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THE EFFECTS OF DISTENSION OF THE PULMONARY VEIN–ATRIAL JUNCTIONS UPON PERIPHERAL VASCULAR RESISTANCE

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SUMMARY

1. Small balloons were inserted through the left pulmonary veins so as to lie at the pulmonary vein–left atrial junctions.

2. Distension of the balloons caused a reflex increase in heart rate. The afferent path was in the vagus nerves and the efferent path was in the cardiac sympathetic nerves.

3. Only small and variable changes in vascular resistance in a perfused hind limb accompanied the increase in heart rate when a steady state had been reached.

4. In about half of the experiments a transient vasodilatation was observed in the perfused hind limb, occurring immediately after distension of the pulmonary vein–atrial junctions and lasting about 22 sec.

5. The transient dilatation was due to a decrease in sympathetic vasoconstrictor nervous activity.

6. Stimulation of left atrial receptors causes an increase of sympathetic nervous activity to the heart but does not cause a corresponding increase in sympathetic nervous activity to the hind limbs.

INTRODUCTION

Stimulation of receptor areas in the heart and pulmonary circulation was generally thought to cause reflex bradycardia and systemic vasodilatation (Aviado & Schmidt, 1955; Heymans & Neil, 1958). More recently it has been shown that distending the left pulmonary vein–left atrial junctions by means of small balloons (Ledsome & Linden, 1964) and increasing the perfusion pressure in an isolated pouch of the left pulmonary

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veins and the adjacent part of the left atrium (Ledsome & Linden, 1967) caused a reflex increase in heart rate. The afferent path of this reflex was shown to be in the vagus nerves and the efferent path solely in the cardiac sympathetic nerves.

The present investigation was designed to determine if any changes in the vascular resistance of a perfused limb accompanied the reflex increase in the heart rate.

METHODS

Dogs of weight 13–21 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., of 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. In some of the dogs both common carotid arteries were dissected free for about 3 cm and a loose string was placed round each.

The chest was opened in the fifth left intercostal space and small balloons were inserted into each of three left pulmonary veins, as described by Ledsome & Linden (1964).

The left femoral artery in the groin was exposed for about 3 cm and any recurring branches were tied. The animal was then given an intravenous injection of Heparin (B.P. mucous; 500 i.u./kg followed by 50 i.u./kg every 30 min). A 3 mm bore stainless-steel cannula was tied into the proximal end of the left femoral artery and the blood thus received was pumped by a roller pump at a constant controlled flow through a 3 mm bore cannula tied in the distal end of the artery. This circuit was used in six dogs. In four other dogs the blood was received through a 3 mm bore nylon cannula which was passed up the left femoral artery so that its tip lay in the abdominal aorta. In these dogs the aorta was occluded just above its bifurcation either by tying the aorta on to the cannula or by injecting 2 ml. saline into a small balloon tied on the end of a length of 1 mm bore nylon tubing passed up the right femoral artery.

In a further five dogs the carotid arteries were perfused at various steady pressures. Blood was received through a cannula tied in the proximal end of the right common carotid artery. Some of this blood was pumped using a roller pump into a chamber at a rate which maintained a constant blood level in the chamber. The pressure of the air above the blood in this chamber was controlled. This provided a pressure-controlled perfusion system, the outlet of which led to a Y-shaped cannula with one limb in the cut distal end of each common carotid artery. Some of the blood obtained was used to perfuse the left hind limb at constant blood flow. The abdominal aorta was occluded at the bifurcation by a balloon.

Pressures in the cardiovascular system were recorded using Statham strain gauges (Model P 23 Gb) attached directly to the perfusion cannulae (femoral and carotid), to a 1·5 mm bore stainless-steel cannula tied in the right femoral or brachial artery

and to a nylon cannula (Portex No. 4, 6 in. long) inserted through the right femoral vein into the inferior vena cava. 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). The frequency response of these systems as measured by the method of Linden (1959) was flat ($\pm 5\%$) to better than 60 c/s. Mean pressures were obtained by passing the output signal from the carrier amplifier through a simple R–C network with a time constant of 1 sec. Mean flow of blood to the limb was measured using a Medicon M-4000 electromagnetic flowmeter (Statham Instruments Inc.) with a cannulating transducer. Zero flow was recorded at intervals during the experiment and the flowmeter was calibrated using the animal's own blood at the end of the experiment. The output from the flowmeter and an e.c.g. obtained from chest-wall leads were also recorded. Heart rate was recorded using a Gilford Cardiotachometer triggered by the systemic arterial pressure pulse.

Arterial pH, P_{a,CO_2} and P_{a,O_2} were measured using the methods described by Norman, Ledsome & Linden (1965). pH was maintained between 7·30 and 7·40 by intravenous infusion of 1 M-$NaHCO_3$. P_{a,CO_2} was maintained between 36 and 40 mm Hg by adjusting the stroke of the respiration pump. P_{a,O_2} was always greater than 160 mm Hg. Oesophageal temperature was maintained at 38° C ± 1° C by adjusting heating lamps under the table.

RESULTS

After completion of the operative procedures, about 30 min were allowed for a steady state to be reached. Then the pulmonary vein–atrial junctions were distended for periods of 2·5 min by injecting 1 ml. saline into each balloon. Values of heart rate, limb perfusion pressure and systemic arterial pressure obtained after 2 min of distension of the pulmonary vein–atrial junctions were compared with the averages of the values obtained immediately before distension and 2 min after release of the distension. Mean values for the pressure readings were estimated over 30 sec and the heart rate was counted over the same period from the electrocardiogram. In five of the ten dogs there were transient changes in arterial pressure and limb perfusion pressure occurring immediately after the balloons were inflated. Results will therefore be presented of measurements made after a steady state had been reached (2 min) and a separate description will be given of changes occurring transiently following distension of the balloons.

The effects of distension of the pulmonary vein–arterial junctions for 2·5 min. Measurements were made of heart rate, arterial pressure and perfusion pressure in the limb in the control periods and during distension of the pulmonary vein balloons as described. The values of the change in heart rate and the percentage change in perfusion pressure to the limb in each test are compared in Fig. 1. This Figure shows the results of the first three balloon distensions made in each of ten dogs. This selection has been made to avoid overweighting the average values with results from those animals in which more tests were made. During distension of the pul-

monary vein–arterial junctions there was always an increase in heart rate compared with the control values. The average increase was 34·5 beats/min (S.E. of mean ± 2·9, range 5–68) from a control heart rate of 127 beats/min (S.E. of mean ± 6·6, range 61–193). Changes in the perfusion pressure to the limb (flow remained constant) were usually small and variable. The average perfusion pressure during distension of the pulmonary vein–atrial junctions was not significantly different from that during the control periods. However, when the values during distension

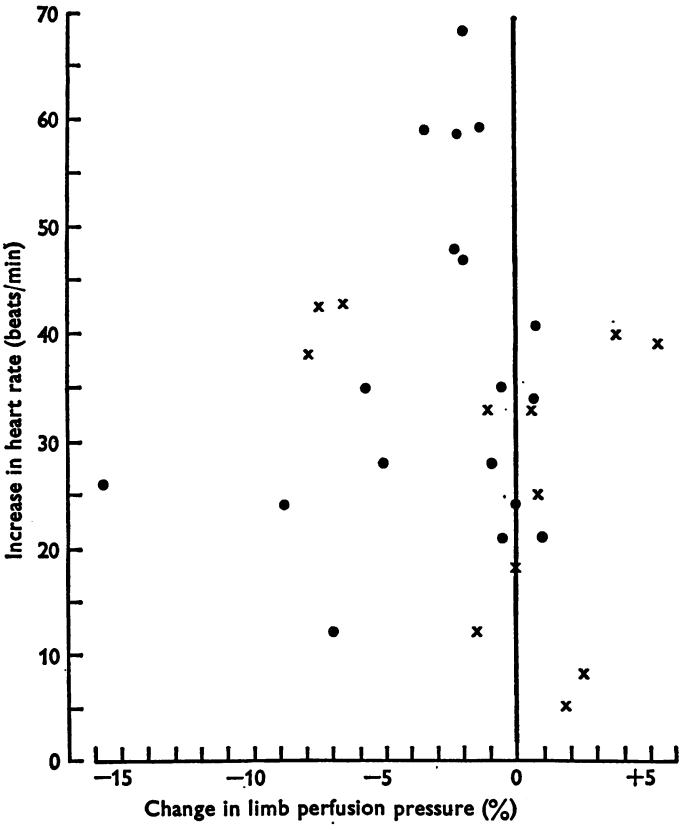

Fig. 1. Effects of distension of the pulmonary vein–atrial junctions; three distensions in each of ten dogs. 'Increase in heart rate' is the heart rate 2 min after distension minus the average of the heart rates immediately before distension and 2 min after release of distension. 'Change in limb perfusion pressure' is the % change in limb perfusion pressure after 2 min of distension of the pulmonary vein–atrial junctions from the average of the values of the perfusion pressure immediately before distension and 2 min after release of the distension. ● denotes observations made in experiments in which the abdominal aorta was not occluded and ×, those in which the aorta was occluded at the bifurcation.

of the pulmonary vein–atrial junctions were expressed as a percentage of the control values (as in Fig. 1), the paired differences between the control and experimental values in each test showed a small but statistically significant difference ($P < 0{\cdot}01$). The average difference was a decrease in perfusion pressure of 2·21 % (S.E.M. of mean ± 0·78, range 15·7 % decrease–5·3 % increase); that is, there was a small decrease in vascular resistance in the limb during distension of the pulmonary vein–atrial junctions. There were no significant changes in mean systemic arterial pressure. The average change was a decrease of 0·8 % (S.E. of mean ± 0·44, range 8·7 % decrease–3·8 % increase). There was an average decrease in systolic pressure of 8·5 mm Hg (S.E. of mean ± 1·4, range 20 mm Hg decrease to 6 mm Hg increase). Pulse pressure decreased by an average of 12·2 mm Hg (S.E. of mean ± 1·5 range 0–32 mm Hg); i.e. diastolic pressure increased.

An example is given in Fig. 2 of parts of the record obtained in one experiment in which a large increase in heart rate occurred on balloon distension. Although the heart rate increased by 68 beats/min, there was only a small decrease (3 mm Hg) in femoral perfusion pressure. Mean systemic pressure remained constant, but there was a decrease in systolic and pulse pressure with an increase in diastolic pressure.

The responses obtained in experiments in which the abdominal aorta was occluded were similar to those obtained with the aorta not occluded (Fig. 1). In experiments in which the aorta was occluded, the pressure in the femoral perfusion cannula fell to the level of the venous pressure when the femoral perfusion pump was stopped, thus demonstrating the absence of significant anastomoses between the systemic arteries and the perfused limb.

Immediate effects of distension of the pulmonary vein–atrial junctions. In five out of the ten dogs there was a transient decrease in limb perfusion pressure and mean systemic pressure immediately following distension of the pulmonary vein–atrial junctions (Fig. 3). In those dogs in which a transient response was observed, it occurred following each test of balloon distension. The average maximum fall in perfusion pressure was 30 mm Hg (range 12–50 mm Hg); this returned to a steady-state value after 22 sec (range 15–50 sec). The changes in systemic pressure were of a similar magnitude and duration. There was no transient heart rate change; this increased and remained faster for as long as the balloons were distended. In about half the cases in which a transient decrease in perfusion pressure occurred, this response followed an abnormally large pulse beat or a series of extrasystoles initiated by the distension of the balloons. However, such extrasystoles followed by heart beats with large pulse pressures occurred in about half the experiments without associated transient responses.

The nature of the reflex mechanism. In five of the dogs the right vagus

was cut in the neck and the left vagus nerve cooled to 5° C (Thermode to 4° C) for 5 min. This abolished all responses to distension of the pulmonary vein–atrial junctions, including the transient responses in the three dogs tested in which these were obtained. After the left vagus had been rewarmed, the increase in heart rate and the transient falls in systemic pressure and limb perfusion pressure were again observed on distension of the pulmonary vein–atrial junctions.

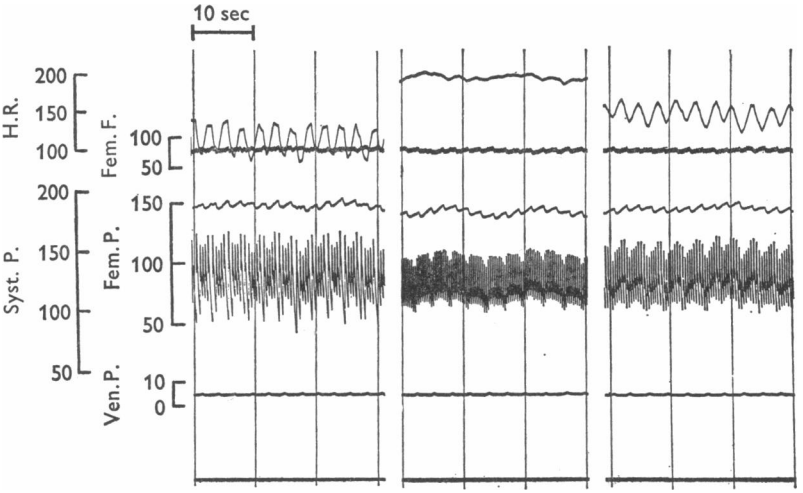

Fig. 2. Effects of distension of the pulmonary vein–atrial junctions in a dog in which a large increase in heart rate occurred. Dog 13 kg. Femoral artery perfusion, aorta not occluded. From above downwards heart rate, femoral perfusion flow, femoral perfusion pressure, systemic arterial pressure (recorded in the right femoral artery) and venous pressure. H.R., heart rate (beats/min); Fem. F., femoral perfusion flow (ml./min); Fem. P., femoral perfusion pressure (mm Hg); Syst. P., systemic arterial pressure (mm Hg); Ven. P., venous pressure (cm H_2O). First column recorded immediately before distension of the pulmonary vein–atrial junctions; second column, after 2 min of distension; third column, 2 min after release of distension.

In two dogs, propranolol (0·5 mg/kg) was given intravenously. In one dog the heart rate increase on distension of the pulmonary vein–atrial junctions was reduced from 38 beats/min immediately before propranolol to 12 beats/min after propranolol. In the other dog the heart rate increase was reduced from 81 beats/min to 16 beats/min. In neither of these experiments was a significant steady-state change observed in the perfusion pressure following balloon distension before or after injection of propranolol. The transient responses of a fall in systemic pressure and a decrease in perfusion pressure in the limb were unaffected by propranolol (two dogs) or an intravenous injection of atropine sulphate, 0·4 mg/kg (two dogs).

They were, however, abolished by an intravenous injection of bretylium tosylate, 10 mg/kg (two dogs).

In six of the dogs both common carotid arteries were clipped simultaneously. This always produced an increase in both systemic pressure and limb perfusion pressure. The average maximum rise in mean systemic pressure was 54 % (range 28–82 %) and the average maximum rise in limb perfusion pressure was 59 % (range 26–105 %).

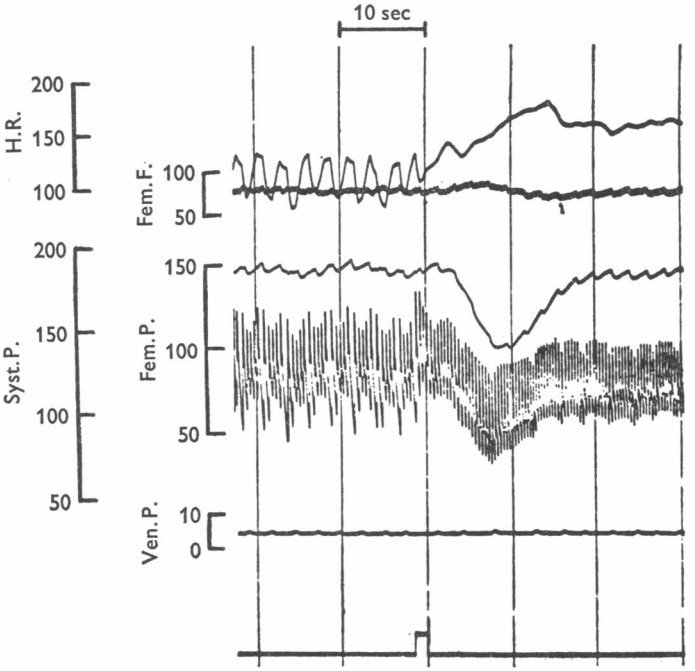

Fig. 3. Changes occurring immediately following distension of the pulmonary vein–atrial junctions. Record from same animal as in Fig. 2. Conventions as in Fig. 2.

Distension of the pulmonary vein–atrial junctions with controlled carotid perfusion. The effects were studied of distension of the pulmonary vein–atrial junctions in five dogs in which both common carotid arteries were perfused at controlled non-pulsatile pressures. The carotid perfusion pressure was set at various levels between 64 and 212 mm Hg. Increasing the carotid perfusion pressure always reduced the femoral perfusion pressure and the systemic arterial pressure. The effect on heart rate was less consistent. A large rise in carotid perfusion pressure always resulted in a transient bradycardia, but often there was little change in heart rate in the steady state. Distension of the pulmonary vein–atrial junctions at all carotid perfusion pressures always caused an increase in heart rate; the

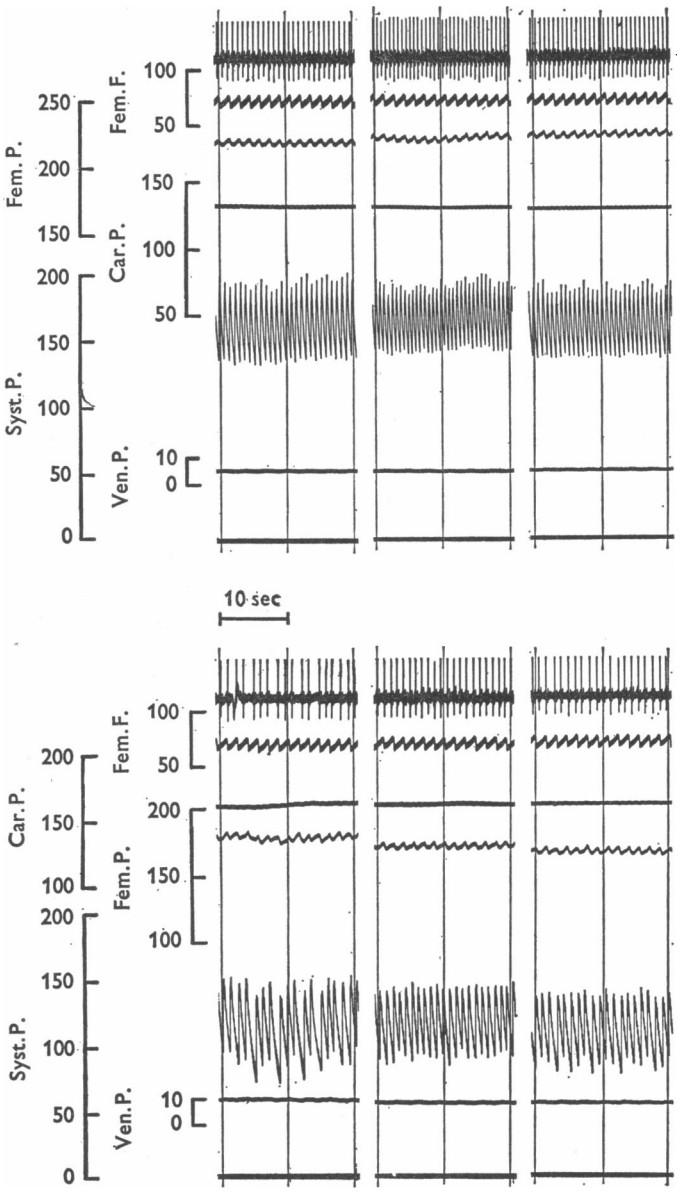

Fig. 4. Effects of distension of the pulmonary vein–atrial junctions at two different constant carotid perfusion pressures. Dog 16 kg. Femoral artery perfusion; aorta occluded at bifurcation. Upper records from above downwards, e.c.g., femoral perfusion flow, femoral perfusion pressure, carotid perfusion pressure, systemic arterial pressure (recorded in right brachial artery), and venous pressure. Lower records, e.c.g., femoral flow, carotid perfusion pressure, femoral perfusion pressure, systemic arterial pressure and venous pressure. Car. P., carotid perfusion pressure (mm Hg). Other conventions as in Fig. 2.

effects on limb perfusion pressure and systemic arterial pressure were always small and variable. Figure 4 shows a record obtained in one experiment in which an increase in heart rate was obtained on distension of the pulmonary vein–atrial junctions at two different carotid pressures. In this experiment, increasing the carotid pressure did reduce the heart rate as well as the limb perfusion pressure and the systemic arterial pressure. Distension of the pulmonary vein–atrial junctions resulted in an increase in heart rate but no definite effect on limb perfusion pressure or systemic arterial pressure at any carotid pressure.

TABLE 1. Effects of distension of pulmonary vein–atrial junctions at controlled carotid perfusion pressures. Results from five dogs in which carotid perfusion pressures were 132 mm Hg and below (sixteen tests) and 138 mm Hg and above (twenty-two tests). Average values given with ranges of individual observations. Control values are the averages of measurements made immediately before, and 2 min after, release of distension. Changes refer to the differences from the control values of measurements made after 2 min of distension

	Low carotid pressure	High carotid pressure
Carotid perfusion pressure (mm Hg)	85 (47–132)	168 (138–212)
Control heart rate (beats/min)	143 (82–207)	132 (54–202)
Change in heart rate (beats/min)	+24 (+9–+42)	+18 (+6–+35)
Control limb perfusion pressure (mm Hg)*	197 (145–232)	137 (90–184)
Percent change in limb perfusion pressure	−0·3 (−7·0–+3·4)	+3·2 (−3·5–+16·2)
Control mean systemic pressure (mm Hg)*	186 (161–202)	122 (82–180)
Percent change in mean systemic pressure	−4·1 (−9·3–+2·0)	−1·3 (−10·7–+9·0)

* Indicates that paired observations in each dog of values obtained at high and low carotid pressures are significantly different ($P < 0{\cdot}01$).

For analysis of the results, the experiments have been divided into those at carotid pressures up to 132 mm Hg (sixteen tests) and those at carotid pressures of 138 mm Hg and over (twenty-two tests). No significant differences were observed between the responses of heart rate, limb perfusion pressure or systemic arterial pressure to distension of the pulmonary vein–atrial junctions at high and low carotid pressures. It should be noted that in these five dogs there was no significant decrease in limb perfusion pressure during distension of the pulmonary vein–atrial junctions at either high or low carotid pressure. In fact, in the experiments carried out at high carotid pressure, the average change on pulmonary vein distension was a small increase in limb perfusion pressure (Table 1).

DISCUSSION

The balloons inserted through the left pulmonary veins were tied and clamped in such a position that distension by 1 ml. saline would distend the pulmonary vein–atrial junctions. The subendocardium at the pulmonary vein–atrial junctions was shown by Coleridge, Hemingway, Holmes & Linden (1957), using combined electrophysiological and histological techniques, to be the site where left atrial receptors were concentrated. Kidd, Ledsome & Linden (1966) showed that these left atrial receptors were strongly stimulated on distension by small balloons and that such stimulation was maintained as long as the distension continued. In the present experiments, the lung roots were tied tightly distal to the insertions of the balloons; it is unlikely that distension of these balloons would interfere with blood flow through the left atrium. It was considered likely that the responses obtained on distension of the balloons would be a result of stimulation of left atrial receptors.

Distension of the pulmonary vein–atrial junctions consistently caused an increase in heart rate. An increase in heart rate was not obtained when the pulmonary vein–atrial junctions were distended following division of the right vagus nerve and cold block of the left vagus nerve. The response was greatly reduced following injection of propranolol (0·5 mg/kg). Propranolol in this dose had been shown to greatly reduce, but not completely prevent, the increase in heart rate caused by stimulation of the cardiac sympathetic nerves (Ledsome, Linden & Norman, 1965). These results, therefore, confirmed the findings of Ledsome & Linden (1964) that distension of the pulmonary vein–atrial junctions caused an increase in heart rate by a reflex with an afferent path in the vagus and an efferent path in the cardiac sympathetic nerves.

In the steady state (after 2 min) the changes in vascular resistance in a perfused hind limb which accompanied the reflex increase in heart rate were variable (Fig. 1). However, there was a small but statistically significant decrease in vascular resistance in the limb. The change in vascular resistance could have been due to stimulation of atrial receptors as a result of the distension of the pulmonary vein–atrial junctions. Equally, the change may have been produced secondary to an increase in the stimulus to the arterial baroreceptors as a result of the increase in heart rate in spite of the decrease in arterial pulse pressure which occurred. It is well known that a decrease in pulse pressure leads to a decreased stimulus to the arterial baroreceptors (Ead, Green & Neil, 1952) but it is impossible to predict in any individual experiment whether the combination of a decrease in pulse pressure accompanied by an increase in heart rate would lead to a greater or lesser stimulation of the arterial baroreceptors. In

those experiments in which carotid arterial pressure was controlled, thus maintaining a constant stimulus to at least some of the arterial baroreceptors, no significant decrease in perfusion pressure in the limb was observed. Also in some experiments (Fig. 1, Table 1) there was an increase rather than a decrease in perfusion pressure in the limb; this was seen most frequently when the carotid perfusion pressure was controlled at high pressure. It cannot therefore be concluded that the small decrease in perfusion pressure observed in the steady state in the first group of experiments represents the direct reflex response to stimulation of left atrial receptors.

The small size of the changes in vascular resistance in the steady state could not have been due to damage to vasomotor nerves to the limb because large changes in vascular resistance occurred immediately following changing the pressure in the carotid arteries either by changing the carotid perfusion pressure or by occluding the common carotid arteries. In the experiments in which the carotid arteries were perfused at different pressures the limb vascular resistance was varied over a wide range. The absence of a reproducible vasomotor response on distension of the pulmonary vein–atrial junctions could not then be explained by the limb vessels being already in a state of maximal dilatation or maximal constriction.

The experiments also emphasize the difference between the relative effects upon the heart and peripheral vessels of distending the pulmonary vein–atrial junctions and of changing the carotid perfusion pressure. Distension of the pulmonary vein–atrial junctions consistently caused an increase in heart rate accompanied by only small and variable changes in vascular resistance; increasing the carotid perfusion pressure always caused a large decrease in vascular resistance and a decrease in heart rate to a usually smaller and more variable extent. These reflex effects of increasing carotid perfusion pressure are similar to the reflex changes induced when pressure is raised in an isolated carotid sinus preparation but it should be noted that in the present experiments pressure changes were induced throughout the cerebral vascular bed.

In about half of the experiments a transient vasodilatation was observed occurring immediately following distension of the pulmonary vein–atrial junctions. The transient vasodilatation was seen as a decrease both in limb perfusion pressure and in systemic arterial blood pressure of approximately equal magnitudes. This response persisted for an average of 22 sec. The occurrence and magnitude of a transient response were not related to the magnitude of the steady-state response of either vascular resistance or heart rate. However, in those experiments in which a transient vasodilatation was observed, it was noted that it occurred each time the pulmonary

vein–atrial junctions were distended. In these experiments, as the blood pressure and limb perfusion pressure fell, the heart rate increased. The heart rate, however, remained faster for as long as the stimulus was applied. The transient vasodilatation was still observed on distension of the pulmonary vein–atrial junctions following the intravenous injection of propranolol (0·5 mg/kg), which greatly attenuated the heart rate response. It was not modified by the intravenous injection of atropine sulphate (0·4 mg/kg) or by both propranolol and atropine. The response was no longer obtained following cutting or cooling both vagus nerves in the neck. It was also prevented by the intravenous injection of bretylium tosylate (10 mg/kg), which is known to block the efferent sympathetic vasoconstrictor nerves (Boura & Green, 1959). The transient vasodilatation following distension of the pulmonary vein–atrial junctions must, therefore, be dependent upon afferent impulses travelling in the vagus nerves and be effected by the release of sympathetic vasoconstriction.

The mechanism responsible for the transient vasodilatation remains in doubt. If the dilatation were due to stimulation of left atrial receptors then the transient nature of the response must be due to mechanisms other than adaptation of the receptors to the stimulus. One such mechanism could be a restoration of systemic pressure by the reflex action of the arterial baroreceptors. If this were the case it would be expected that the magnitude and duration of the vasodilatation would have been greater when carotid arterial pressure was maintained constant. It is possible that distension of the balloons caused temporary stimulation of receptors other than those at the pulmonary vein–atrial junctions. If there was excessive traction on the balloon catheters distension of the balloons could cause a small movement of the whole heart. Also injection of 3 ml. fluid into the balloons effectively increases the volume of the atrial contents and could lead to a temporary increase in ventricular volume, so that immediately at the time of distension the stimulus may not have been limited to the pulmonary vein–atrial junctions. Extrasystoles and an abnormally large pulse beat were sometimes observed at the time of balloon distension but the incidence of such changes was no higher in those tests in which a transient vasodilatation occurred than in those tests in which it did not occur. Sleight & Widdicombe (1965*a*, *b*) have described receptors in the epicardium and pericardium the discharge of which is stimulated by distension of the ventricle. It is possible that such epicardial or pericardial receptors could be stimulated on balloon distension; stimulation of epicardial receptors is said to cause bradycardia and hypotension; there is no knowledge of the reflex effects of stimulating pericardial receptors.

The mechanism responsible for causing a transient vasodilatation in some of the experiments thus remains a matter for speculation; it is

believed that it may not be due to stimulation of left atrial receptors. It may be relevant that in experiments performed by earlier investigators (Daly, Ludány, Todd & Verney, 1937; Aviado, Li, Kalow, Schmidt, Turnbull, Peskin, Hess & Weiss, 1951) in which hypotension was obtained on increasing left atrial and pulmonary venous pressures, the stimuli were applied for a short duration (20 sec) and responses of short duration resulted. Although in many cases the responses were capable of alternative explanations, it is possible that in some cases the hypotension reported may have been caused by stimulation of receptors similar to those responsible for causing the transient vasodilatation reported in the present experiments, i.e. they may not have been the result of stimulation of left atrial receptors. In these earlier experiments a slowing of the heart rate was obtained associated with the hypotensive response. It must be emphasized that, in the present experiments, even though a transient hypotension occurred in half the experiments, there was never even a transient bradycardia; the heart rate always increased following distension of the pulmonary vein–atrial junctions.

Distension of the pulmonary vein–atrial junctions has been shown to cause a reflex increase in heart rate as a result of an increase in sympathetic nervous activity to the heart. No evidence has been found of concomitant changes in the activity of sympathetic vasomotor nerves to the hind limb. There was no convincing evidence that the transient vasodilatation sometimes observed was caused by the same mechanism which is thought responsible for the increase in heart rate, that is, stimulation of left atrial receptors. The results are significant in that they demonstrate that the effects of stimulation of atrial receptors are unlike those of stimulation of other cardiovascular stretch receptors. This conclusion contradicts an opinion formerly held (Aviado & Schmidt, 1955; Heymans & Neil, 1958) that stimulation of all cardiovascular stretch receptors would be likely to result in similar responses. Also, this is believed to be the first example reported of a reflex response which causes an increase in activity in the cardiac sympathetic nerves and not in the vasomotor nerves to the limbs.

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REFERENCES

Aviado, D. M., Jun., Li, T. H., Kalow, W., Schmidt, C. F., Turnbull, G. L., Peskin, G. W., Hess, M. E. & Weiss, A. J. (1951). Respiratory and circulatory reflexes from the perfused heart and pulmonary circulation of the dog. *Am. J. Physiol.* **165**, 261–277.

AVIADO, D. M., JUN. & SCHMIDT, C. F. (1955). Reflexes from stretch receptors in blood vessels, heart and lungs. *Physiol. Rev.* **35**, 247–300.

BOURA, A. L. A. & GREEN, A. F. (1959). The actions of bretylium: adrenergic neurone blocking and other effects. *Br. J. Pharmac. Chemother.* **14**, 536–548.

COLERIDGE, J. C. G., HEMINGWAY, A., HOLMES, R. L. & LINDEN, R. J. (1957). The location of atrial receptors in the dog: a physiological and histological study. *J. Physiol.* **136**, 174–197.

DALY, I. DE B., LUDÁNY, G., TODD, A. & VERNEY, E. B. (1937). Sensory receptors in the pulmonary vascular bed. *Q. Jl exp. Physiol.* **27**, 123–146.

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 baroceptors in the cat. *J. Physiol.* **118**, 509–519.

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

KIDD, C., LEDSOME, J. R. & LINDEN, R. J. (1966). Left atrial receptors and the heart rate. *J. Physiol.* **185**, 78–79*P*.

LEDSOME, J. R. & LINDEN, R. J. (1964). A reflex increase in heart rate from distension of the pulmonary vein–atrial junctions. *J. Physiol.* **170**, 456–473.

LEDSOME, J. R. & LINDEN, R. J. (1967). The effect of distending a pouch of the left atrium on the heart rate. *J. Physiol.* **193**, 121–129.

LEDSOME, J. R., LINDEN, R. J. & NORMAN, J. (1965). The use of sympathetic β-receptor blocking agents in the investigation of reflex changes in heart rate. *Br. J. Pharmac. Chemother.* **24**, 781–788.

LINDEN, R. J. (1959). Methods of determining the dynamic constants of liquid-containing membrane manometer systems. *J. scient. Instrum.* **36**, 137–140.

NORMAN, J., LEDSOME, J. R. & LINDEN, R. J. (1965). A system for the measurement of respiratory and acid-base parameters in blood. *Br. J. Anaesth.* **37**, 466–479.

SLEIGHT, P. & WIDDICOMBE, J. G. (1965*a*). Action potentials in fibres from receptors in the epicardium and myocardium of the dog's left ventricle. *J. Physiol.* **181**, 235–258.

SLEIGHT, P. & WIDDICOMBE, J. G. (1965*b*). Action potentials in afferent fibres from pericardial mechanoreceptors in the dog. *J. Physiol.* **181**, 259–269.