J. Physiol. (1963), **169**, *pp.* 116–136
With 11 *text-figures*
Printed in Great Britain

NATURAL STIMULATION OF TYPE B ATRIAL RECEPTORS

By A. S. PAINTAL

From the Physiology Department, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-16, *India*

(*Received* 28 *January* 1963)

Recently, Langrehr (1960*a*, *b*) published two papers in which he concluded that the type B atrial receptors, which discharge a late systolic burst of impulses with each heart beat, are stimulated primarily by ventricular contractions pulling on the atrial wall. This conclusion contrasts with the generally accepted view that the intensity of the discharge is determined by the degree of atrial filling (see Heymans & Neil, 1958). The latter belief is based on the unequivocal demonstration that the activity in left atrial endings depends on the volume of fluid introduced into isolated *in situ* left atria, the two being linearly related (Paintal, 1953*a*). Further, the discharge so produced is slowly adapting in most receptors (Paintal, 1953*a*), an observation that has also been confirmed in dogs by Mühl (see Kramer, 1959).

However, in view of Langrehr's conclusion it was necessary to reinvestigate the problem in order to determine the manner in which ventricular contractions influence the type B endings. Results which contradict the findings of Langrehr (1960*b*) and confirm the earlier conclusions (Paintal, 1953*a*) are reported in this paper. In this connexion the relation of the discharge of impulses to the V wave of the atrial pressure curve has also been studied carefully since this rise in pressure at the V wave or its cause, atrial filling, are the only other factors that could possibly be responsible for the normal late systolic burst of impulses in these endings.

METHODS

Experiments were carried out on cats as described previously (Paintal, 1953*b*, 1962). In all experiments, after identifying a particular afferent fibre as arising from a type B atrial ending, the chest was opened and retracted widely. The receptor was then located in one of the two chambers, as described already (Paintal, 1953*a*; Henry & Pearce, 1956; Coleridge, Hemingway, Holmes & Linden, 1957; Langrehr, 1960*a*).

A polyethylene catheter with a bore of 1·5 mm was then introduced into the chamber concerned for recording atrial pressure by means of a pressure transducer, whose output was displayed on one beam of the oscilloscope after suitable amplification. In the earlier half of the experiments this catheter was 21 cm long and it was connected to a P23D Statham pressure transducer. Movements of this catheter were prevented by tying it to

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

rigid structures. The damped natural frequency of the whole system, which was determined during some experiments, ranged from 40 to 60 c/s. The degree of damping was determined at the end of this series and from the measurements made it may be assumed to have ranged from 0·1 to 0·2 of critical damping. Samples of records obtained from this series are shown in Figs. 3 and 6. Since the catheter was 21 cm long, the time taken for the transmission of the pressure pulse from its tip to the transducer was determined by applying a pressure pulse near the tip by means of a vibrator (Goodmans). As expected (cf. Van Citters, 1960) this time was about 2 msec.

In the remaining half of the experiments the length of the catheter was reduced to 6 cm and it was connected to a P 23 G pressure transducer (Statham), care being taken to ensure that the whole recording system was free of air bubbles by using boiled NaCl solution, 0·9 g/100 ml. The damped natural frequency and the degree of damping were determined from observation of the free vibrations following the application of a transient pressure as described by Hansen & Warburg (1950) and McDonald (1960); this was done at the beginning and end of each experiment. The damped natural frequency ranged from 134 to 145 c/s and the degree of damping ranged between 0·06 and 0·1 of critical. Samples of records obtained from such experiments are shown in Figs. 1, 2, 4 and 7. The ventricular pressure was also recorded in these experiments with a 16-gauge needle connected to a pressure transducer (Statham, type P 23 D). The connecting stopcocks and the needle were filled by boiling them in distilled water. The natural frequency of this system varied from 135 to 314 c/s, the degree of damping was 0·08–0·09 of critical. It is therefore clear that the characteristics of the pressure-recording systems in the latter series of experiments were adequate for recording the amplitude and wave form of the atrial and ventricular pressure pulses without any distortion or phase lag (cf. Wiggers, 1928, pp. 5–14; McDonald, 1960).

Sometimes there appeared in the pressure tracing obvious artifacts due to partial blockage of the needle or catheter tip during some part of the cardiac cycle. Such records were discarded, although this is not a desirable practice because it leads to selection of results on an uncertain basis. However, there is really no good criterion for ascertaining whether an atrial pressure tracing is a faithful record of the actual pressure changes in the atrium, other than its appearance and the fact that blood can be aspirated freely throughout the cardiac cycle. In the case of right and left ventricular pressures, however, one can be certain that a particular pressure tracing is genuine if its shape during the ejection phase conforms to the respective pulmonary or aortic pressure pulse (Wiggers, 1928, p. 46). This criterion was used in one experiment in which the aortic pressure was recorded through a catheter connected to a P 23 G transducer (Statham).

The total conduction time for the impulses from the endings to the recording electrodes, which amounted to 6–21 msec in different fibres, was determined by local electrical stimulation after opening the chest. Although this method may not give a reliable index of the actual total conduction time with intact chest (Paintal, 1962) it was the method of choice in the present experiments, since nearly all the observations were made after opening the chest.

Ectopic atrial contractions were produced by stimulating any part of the atrium electrically in order to study the effects of premature ventricular contractions on the endings. With open chest this was easily done by applying a pair of stimulating electrodes to either atrium and stimulating it with pulses of 1 msec duration. For stimulating the right atrium with the chest intact a steel wire (cathode) was passed down a catheter whose tip lay in the right atrium; this catheter was inserted through the external jugular vein. The other electrode was placed in the abdomen as it yielded the smallest artifact when it was located here. The position of the catheter was adjusted so as to yield ectopic contractions with the weakest stimulus. This catheter was also used for injecting fluids or drugs.

In the initial experiments nerve impulses and the e.c.g. (Lead II) were recorded on one

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

double-beam cathode-ray tube and the pressures on another tube. The amount of non-alignment between the four beams of the two tubes was always determined by recording a signal simultaneously on both cathode-ray tubes, and an allowance was made for it in the calculations. However, in spite of all care some errors amounting to about 5 msec at a paper speed of 7 cm/sec were observed. In order to eliminate this error all four traces were recorded on one cathode-ray tube by using suitable electronic switches.

RESULTS

All the type B receptors studied in this investigation showed only a late systolic burst of impulses with intact chest, with characteristic respiratory fluctuations. The minimum latency of the first impulse of the burst after the Q wave of the e.c.g. ranged from 127 to 279 msec during inspiration; the maximum latency of the first impulse for the same fibres during expiration, when the discharge is reduced, was 155–292 msec. It is therefore clear that the fibres studied in this investigation arose from typical type B atrial receptors (cf. Paintal, 1953*a*).

Role of ventricular contractions

In order to determine the role of ventricular contractions, atrial pressure and the corresponding ventricular pressure were recorded simultaneously with the discharge of impulses (Fig. 1) and changes in ventricular and atrial pressures were produced by various procedures such as injecting saline (Fig. 1), occluding the aorta (Fig. 2) or pulmonary artery, or by injecting pentobarbitone (Fig. 7) which is known to have a marked depressant action on the myocardium.

When fluid was injected through the catheter in the right atrium, there was an increase in discharge in right and left atrial receptors along with an increase in the V wave of the atrial pressure tracing and an increase in ventricular pressure (e.g. Fig. 1). However, in most cases the increase in discharge preceded the rise in ventricular pressure by one or more cycles. Thus in Fig. 1*A* it is clear that the discharge started increasing in the 3rd cycle before there was any visible increase in left ventricular pressure which appeared in the 4th cycle. This lag in the change in ventricular pressure is also noticeable in Fig. 1*C*, which shows that the discharge decreased before there was any clear fall in ventricular pressure. In the case of left atrial receptors similar observations have been made after releasing a temporary occlusion of the pulmonary artery.

In some experiments two catheters were introduced into an atrium, one for recording pressure and the other for injecting small amounts of fluids rapidly. Such experiments showed that a sudden marked rise of atrial pressure lasting only one or two cycles was accompanied by marked increase in the discharge of impulses without any simultaneous change in ventricular pressure. Conversely, when the aorta or pulmonary artery

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

was occluded briefly there followed a rise in ventricular pressure before there was an increase in the discharge of impulses. Figure 2 shows this lag in the discharge. In some experiments there was a marked increase in the strength of ventricular contractions with little or no increase in receptor activity.

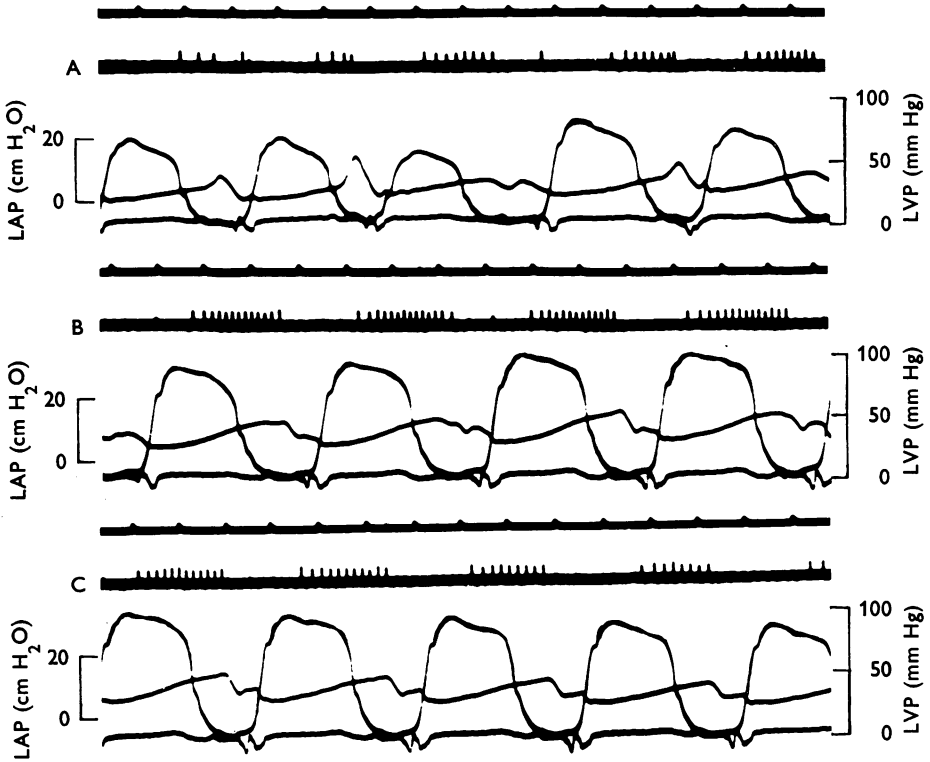

Fig. 1. Effect of injecting 10 ml. 0·9 % NaCl solution into the right atrium on the activity of a left atrial type B receptor. The injection was started at the beginning of *A* and it ended at the beginning of *B*. From above downwards in each record: 0·1 sec time markers; impulses in the fibre; left atrial pressure; left ventricular pressure and e.c.g., lead II. Note that increased activity in the 3rd cycle in *A* is associated with a fall in left ventricular pressure and that the marked increase of the latter in the 4th cycle does not affect the ending. *A*, *B* and *C* are continuous. Most of the points plotted in the graphs of Figs. 9, 10 and 11 were obtained from this record. The chest was open. Total conduction time in the fibre was 7·1 msec. Improved pressure recording systems were used.

Effect of premature ventricular contractions on left atrial receptors. Proof that ventricular contractions do not influence type B atrial endings directly was obtained by producing ectopic beats by stimulating the atrium electrically (Figs. 3 and 4). Since it is well known that premature ventri-

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

cular contractions are much weaker than normal ones, it would be expected that the discharge from the endings would be less during premature ventricular contractions. Quite the opposite was observed in left atrial endings, as is shown in Fig. 3, in which it is clear that the increased activity during the premature cycle is due to the accumulated blood in the atrium owing to incomplete emptying of the atrium due to the premature contraction. This behaviour was noted in each one of the twelve left atrial endings examined. The increase in discharge was evaluated in relation to the normal activity of the ending. In any receptor the total number of impulses during the premature contraction depended on the number of impulses appearing during normal cycles; the greater the discharge in normal cycles, the greater the discharge during premature ventricular contractions.

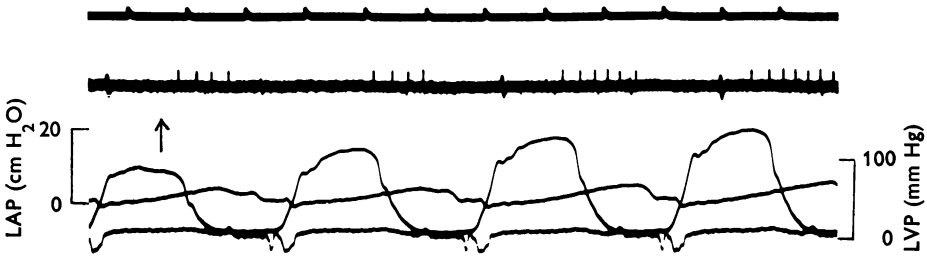

Fig. 2. Effect of brief occlusion of the aorta on the activity of the receptor shown in Fig. 1. The occlusion was begun at the arrow. From above downwards: 0·1 sec time markers; impulses in the fibre; left atrial pressure; left ventricular pressure and e.c.g. The three broad diphasic impulses are from another fibre (non-myelinated). Improved pressure recording systems were used.

It was also found consistently that the earlier the ectopic stimulus was applied the greater was the discharge; i.e. the weaker the premature contraction (cf. Wiggers, 1928, pp. 170–171), the greater was the discharge. Thus in Fig. 3 the discharge increases from record *A* to record *C*. Figure 5*A* shows graphically the response in another fibre. The above relation was seen consistently in nine left atrial receptors; in three of these similar observations were made with the chest intact. However, there was one exception resulting from unusual experimental conditions leading to very low systemic blood pressure and a very low heart rate. Here, as is shown in Fig. 4, the earlier application of the stimulus led to reduction or absence of the discharge because of the gradual rise in pressure, i.e. the rate of rise of pressure was so small that it failed to stimulate the ending owing to accommodation, although the peak pressure attained before the next *a* wave was higher than the normal threshold pressure required to stimulate

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

the ending, as shown in the first control cycle of Fig. 4*B*. This is consistent with Landgren's observations on carotid baroreceptors (Landgren, 1952).

Effect on right atrial receptors. In contrast to the left, five out of seven right atrial endings examined showed the opposite response, i.e. a reduc-

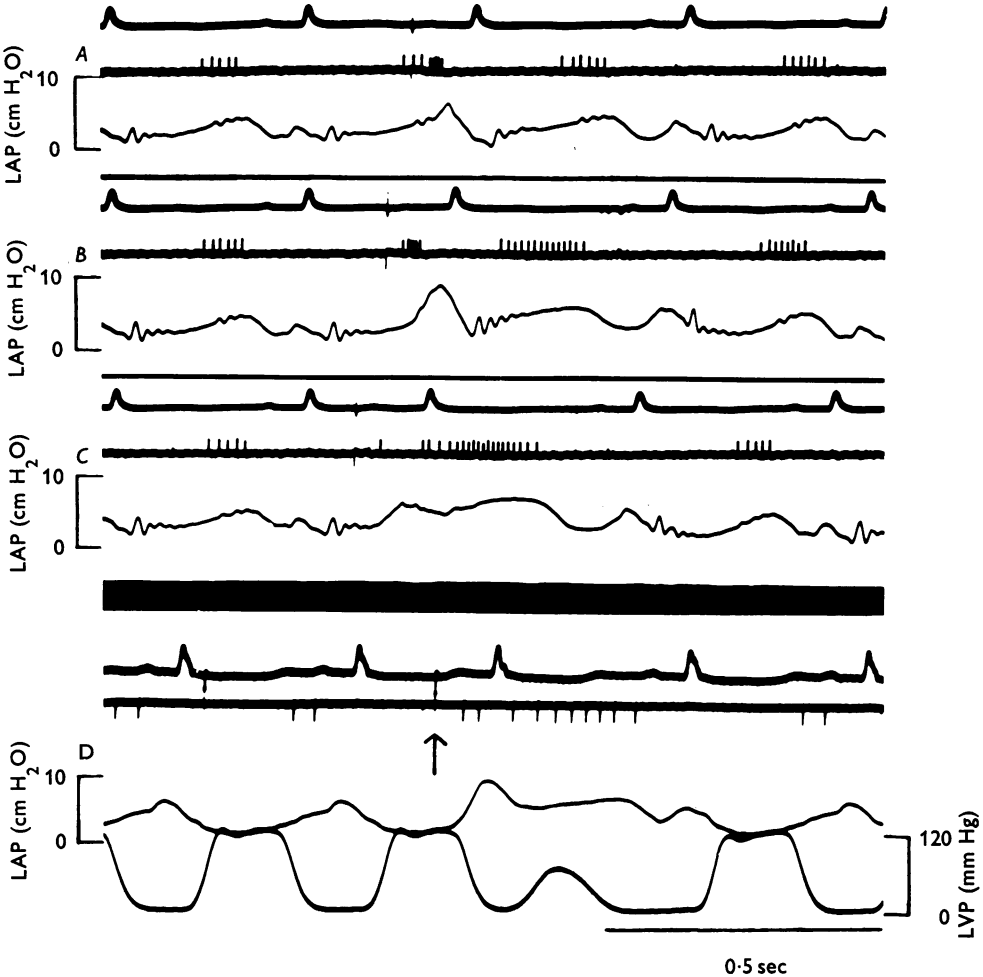

Fig. 3. Effect of premature ventricular contractions on the activity of 2 left atrial type B receptors. Records *A*, *B* and *C* show that the earlier the application of the stimulus to the atrium in the 2nd cycle, the greater is the increase in activity during premature ventricular contraction; this is related to the rise in left atrial pressure. Total conduction time in this fibre was 10·0 msec. *D* is a record of another fibre with a left ventricular pressure tracing; the stimulus was applied at arrow. Total conduction time in this fibre was 11·0 msec. From above downwards in each record: e.c.g.; impulses in a fibre; left atrial pressure and in *D* left ventricular pressure. Left atrial pressure was recorded with a 21 cm long catheter in both experiments.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

Fig. 4. Records showing the effect of accommodation on the activity of a left atrial type B receptor. In both *A* and *B* the right atrium was stimulated at the arrows. This was not followed by ventricular contraction, so that there is no rise in left ventricular pressure, but in *A* the left atrial pressure rose at sufficient rate to stimulate the ending. In *B* the rate of rise was inadequate to stimulate the ending, although the peak pressure attained before the next *a* wave was higher than the threshold pressure needed to stimulate the ending normally. From above downwards in each record; 0·1 sec time marker; impulses in a fibre; left atrial pressure; left ventricular pressure and e.c.g. Improved pressure recording systems were used.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

tion of activity during premature ventricular contractions (Fig. 6); sometimes there was no change in activity and quite infrequently in these five endings there was an unpredictable increase in discharge if the ectopic stimulus was applied late in the cardiac cycle (Fig. 5*B*). Only two right atrial endings behaved like left atrial ones. The difference between the right and left atrial endings is possibly due to the difference in the level of

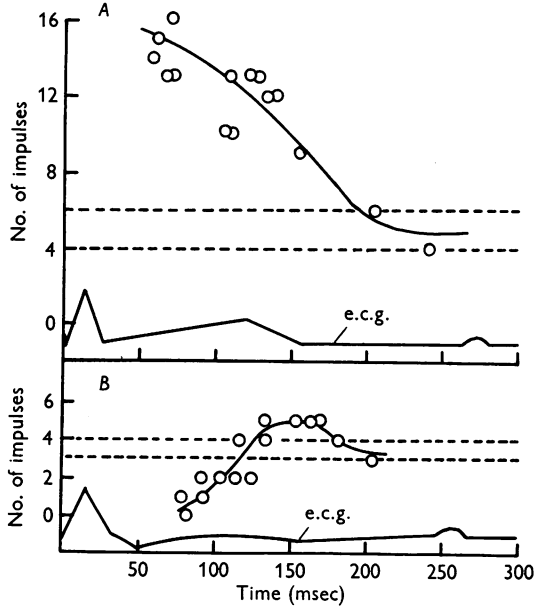

Fig. 5. Graphs showing how the activity of left (*A*) and right (*B*) atrial type B receptors during premature ventricular contraction varies with the position of the ectopic stimulus in the cardiac cycle. Abscissa indicates the interval between the QRS complex of the e.c.g. and the stimulus to the right atrium. The ordinates indicate the number of impulses during premature ventricular contraction. The interrupted lines represent the range of normal activity.

pressure developed in the two ventricles, because in the case of the right ventricle (unlike the left) the pressure developed during premature contractions may not be high enough to keep the auriculoventricular valves closed, so that the blood flows out of the atrium into the right ventricle, as shown by the down slope in the right atrial pressure record (Fig. 6*B*). However, this down slope is not a consistent observation (Fig. 6*A*) but in every instance where the discharge was reduced it was consistently noted that the V wave of the pressure record was clearly reduced (Fig. 6). This could be partly due to the outflow of blood into the right ventricle, but it could also be due to a reduction in the suction force (*vis a fronte*) exerted by the ventricle (Brecher, 1954, 1956).

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

The earlier in the cycle the stimulus was applied the weaker was the discharge during premature ventricular contractions (Fig. 5*B*). This behaviour, which is the opposite of that seen in left atrial receptors (Fig. 5*A*) was noted in five out of seven endings studied. In two the behaviour was typical of left atrial receptors when the effects of ectopic stimuli were examined with the chest intact; in one of these the response became typical of right-sided endings after opening the chest, in the other the response remained unchanged.

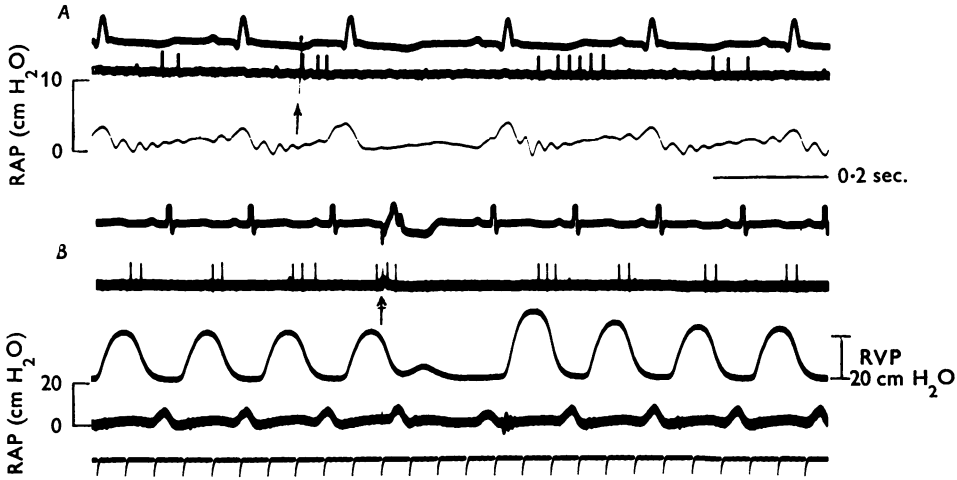

Fig. 6. Records showing that the activity of two right atrial type B receptors (*A* and *B* respectively) is abolished during premature ventricular contraction produced by stimulating the right atrium at arrows. Note increased activity in post-extrasystolic beat in *A* and that right atrial pressure falls during premature ventricular contraction in both *A* and *B*. From above downwards in *A*: e.c.g., impulses in a fibre and right atrial pressure; in *B*: e.c.g., impulses in a fibre; right ventricular pressure, right atrial pressure and 0·1 sec time markers. Total conduction time in *A* was 9·5 msec; in *B*, 14·0 msec. Left atrial pressure was recorded with a 21 cm long catheter in both experiments.

Following the reduction in discharge during premature ventricular contractions there was in several instances an increase during the post-extrasystolic beat (Fig. 6*A*). This increase was associated with the increased strength of ventricular contractions that is known to occur at this time (Fig. 6*B*) and was due to the increase in the V wave which is visible in Fig. 6*A*. However, as Fig. 6*B* shows there were also some exceptions; in such cases there was no increase in the V wave either. In contrast, the left atrial endings as a rule did not show increased activity during the post-extrasystolic beat (Fig. 3); neither was there an increase in the V wave.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

Effect of pentobarbitone. Langrehr found that the discharge in type B atrial receptors fell after injection of 'Inactin', a substance believed to cause myocardial weakness (Langrehr, 1960*b*). In order to see if the same effect could be produced by other drugs, Nembutal (sodium pentobarbital, Abbott Laboratories), which in addition to other effects is known to have a marked depressant effect on the myocardium (Goodman & Gilman, 1955), was injected into the right atrium and its effect studied on seven left and three right atrial type B endings. In some of these experiments the corresponding atrial and ventricular pressures were recorded simultaneously. The quantities injected ranged from 18 to 50 mg.

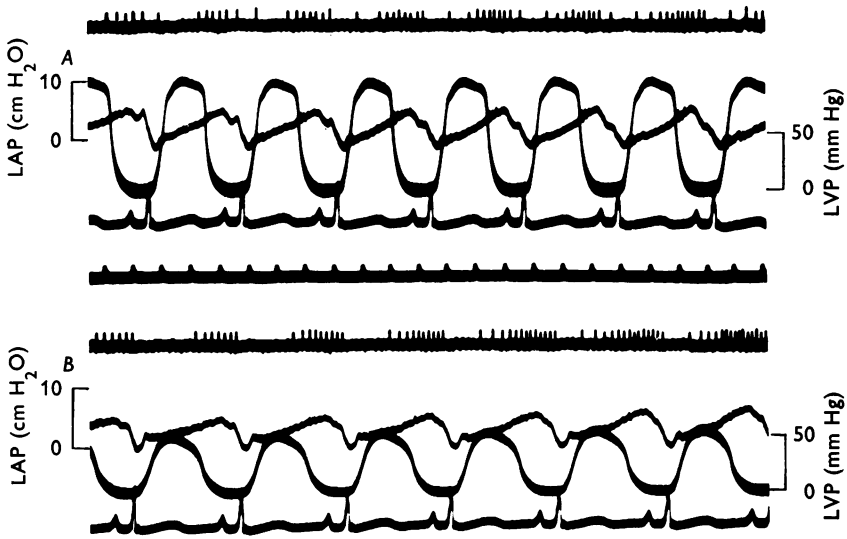

Fig. 7. Effect of 40 mg Nembutal injected into the right atrium on a left atrial type B receptor, *A*, 0·5 sec after end of injection. *B* is a sample of the same record 12 sec after the injection showing a clear increase in the activity of the ending during the fall in left ventricular pressure. From above downwards in both records (taken in the same part of the respiratory cycle): impulses in a fibre; left atrial pressure; left ventricular pressure and e.c.g. Between *A* and *B* is a trace of 0·1 sec time markers. Improved pressure recording systems were used.

Langrehr's observations have been confirmed in one left atrial ending; in two right atrial endings there was no obvious change following Nembutal. In these experiments Nembutal caused a marked fall in ventricular pressures and mean atrial pressure, and a reduction in the amplitude of the V wave. In the remaining seven receptors (6 left, 1 right), the response was quite the opposite. In these the left ventricular pressure fell markedly, but the activity in the ending increased (Fig. 7*B*), quite considerably in some fibres. This increase could be attributed to the increase in the

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

amplitude of the V wave. Figure 7*B* shows a moderate increase in activity after Nembutal.

The increase in the activity of left atrial receptors following Nembutal depended on the level of systemic arterial pressure. If this was high before injection, the increase in activity was much greater. This is because the diastolic volume of the left ventricle will increase more if the myocardium is weakened at a time when aortic pressure is higher. In all fibres the activity was reduced about 0·5–2 min after injecting Nembutal. This is in complete agreement with Langrehr, who reports observations made more than 2 min after 'Inactin'. However, the reduction in the activity of the ending is not due primarily to weak ventricular contractions but to the reduced amplitude of the V wave.

Conclusion. All the foregoing observations demonstrate conclusively that ventricular contractions do not in any way influence type B atrial receptors directly. Therefore the only other event that can possibly stimulate the endings during the latter part of systole is the increase in atrial volume reflected in the V wave.

Relation of the discharge to the V *wave*

It has been repeatedly demonstrated that the introduction of fluids into the atrium is always accompanied by an increase in the discharge from type B atrial receptors (Paintal, 1953*a*; Henry & Pearce 1956; Pearce, Henry & Chapman, 1956; Coleridge *et al.* 1957). This increase is accompanied by increase in mean atrial pressure, peak pressure of the V wave and the amplitude of the V wave. All these three factors which depend on atrial filling are co-variant, but their quantitative relation to each other is different in different circumstances. Thus the relation between initial pressure of the V wave (or mean atrial pressure) and the amplitude of the V wave depends on whether the pressure is rising or falling (Fig. 10).

In the following analysis of the results the initial pressure of the V wave was taken to be the pressure at the foot of the V wave, i.e. the point from where the V wave begins soon after the C wave (Figs. 1–4, 7); the amplitude to be the difference between the pressure at the peak of the V wave and the initial pressure; and mean atrial pressure tc be the average of the two. All the later experiments in which improved pressure recording systems were used (see Methods) are included in this analysis. Some of the earlier experiments with the 21 cm long catheter have also been included provided the pressure records were satisfactory (e.g. Fig. 3); records with too many artifacts (e.g. Fig. 6*A*) or with inadequate amplification (e.g. Fig. 6*B*) have not been included in the following analysis.

The relation between peak V pressure and the peak frequency of discharge or the number of impulses per cardiac cycle in a left atrial receptor

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

is shown in Fig. 8*C* and *D* respectively. These graphs were plotted from a single record obtained after releasing a temporary occlusion of the pulmonary artery, and it is clear from both that for a given peak pressure the

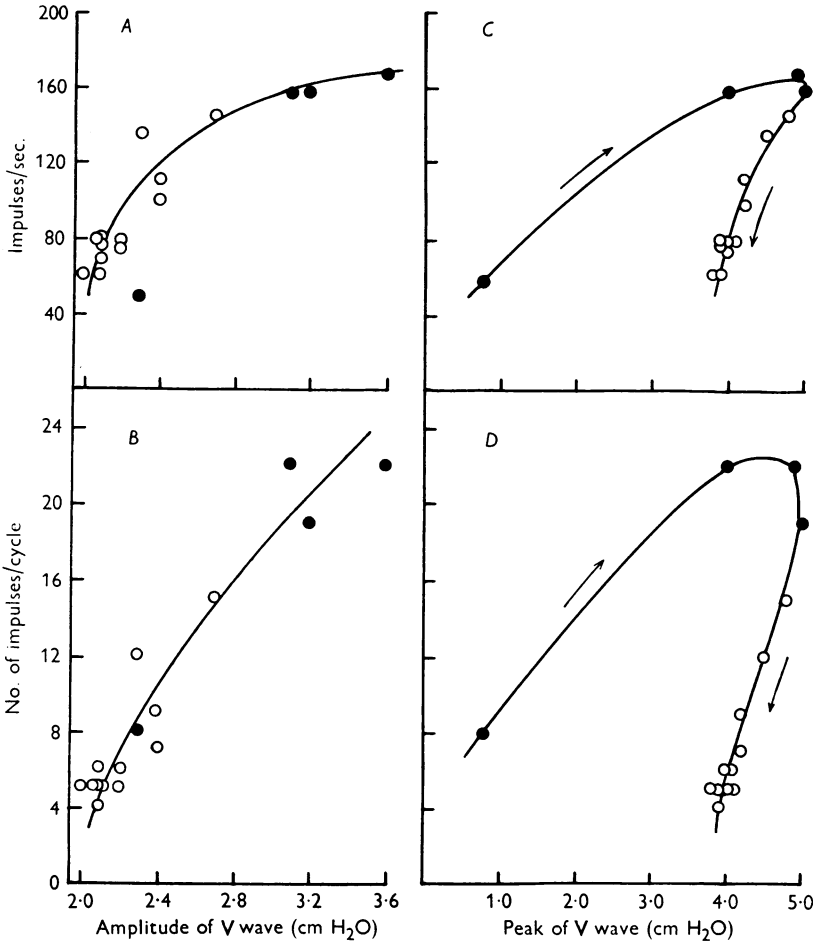

Fig. 8. Relation of activity in a left atrial receptor to peak pressure of the V wave (*C* and *D*) and amplitude of the V wave (*A* and *B*). The filled and open circles are the values obtained when atrial pressure was rising and falling respectively. The ordinates for *A* and *C* represent the peak frequency of discharge. Note that the marked *deviation* of the curves in *C* and *D* is absent in *A* and *B*. All the points shown in the four graphs were obtained from the same record after releasing a temporary occlusion of the pulmonary artery. A small error may be assumed to be present in the measurements of peak pressure and the amplitude of the V wave because the damped natural frequency of the pressure recording system was 50/sec (damping, 0·1 to 0·2 of critical). This error will merely shift the curves in *C* and *D* a little to the right or the left. The left atrial pressure tracing in Fig. 3*A–C*, obtained from the same experiment, is representative of that used for plotting the graphs.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

activity in the ending was greater when peak pressure was rising than when it was falling. The graphs on the rising and falling phases therefore deviate from each other (Fig. 8*C*, *D*). Such *deviations*, which varied in different endings, were present in all five other receptors studied in this way. The curves obtained by substituting mean atrial pressure for peak pressure on the abscissa were similar in shape (Fig. 11), but when the activity in the fibre was plotted against the amplitude of the V wave the deviation was eliminated or was hardly visible (Fig. 8*A*, *B*)

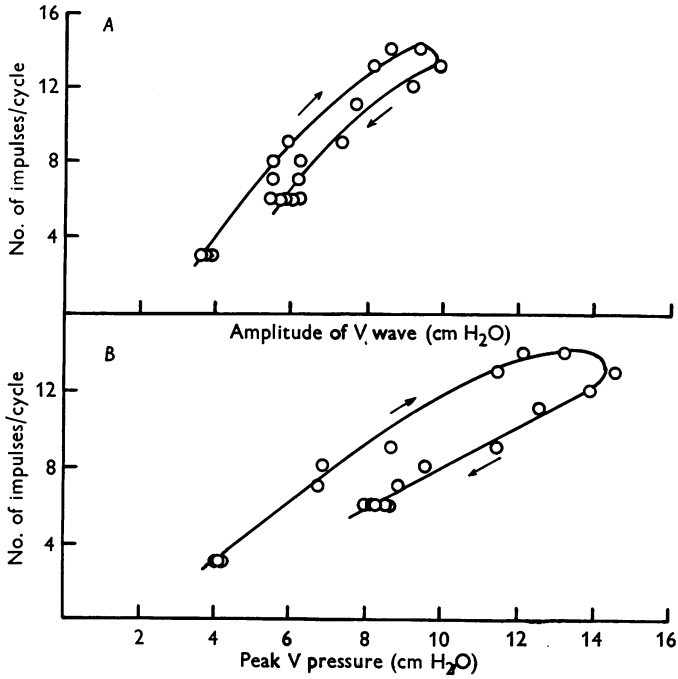

Fig. 9. Relation of activity in a left atrial receptor to amplitude of the V wave (*A*) and peak pressure of the V wave (*B*). Arrows indicate direction of change of atrial pressure. Note that the deviation between the rising and falling curves is less in *A*. The graphs were plotted largely from the records of Fig. 1.

Figure 8*B* also shows that the total number of impulses in a cycle is roughly linearly related to the amplitude of the V wave. Such a relation was found in five out of the six fibres studied and in three the scatter of the points was less than that shown in Fig. 8*B*. In these fibres no *deviation* was seen. In the sixth there seemed to be a small *deviation* (Fig. 9*A*).

Comparison of Fig. 8*B* with 8*D* shows that the *deviation* in the case of peak pressure (Fig. 8*D*) is due to the fact that for a given level of initial V pressure, the amplitude of the V wave is less when atrial pressure is falling

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

than when it is rising. This is well illustrated in the case of another left atrial fibre (Fig. 9) which, unlike that shown in Fig. 8, is more suitable for analysis because it has more points on the rising part of the curve. The fibre shown in Fig. 9 has been chosen for illustration also because it was the only one of the six in which the activity showed a small *deviation* when it was plotted against the amplitude of the V wave (Fig. 9*A*). However, the *deviation* is much greater when the discharge of impulses is plotted against

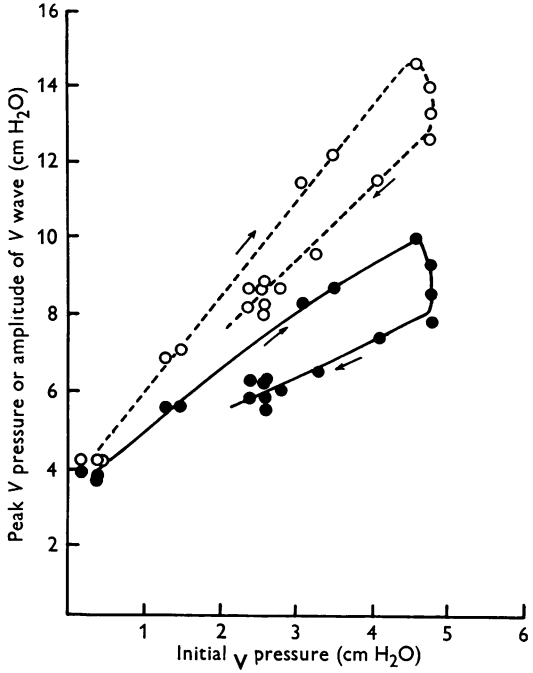

Fig. 10. Graphs showing relation of peak V pressure (○) and amplitude of the V wave (●) to initial pressure of the V wave (abscissa). Arrows indicate direction of change of atrial pressure. The points were plotted from Fig. 1 and from a continuation of Fig. 1*C*.

peak pressure (Fig. 9*B*). The increased *deviation* in Fig. 9*B* is explained completely by the relatively greater reduction in the amplitude of the V wave when atrial pressure is falling, a fact clearly shown in Fig. 10 which was obtained from the same record as that of Fig. 9. This point will become clear if the three figures, i.e. Fig. 9*A* and *B* and Fig. 10, are considered together. Thus Fig. 9*B* shows that for a given peak pressure of say 11 cm H_2O the number of impulses is about 13 when atrial pressure is rising and 9 impulses when it is falling, the difference between the two being about 4 impulses. Figure 10 shows that at a peak pressure of 11 cm H_2O on the rising curve, the amplitude of the V wave was about 8 cm

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

H_2O whereas at a peak pressure of 11 cm H_2O on the falling curve, the amplitude was 7 cm H_2O. On substituting these figures in Fig. 9*A* it is seen that the number of impulses yielded by an amplitude of the V wave of 8 cm H_2O is about 13 impulses when atrial pressure is rising, and that yielded by 7 cm H_2O when it is falling is 9 impulses. It is therefore clear that the deviation in the curves shown in Fig. 9*B* is due to the variation in the amplitude of the V wave and that the activity of the ending is apparently related to peak pressure because of the primary relation between the amplitude of the V wave and the activity of the ending.

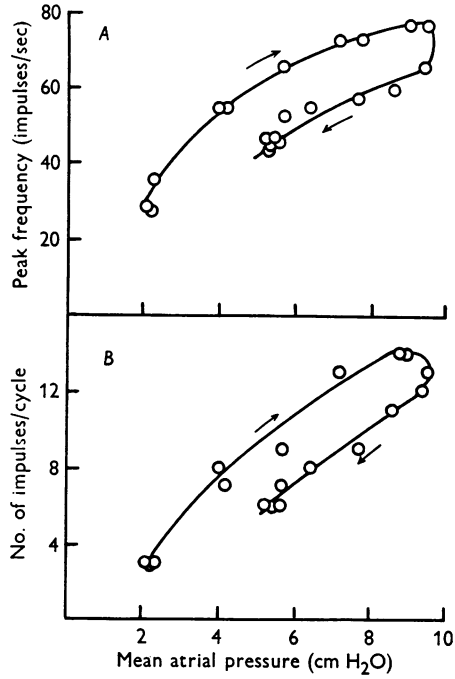

Fig. 11. Relation of activity in a left atrial type B receptor to mean left atrial pressure. Arrows indicate direction of change of atrial pressure. In *A* ordinate represents peak frequency of discharge; in *B*, number of impulses per cycle.

The activity of the ending is related to mean atrial pressure but there is a marked *deviation* between the rising and falling curves as shown in Fig. 11 and is to be expected from Fig. 8*C*, *D*. Ignoring the rising and falling phases of atrial pressure one could in Fig. 11*B* establish a linear relation between mean atrial pressure and the number of impulses per cycle, as noted by Langrehr (1960*b*). However, this is deceptive because the relation between the two when mean atrial pressure is rising is different

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

from that when it is falling (Fig. 11*B*). This might account for the large scatter of the points for a given level of mean atrial pressure shown in Fig. 3 of Langrehr's paper (1960*b*), e.g. at a mean atrial pressure of 5 cm H_2O the number of impulses ranges from 2 to 18 impulses.

The minimum amplitude of the V wave needed to produce about 2 impulses per cycle varied in different endings. In the present sample of six endings it ranged from 1 to 4 cm H_2O (mean = 2·5; S.D. = 1·2). From this it may be concluded that if the amplitude of the V wave is less than 1 cm H_2O there will be practically no activity in type B receptors. The sensitivity of the endings also varied considerably, an increase in the amplitude of the V wave by 1 cm H_2O causing an increase in the discharge by 2–4 impulses per cycle in five endings (e.g. Fig. 9*A*) and by 12 impulses in one ending (Fig. 8*B*).

The V wave starts just after the C wave, i.e. with the beginning of ventricular systole, and it reaches its peak just after the end of systole, when it falls as soon as the auriculoventricular (a-v) valves open (Figs. 1, 3). The V wave is therefore somewhat triangular in shape with moderate and slow heart rates when there is a clear interval between the opening of the a-v valves and the onset of atrial contraction (Figs. 1, 3). Since the duration of ventricular systole is constant, a variation in the amplitude of the V wave results in a variation of the rate of rise of pressure. This variation causes a variation in the onset of discharge in the receptor. Thus, as is to be expected, the first impulse is initiated at a higher pressure when the rate of rise of pressure is lower. For example, the pressure at which the first impulse is initiated is higher in cycle no. 4 of Fig. 1*C* than in cycle no. 5 of Fig. 1*A*, although the initial pressure of the V wave is the same in both cases. This effect, as shown by Landgren (1952) in the case of carotid baroreceptors, is due to accommodation of the ending. A clearer example of accommodation is shown in Fig. 4. Further, it has been noted that the greater the rate of rise of pressure, the greater is the starting frequency of discharge, but this needs to be studied further under better conditions.

DISCUSSION

Contrary to Langrehr's conclusions (1960*b*) the results have shown unequivocally that ventricular contractions have no primary effect on type B atrial receptors under the several conditions examined. Thus, increase in the strength of ventricular contractions may be accompanied by reduced, increased or unchanged activity in the endings. Procedures that lead to increase in activity of the endings, e.g. injection of fluids, also lead to increase in strength of ventricular contractions, but there is often a clear lag of 1–2 cycles between the increase in activity of the ending and the increase in the contraction of the corresponding ventricle.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

However, the best evidence that ventricular contractions do not influence the endings directly comes from the response of the left atrial endings during premature ventricular contractions, when their activity is invariably increased. In fact, the weaker the contraction, the greater is the discharge (Figs. 3, 5). This inverse relation is because of the direct relation between atrial emptying and the strength of ventricular contractions. Thus if an ectopic atrial contraction occurs in the early part of the cardiac cycle, the atrium will be contracting against closed a-v valves and can therefore empty itself only in the retrograde direction. The succeeding premature contraction will therefore be weak, but there will be increased activity in the receptor at this time owing to the accumulated blood in the atrium (Fig. 3*C*). On the other hand, if an ectopic atrial contraction occurs just before a normal one, then emptying will be nearly complete, the premature ventricular contraction will be much stronger than in the previous case and there will be little extra excitation of the receptor (Fig. 3*A*).

The response of the right atrial endings during premature ventricular contractions shows important differences from the left atrial ones, and a superficial examination of the records, especially if atrial and ventricular pressures have not been recorded simultaneously, will lead one to the erroneous conclusion that the activity of right atrial endings depends on the strength of ventricular contractions (Fig. 4). No doubt such a relation between the two does exist in the majority of right atrial receptors, but this is not due to a direct influence of ventricular contractions on the endings, as is shown by the effects of introduction of fluids or occlusion of the pulmonary artery. During such procedures increased or reduced strength of ventricular contractions do not keep in step with increase or reduction in activity of the endings. Further, not all right atrial endings show this relation, because some behave just like left atrial ones, and there are some that may show a reduction of activity during premature ventricular contractions at one time and an increase at another.

Two simultaneous changes have always been noted whenever there was reduction of activity in right atrial receptors during premature ventricular contractions; a reduction in right ventricular pressure and a reduction in the amplitude of the V wave (Fig. 6). Since the reduction in the discharge cannot be due to reduced strength of ventricular contractions it follows that it may be related to a reduction in the amplitude of the V wave which in turn is probably due to reduced atrial filling.

The foregoing considerations lead to the conclusion that ventricular contractions influence the right and left atrial endings by their influence on venous return.

There may be several explanations for Langrehr's conclusion that the

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

discharge in type B endings is brought about directly by ventricular contraction (Langrehr, 1960*b*). One is that he used different criteria for identifying the endings, so that many of his type B endings cannot be compared with those studied by others, especially since most of them had more than one burst of impulses (see Table 1 in Langrehr, 1960*a*). By definition a type B receptor is one which has only a late systolic burst of impulses (Paintal, 1953*a*). Further, confusion is bound to arise if no distinction is drawn between responses obtained under control conditions and those obtained during abnormal cardiac rhythms, especially if intraventricular pressure is not recorded simultaneously.

Clearly the activity in these endings is best related to the amplitude of the V wave; there is almost a linear relation between the number of impulses per cycle and the amplitude of the V wave under varying conditions of mean atrial pressure or peak pressure of the V wave. However, the amplitude of the V wave itself depends on at least two factors, namely, the amount of blood flowing into the atrium and the compliance of the atrial wall. Since the pressure developed is linearly related to atrial volume in isolated or intact heart preparations, provided the volumes used are not excessively large (Opdyke, Duomarco, Dillon, Schreiber, Little & Seely, 1948; Little, 1949, 1960; Irisawa, Greer & Rushmer, 1959) it follows that the amplitude of the V wave is a measure of the amount of blood entering the atrium during this part of the cycle. With this assumption it may therefore be reasoned that the activity of the endings is linearly related to atrial volume in normally beating hearts, thus confirming the conclusion obtained from isolated *in situ* preparations (Paintal, 1953*a*).

Under ordinary conditions the normal discharge in type B endings is largely a result of the dynamic response of the endings (cf. response of muscle spindles, Katz, 1950), because under ordinary conditions the changes in atrial volume are of a pulsatile nature and there is no occasion when a particular level of atrial volume can be maintained in hearts with a normal rhythm. The static response can be conveniently studied as has already been done by using isolated atrial preparations (Paintal, 1953*a*; Mühl, quoted by Kramer, 1959).

The behaviour of the type B endings which are slowly adapting stretch receptors (Paintal, 1953*a*) is similar to the behaviour of systemic arterial baroreceptors (Bronk & Stella, 1932; Ead, Green & Neil, 1952; Landgren, 1952; Heymans & Neil, 1958). Thus in both the adequate stimulus is a pulsatile change, pulse pressure in the baroreceptors, and increase in volume (or amplitude of the V wave) in the atrial receptors. In both activity tends to increase with mean pressure, but not if the pulsatile stimulus falls simultaneously. Both sets of endings accommodate to

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

slowly rising stimuli and in both the starting frequency of discharge varies with the rate of rise of the stimulus (see Results).

The results of this investigation should be of help in establishing the reflex effects of type B atrial receptors, since it is now known that their adequate stimulus is the pulsatile increase in atrial volume which is reflected in the amplitude of the V wave. At present there are contradictory views regarding the reflex effects of these endings (Henry & Pearce, 1956; Gauer & Henry, 1956; Heymans & Neil, 1958; Doutheil & Kramer, 1959; Ledsome, Linden & O'Connor, 1961; Ledsome & Linden, 1962; O'Connor, 1962). Much of this confusion has arisen because no attempts have been made to differentiate the reflex effects of type A and type B endings, which differ from each other considerably with regard to their adequate stimulus (Paintal, 1963) and because of uncertainty about the proper index of activity in these endings. Thus it is now easy to understand that stroke volume, cardiac output, mean or peak atrial pressure may under certain conditions provide some index of activity in type B endings and fail to do so under others (Langrehr & Kramer, 1960).

SUMMARY

1. The responses of type B atrial receptors of cats were studied with simultaneous records of ventricular and atrial pressures under varying conditions after opening the chest. Procedures that increased ventricular pressure also increased the sensory discharge but there was a lag between the two.

2. It was proved that ventricular contractions do not directly influence the endings by showing that left atrial endings were markedly stimulated during premature ventricular contractions; the weaker the contraction, the greater the discharge. The response of the right atrial endings was variable but in most of them the activity fell along with a fall in the V wave during premature ventricular contractions. The difference between the right and left atrial endings is attributed to the difference in the level of ventricular pressures in the two ventricles and to the differences in the forces responsible for the venous return in the two atria.

3. The pattern of discharge was closely related to the V wave. The relation of the discharge to peak pressure of the V wave or mean atrial pressure while atrial pressure was rising was different from the relation when it was falling. This variation was absent when the activity was related to the amplitude of the V wave; the relation between the two was practically linear in all endings studied, an increase of 1 cm H_2O causing an increase of 2–4 impulses per cycle in most endings. The threshold amplitude of the V wave varied from 1 to 4 cm H_2O.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

4. The ways in which the endings resemble the arterial baroreceptors have been pointed out.

5. It is concluded that ventricular contractions influence the endings indirectly by varying the venous return and that in agreement with earlier conclusion (Paintal, 1953*a*) the adequate stimulus for the endings is the pulsatile increase in atrial volume which is reflected in the amplitude of the V wave.

I wish to thank Professor M. Taylor, University of Sydney, for valuable discussions on calibration of manometers. Part of this investigation was aided by a grant from the Atomic Energy Commission, India.

REFERENCES

BRECHER, G. A. (1954). Cardiac variation in venous return studied with a new bristle flowmeter. *Amer. J. Physiol.* **176**, 423–430.

BRECHER, G. A. (1956). *Venous Return*, pp. 104–107. New York: Grune and Stratton.

BRONK, D. W. & STELLA, G. (1932). Afferent impulses in the carotid sinus nerve. I. The relation of the discharge from single end organs to arterial blood pressure. *J. cell. comp. Physiol.* **1**, 113–130.

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.

DOUTHEIL, U. & KRAMER, K. (1959). Über die Differenzierung kreislaufregulierender Reflexe aus dem linken Herzen. *Pflüg. Arch. ges. Physiol.* **269**, 114–129.

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.

GAUER, O. H. & HENRY, J. P. (1956). Beitrag zur Homöostase des extraarterielen Kreislaufs. *Klin. Wschr.* **34**, 356–366.

GOODMAN, L. S. & GILMAN, A. (1955). *The Pharmacological Basis of Therapeutics*, p. 131. New York: The Macmillan Co.

HANSEN, A. T. & WARBURG, E. (1950). The theory for elastic liquid-containing membrane manometers. General part. *Acta physiol. scand.* **19**, 306–332.

HENRY, J. P. & PEARCE, J. H. (1956). The possible role of cardiac atrial stretch receptors in the induction of changes in urine flow. *J. Physiol.* **131**, 572–585.

HEYMANS, C. & NEIL, E. (1958). *Reflexogenic Areas of the Cardiovascular System*, pp. 205–208. London: Churchill.

IRISAWA, H., GREER, A. P. & RUSHMER, R. F. (1959). Changes in the dimensions of the venae cavae. *Amer. J. Physiol.* **196**, 741–744.

KATZ, B. (1950). Depolarization of sensory terminals and the initiation of impulses in muscle spindle. *J. Physiol.* **111**, 261–282.

KRAMER, K. (1959). Die afferente Innervation und die Reflexe von Herz und venösem System. *Verh. dtsch. Ges. Kreis.-Forsch.* **25**, 142–163.

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

LANGREHR, D. (1960*a*). Entladungsmuster und allgemeine Reizbedingungen von Vorohofsreceptoren bei Hund und Katze. *Pflüg. Arch. ges. Physiol.* **271**, 257–269.

LANGREHR, D. (1960*b*). Beziehungen zwischen Vorhofsreceptoraktivitäten und Herzmechanik von Hund und Katze bei verschiedenen Kreislaufzuständen. *Pflüg. Arch. ges. Physiol.* **271**, 270–282.

LANGREHR, D. & KRAMER, K. (1960). Beziehungen der mittlern Impulsfrequenz von Vorhofsreceptoren zum thorakalen Blutvolumen. *Pflüg. Arch. ges. Physiol.* **271**, 797–807.

LEDSOME, J. R. & LINDEN, R. J. (1962). The effects of distension of the junctional regions of the pulmonary veins and left atrium. *J. Physiol.* **165**, 44–45*P*.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011

LEDSOME, J. R., LINDEN, R. J. & O'CONNOR, W. J. (1961). The mechanisms by which distension of the left atrium produces diuresis in anaesthetized dogs. *J. Physiol.* **159**, 87–100.

LITTLE, R. C. (1949). Volume elastic properties of the right and left atrium. *Amer. J. Physiol.* **158**, 237–240.

LITTLE, R. C. (1960). Volume pressure relationships of the pulmonary-left heart vascular segment. *Circulation Res.* **8**, 594–599.

MCDONALD, D. A. (1960). *Blood Flow in Arteries*, pp. 234–257. London: Edward Arnold.

O'CONNOR, W. J. (1962). *Renal Function*, pp. 217–220. London: Edward Arnold.

OPDYKE, D. F., DUOMARCO, J., DILLON, W. H., SCHREIBER, H., LITTLE, R. C. & SEELY, R. D. (1948). Study of simultaneous right and left atrial pressure pulses under normal and experimentally altered conditions. *Amer. J. Physiol.* **154**, 258–272.

PAINTAL, A. S. (1953*a*). A study of right and left atrial receptors. *J. Physiol.* **120**, 596–610.

PAINTAL, A. S. (1953*b*). The conduction velocities of respiratory and cardiovascular afferent fibres in the vagus nerve. *J. Physiol.* **121**, 341–359.

PAINTAL, A. S. (1962). Determination of intrathoracic conduction time in cardiovascular afferent fibres of the vagus nerve. *J. Physiol.* **163**, 222–238.

PAINTAL, A. S. (1963). Vagal afferent fibres. *Ergbn. Physiol.* **52**, 73–156.

PEARCE, J. W., HENRY, J. P. & CHAPMAN, K. M. (1956). The behaviour and possible functions of cardiac atrial stretch receptors. *Abstr. XX int. physiol. Congr.* 711–712.

VAN CITTERS, R. L. (1960). Pulse wave velocity through polyethylene tubing. *J. appl. Physiol.* **15**, 184–185.

WIGGERS, C. J. (1928). *The Pressure Pulses in the Cardiovascular System.* London: Longmans, Green and Co.

Downloaded from J Physiol (jp.physoc.org) by guest on April 20, 2011