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INOTROPIC RESPONSES OF THE LEFT VENTRICLE TO CHANGES IN AORTIC ARCH PRESSURE IN ANAESTHETIZED DOGS

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SUMMARY

1. Inotropic changes in the left ventricle in chloralose anaesthetized dogs were determined in response to changes in non-pulsatile pressure perfusing the vascularly isolated aortic arch.

2. Inotropic responses were assessed by measuring the maximum rate of change of left ventricular pressure (dP/dt max) in preparations in which heart rate, mean ascending aortic pressure and brachiocephalic (i.e. carotid sinus and cerebral) perfusion pressure were held constant.

3. dP/dt max increased (average +43%) when aortic pressure was reduced from a level above that which produced maximum depression of the myocardium to a level below which no further responses could be obtained; responses occurred as aortic arch pressure was changed between 250 and 90 mm Hg.

5. In the same preparations changes in the brachiocephalic artery perfusion pressure with aortic arch pressure held constant resulted in similar inotropic responses.

6. It is suggested that aortic arch baroreceptors may be of importance in the control of the inotropic state of the heart.

INTRODUCTION

Recently, perfusion techniques have been devised which have enabled the aortic arch to be vascularly isolated and studies made of the reflex effects of changes in aortic pressure on vascular resistance and heart rate (Daly & Daly, 1959; Daly, Hazzledine & Howe, 1965; Levy, Ng & Zieske, 1966; Hainsworth, Ledsome & Carswell, 1970; Angell James & Daly, 1970; Donald & Edis, 1971). These investigations have shown that vasomotor and heart rate responses from stimulation of baroreceptors in the

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aortic arch are qualitatively similar to those resulting from stimulation of carotid sinus baroreceptors (Heymans & Neil, 1958). However, there is little information about the inotropic responses of the heart which result from stimulation of aortic arch baroreceptors. Some observations on the effects of stimulation of aortic baroreceptors on peak left ventricular pressure were made by Levy *et al.* (1966), but since then Furnival, Linden & Snow (1970) showed that measurements of peak left ventricular pressure did not provide a sensitive or quantitative index of inotropic changes and that a much better index could be provided from measurements of the maximum rate of change of left ventricular pressure (dP/dt max). To study reflex inotropic responses it is necessary to maintain both heart rate and mean aortic pressure constant, since changes in these variables also cause changes in dP/dt max. In the present study the pressure in the aortic arch was varied independently of pressure in other parts of the circulation and the rate of change of left ventricular pressure was measured with heart rate, ascending aortic pressure and brachiocephalic artery pressure (i.e. the pressure perfusing carotid sinuses and brain) held constant.

A preliminary report of these experiments has already been given (Hainsworth & Karim, 1969).

METHODS

Dogs of weight 15–24 kg were given a subcutaneous injection of morphine sulphate (0·5 mg/kg). About 1 hr later under local anaesthesia (decicain 2%) a catheter was passed through a saphenous vein so that its tip lay in the inferior vena cava. The animals were anaesthetized by the infusion through this cannula of chloralose (0·1 g/kg; British Drug Houses). The chloralose was dissolved to make a solution, 1 g/100 ml., in sodium chloride solution (0·9 g/100 ml.). A state of light surgical anaesthesia was maintained during the experiment by further infusions of chloralose (about 10 mg/kg every 15 min). Following induction of anaesthesia the neck was opened in the mid line, the trachea cannulated and positive pressure ventilation started by means of a Starling 'Ideal' pump using air enriched to contain 40% oxygen and humidified at room temperature. The rate of the pump was 18 strokes/min and the stroke volume was approximately 50 ml./3 kg body weight. When the pleura was opened a resistance to expiration was inserted equivalent to 3 cm water.

The chest was opened widely by removing the fifth left rib. The upper lobe of the left lung was tied at its root and removed to expose the descending aorta which was mobilized by tying and dividing the upper four intercostal arteries on both sides. About 1 cm of the brachiocephalic and left subclavian arteries were dissected free of their attachments. The pericardium was opened and a strong thread was loosely passed round the ascending aorta using an aneurism needle pushed between the ascending aorta and the pulmonary artery.

The dog then received heparin 500 i.u./kg (Pularin, Evans Medical Ltd.) and was connected to the perfusion circuit (Fig. 1). The circuit was primed with heparinized blood obtained from a large donor dog bled the same day. A long 7 mm i.d. cannula connected to the atrial reservoir was inserted into the left atrium through the appendage. A curved stainless-steel cannula was then inserted up through the descending aorta and passed round into the aortic arch. The aortic cannula had a

curvature and diameter similar to that of the aorta of a 20 kg dog. It was connected by 1 cm i.d. tubing to a closed 2 l. polyethylene reservoir connected to a constant pressure system maintained at about 132 mm Hg (see Hainsworth *et al.* 1970 for further details). Next, cannulae were inserted in the distal end of the brachiocephalic artery and the proximal end of the left subclavian artery which were immediately perfused using independent constant pressure systems. Silver pacing electrodes were sewn on to the right atrial appendage; in two experiments electrodes were also sewn

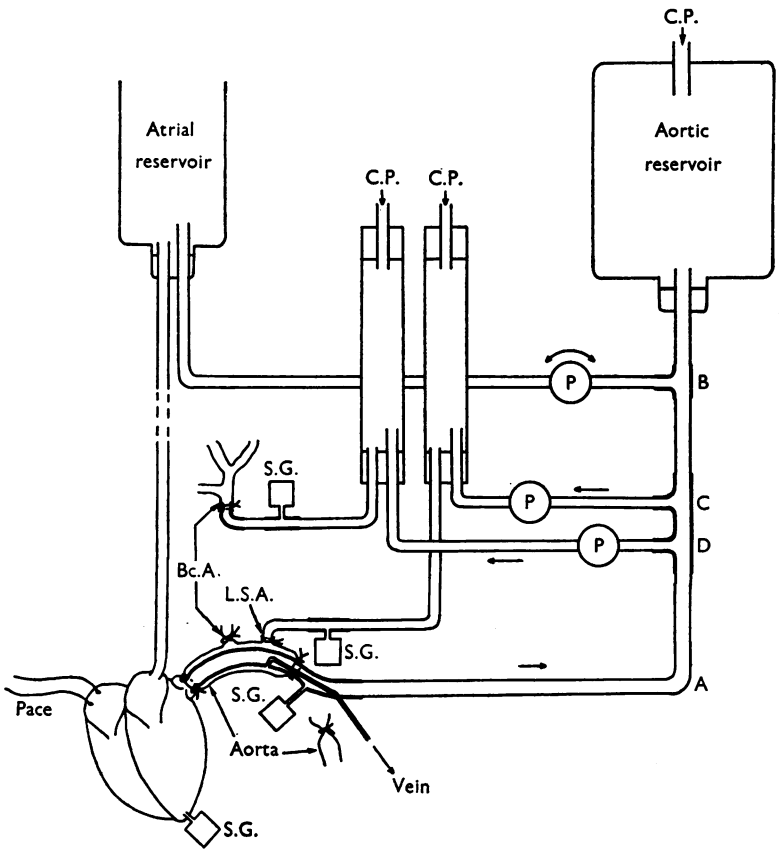

Fig. 1. Diagram of the experimental preparation. Bc.A., brachiocephalic artery; L.S.A., left subclavian artery; S.G., strain gauge; C.P., constant pressure; P, roller pump. For explanation of circuits A, B, C and D see text.

on to the right ventricle. A stainless-steel cannula (length 5 cm, bore 1·5 mm) was inserted into the left ventricle through its apex and clamped firmly in position. Finally, the thread previously placed round the ascending aorta was passed through strong polyethylene tubing to form a snare which was then located in the proximal groove in the aortic cannula, tightened and firmly clamped. Thus a pouch of the aortic arch was formed on the outside of the cannula; the entire aortic blood flow passed through the lumen of the cannula and thence to the aortic reservoir (A in Fig. 1). This blood was distributed by the three independent perfusion systems: B, blood was

pumped either way between the aortic and the atrial reservoirs using a large reversible roller pump. By adjusting the height of the atrial reservoir and the rate and direction of the pump it was possible to control left ventricular filling, as indicated by left ventricular end-diastolic pressure; C, blood was pumped using a roller pump (Watson Marlow Ltd, model M.H.R.E.) into a constant pressure chamber, the outflow of which led to the cannula in the left subclavian artery, to control the pressure in the pouch of the aortic arch; the rate of the pump was adjusted to maintain a constant level of blood in the chamber. The outflow from the aortic arch passed through a small tube opening to the pouch side of the aortic cannula and connected to a systemic vein; D, a similar system perfused the brachiocephalic artery. The descending aorta was not perfused.

Pressures were recorded using Statham strain gauges (Model P23 Gb) attached to the perfusion cannulae and the left ventricular cannula. After amplification by a carrier amplifier (S.E. Laboratories, Feltham, Middlesex) the pressure signals were recorded on photographic paper by a direct-writing ultra-violet light recorder (S.E. Laboratories). Mean pressures were obtained by passing the output signals from the strain gauge amplifiers through simple R–C networks with time constants of 2 sec. Zero pressures were recorded at the end of the experiments as the pressures with the cannula tips free in air.

The output from the carrier amplifier for the left ventricular pressure transducer was distributed four ways: (1) through a variable series resistance to a galvanometer to record left ventricular pressure at normal arterial calibration (20 mm Hg = 10 mm paper), (2) directly to a galvanometer to record left ventricular end-diastolic pressure at greater sensitivity (10 cm H_2O = 10 mm paper), (3) to a digital cardiotachometer (Gilford Instruments Inc.), and (4) to an analogue differentiator to provide a signal of dP/dt which was amplified and recorded.

The differentiator was calibrated using the method of Neal, Halpern & Reeves (1960). The frequency response of the left ventricular pressure system and differentiator was flat ($\pm 5\%$) to better than 60 c/s.

The heart was paced at a constant rate by means of a Grass stimulator (model S4) connected to the atrial electrodes; in two dogs the right atrium and ventricle were sequentially paced using two stimulators synchronized with a constant A–V delay of 65–90 msec.

A thermistor probe (Yellow Springs Instruments Inc.) recorded oesophageal temperature which was maintained at 37–39° C by using heating lamps under the operating table. Blood in the perfusion circuit was prevented from cooling by heating tapes applied to the sides of the reservoirs. Arterial P_{O_2}, P_{CO_2} and pH were determined frequently during the experiment using the method of Norman, Ledsome & Linden (1965). Since during the experimental procedures the dogs breathed 40–100% oxygen, arterial P_{O_2} was always greater than 160 mm Hg. P_{CO_2} and pH were adjusted to 35–40 mm Hg and 7·35–7·42 respectively by adjustments of the stroke of the respiratory pump and intravenous infusion of 1 M-$NaHCO_3$.

Experimental procedure

At the beginning of each experiment, the pressure in the aortic cannula was set by adjusting the pressure in the aortic reservoir. The aortic pressures had a mean value of 132 mm Hg (Table 1). This pressure was held constant throughout the entire experiment; any small changes which occurred were corrected before any measurements were made. The heart was paced at a rate in excess of that occurring with a low pressure in both aortic pouch and brachiocephalic artery. Aortic pouch pressure was set to a value below threshold for responses and brachiocephalic artery perfusion pressure was raised in steps of about 10 mm Hg from about 70 mm Hg

until there was a reduction of 10–20% in dP/dt max. The brachiocephalic artery was perfused at this pressure (average 117 mm Hg) throughout the rest of the experiment of changing aortic pouch pressure.

Aortic pouch pressure was set at a high value (Table 1) which should have produced a maximum stimulation of all the baroreceptors within the pouch and was then decreased either in a single large step or a series of smaller steps to a level below threshold for most aortic baroreceptors (Ninomiya & Irisawa, 1967; Angell James, 1971). Finally, aortic pouch pressure was increased to its previous high value. Throughout these steps, heart rate, mean aortic cannula pressure and brachiocephalic artery perfusion pressure remained constant. At each step, fast records were obtained after at least 1 min when all the measured variables had reached steady states.

RESULTS

The effects of large step changes in aortic pouch pressure on dP/dt *max*

In thirty tests in twelve dogs a decrease in aortic pouch pressure from a mean of 365 mm Hg to a mean of 71 mm Hg always resulted in an increase in dP/dt max. The average of the responses from all the dogs was an increase in dP/dt max of 1174 mm Hg/sec; i.e. +43%. The average responses from each dog are given in Table 1.

An example of the responses obtained on changing aortic pouch pressure is shown in Fig. 2. In addition to the increase in dP/dt max as aortic pouch pressure decreased, there was also an increase in peak left ventricular pressure and a decrease in left ventricular end-diastolic pressure although the changes in end-diastolic pressure were reduced by changing the level of the atrial reservoir.

The effects of graded changes in aortic pouch pressure on dP/dt *max*

Five tests were done in five dogs. The results showing the responses to changing aortic pouch pressure in steps of about 50 mm Hg are plotted in Fig. 3. Responses were first obtained as aortic pouch pressure decreased to 250 mm Hg (range 295–230) and little change occurred when aortic pouch pressure was reduced below 90 mm Hg. The aortic pouch pressure corresponding to the value of dP/dt max, mid-way between the maximum and minimum was read off each plot to give the middle of the operating range of the aortic arch baroreceptors for this reflex. These values were 150, 152, 155, 190 and 200 mm Hg in the five experiments.

Effects of vagal section or cold blockade on responses to changing aortic arch pressure

In two dogs the right vagus nerve was cut in the neck and the left vagus placed on a silver-plated copper block which was cooled by a thermoelectric module (De La Rue Frigistor Ltd.). The temperature at the surface of the nerve was recorded using a miniature thermistor probe (Yellow

TABLE 1. Inotropic responses from large step changes in aortic pouch pressure, with brachiocephalic artery pressure, aortic cannula pressure and heart rate maintained constant. Mean values given from each dog

Dog no.	Ao.P.P. (mm Hg) A	Ao.P.P. (mm Hg) B	dP/dt max (mm Hg/sec) A	dP/dt max (mm Hg/sec) B	% incr. in dP/dt max	L.V.E.D.P. (cm H_2O) A	L.V.E.D.P. (cm H_2O) B	Bc.P. (mm Hg)	Ao.C.P. (mm Hg)	H.R. (beats/min)
1	360	84	3000	5000	67	12·0	10·0	139	157	130
2	334	88	2400	3250	35	18·0	17·0	120	143	150
3	339	93	2830	3530	25	13·8	11·8	129	112	150
4	375	72	1770	2300	30	11·7	8·1	117	127	160
5	357	54	3460	4160	20	8·6	5·6	98	144	198
6	376	91	3650	4600	26	7·2	5·0	133	109	168
7	348	64	1700	3000	76	15·0	13·0	95	116	180
8	366	65	3530	5790	64	11·7	8·3	105	155	240
9	350	70	2000	2600	30	12·0	10·5	143	119	160
10	389	55	3270	3680	12	7·4	6·1	135	126	160
11	373	61	4050	5900	46	6·4	4·4	93	141	207
12	418	52	2300	4240	84	9·1	6·3	93	140	187
Mean	365	71	2830	4004	43	11·1	8·8	117	132	174
S.E.	6·7	4·3	227	337	6·9	1·0	1·1	5·5	4·7	8·7
Range	334–418	52–93	1700–4050	2300–5900	12–84	6·4–18·0	4·4–17·0	93–143	109–157	130–240
P			< 0·0005			< 0·0005				

Bc.P., brachiocephalic perfusion pressure; dP/dt max, maximal rate of rise of left ventricular pressure; L.V.E.D.P., left ventricular end-diastolic pressure; Ao.P.P., aortic pouch pressure; Ao.C.P., aortic cannula pressure; H.R., heart rate; A, average of high aortic pouch pressures before and after lowering pressure; B, low aortic pouch pressure. P denotes level of significance for paired observations.

Springs Instruments Inc.). Responses to decreasing aortic pouch pressure were tested with the left vagus warm and then cooled to 5° C (surface temperature). In these dogs, with the vagus warm, decreasing aortic pouch pressure resulted in increases in dP/dt max of 1300 and 1650 mm Hg/sec. With the vagus cooled a similar decrease in aortic pressure resulted in a decrease of 8 and an increase of 40 mm Hg/sec. In one of the dogs, aortic

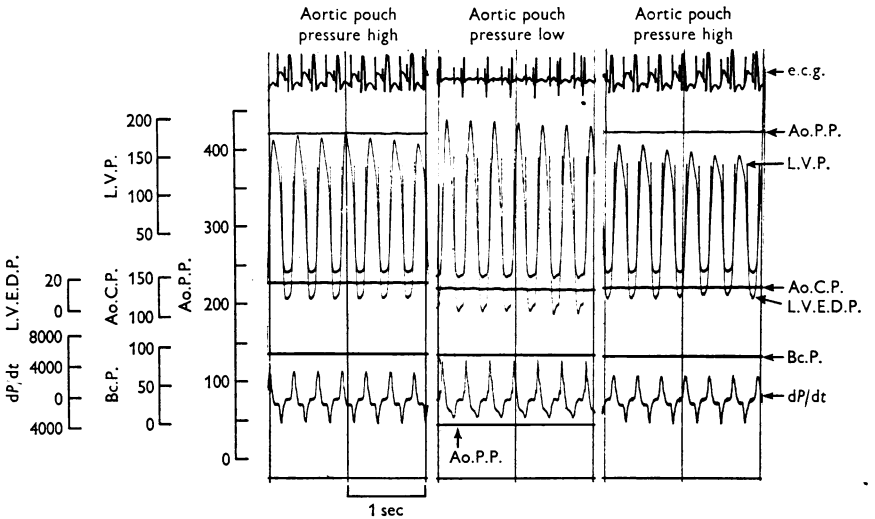

Fig. 2. Effects of large step change in aortic pouch pressure from 420 to 50 mm Hg (dog no. 12). Heart paced at 190 beats/min (atrio-ventricular pacing). Mean aortic cannula pressure and brachiocephalic artery pressure constant throughout. Ao.P.P., aortic pouch pressure (mm Hg); L.V.P., left ventricular pressure (mm Hg); L.V.E.D.P., left ventricular end-diastolic pressure (cm H_2O); Ao.C.P., aortic cannula pressure (mm Hg); Bc.P., brachiocephalic artery perfusion pressure (mm Hg); dP/dt, first differential of left ventricular pressure (mm Hg/sec). (In this dog, see also Figs. 4 and 5, a positive inotropic response of the heart was accompanied by a change in the e.c.g. With atrio-ventricular pacing and non-standard e.c.g. leads this is difficult to explain but it may be associated with the changed heart size (end-diastolic pressure changes) or the rate of impulse conduction over the heart.)

arch pressure was changed on re-warming the nerve to body temperature; responses were again obtained. In a third dog responses were abolished by cutting both vagi in the neck.

Effects of cardiac sympathetic nerve blockade with propranolol on responses to changing aortic pouch pressures

After propranolol (0·5 mg/kg I.V.), the average value in three dogs for dP/dt max at high aortic pressure was reduced from 3500 mm Hg/sec to 2100 mm Hg/sec. The increase in dP/dt max resulting from a large step

decrease in aortic pouch pressure was abolished or greatly reduced after propranolol. In these dogs, the average response before propranolol was an increase of 1430 mm Hg/sec and, after propranolol, an increase of 40 mm Hg/sec (e.g. Fig. 4).

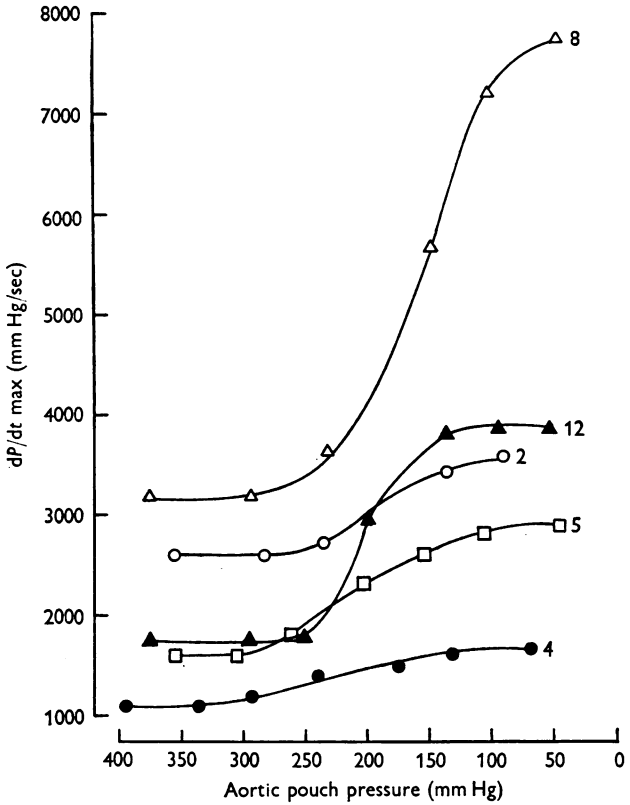

Fig. 3. Effects of stepwise reduction in aortic pouch pressure on dP/dt max in five experiments. Each symbol represents results obtained from one experiment. Mean aortic cannula and brachiocephalic perfusion pressure and heart rate were held constant throughout each series of observations.

The effect of large step changes in brachiocephalic artery perfusion pressure on dP/dt *max*

In these experiments, performed on five of the dogs, aortic pouch pressure was set to a constant level below that which induced reflex changes in dP/dt max and, with heart rate and mean aortic cannula pressure also held constant, brachiocephalic artery pressure was decreased in a large single step within the 'buffering' range of the carotid baroreceptors (Heymans & Neil, 1958). A decrease in brachiocephalic artery pressure from a mean value of 156 mm Hg to a mean value of 74 mm Hg resulted in an increase

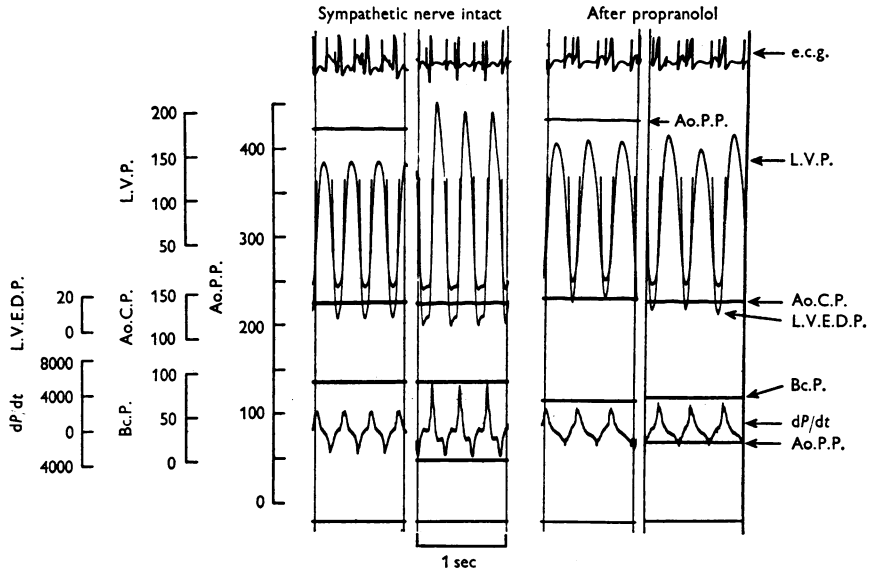

Fig. 4. The effect of a decrease in aortic pouch pressure on the inotropic state of the heart before and after propranolol (0·5 mg/kg I.V.) Conventions as in Fig. 2.

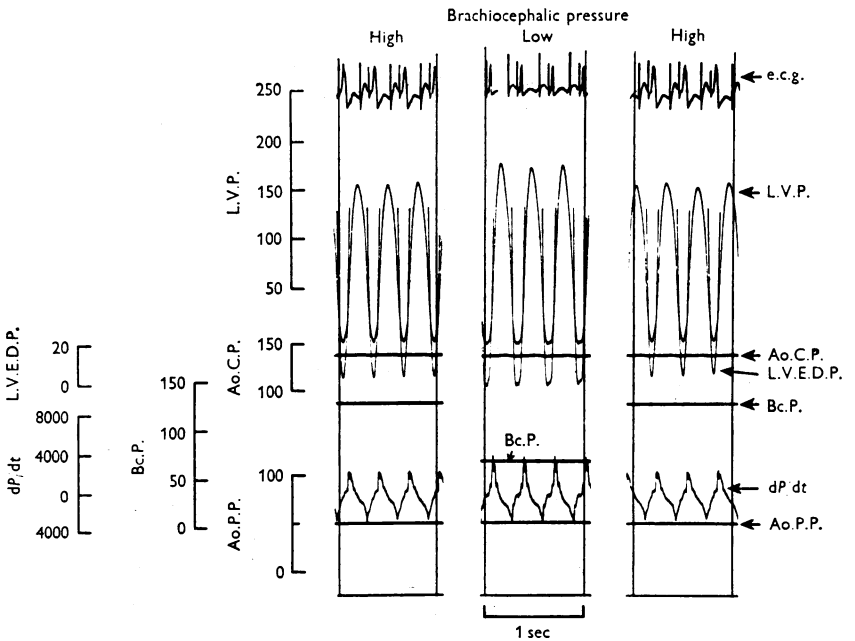

Fig. 5. Effects of step change in brachiocephalic artery perfusion pressure from 130 to 70 mm Hg. Records obtained from same dog as in Fig. 2. Conventions as in Fig. 2. Heart rate paced at 190 beats/min.

TABLE 2. Inotropic responses from large step changes in brachiocephalic artery perfusion pressure with aortic pouch pressure, aortic cannula pressure and heart rate held constant

Mean values obtained from each dog.

Dog no.	Bc.P. (mm Hg) A	Bc.P. (mm Hg) B	dP/dt max (mm Hg/sec) A	dP/dt max (mm Hg/sec) B	% incr. in dP/dt max	L.V.E.D.P. (cm H_2O) A	L.V.E.D.P. (cm H_2O) B	Ao.P.P. (mm Hg)	Ao.C.P. (mm Hg)	H.R. (beats/min)
1	178	72	1157	1700	47	10·7	7·5	39	127	130
5	146	88	2600	3115	20	18·0	15·5	89	162	180
8	144	70	4924	6662	35	9·5	7·0	71	161	240
9	176	75	2919	4133	42	16·7	15·2	80	137	180
12	136	69	2000	3912	96	7·0	3·9	52	146	190
Mean	156	74	2720	3904	48	12·3	9·8	66	147	184
S.E.	8·7	3·4	627	810	12·8	2·1	2·3	9·1	6·8	17·5
Range	136–178	69–88	1157–4924	1700–6662	20–96	7·0–18·0	3·9–15·5	39–89	127–162	130–240
P			< 0·01			< 0·0025				

Conventions as in Table 1. A, average of high brachiocephalic perfusion pressures before and after lowering pressure. B, low brachiocephalic perfusion pressure.

in dP/dt max from 2720 mm Hg/sec to 3904 mm Hg/sec; an increase of 48% (Fig. 5, Table 2). These changes are similar to those obtained on changing aortic pouch pressure (Fig. 2, Table 1).

DISCUSSION

Method used to assess inotropic responses

Measurements of maximum rate of change of left ventricular pressure were used to study inotropic responses since these have been shown to provide a sensitive and quantitative index of inotropic responses to catecholamine infusion (Furnival *et al.* 1970, 1971) and cardiac sympathetic nerve stimulation (Furnival *et al.* 1968). However, since changes in heart rate and mean aortic pressure also result in inotropic responses as assessed by measurements of dP/dt max (Furnival *et al.* 1970), to study *reflex* responses it is essential to keep these other variables constant. Wallace, Skinner & Mitchell (1963) in preparations in which heart rate and mean aortic pressure were held constant also found that increases in left ventricular end-diastolic pressure resulted in small variable increases in dP/dt max in the left ventricle. However, Furnival *et al.* (1970), from the results of their experiments, concluded that left ventricular end-diastolic pressure changes did not cause significant changes in dP/dt max. In the preparation used in the present study, left ventricular end-diastolic pressure decreased slightly as dP/dt max increased. This decrease must have been the result of the positive inotropic response of the ventricle. It is unlikely that a decrease in end-diastolic pressure significantly influenced the responses; if any effect occurred it would be to reduce the measured responses.

Other factors known to be of importance in influencing the inotropic state of the left ventricle are the coronary perfusion pressure and blood flow (Salisbury, 1955; Salisbury, Cross & Rieben, 1960, 1962; Cross, Rieben & Salisbury, 1961; Arnold, Morgenstern & Lochner, 1970; Abel & Reis, 1970). In the present series of experiments coronary flow was not measured, and changes in this due to changes in coronary vascular resistance may have influenced the responses. Changes in coronary vascular resistance might occur either as a result of metabolic changes due to the changed inotropic state or as a result of the direct action of the cardiac sympathetic nerves on the coronary vessels. The effect of this second mechanism is at present unknown and opinion as to whether sympathetic nerves dilate or constrict coronary arteries is divided (Eckstein, Stroud, Eckel, Downing & Pritchard, 1950; Denison & Green, 1958; Szentivanyi & Juhasz-Nagy, 1959, 1963; Berne, DeGeest & Levy, 1965). In these experiments the aortic cannula pressure, which is the pressure perfusing the coronary arteries, was kept

constant during each test. This procedure has the advantage of also maintaining a constant afterload to the left ventricle (see Furnival *et al.* 1970). The alternative approach would have been to control coronary artery flow, but because of increased cardiac work as the sympathetic nerves became more active, such a technique might have limited the responses. However, responses at constant coronary perfusion pressure and constant coronary flow are likely to be similar since De Geest *et al.* (1964) used both techniques in assessing inotropic responses to changes in carotid sinus pressure and found little difference.

Inotropic responses from changes in aortic arch pressure

In all these experiments, a decrease in the pressure in the vascularly isolated aortic arch invariably resulted in a positive inotropic response of the left ventricle as assessed by measurements of dP/dt max. The magnitude of the responses varied considerably between dogs and in some tests dP/dt max at low aortic pressure was twice its value at high aortic pressure. At the high level of aortic pouch pressure, which should have caused maximum stimulation of all the baroreceptors within the pouch, dP/dt max was reduced to levels which indicated that there was little or no sympathetic activity to the heart. The values recorded for dP/dt max at high aortic pouch pressure (mean 2830 mm Hg/sec) were similar to those recorded from a denervated heart by Furnival *et al.* (1970) (mean 3105 mm Hg/sec). However, the actual values obtained depend on the preparation used and in three dogs after β-adrenergic blockade with propranolol, values for dP/dt max of only 2000–2400 mm Hg/sec were recorded. The values for dP/dt max at low aortic pouch pressure also were variable. In one dog dP/dt max increased to nearly 8000 mm Hg/sec when aortic pouch pressure was reduced (Fig. 3) and in two other dogs values of over 5000 mm Hg/sec were recorded (Table 1). However, the average value of dP/dt max at low aortic pressure (4009 mm Hg/sec) is lower than that obtained by Furnival *et al.* (1970) during infusion of isoprenaline at 10 μg/min (6041 mm Hg/sec) or by ourselves (unpublished observations) on supramaximal stimulation of the left ansa subclavia using a preparation similar to that used in the present study (9000 mm Hg/sec).

The response of dP/dt max to changing aortic pouch pressure must depend on the number of active baroreceptors within the pouch. Only the receptors in the aortic arch would be stimulated and receptors in the ascending aorta and the brachiocephalic and right subclavian arteries would not be affected. Also, there is a possibility that some of the receptors in the aortic arch may have been damaged during the initial dissection.

These experiments have shown that inotropic responses from aortic baroreceptors are qualitatively similar to responses described by others

resulting from stimulation of carotid baroreceptors (Sarnoff, Gilmore, Brockman, Mitchell & Linden, 1960; DeGeest, Levy & Zieske, 1964). The maximum responses obtained were qualitatively similar to the responses resulting from changes in brachiocephalic artery pressure in the present experiments and the responses to changing only carotid sinus pressure in another series of experiments (Hainsworth & Karim, 1971). The observation that maximum inotropic responses were of a similar magnitude when either aortic pouch or carotid pressure was changed contrasts with recent findings using an identical aortic arch preparation when it was noted that maximum heart rate and vasomotor responses were about three times greater for carotid pressure changes than for aortic pressures changes (Hainsworth *et al.* 1970). In the present study we found that inotropic responses were obtained when aortic pouch pressure was changed between 90 and 250 mm Hg (average), whereas in the earlier study the corresponding ranges of aortic pressure for heart rate and vasomotor responses were 163 to about 350 mm Hg and 143–276 mm Hg, respectively. The range of aortic pouch pressures which induced inotropic responses was actually similar to that required in the carotid sinuses to induce similar responses (Hainsworth & Karim, 1971). It is possible that inotropic responses would have been obtained at even lower aortic pouch pressures if these had been pulsatile since studies in the carotid sinus have shown that pulsatile pressures are more effective than steady pressures at the same mean value (Ead, Green & Neil, 1952; Spickler & Kezdi, 1967). However, Angell James & Daly (1970) did not observe appreciable differences in vasomotor responses when the aortic arch was perfused at pulsatile pressures rather than steady pressures at the same mean value.

The vaso-sensory area investigated contains not only aortic baroreceptors but also chemoreceptors which are known to be stimulated as a result of a fall in perfusion pressure to the area (Lee, Mayou & Torrance, 1964). However, the same authors showed that the activity in aortic chemoreceptors did not increase greatly until the pressure was reduced to below 100 mm Hg and that if the animal (cat) was breathing an increased concentration of oxygen the activity in chemoreceptor fibres was low even at perfusion pressures of 60 mm Hg. Landgren & Neil (1951) also found little change in carotid body chemoreceptor discharge until the brachiocephalic pressure was reduced to below 30 mm Hg. It is unlikely that stimulation of aortic chemoreceptors contributed significantly to the responses resulting from decreasing pressure in the aortic arch in the present experiments since P_{a,O_2} was always greater than 160 mm Hg, aortic pressure was not reduced to very low levels (average 71 mm Hg) and at this pressure changes in aortic pouch pressure did not induce large reflex changes in dP/dt max. The influence of chemoreceptor stimulation on the

inotropic state of the heart is in any case uncertain (Kahler, Goldblatt & Braunwald, 1962; Downing, Remensnyder & Mitchell, 1962; Berne & Levy, 1964).

The results from the present study suggest that the aortic baroreceptor reflex is likely to be of importance in the control of the inotropic state of the heart. A change in the stimulus to only those baroreceptors in the arch of the aorta produced significant inotropic responses. Furthermore, unlike the heart rate and vasomotor responses previously described (Hainsworth *et al.* 1970) inotropic responses occurred on changing aortic pressure within the normal physiological range.

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