Electrically Induced Ventricular Fibrillation.

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Ventricular fibrillation (VF) is one of the prime causes of death in myocardial infarction in humans. The effective prevention of VF in patients with acute myocardial infarction is therefore a most important aspect of cardiac therapy. Knowledge in relative effectiveness of various antidysrythmic agents against VF is imperative.

In screening antidysrhythmic drugs for their antifibrillatory activity, a consistent and major problem has been the lack of suitable in vivo model. Various in vitro models for the screening of antidysrhythmic agents were described (Vaughan Williams and Szekeres, 1961, Handmark and Refsun, 1973, Lubbe, et al., 1975), and in vivo (Baum, et al., 1971, Wellens & Wauters, 1973, Lawson and Wojciechowski, 1974).

In vivo techniques have been based mostly on dogs in which thoractomy was necessary and defibrillation was used. In the present study a simple model for inducing VF by electrical stimulation in closed-chest cats is described and the effects of this technique on general haemodynamic functions are evaluated.

METHODS

Cats of either sex weighing 1.6—3.0 Kg were anaesthetized with pentobarbitone sodium (30 mg/Kg intrathoracically, upper right diaphragmatic area using a fine short needle). The trachea was cannulated to facilitate spontaneous and artificial respiration when required. The right cephalic vein and left femoral artery were respectively cannulated for the injection of small (3 mg) maintenance doses of anaesthetic and recording the blood pressure. The E.C.G. was recorded from needle electrodes inserted subcutaneously. Lead II (2 cm=1 mv) being monitored continuously throughout each experiment.

A fine insulated copper wire (S.W.G. 40 0.75 Ohm resistance) was passed through a polythene cannula (Protex 200/300/040 O.D 1.34 mm). The wire cathoder being fixed to the catheter tip at which point the wire was cleared of its insulation. A hypodermic needle was positioned subcutaneously over the region of the left ventricle on the left side of the chest and served as the anode.

This polythene Catheter and wire within it was passed retrogradely into the left ventricle

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via left carotid artery and was used for passing the fibrillatory current and recording the left ventricular pressure. The E.C.G., left ventricular pressure and its first derivative (peak dp/dt), blood pressure through femoral artery, heart rate, cardiac out-put guide (Systolic-diastolic BP x heart rate) and cardiac effort index (Left ventricular pressure x heart rate) were recorded using a grass polygraph 7.

Animals were left for 30 minutes after surgery for stabilization of the haemodynamic parameters before applying the electrical stimulation. All basal cardiovascular data were recorded prior to experimental procedures. Animals were respired artificially where necessary (Stroke rate 26/min., stroke volume 50-75 c.c.) using a palmer ideal pump. Electrical stimulation was provided with SRI stimulator using a frequency of 20Hz and pulse duration of 1.0 ms and increasing voltaage to precipitate V.F. with a total stimulation period of 8 seconds.

The voltage necessary to induce fibrillation varied between animals. If fibrillation could not be induced at certain voltage; the stimulus voltage was increased until the condition appeared. After each stimulation period, the preparation was left for 10 minutes to reestablish as nearly as possible pre-fibrillatory condition. The control or threshold fibrillatory voltage was established three times in each animal.

RESULTS

The control voltage necessary to induce VF ranged from 10V-30V in these experiments. The effects of drugs on the ventricular fibrillating threshold (V.F.T.) have been described in detail elsewhere (Rashid, 1976).

(i) Effect of Electrical Induced Fibrillation on ECG:

After stimulation, the changes characteristic of ventricular fibrillation (Fig. 1) occured in the configuration of the E.C.G. wave form in lead II (Fig. 1) at appropriate voltage but normal E.C.G. configuration reappeared in all animals within 30 seconds after cessation of stimulation and no irregularities of cardiac rhythm were observed. Repeated episodes of VF induced by electrical stimulation produced similar reversible changes in the E.C.G. in these experiments.

(ii) Effect of Electrically Induced Fibrillation on Haemodynamics:

The mean results for 30 experiments showing the changes in cardiovascular parameters recorded 25 minutes after the last episode of control fibrillation are shown in Fig. 2. No significant changes were seen in blood pressure after recovery from the VF episodes. Similarly no changes in heart rate (H.R.) or left ventricular contractility (L.V.C.) were observed. Cardiac output guide (C.O.) slightly decreased (—5%) though not significantly from the control data while cardiac effort index (C.E.I.) was unchanged.

DISCUSSION

Electrical stimulation of the myocardium and the subsequent achievement of VF can be performed by two methods.

(1) The application of a single shock stimulus of high intensity directly to the myocardium during the last part of the systole which is called vulnerable period was first described by Wiggers and Wegria in 1940. The application of electrical stimulus in the last

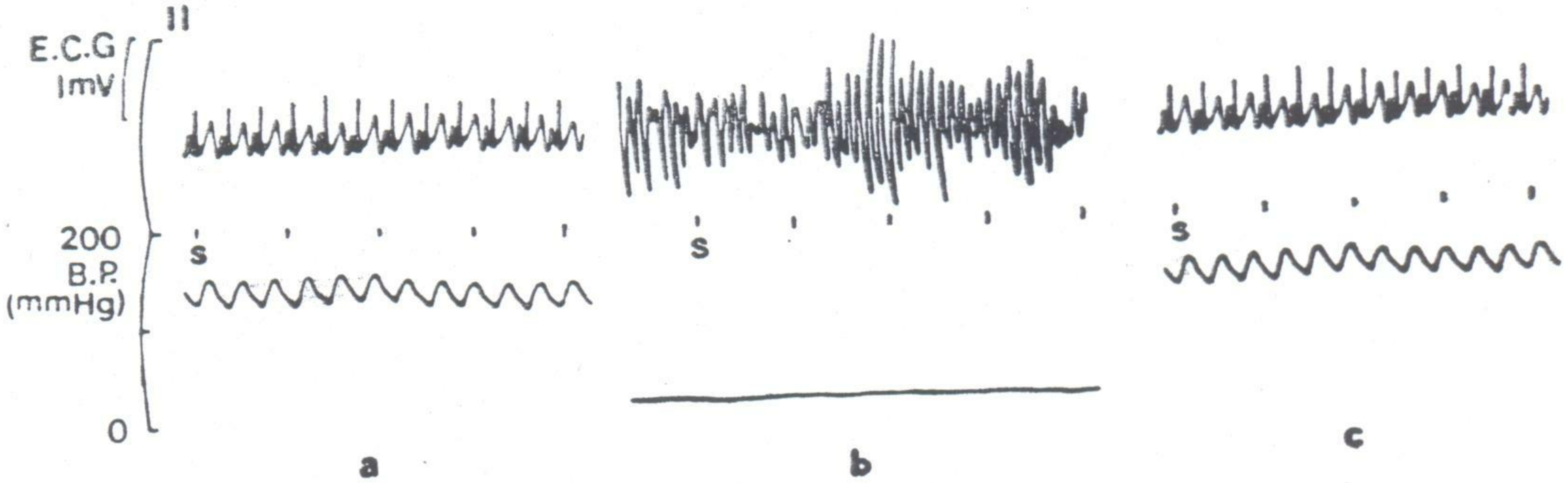

Fig. 1:-Showing (a) Control electrocardiogram (E.C.G.) in lead II and blood pressure (B.P.) pentobarbitone anaesthetized cat. After electrical stimulation for 8 seconds a typical ventricul fibrillation developed (b) which reverted spontaneously after 25 seconds. No adverse effec on E.C.G. or B.P. were seen (c) after 10 minutes of rest period before the other stimulus was give

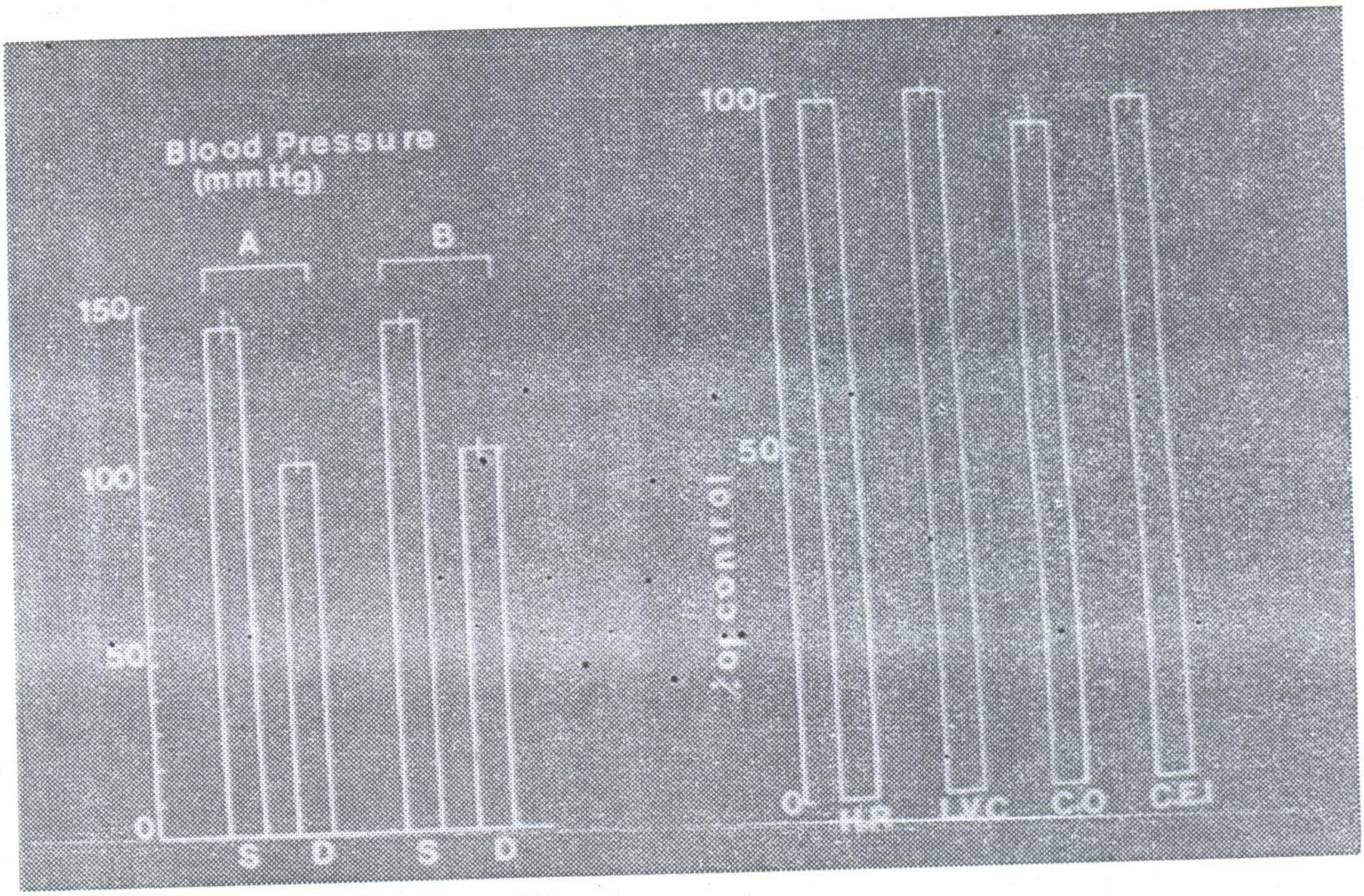

Fig. 2:-Changes in haemodynamic parameters are shown in this figure. Blood pressure (mm/H did not show any change before (A) and (B) 25 minutes after the last period of electrica induced ventricular fibrillation. Other parameters were also taken at the same time and shown as of control. Vertical bars represent meant ±S.E. of 30 experiments.

S —Systolic blood pressure
D —Diastolic blood pressure
C.E.I. —Cardiac Effort Index
C.O. —Cardiac output guide
H.R. —Heart Rate
L.V.C. —Left Ventricular Contractility.

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part of systole resulted in the induction of fibrillation in dogs.

(2) The use of Successive Shocks at high frequency directly to the myocaridum has also been demonstrated (Wegria and Wiggers, 1940).

The latter method appears to be more acceptable experimental system for induction of VF (Szekere and Papp, 1971) and has been found to be convenient for estimation of anti-arrhythmic drug action (Dipalma, et al., 1950). In recent years the application of Serial Shock with increasing voltage has been extrensively used (Baum, et al., 1971), Wellen and Wauters, 1972, Kniffen, et al., 1972, Wellen & Wauters, 1973), in experimental work. Few workers have favoured the single shock method presumably because of extensive damage to the myocardium (Shumway, Johnson & Stish, 1957, Ventyn & Maclean, 1961). Disadvantages of using single shock stimulus have been described such as that in this method a fairly powerful stimulus is required to affect myocardium which may severely injure the cardiac tissue. Secondly the vulnerable period does not exist as a single point of time in the Q.R.S. Complex but is considered a phase of certain duration within which the fibrillation threshold is constantly changing, therefore, in order to find the lowest intensity that may produce fibrillation, practically the whole of the vulnerable period has to be 'Surveyed' under varying circumstances (e.g. prior to and following the administration of drug). Thus, a slight change in the duration of action potential may shift the position of the Vulnerable period within the cycle and in the case of a shock applied at a fixed time from the beginning of the cardiac cycle may result in false fibrillation threshold value. This technique also needs an elaborate fibrillation-defibrillation equipment as well as being experimentally much more difficult to determine. In the alternative method described in the present studies for inducing V.F. it has been found that cat is capable of reverting spontaneously from the state of ventricular fibrillation.

Very little work has been reported on the effect of electrically induced V.F. and subsequent spontaneous or defibrillated assisted recovery on general haemodynamics responses prior to the administration of an anti-dysrhythmic agent. Lawson and Wojeiechowski (1974) reported a reduction of 15 mm Hg in the systolic and diastolic blood pressures in the dog 15 mins., after the induction of the fibrillation and subsequent defibrillation. Sarin and Nickle (1974) studied the effect of electrical stimulation on dogs and found that blood pressure, coronary blood flow and coronary resistance were unchanged after recovery. These results are analogous to those observed in the present studies where no significant changes were found in blood pressure (Fig. 2), but differ from Lawson & Wojciechowski (1974) perhaps due to the longer recovery period after stimulus (25 minutes) given in present studies compared with 15 minutes given in other experiments (Lawson & Wojciechowski, 1974), or may be the species difference.

An investigation has been described in which paired electrical stimulation was applied to man (Braunwald, et al., 1964), in order to characterize the effect of this intervention on human heart. These authors reported, slowing of the heart, augmentation of contractility and increase in rate of rise of intra-ventricular pre-

sure but did not observe consistent changes in ventricular diastolic pressure or cardiac output.

It appears therefore that electrically induced V.F. technique has certain advantages as described by Baum, et al. (1971). This method of experimentally determined fibrillatory threshold better fulfills the requirements of a basic screen for potential antifibrillatory drug detection even though its clinical counter-part may not be as obvious as that of Oubain.

The present technique using cats has an advantage over using dogs in that no defibrillation equipment is required. The other advantage is that the application of electrodes directly to the myocardium and the need for open heart surgery is not necessary and so the damage to the surface tissue is prevented. Thoractomy is also not required.

As it has been shown that no adverse effects were seen on the general haemodynamics 25 minutes after repeated intermittent episodes of electrical stimulation, the true cardiovascular effect of a drug compound can be seen and if a drug can be shown to have no adverse effect on general haemodynamic function and is also capable of raising V.F.T., it is possible that this drug may be useful for antidysrhthmic purposes.

SUMMARY

A simple technique for induction of ventricular fibrillation (V.F.) by electrical stimulation for purposes of screening antifibrillating agents in closed-chest cats is described. A fine insulated copper wire was passed through the catheter and its tip near the end of the catheter was cleaned from insulation. This catheter was introduced retrogradely into the left ventricle in cat. The wire tip in the ventricle served as the cathode while a hypodermic needle positioned subcutaneously over the chest served as the anode.

This technique neither requires thoracotomy nor elaborate equipment for defibrillation as it cats a spontaneous defibrillation occurs. The merit and the effect of this technique on general haemodynamic function is discussed.

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