressure. The impulse activity in a 1 sec period or per cycle length of time will be increased in Condition 1, decreased in Condition 2, and remain constant in Condition 3. In the whole nerve the net result will be a combination of all three conditions due to the variation of threshold pressures of different baroreceptors.

The effect of increasing the mean pressure at constant pulse pressure

When the mean pressure is increased in steps the pulse pressure remaining constant, it was found in few- and multi-fibre preparations that at relatively low initial mean pressures the total impulse activity per cycle and per 1 sec period increased. This is due to two factors. First, in individual fibres there is an increase in the maximum impulse frequency and

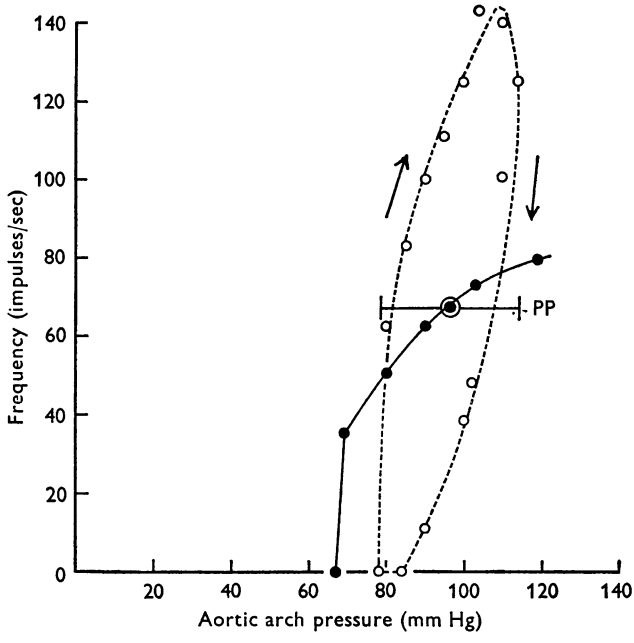

Fig. 5. The relationship between impulse activity and aortic arch pressure. Single fibre preparation of the left aortic nerve. *Continuous line, filled circles* (●—●), non-pulsatile pressure perfusion of the aortic arch under steady state conditions. *Interrupted line, open circles* (○ - - - - ○), pulsatile perfusion of the aortic arch. The impulse frequency-aortic arch pressure relationship during one pressure cycle, the direction of which is indicated by the arrows. *Large open circle* (○) represents the number of impulses in a one second period during pulsatile perfusion plotted at the mean of the pulse pressure. (——*PP*), demarcates systolic and diastolic pressures. The *filled circles* within the *large open circle* represents the impulse frequency during non-pulsatile perfusion at a pressure corresponding to the mean of the pulse pressure.

number of impulses during systole and in the minimum impulse frequency and number of impulses during diastole. This was confirmed in single-fibre preparations. And, secondly, there is recruitment of other fibres as the phasic pressure passes their threshold pressures.

At higher levels of mean pressure an increment of mean pressure produces little or no change in impulse activity per cycle or per 1 sec period. At these levels of pressure the curves relating the non-pulsatile pressure and impulse frequency have reached a plateau or in some cases have begun to descend (Angell James, 1968, 1969, 1971), so that with an incremental increase in mean pressure the impulse activity during the pressure cycle may increase in some fibres, and decrease or remain unchanged in others. If the pressure is such that the threshold of all the fibres is exceeded in all phases of the pressure cycle no recruitment of fibres takes place.

Effects of increasing the pulse pressure

The response of the baroreceptors to increasing pulse pressure was studied in fourteen tests on thirteen fibres in four experiments. Pulsatile pressures with pulse pressures varying from 10 to 70 mm Hg were superimposed on non-pulsatile pressures at a constant mean pressure varying from 30 to 135 mm Hg in different tests and the impulse activity in single- and few-fibre preparations was studied under the same conditions as shown in Fig. 1.

Condition 1. There is an absence of recordable impulses when the aortic arch is perfused at a non-pulsatile pressure which is below the threshold pressure for that fibre. This is illustrated in Fig. 3*A* for the larger fibre. On superimposing a pulsatile pressure at the same mean pressure impulses are recorded during the systolic phase only when the pressure exceeds the threshold pressure (Fig. 3*B*). Increasing the pulse pressure (Fig. 3*C*) results in additional discharge from the recruited fibre as the systolic phase of the pressure cycle remains above the threshold pressure for a longer period of time. The peak frequency also increases with the increased systolic pressure and rate of change of pressure. Under these conditions the total number of impulses per cycle increased due to recruitment in multifibre preparations (Fig. 3).

Condition 2. When the mean and systolic pressures exceed the threshold pressure for the particular fibre, firing ceases only in the diastolic phase (Fig. 4*C* and *D*).

In Fig. 4 the impulse discharge in *A* is continuous during non-pulsatile perfusion. In *B* during pulsatile pressure perfusion (pulse pressure, 16 mm Hg) there is an increase in peak frequency during systole and a reduced frequency during diastole, but the number of impulses per 1 sec period remains the same, i.e. 17 impulses/sec. In *C* and *D* the pulse pressure is increased to 22 and 32 mm Hg respectively and now there occurs a pause in the discharge during diastole when the pressure falls below the threshold pressure for the fibre. As the pulsatile pressure is increased, the length of time during which the diastolic pressure falls below the threshold is

greater and it will be seen in this experiment that the diastolic pause is correspondingly increased (Fig. 4*C* and *D*). An alternative interpretation of this temporary cessation of discharge is that it is due to the 'off effect', because the pressure during diastole is falling at a greater rate from a higher systolic pressure.

Another characteristic which occurs on increasing the pulse pressure is that the level of pressure at which impulse activity commences during the systolic phase of the cycle may be lower than the threshold to a steady pressure. At the same time the 'cut-off' pressure may be elevated, as illustrated in Fig. 4*C* and *D*, in which increasing the pulse pressure from 22 to 32 mm Hg reduced the threshold pressure from 118 to 113 mm Hg. At the same time the pressure at which the impulses ceased during the diastolic phase of the pressure cycle was elevated from 120 to 128 mm Hg. In other fibres the threshold pressure and the 'cut-off' pressure were unaffected by changes of pulse pressure.

A large increase of pulse pressure sometimes resulted in impulses appearing when the aortic arch pressure was at its lowest point (Fig. 3*D*). This may be due to distortion of the arterial wall at a low diastolic pressure.

Condition 3. It was found in nine single-fibre preparations that when the pulse pressure was increased and remained threshold above at all phases of the pressure cycle, the peak frequency increased during the systolic phase of the cycle. The greater the increase of pulse pressure, and hence the rate of change of pressure, the higher was the peak frequency. On the other hand during the diastolic phase of the cycle there was a reduced minimum frequency which became progressively lower as the pulse pressure was increased. The over-all effect was that the number of impulses per cycle and per 1 sec period remained constant (Fig. 4*A*, *B* and Fig. 3 (smaller action potential)).

The relationship between the instantaneous impulse frequency and the aortic arch pressure for a fibre at two different pulse pressures is shown in Fig. 6. At a pulse pressure of 10 mm Hg (*open circles, interrupted line*) an elliptically shaped curve is produced around a point which is the frequency of impulse discharge for a non-pulsatile pressure at the same mean pressure. The second elliptical curve (*circles, continuous line*) was obtained at a pulse pressure of 20 mm Hg. The peak frequency does not coincide with the maximum pressure attained during the pressure cycle but leads it by 8° when the pulse pressure is 20 mm Hg. However, at a pulse pressure of 10 mm Hg, there was no demonstrable phase lag. Doubling the pulse pressure resulted in an increase of the maximum peak frequency during systole from 55·5 to 62·5 impulses/sec; during diastole, there was a fall in the minimum frequency from 45 to 43·5 impulses/sec. The number of impulses during a 1 sec period remained constant at 50 impulses.

Fig. 7 shows the peak impulse frequencies during systole and during diastole for six fibres. A line drawn through these points describes an S-shaped curve in five of the six fibres. This Figure also illustrates the variation in the response of different baroreceptors to increasing pulse pressures. At the higher pulse pressures the maximum peak frequency during systole may be greater, the same or less than the maximum peak frequency which occurred at a smaller pulse pressure when the systolic

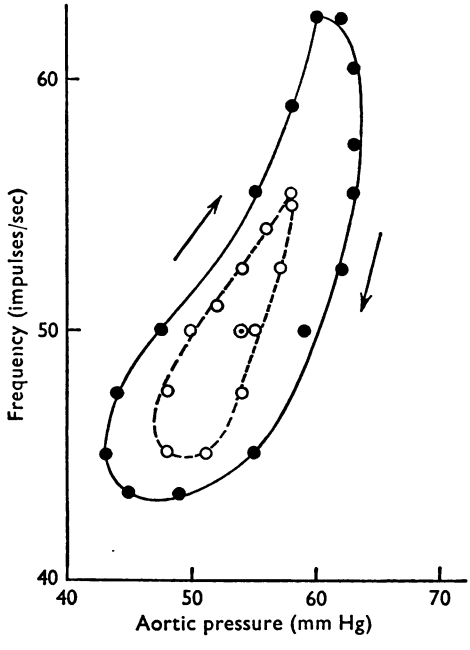

Fig. 6. The relationship between instantaneous impulse frequency in a fibre of the left aortic nerve and aortic arch pressure in an isolated perfused aortic arch preparation perfused by Krebs–Henseleit solution at pulse pressures of 10 mm Hg (*open circles*, ○– –○) and 20 mm Hg (*filled circles*, ●—●). ⊙ Impulse frequency during non-pulsatile pressure perfusion at the same mean pressure as with pulsatile pressure perfusion. The arrows indicate the direction of the pressure cycle.

pressure was lower. In the latter case it is possible that at these higher pressures the pressure during systole exceeds that pressure at which the maximum peak frequency occurs.

The effects of altering the pulse frequency

The frequency of the pulse pressure cycles was altered between 110 and 450 c/min in sixteen tests performed on thirteen fibres in five experiments while maintaining the pulse pressure constant.

The results obtained on five single-fibres in four experiments under conditions in which the pressure remained above threshold during all phases of the cycle are represented graphically in Fig. 8 which shows that as the pulse frequency is increased there is a reduction in the number of impulses/cycle.

The results of one experiment are illustrated in Fig. 9. It will also be

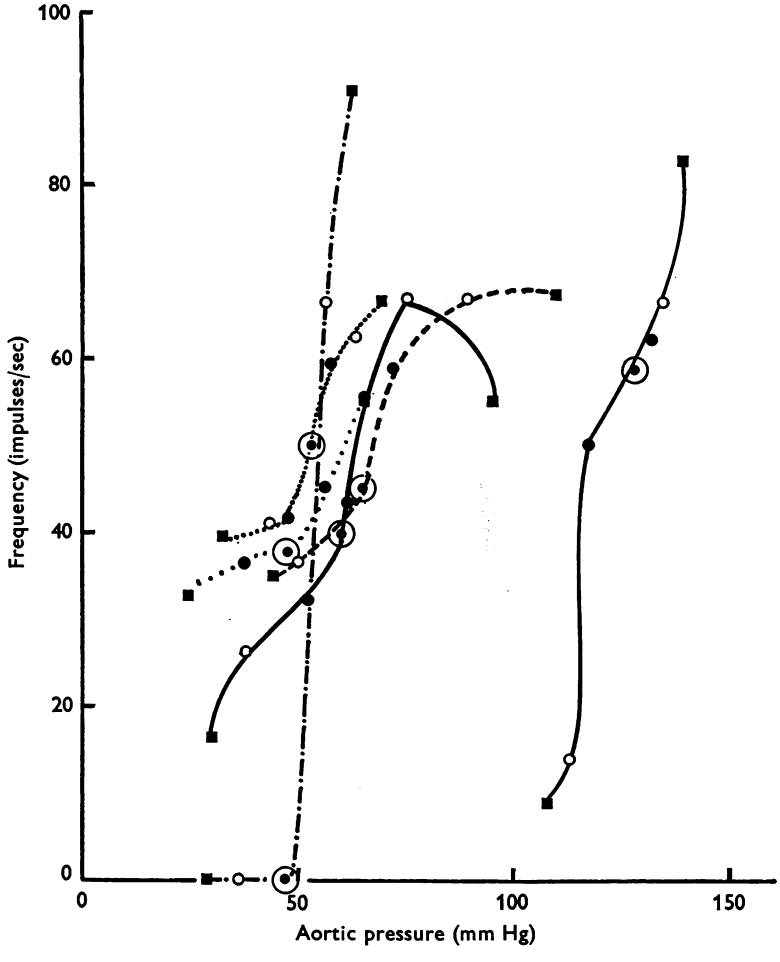

Fig. 7. Graph showing the relationship of the maximum and minimum peak impulse frequency to the systolic and diastolic pressures during pulsatile perfusion of the aortic arch preparation. Recordings from six fibres of the aortic nerves in five experiments. ● (*filled circles*), smallest pulse pressures; ○ (*open circles*), medium pulse pressures; ■ (*filled squares*), largest pulse pressures ⊙ (*large circle around small filled circle*), impulse frequency during non-pulsatile perfusion at the mean pressure of the pulsatile perfusion pressure.

observed that during the systolic phase of the pressure cycle in *B* there was recruitment of another fibre whose threshold pressure to non-pulsatile perfusion was higher than the mean pressure (Fig. 9*A*). Its response to increasing the pulse frequency from 110 to 210 c/min was a reduction in the number of impulses/cycle, although the number of impulses per 1 sec period remained the same.

A graphical representation of the relationship between the instantaneous peak impulse frequency and aortic arch perfusion pressure for the two fibres depicted in Fig. 9 is shown in Fig. 10. The fibre giving rise to the

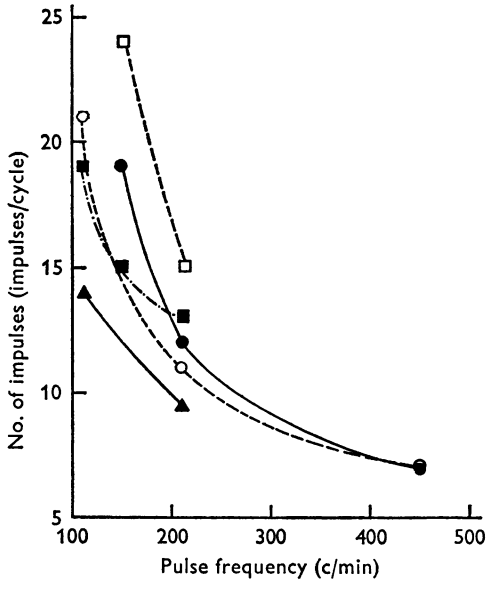

Fig. 8. Graph relating the impulses/cycle in single-fibre preparations from the aortic nerve to the frequency of the pressure cycles during pulsatile perfusion in an isolated perfused aortic arch preparation. Five fibres in four experiments. Each symbol represents a different fibre.

larger action potential was discharging during all phases of the pressure cycle and the plot at a pulse frequency of 110 c/min (*continuous line*) formed an ellipse around a point which represented the number of impulses in a 1 sec period. It also corresponded to the impulse frequency during non-pulsatile perfusion at the same mean pressure. Increasing the frequency of the pressure cycle from 110 to 210 c/min resulted in the maximum peak frequency during systole being elevated and the minimum frequency during diastole being reduced (*interrupted line*). The peak frequency does not coincide with the peak pressure but precedes it by 8° at a pulse frequency of 210 c/min. The smaller action potential which appeared

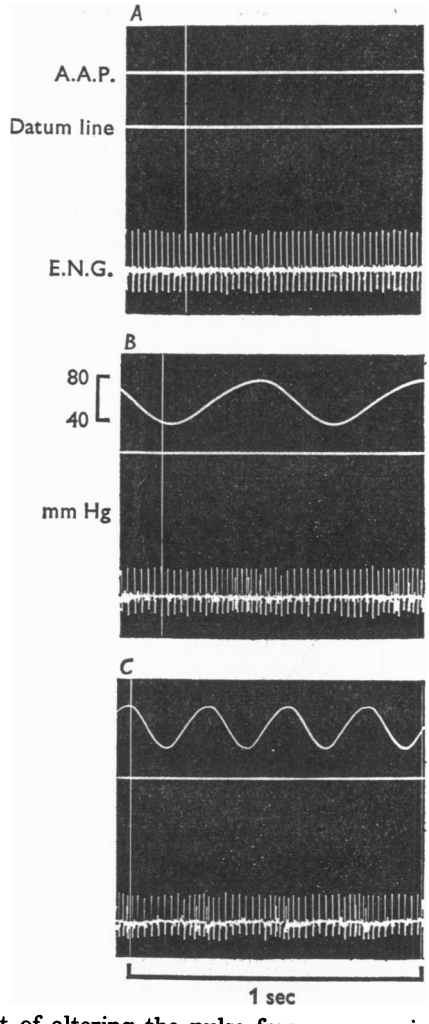

Fig. 9. The effect of altering the pulse frequency on impulse frequency. Isolated perfused aortic arch from a rabbit 2·5 kg. Recordings from the left aortic nerve. A two-fibre preparation perfused at a constant mean pressure of 54 mm Hg and pulse pressure of 28 mm Hg. 1 and 2 refer to the large and small action potentials respectively. A.A.P., aortic arch pressure; E.N.G., electroneurogram.

			Impulse frequency (impulses/sec)		Impulses total/sec
A	Non-pulsatile perfusion	1	50		50
		2	0		0
			Max.	Min.	
B	Pulse frequency (110 c/min)	1	62·5	43·5	50
		2	22·0	0	7
C	Pulse frequency (210 c/min)	1	67	40·8	50
		2	28·5	0	7

only during the systolic phase of the pressure cycle, was recruited at an aortic arch pressure of 62 mm Hg during pulsatile perfusion at a pulse frequency of 110 c/min, but this pressure was not lowered by increasing the frequency of pulse pressure to 210 c/min. This implies that in this particular fibre increasing the rate of change of pressure did not alter the pressure at which the fibre was recruited.

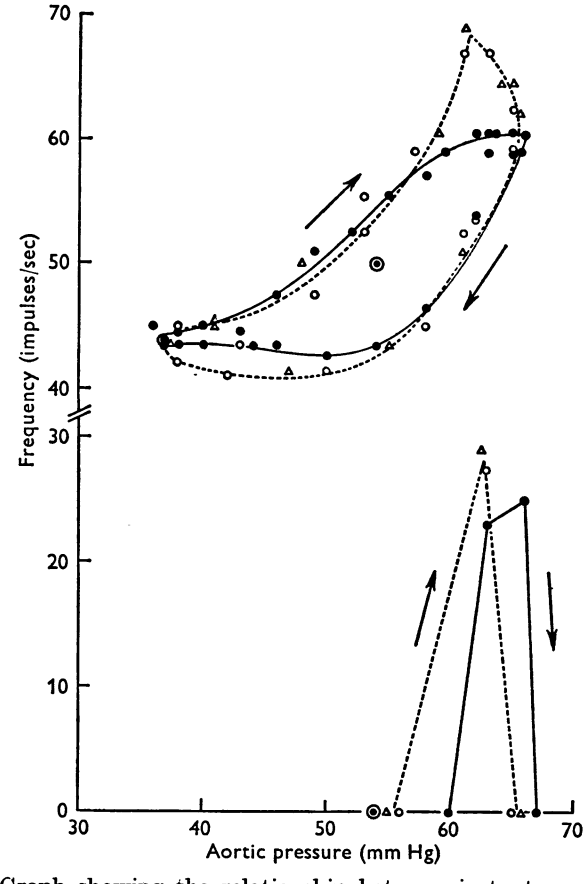

Fig. 10. Graph showing the relationship between instantaneous impulse frequency and aortic arch pressure in a two-fibre preparation from the left aortic nerve. Isolated aortic arch perfused with Krebs–Henseleit solution (37·5° C) at a mean pressure of 54 mm Hg. Pulse pressures of 28 mm Hg were superimposed at a frequency of 110 c/min (○, *filled circles*) and 210 c/min (○, △, *open circles and open triangles*). ● (*large open circle around a filled circle*), the impulse frequency with the aortic arch perfused at the same mean pressure (54 mm Hg) during non-pulsatile perfusion. During pulsatile perfusion the larger action potential showed a continuous discharge (upper part of graph) whereas the smaller one discharged only during systole (lower part of graph). The arrows indicate the direction of the pressure cycle.

It was found in all fibres studied that as the pulse frequency increased so the number of impulses/cycle diminished. However, the number of impulses per 1 sec period remained constant provided the threshold pressure was exceeded at all phases of the pressure cycle. The value was the same as that obtained for non-pulsatile perfusion at the same mean pressure.

In few- or multi-fibre preparations bursts of impulse activity, due to recruitment, occurred more frequently in a one second period with increasing pulse frequency. There was also a slight reduction of the threshold pressure of some fibres produced by the increased rate of change of pressure with increasing pulse frequency, which produced additional recruitment of fibres previously inactive. In some cases the impulse activity, in a 1 sec period of recruited fibres increased with increasing pulse frequency. The total effect on the baroreceptors resulted in a small increase in the total impulse activity in a one second period with increasing pulse frequency.

DISCUSSION

Effects of pulsatile pressure

When a non-pulsatile pressure is converted to a pulsatile pressure at the same mean pressure, the discharge in single fibres of the aortic nerves becomes phasic, the peak frequency of impulses preceding the peak of the systolic pressure wave by up to 8° in this series, and coinciding with the maximum rate of change of pressure. The phasic nature of the aortic baroreceptor impulse activity was noted by both Adrian (1926) and Einthoven (1908) and by other workers who have recorded changes in electrical activity from the aortic nerves synchronous with each pulse in the intact animal.

Substitution of a pulsatile pressure for a non-pulsatile pressure at the same mean pressure had no effect on the total number of impulses per cycle time for a single fibre provided all phases of the pulse pressure wave were above the threshold pressure for that fibre, as demonstrated by Ead *et al.* (1952) in single fibres of the carotid sinus nerve. This is termed Condition 3 (Fig. 1). In this circumstance the total number of impulses per cycle is independent of pulse frequency, and pulse pressure provided the mean pressure remains constant.

However, the total number of impulses in the whole nerve on substituting a pulsatile for a non-pulsatile pressure is dependent on the algebraic sum of the changes occurring in individual fibres under the three conditions stated above. Fibres in Condition 3 will not alter their number of impulses per cycle time, those in Condition 2 will reduce the number, whereas those in Condition 1 will increase the number of impulses due to

recruitment. From these results and from evidence obtained on the carotid sinus nerve it appears likely that the increased whole nerve activity during pulsatile perfusion (Trank & Visscher, 1962; Spickler & Kezdi, 1967; Koushanpour & McGee, 1969) is due largely to recruitment of fibres.

The relationship between the instantaneous impulse frequency and aortic arch pressure observed during pulsatile perfusion is in sharp contrast to that which occurs during non-pulsatile perfusion over the same pressure range (Fig. 5). When the elliptiform plot for one pressure cycle is compared with the curve obtained for the same range of pressure during non-pulsatile perfusion, it is found that the impulse frequency during pulsatile perfusion is higher in systole and lower in diastole than at the corresponding pressure during non-pulsatile perfusion. Thus the aortic baroreceptors respond to rate of change of pressure as well as to absolute pressure, as do the carotid sinus baroreceptors (Bronk & Stella, 1932, 1935; Landgren, 1952*a*) and other mechanoreceptors such as muscle spindles (Adrian & Zotterman, 1926*a*; Matthews, 1931, 1933), Pacinian corpuscles (Adrian & Zotterman, 1926*b*; Gray & Matthews, 1951*a*, *b*) and touch receptors (Gray & Malcolm, 1951). The underlying mechanisms have been discussed by several workers (Matthews, 1931, 1933; Katz, 1950; Loewenstein, 1956; Lippold, Redfearn & Vuco, 1958; Lippold, Nicholls & Redfearn, 1960; Matthews, 1964). The present theory of these responses of mechanoreceptors is that they are basically a mechanical property of the gross or finer structure of the nerve endings and of the surrounding tissue to which they are attached.

It was observed in the present experiments that during pulsatile perfusion at a given mean pressure, the impulse frequency during the descending phase of the pressure wave is diminished in spite of the aortic diameter being greater (Remington, 1955). This phenomenon may be similar to that described for static impulse frequency–pressure loops and have a similar underlying mechanism (Angell James, 1971).

In contrast to the marked difference between the impulse activity in single baroreceptor fibres during the systolic and diastolic phases of the pressure cycle at low mean pressures there is much less difference in the impulse activity during the pressure cycle at higher mean pressures. This can be related to the differences in the slope of the impulse frequency–pressure curve for non-pulsatile pressures (Angell James, 1968, 1969, 1971, this paper) and to the diminished recruitment that occurs as the threshold pressure of the majority of the fibres has been exceeded. Aars (1968) using whole nerve recording also observed a more constant impulse activity at high arterial pressures in the intact animal. The phasic discharge occurring at low pressures is likely to be due to variations in impulse frequency in individual fibre and to recruitment of others.

Effects of changes in pulse pressure

With increasing pulse pressure the curve relating impulse activity to pressure becomes more elliptical and the impulse frequency during systole increases progressively while that during diastole decreases and finally reaches zero. At least two factors are responsible for this phenomenon. One is that the higher systolic pressure distends the aortic arch more and secondly the increased rate of change of pressure produces an additional increase in impulse frequency (the 'on' effect). This may be related to the larger aortic diameter which occurs at any pressure when the amplitude of stretch is increased (Remington, 1955), or to additional stiffness of the wall which occurs with increasing rate of change of pressure (Peterson, 1960). At high pulse pressures the increase of peak frequency during systole with increasing pulse pressure becomes progressively less in some fibres despite an increase of rate of change of pressure. In a similar way the increase of baroreceptor impulse activity with increased non-pulsatile pressure is less evident at these high pressures and it is probable that the underlying mechanism is the same (Angell James, 1969, 1971).

Increasing the rate of change of pressure to which the aortic baroreceptors were subjected only decreased their threshold pressure by a very small amount in some cases and in others it had no effect at all. This in contrast to the carotid sinus baroreceptors whose threshold pressures were considerably depressed by increasing the rate of change of pressure (Landgren, 1952*a*). The difference between the carotid sinus and the aortic arch baroreceptors may be due to differences of the local mechanical properties of the two vasosensory areas or to the attachment of individual baroreceptors to the tissues of the walls. The mechanism underlying these effects has not been fully explained but is discussed in a separate paper (Angell James, 1971).

In a few-fibre or whole nerve recording of the aortic nerve the most striking effect of increasing the pulse pressure is the recruitment which occurs during systole as a result of the pressure exceeding the threshold pressure of other baroreceptors. This results in an increase in the total impulse activity per cycle although the number of impulses in 1 sec period of fibres whose threshold are below the pressure at all phases of the pressure cycle will remain constant.

These studies are consistent with those in which it has been shown that an increase in aortic arch pulse pressure causes reflexly a reduction in systemic vascular resistance (Angell James & Daly, 1970*b*). Gero & Gerová (1962) had previously shown that an increase in pulse pressure in the carotid sinus evoked a reflex reduction in blood pressure.

Effects of changes in pulse frequency

The relative constancy of the number of impulses/cycle with increasing pulse frequency is in contrast to the changes in peak impulse frequency/cycle. With increasing pulse frequencies this progressively increased during the systolic phase of the cycle and decreased during the diastolic phase. The increase in impulse frequency during systole occurred even though the frequency during diastole had reached zero. Two mechanisms probably contribute to the elliptiform shape of the curve relating instantaneous impulse frequency to aortic pressure (Fig. 10). First, a change in the state of the wall during the pressure cycle due to hysteresis. This fact is well documented (see Remington, 1963) and when the pulse frequency is increased, although the hysteresis diminished, the volume of the aorta during systole at any given pressure is slightly increased (Remington, 1955). This would increase the peak impulse frequency. Secondly, the pulse frequency is closely related to the rate of change of pressure both during systole and diastole. Thus with increasing pulse frequency, and hence rate of change of pressure, the augmented peak frequency of impulses during systole could be due to the 'on-effect' (Matthews, 1931, 1933; Landgren, 1952*a*), and conversely a decrease in frequency during diastole to the 'off-effect'. The other possibility is that these effects are related to accompanying changes in wall stiffness (Peterson, 1960), or distensibility (Landgren, 1952*b*).

The threshold pressure of the majority of fibres remains remarkably constant with alterations of the rate of change of pressure, but increasing the pulse frequency reduced the threshold pressure by up to 9 mm Hg in a few fibres studied. This is in contrast to the striking effects observed by Landgren (1952*a*) on applying a rapid pressure transient to the carotid sinus in which a considerable lowering of the threshold was observed. However the rate of change of pressure in his experiments was greater than those applied to the aortic arch by the pulse pressure pump in the present series. A lowering of the threshold pressure with increasing pulse frequency can also be seen in the records of carotid sinus nerve action potentials in Fig. 4 of the paper by Gero, Gerová & Filistovichová (1963), though they do not comment on it.

These findings must now be considered in relation to impulse activity in the whole nerve. The foregoing discussion is based on an example in which all phases of the pressure cycle are above the threshold pressure, and therefore only applies to a certain number of fibres in the nerve. With the remaining fibres part or all of the pressure cycle falls below their threshold pressures. In the latter case there will be recruitment of fibres during systole as the pressure rises above their threshold pressures. But

with increasing pulse frequency the length of time the pressure remains above the threshold pressure during each pressure cycle diminishes, so that the number of impulses per cycle diminishes although the number per unit time may remain about the same. The higher the pulse frequency the more often a given number of fibres will be recruited, and furthermore additional recruitment of other fibres may occur from the depression of the threshold by the increased rate of change of pressure. Thus a larger total number of impulses in the whole nerve per unit time will reach the medullary centres. In this connexion, whole nerve recordings by Spickler & Kezdi (1967) showed an increase in the ratio of the amplitude of the averaged nerve action potentials to the carotid sinus pressure ('relative gain'). This finding is consistent with those of other workers who demonstrated that increasing the carotid sinus pulse frequency caused a reduction in arterial blood pressure (Gero & Gerová, 1962; Gero *et al.* 1963; Scher & Young, 1963; Levison, Barnette & Jackson, 1966) and a reduction in systemic vascular resistance (Angell James & Daly, 1970*b*). An increase in aortic arch pulse frequency also produces reflex vasodilatation (Angell James & Daly, 1970*b*).

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