

# THE USE OF PERICARDIAL SAC AS A CARDIOMETER-A TECHNIQUE FOR RECORDING THE EFFECTS OF DRUGS ON HEART IN SITU

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A technique to record the effects of drugs on heart in situ is described.

The technique seems to give faithful information as has been shown by the use of conventional cardioactive agents. An attempt has been made to study if this technique gives information regarding both auricular and ventricular activity in the same tracing.

When one is interested in the study, particularly the screening, of cardioactive agents, one needs to have the information on the effects of the concerned drug on (i) the rate, (ii) rhythm, (iii) force of contraction and (iv) output of the heart. The methods commonly used to study the effects of drugs on the heart in situ are Cushny's myocardiograph, glass cardiometry and electrocardiography (3). Cushny's myocardiography gives dependable information on the force and the rate of contraction of both auricles and the ventricles but volume changes can not be studied. The electrocardiography records information on the rate and the rhythm of auricles and ventricles. But it can not be routinely employed particularly in the screening of cardioactive agents. Moreover, it does not give any information regarding the cardiac output and the force of contraction. The glass cardiometry provides information regarding the ventricular volume changes, the rate of ventricles and perhaps indirectly the force of contraction. It may also provide some gross information regarding the presence of some irregularity. Thus, of the three commonly employed methods, the glass cardiometry appears to give a greater information about the drug effect on the heart. It was thought whether the principle of glass cardiometry which is applicable to ventricles only, can be extended to the entire heart by putting a cannula in the pericardial sac. We therefore wish to report the working of this technique. We have not so far come across any reference to this technique in the literature.

## MATERIALS AND METHODS

The present study was carried out on cats anaesthetised with pentobarbitone 35 mg./kg. body weight intraperitoneally. The blood pressure was recorded by conventional carotid cannulation. After cannulating the trachea thoracotomy was done by splitting the sternum and artificial respiration was started simultaneously.

The pericardium was picked up, freed of its surroundings and the fat on the pericardium was carefully removed. An area midway between the apex and the base of

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the heart on its anterior surface was selected and lifted from the myocardium with the help of three forceps. A small nick was made in this area and the pericardial fluid was drained and dabbed with cotton wicks. A cannula (see below) was introduced into the pericardial sac and a tight ligature passed round the constriction on the cannula to prevent leakage of air. The position of the cannula was so adjusted as to give good tracings and clamped in that position. The cannula was connected to the Mary's tambour and the chest closed. The drugs were administered through a cannulated femoral vein.

The following drugs were used to see whether the technique gives faithful results- (1) Saline 10 mls., (2) Adrenaline 20  $\mu$ g., (3) Noradrenaline 20  $\mu$ g., (4) Acetylcholine 5, 3 and 10  $\mu$ g. respectively, (5) Carbachol 2  $\mu$ g., (6) Pentobarbitone 15 mg., (7) Caffeine 5 mg. and (8) Digitalis 200 and 500  $\mu$ g. respectively.

*Cannula*: The pericardial cannula was prepared by using a 'L' shaped tube with a bore of about 5 mm. diameter. The limb modelled to have a circular constriction about 2mm. from the edge was always introduced into the pericardial sac.

## RESULTS

(1) *Saline*: Ten ml. of physiological saline were rapidly infused. After the infusion the tracings showed an upward shift (Fig. 1). Though the baseline was shifted upwards there was no decrease in the total excursion of the writing point. Indeed, the measurement showed that the distance between the limits of the tracings was increased from 1.6 cm. to 2.0 cms. The blood pressure was also raised after the infusion of the saline.

(2) *Adrenaline*: Injection of 20  $\mu$ g. of adrenaline caused an increase in the downward as well as upward excursion of the lever. The distance between the upper and the lower limits of the tracings was also significantly increased. The changes occurring in the heart tracings coincided with the rise of blood pressure. The heart tracing and the blood pressure tracing returned to control levels simultaneously (Fig. 2).

(3) *Noradrenaline*: The tracings obtained after 20  $\mu$ g. of noradrenaline are qualitatively similar to those seen with adrenaline. The time relationship between the heart and the blood pressure tracings was maintained (Fig. 3).

(4) *Acetylcholine*: Injection of 5,3 and 10  $\mu$ g. of acetylcholine showed diminished excursion of the lever and the baseline was shifted up. The total distance between the upper and the lower limits of the tracings was also decreased. The fall in blood pressure coincided each time with the changes in the heart tracings (Fig. 4).

(5) *Carbachol*: Tracings obtained after 2 mcg. of carbachol were qualitatively similar to those observed after the injection of acetylcholine. The effects were however more prolonged (Fig. 5).

(6) *Pentobarbitone*: When 15 mg. of pentobarbitone were injected rapidly intravenously the heart tracings showed an upward shift of the baseline and a decrease in the total width of the tracings was observed. The blood pressure showed a fall and the tracings of the heart as well as blood pressure returned to control level after about 5 minutes (Fig. 6).

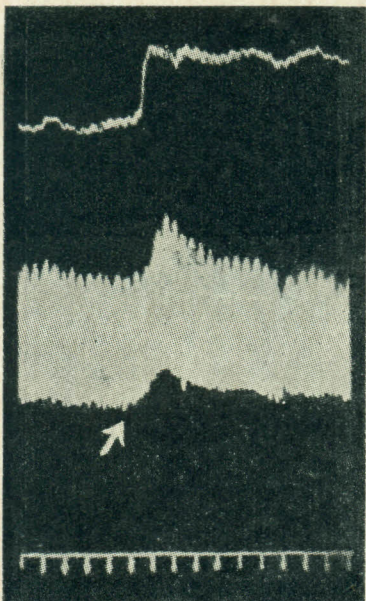


Fig. 1. Effect of rapid infusion of 10 ml. of normal saline. Tracings from above downwards:—carotid pressure, heart tracings and time 10 sec. Arrow indicates the saline infusion.

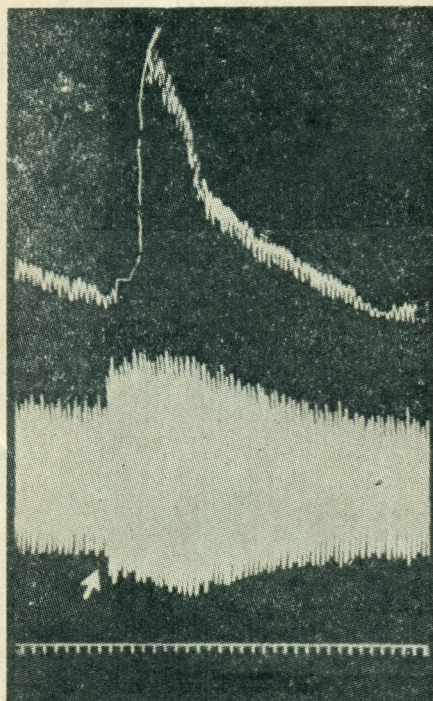


Fig. 2. Effect of 20  $\mu$ g. of adrenalin. Tracing from above downwards:—carotid pressure, heart tracings and time 10 sec. Arrow indicates the injection of Adrenaline.

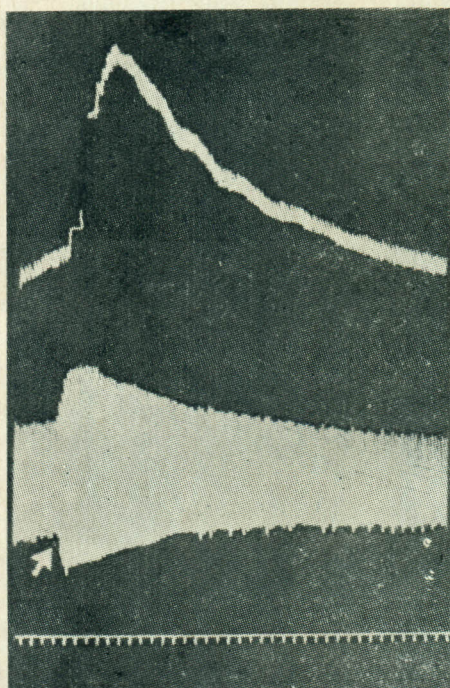


Fig. 3. Effect of 20  $\mu$ g. of noradrenaline. Tracing from above downwards:—carotid pressure, heart tracings and time 10 sec. Arrow indicates the injection of Noradrenaline.

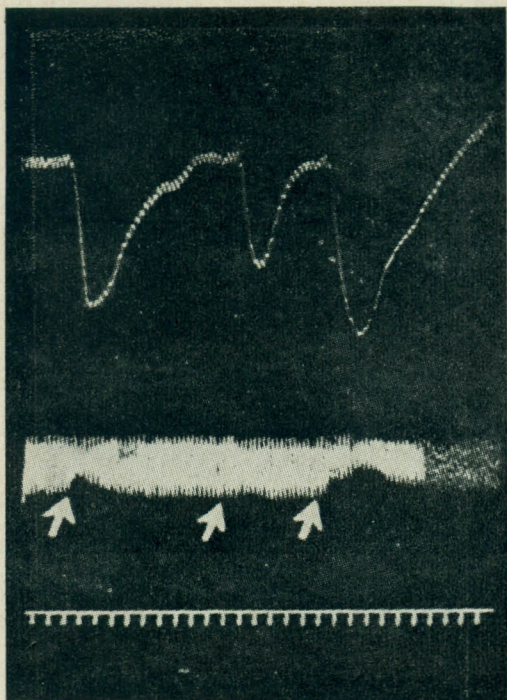


Fig. 4.  
Effect of Acetylcholine.  
Tracings from above downwards :—Carotid pressure, heart tracings & time 10 sec. Arrow indicates the injection of 5, 3 and 10  $\mu$ g. of Acetylcholine respectively.

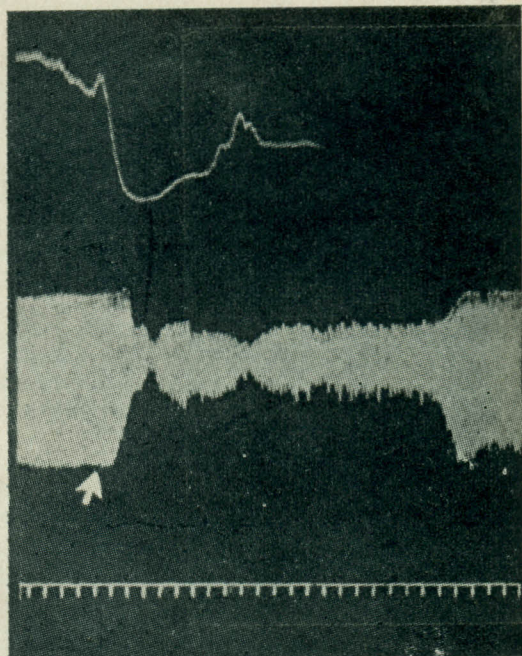


Fig. 5. Effect of 2  $\mu$ g. of carbachol.  
Tracing from above downwards :—carotid pressure heart tracings and time 10 sec. Arrow indicates injection of Carbachol.

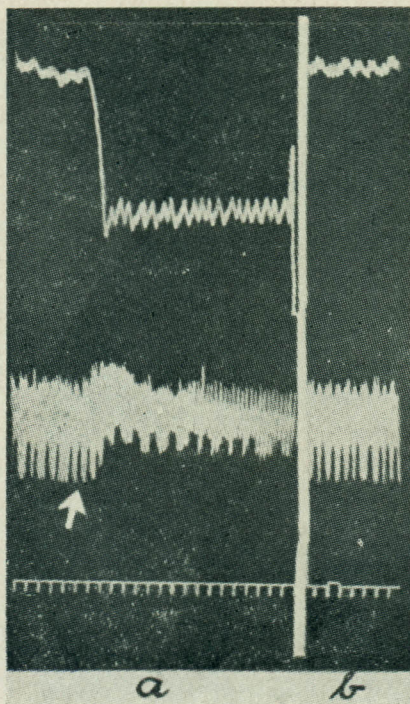


Fig. 6.  
Effect of 15 mg. of Pentobarbitone.  
Tracings from above downwards :—carotid pressure, heart tracings and time 10 sec. Arrow in (a) indicates the injection of Pentobarbitone (b) tracings 15 mts. after the drug showing the recovery from the effect.

(7) *Caffeine* : The injection of 5 mg. of caffeine elicited a small but significant increase in the downward excursion of the lever. The upward excursion was however not influenced. The total distance between the limits of the tracings was increased. There was a rise in blood pressure corresponding with the changes in the heart (Fig. 7).

(8) *Digitalis* : When 200  $\mu$ g. of Cedilanid were injected there was a significant increase in the downward excursion. These were recorded on fast and slow moving drum (Fig. 8b). A further injection of 500  $\mu$ g. of Cedilanid produced depression of the heart and its ultimate arrest in the diastole along with a fall of blood pressure to zero (Fig. 8c). The tracings in the Fig. 8c show some irregularity in the heart before it came to standstill.

#### DISCUSSION

This technique essentially records the volume changes within the pericardial sac. With each contraction of the heart the pressure within the enclosed cavity falls and the lever of the Mary's tambour moves down. The reverse occurs in the diastole.

The tracings can be read, we believe, to give the following information :-

1. *Stroke volume* : The upper limit of the tracing represents the diastolic volume and the lower limit the systolic volume. The difference between the two limits indicates the volume of the blood ejected out i.e. stroke volume. Thus, it can be inferred that a widening of the tracing indicates an increase in the stroke volume while a narrowing of the tracing a decrease in the stroke volume. Unless the graph is calibrated the tracings can not give any quantitative information and the changes in the width of the tracing will give only qualitative results.

2. *Rate of contraction* : This can be counted with the help of a stop watch when the tracings are on a slow drum but can be read directly from the graph recorded with the time tracing on a fast drum.

3. *Force of contraction* : Though there is no direct information as in Cushny's myograph, a sufficiently reliable information can be obtained indirectly from the tracings. If under the influence of a drug the downward pull is greater than in the control recording it means that systolic size of the heart is decreased, in other words the force of contraction has increased. The reverse will indicate a decrease in the force of contraction of the heart.

4. *Rhythm* : If tracings are taken on a fast drum one may be able to decipher alterations in the rhythm. No doubt, the information afforded will be gross one and it may not furnish any information regarding the nature of the arrhythmia.

The trustworthiness of the technique was assessed by comparing the known effects of the various cardioactive drugs with the results obtained by this technique.

(1) *Saline* : (Fig. 1). A rapid infusion of 10 mls. of saline produced a temporary dilatation of the heart as shown by an upward shift of the baseline. This is an expected result because "when venous inflow increases the ventricles undergo progressive

dilatation i.e. they fail initially to discharge as much blood as they receive" (8). Though the baseline is shifted upwards the total excursion of the lever has increased by 4 mm. This means that the cardiac output has increased. This is also in accordance with the observation that "the increased stretch of the muscle fibre during diastole leads to increased force of contraction; when compensation is fully established the cardiac output is increased" (8).

(2) *Adrenaline* : (Fig. 2). The increased downward excursion of the lever after 20  $\mu$ g. of adrenaline can be interpreted as indicative of increased force of contraction. The increased upward excursion may be due to better cardiac filling and may partly be due to the mechanical reasons. The distance between the two limits of the tracing is obviously increased indicating a marked increase in the stroke volume. Thus, information obtained from the tracing that the force of contraction and the stroke volume are increased by adrenaline is in accordance with the known effects of the drug.

(3) *Noradrenaline* : (Fig. 3). Under the effects of 20  $\mu$ g. of noradrenaline the downward and upward excursions of the lever are increased showing an increase in the force of contraction and the stroke volume. These are the known effects of noradrenaline (4).

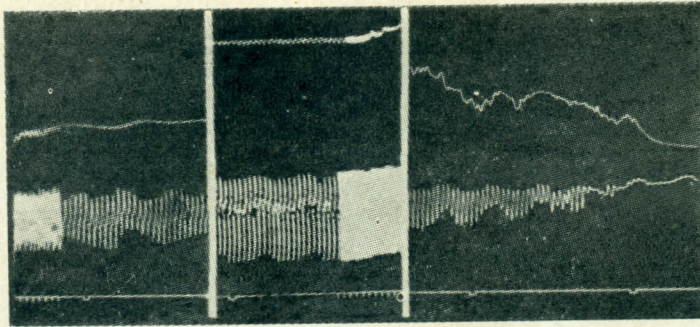
(4) *Acetylcholine* : (Fig. 4). The upward shift of the baseline and the narrowing of the tracing indicate a decrease in the force of contraction and a decrease in the stroke volume. The decrease in the force of contraction is an expected result for "parasympathetic stimulants, acetylcholine, muscarine, physostigmine and pilocarpine weaken and slow the heart... .." (5). The reduction in the stroke volume may be due to the decreased force of contraction and perhaps, decreased venous return.

(5) *Carbachol* : (Fig. 5). The anticipated reduction in the force of contraction and the stroke volume of a duration longer than that of acetylcholine, are clearly suggested by a decrease in the downward excursion of the lever and narrowing of the tracing.

(6) *Pentobarbitone* : (Fig. 6). Intravenous pentobarbitone causes precipitous fall in blood pressure (2) and barbiturates in high doses have been reported to produce direct myocardial depression (1). The narrowing of the cardiac tracing and an upward shift of the baseline suggest the depressant effect on the heart.

(7) *Caffeine* : (Fig. 7). The tracings obtained after caffeine suggest that there is an increased force of contraction (increased downward excursion) and an increase in the stroke volume (widening of the tracings). This is an anticipated result as "caffeine in small and moderate doses upto 20 mg./kg body weight generally produces a rise in blood pressure with more or less increase in heart rate, the tonus of the heart is increased and amplitude of its excursion may be greater. This and the faster rate raise the output of the heart" (6).

(8) *Digitalis* : (Fig. 8). A comparison of Fig. 8b with Fig. 8a. shows that there is an increase in the force of contraction and stroke volume. This is in accordance with



(a) (b) (c)

Fig. 8. Effect of Cedilanid.  
Tracings from above downwards:—carotid pressure, heart tracings and time 10 sec.  
(a) Normal tracings on slow and fast drum.  
(b) 5 mts. after 200  $\mu$ g. of Cedilanid. Tracing on fast and slow drums.  
(c) 10 mts. after another 500  $\mu$ g. of Cedilanid. Tracings on fast drum.

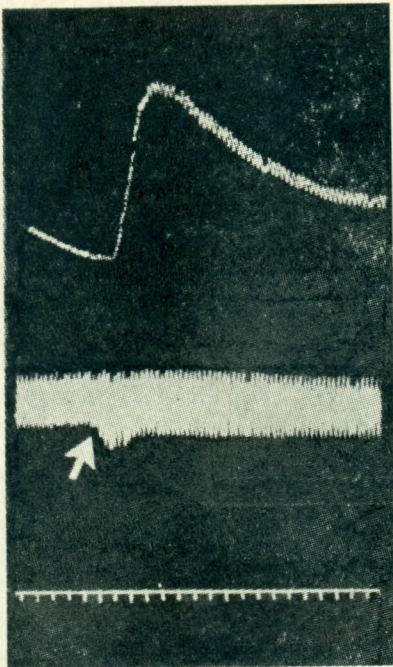


Fig. 7. Effect of 5 mg. of Caffeine.  
Tracings from above downwards: carotid pressure, heart tracings and time 10 sec.  
Arrow indicates the injection of Caffeine.

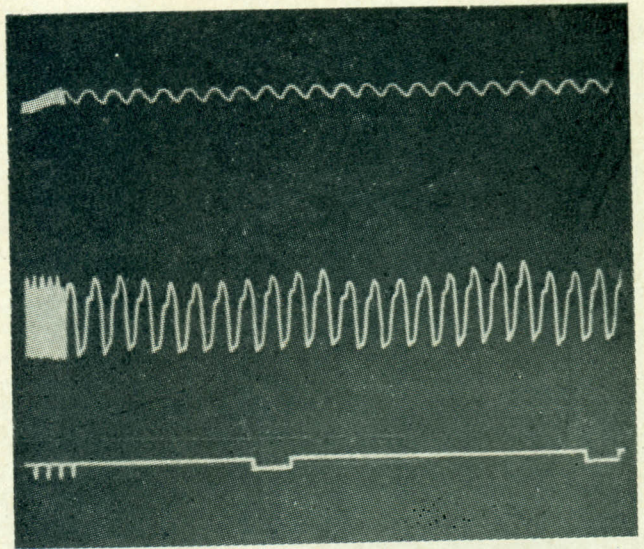


Fig. 9. Normal tracing at slow and fast drums.  
Tracings from above downwards:—carotid pressure heart tracings and time 5 sec.

the known effects of digitalis. The toxic effects of digitalis such as decrease in the amplitude of contraction, irregularity and cardiac arrest are suggested by tracings in Fig. 8c. The figure suggests, however, that the heart has stopped in diastole. Though the heart is expected to stop in systole in digitalis poisoning, "the terminal changes may lead to first the auricular and then ventricular fibrillation and arrest of the circulation; the chambers stop in median position and gradually become greatly dilated" (7).

In all these tracings we recorded simultaneously the blood pressure to ascertain whether the changes in the heart tracings coincide in time with the changes in blood pressure; and as can be seen from all the graphs there is definite time relationship between the two tracings.

In this technique the pericardial sac functions as a cardiometer. So we thought that the tracing may reflect the auricular as well as ventricular events. To see this the tracings were taken on a fast moving drum. As can be seen from Fig. 9, there is a continuous downward descent which probably indicates the ventricular contraction. At the end of this descent there is a small ascent which may represent auricular diastole or filling phase; and this is soon taken over by a prominent upstroke probably due to ventricular diastole or rapid filling phase; in this upstroke there is a small notch or step which probably is due to auricular systole which occurs a little earlier than ventricular systole. The prominent downward as well as upward strokes must be representing the systole and the diastole respectively of the ventricles; but we do not know whether other undulations (notches, steps etc.) recorded, reflect the auricular events or are merely mechanical. The above interpretations of these are the most probable ones but can only be valid if there is a relationship between these and a simultaneously recorded electrocardiogram or intraluminal pressure changes.

The technique seems to provide a reliable data regarding the effects of drugs on the various aspects of cardiac activity. It needs stressing that the information given by this technique is qualitative.

Among the few difficulties involved in this procedure the respiratory interferences are the most common but these could be minimised by controlling the ventilation at a level just sufficient to maintain oxygenation. Sometimes the pericardial fluid froths within the cannula; this can be overcome by removing the pericardial fluid as far as possible and by employing a wider mouth cannula. Occasionally, it may be necessary to adjust the air pressure in the enclosed system to get a satisfactory amplitude of the lever movement. Excessive injection of air into the system may give a good tracing but it embarrasses the heart and the blood pressure falls. Therefore, the pressure inside the closed system should be so adjusted as to give a good tracing of both the blood pressure and the intrapericardial volume changes. The hole in the pericardium should be sufficiently away from the apex which during contraction can slap against the cannula and close it.

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