THE REFRACTORY PERIOD OF THE NORMALLY-BEATING DOG'S AURICLE; WITH A NOTE ON THE OCCURRENCE OF AURICULAR FIBRILLATION FOLLOWING A SINGLE STIMULUS

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Plate 8

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In all previous determinations of the refractory period of the mammalian auricle two factors influencing the accuracy of the measurements obtained have been necessarily present as a part of the technique of the experimental procedure. In order to control the exact time in the cardiac cycle at which the interrupting stimulus is introduced it has hitherto been necessary to drive the heart by a series of break induction shocks at a rate more rapid than that of the spontaneous rhythm. The local stimulating effect of these repeated shocks upon the vagus endings of the myocardium has made accurate measurements possible only upon the atropinized heart, and in many instances has also led to an irregular failure of response at a level above the true refractory period. The occasional interruption of the rhythm by false responses, upsetting the essential order of at least several sequential cycles preceding that one during which the refractory period is determined, has also been unavoidable.

A second cause influencing the accuracy of the results previously obtained has arisen from the fact that it has been impossible to record the refractory period from the exact point of stimulation. In all such experimental observations there has necessarily been a small gap between the stimulating and the recording electrodes. It is a reasonable assumption that changes in this small area of musculature, as a result of the repeated induction shocks, may modify the measurement considered as the true refractory period of the auricular muscle. Even

when using the method first described by Lewis, Drury and Bulger (1) in which the shocks, which control the rhythmic beats of the heart, and those which test the refractory period, enter the muscle at precisely the same place, there is a gap of about 15 millimeters between the stimulating and the recording electrodes. This procedure has been necessary owing to the danger to the galvanometer string when the stimulating electrodes are placed too close to the leading-off point. As a result what has actually been measured has been the refractory period at the point of stimulation plus the interval required for the excitatory process to spread from this point to the recording electrodes. In the absence of any added experimental procedure, and under conditions in which both the refractory period and conductivity may be altered in the same sense, such results may be at least proportional to the true refractory period. The instant, however, that one attempts observations under the influence of pressure, cold, certain drugs or changes in the hydrogen-ion concentration of a perfusate, the possible effect of conduction with a decrement throughout this gap, can not be avoided (2). Under these circumstances, in some of which the refractory period may be shortened and conductivity remain unchanged or depressed, the error may be considerable.

By means of a balanced circuit with a double induction coil as the source of stimulus (as suggested by Bishop (3) and applied by Gilson (4)) it has been possible, in these experiments, to place the stimulating electrodes actually astride the proximal lead, thus avoiding any gap, and with no more disturbance of the galvanometric record than is shown in the accompanying curves (Fig. 1). Using a specially designed apparatus (See Appendix) the refractory period of the normally beating dog's auricle has been determined in the following manner.

The animals are anaesthetized with morphia (16 mg.) and urethane (1.0 gm. per kilo). The heart is exposed in situ, the pericardium opened and sewn back against the retracted ribs and a ligature is fastened to the tip of the right auricle drawing it toward the left chest wall. The action-current is led off from the auricular appendix by means of kaolin-paste copper-sulphate electrodes, amplified to 12 to 20 volts and applied to a light relay. Activation of this relay releases a pendulum, which, in turn, throws in a single break induction shock at a time interval determined by the position of a trip-switch along its arc, the normal excitatory process alone controlling the timing of the interrupting shock. The arm

bearing the trip-switch carries an accurately calibrated protractor scale etched upon its face. The local effect of a bombardment with induction shocks is thus avoided and there is the added advantage that the R-S interval may be accurately altered or exactly reproduced.

The threshold of current strength was first determined roughly by watching the heart and the galvanometer string, the point at which a response occurred being noted. The current strength was then doubled and a duplicate series of observations recorded from a time interval well above the observed refractory period to one well below. The refractory period was then always checked in the opposite direction; i.e. if the first determination was made with decreasing intervals, a second series was carried out with increasing intervals. It is of interest that the refractory periods so determined checked within a few thousandths of a second.

TABLE I

Refractory Period of the Dog's Auricle. Spontaneous Rhythm. (R-S Intervals in Seconds)

Dog No.	15		22		17	
Auricular rate	170		150		185	
Refractory period	0.1408					
	0.1305	0.1385	0.1245		0.0978	0.1078
	0.1265↓	0.1316↑	0.1190↓	0.1153↑	0.0940↓	0.1008↑
	0.1250	0.1299	0.1159	0.1123	0.0895	0.0924
	0.1245	0.1275	0.1107	0.1100	0.0858	0.0878
	0.1210	0.1207	0.1095	0.1064	0.0781	0.0790
	0.1195↓	0.1144↑	0.1067↓	0.1037↑	0.0740↓	0.0774↑
	0.1160	0.1097	0.0978	0.1015	0.0685	0.0716
	0.1140	0.1021				0.0652

↓ with decreasing, and ↑ with increasing, intervals.

In a series of twenty experiments in which the refractory period was measured before stimulation of the vagus, the administration of atropine or adrenalin, values were obtained varying from between 0.0781 and 0.0858 to between 0.1392 and 0.1410. All measurements were made from the appearance of the excitatory process (R), to the onset of the interrupting stimulus (S)—the R-S interval.* The close agreement of the two values obtained by the method outlined is well shown in Table I.

* All measurements were made with a Lucas Comparator.

In ten animals the right vagus was then exposed in the neck and stimulated with a faradic current of sufficient strength to slow, but not to inhibit completely, the spontaneous rhythm of the auricle. Stimulation of the nerve was commenced a few cycles before the introduction of the induction shock and was continued for less than two seconds unless an abnormal rhythm developed. Typical observations are shown in Table II. Stimulation of the vagus brought about a conspicuous shortening of the refractory period. In no

TABLE II

Refractory Period of the Dog's Auricle. Spontaneous Rhythm. Influence of Vagus and Atropine. (R-S Intervals in Seconds)

Dog No.....	19		16		32		29	
Auricular rate.....	156	70*	167	48*	140	168	187	169
	Control	During vagal stimulation	Control	During vagal stimulation	Control	After atropine	Control	After atropine
Refractory period				0.0848				
			0.1418	0.0771		0.1400	0.1065	
	0.1306	0.0806	0.1312	0.0685	0.1044	0.1333	0.1048	0.1210
	0.1270	0.0737	0.1175	0.0608	0.1013	0.1298	0.0985	0.1150
	0.1245	0.0655	0.1063	0.0559	0.0964	0.1280	0.0918	0.1108
	0.1195	0.0595	0.0992	0.0530	0.0950	0.1257	0.0874	0.1067
	0.1182	**0.0486**	**0.0966**		**0.0938**	**0.1225**	**0.0863**	**0.1041**
	0.1170	**0.0437**	**0.0946**		**0.0880**	**0.1214**	**0.0835**	**0.1012**
	0.1124		**0.0890**		**0.0820**	**0.1155**	**0.0790**	**0.0955**
			0.0816				**0.0760**	

* Average rate.

instance did the refractory period under vagus stimulation exceed in length 0.0629 sec. Indeed in six experiments it lay below the minimum range of the stimulating pendulum (0.0475 sec.). These results agree with those of Lewis, Drury and Bulger (1).

The refractory period was measured in seven hearts after the intravenous injection of atropine (0.001 gm. per kg. body weight). Under the action of this drug it was prolonged well beyond the value obtained in the control observations. The average increase in length amounted to about 20 per cent (See Table II).

TABLE III

Refractory Period of the Dog's Auricle. Spontaneous Rhythm. Influence of Adrenalin after Atropine. (R-S Intervals in Seconds)

Dog No.	21			27		
Auricular rate	82*	167	215	135	145	190
	During vagal stimulation	Control	After atropine followed by adrenalin	After atropine	Control	After atropine followed by adrenalin
Refractory period	0.0765		0.0916		0.1312	
	0.0714		0.0887	0.1604	0.1278	0.0903
	0.0670	0.1165	0.0845	0.1587	0.1248	0.0854
	0.0609	0.1142	0.0806	0.1567	0.1215	0.0787
	0.0545	0.1095	0.0752	0.1503	0.1206	0.0739
		0.1063	**0.0710**	**0.1454**	**0.1155**	**0.0701**
		0.1030	**0.0655**	**0.1425**	**0.1105**	**0.0656**
		0.0984	**0.0619**	**0.1412**	**0.1078**	**0.0624**
				0.1365		

* Average rate.

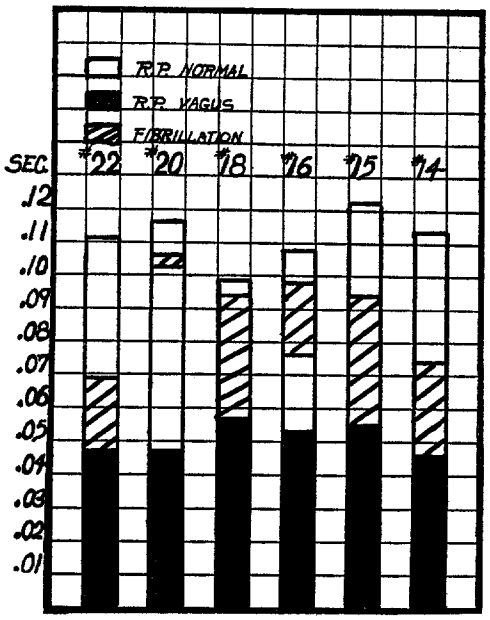
TABLE IV

Refractory Period of the Dog's Auricle. Spontaneous Rhythm. Influence of Vagus, Atropine and Adrenalin. (R-S Intervals in Seconds)

Dog No.	20			
Auricular rate	120	54*	118	176
	Control	During vagal stimulation	After atropine	After adrenalin
Refractory period	0.1314			
	0.1276	0.0870		0.0906
	0.1238	0.0800		0.0887
	0.1222	0.0670	0.1482	0.0828
	0.1190	0.0540	0.1435	0.0819
	0.1165	0.0475	0.1396	0.0806
	0.1114		**0.1340**	**0.0735**
	0.1092		**0.1307**	**0.0693**
	0.1012		**0.1245**	

* Average rate.

A slow intravenous infusion of adrenalin (1/1,000,000 in normal saline) after the vagus endings had been paralysed with atropine, caused acceleration of the spontaneous rhythm and shortening of the refractory period. Six such observations were made. The refractory period showed an average reduction of 40 per cent as compared with the control measurements but was never shortened to the extent



TEXT-FIG. 1. R-S intervals, at which auricular fibrillation followed a single stimulus, compared with the control refractory period and that under vagal stimulation.

produced by vagus stimulation (See Table III). In Table IV are shown the alterations in the refractory period in a single auricle produced successively by vagal stimulation, by atropine and by adrenalin.

It was repeatedly observed that a stimulus introduced during vagal stimulation, shortly after the end of the refractory period, was followed not by a single response, but by auricular fibrillation. This was not encountered in the control observations before stimulation of the vagus or following atropine or adrenalin.

Such results have been previously reported by DeBoer (6) and others in hearts deprived of their blood supply or poisoned with various drugs. Lewis, Drury and Bulger (1) have called attention to the occasional occurrence of such a disorder of rhythm during refractory period determinations while the vagus is being stimulated. The development of this irregularity in our series of experiments following a stimulus applied well out on the auricular appendix is of particular interest. The fact that there is no measurable gap between the stimulus and the beginning of the re-entrant rhythm (as shown in Fig. 2) indicates, we believe, that it rises at that point and not in a ring of muscle at the base of the auricle.

Moreover this rhythm consistently followed stimuli which, in the absence of vagus stimulation would have fallen within the refractory period, Text- fig. 1. Due, however, to the shortening of the refractory period consequent upon stimulation of the vagus, they fell upon tissue which was excitable but in which conductivity had, presumably, not yet returned to normal. Hence as long as vagal stimulation was continued there existed in the auricular musculature conditions favorable to a re-entrant rhythm. The fact that, in the normal heart under conditions of increased vagal tone, an extrasystole occurring early in diastole may set up a re-entrant rhythm suggests to us a possible explanation, in some instances at least, for the genesis of auricular fibrillation.

SUMMARY

1. A method is described for determining the refractory period of the dog's auricle during the normal sinus rhythm. The advantages of the method are:

(a) The total stimulating effects of repeated induction shocks are avoided.

(b) The action current is recorded from a point one millimeter or less from the point of stimulation.

(c) Alterations in the spontaneous rate of the auricle do not interfere with the accurate determination of the refractory period.

2. The values obtained for the normal refractory period and the changes produced by atropine and by stimulation of the vagus agree closely with those of previous observers.

3. The automatic features of the method make possible the determination of the refractory period under adrenalin. This drug brings about a distinct shortening of the refractory period but less than that produced by stimulation of the vagus.

4. During vagal stimulation a single induction shock, introduced soon after the end of the refractory period, frequently produces auricular fibrillation. The cause of this irregularity is discussed and its relation to clinical auricular fibrillation is suggested.

APPENDIX

Amplifier and Timing Device

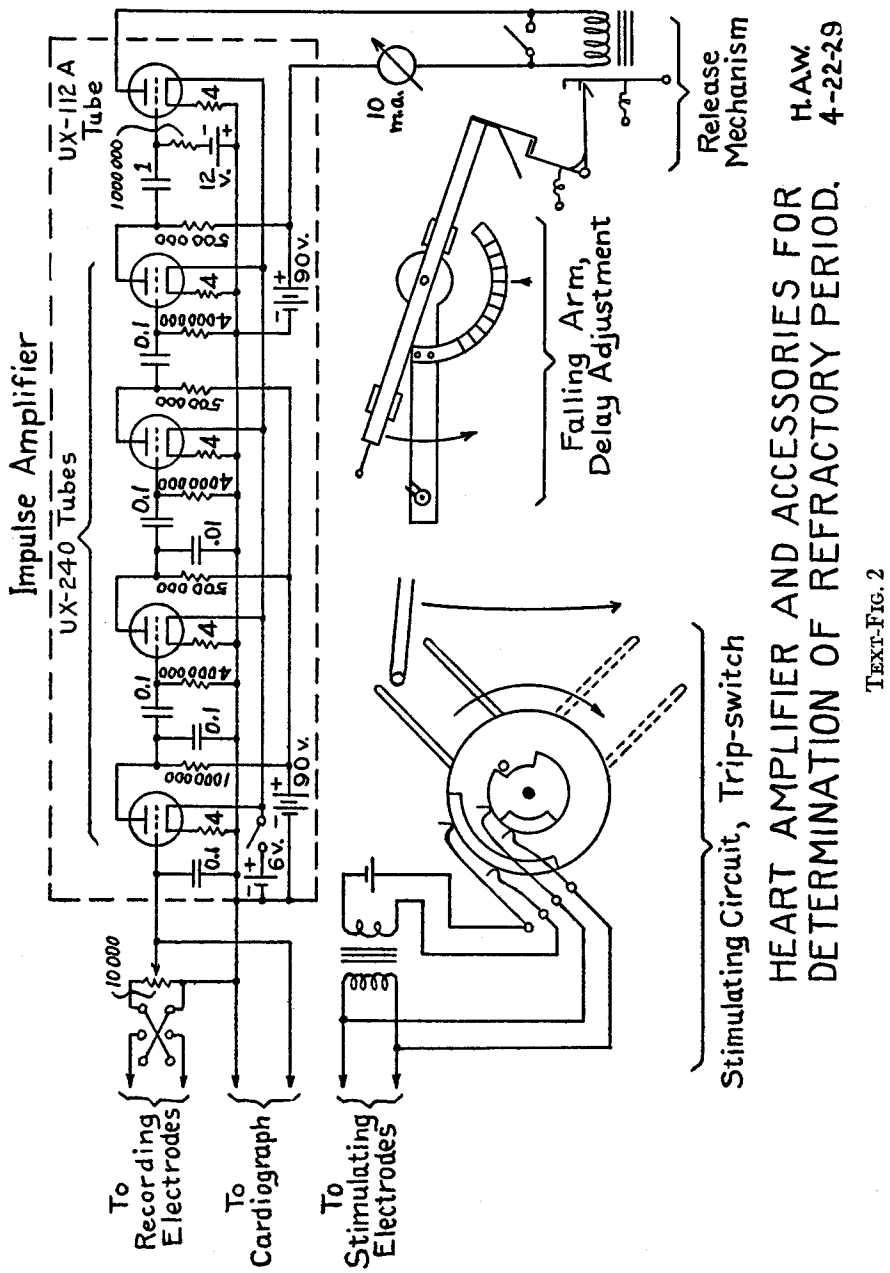
By HAROLD A. WHEELER, Ph.D.

The complete apparatus comprises a five-stage resistance-coupled vacuum-tube amplifier, greatly amplifying the cardiac action-currents, together with a magnetically-actuated mechanical system automatically introducing a stimulating induction shock. The arrangement of the apparatus is illustrated schematically in Text-fig. 2. The resistance values are given in ohms, the capacitance values in microfarads. A six-volt storage battery and two 90-volt dry batteries supply the necessary power. The recording electrodes are connected to the electrocardiograph through an intermediate 10,000-ohm resistor. Independently of the amplifier, the action-current deflection on the galvanometer is adjusted to a value between one-half and two millivolts, the apparatus being designed to operate on this terminal voltage of the galvanometer without further adjustment. The galvanometer string is at no time exposed to the output of the amplifier.

The apparatus performs two functions at the same time; it amplifies the action current to a value of more than 20 volts, and stores, and slowly discharges, energy so that the amplified voltage has a duration of approximately 1/10 second as compared with the 1/50 second duration of the unamplified action current. The amplification of the potential difference applied is thus about 200,000 times, and represents about 10,000,000 times the energy of the action currrent.

The amplified current flows through a 10-milliampere meter and a 10,000-ohm magnet. During adjustment for operation, a switch across the magnet is closed and the magnet is not actuated. The amplifier responds only to a positive potential applied to the first amplifier tube; the reversing switch in the recording electrode circuit must, therefore, be adjusted by trial to give the sharpest deflection of the meter pointer.

The mechanical system is activated upon opening the magnet switch. Each amplified action-current impulse thereafter instantly moves the magnet armature. This armature carries an escapement such that the second impulse releases a hook, which, in turn, sets free a falling arm. The falling arm operates a trip-switch,



TEXT-FIG. 2

opening the primary circuit of an induction coil. The stimulating electrodes thereupon receive a shock from the secondary circuit of the induction coil. The interval between the second action-current impulse and the induction shock can be adjusted to any value between 1/20 and 1 second. The speed of the falling arm is determined by the position of two balancing weights. The angular position of the trip-switch is also adjustable so that the switch can be operated at any time during the period of the falling arm. For the present experiments, a calibration curve was prepared showing the interval at all angular positions of the trip-switch.

The instrument is designed to actuate the magnet armature in response to an action-current impulse of 1/2 millivolt for 1/50 second. The grid condensers and grid resistors thus give the entire amplifier a discharging time constant of about 1/10 second, which is sufficiently short to restore the amplifier to normal very quickly after a short impulse of several millivolts.

The condensers in parallel with the first two plate circuits are proportioned to give the amplifier a charging-time-constant of about 1/50 second. This is sufficiently short to respond quickly but sufficiently long to prevent disturb, ances in the amplifier at audio or radio frequencies. These parallel condensers also serve to increase the duration of the amplified impulse to about 1/10 second-giving the magnet ample time to respond and preventing a quick rebound of its armature. A 90-volt battery common to all five plate circuits would give feedback-coupling from the fifth to the first plate circuits with resulting low frequency oscillations; therefore two separate 90 volt batteries are necessary. With a normal grid bias on the last tube, the magnet may be actuated by random fluctuations in the plate current of the first tube ("flicker effect") amplified to a high degree. This grid bias is, therefore, operated at a high negative value, giving a normal plate current of about 1/2 milliampere. The magnet armature is adjusted to respond only to 2 milliamperes or more, so that it is not actuated by fluctuations. Some difficulty may be experienced with radio-frequency disturbances picked up by the wires connected to the first grid. This is prevented by the condenser shunting the first grid circuit, and by enclosing the entire amplifier with its batteries in a galvanized-iron box. This condenser, and the filament circuit of the first tube, are connected to the box by a short wire. Mechanical agitation has no effect upon the amplifier.

The release mechanism comprises the magnet with its armature, escapement, and trip-switch, shown schematically in Text-fig. 2. The magnet has a laminated "E" core. The middle leg of the core has a cross section of one square inch and carries a 10,000 ohm coil of 40 gauge copper wire. The armature is made of 1/32 inch iron sufficiently large to cover the three poles and is supported at its base on a horizontal pin parallel to the line of poles. It carries an escapement which, on the second impulse, releases a light hook. This release on the second impulse is important because it avoids the confusion which might occur if the magnet switch were opened during the first impulse.

The falling arm is of light construction, one foot long, and pivoted at the center. It carries two weights, whose positions are adjustable by a threaded rod along the

length of the arm. A shock-absorber catches the arm after a 90 degree fall from its initial position. The arm, when released from the hook by the magnet, engages the trip-switch. The angular position of this switch is adjustable and is indicated on a circular scale.

The trip-switch details are shown schematically on an enlarged scale. It is made up of two insulated cylinders carrying metal contact segments. The primary contactor is engaged directly by the falling arm. The secondary contactor floats on the same pin, but is engaged by a pin on the former, and moves only during the latter part of the motion of the primary contactor. When the arm is raised the primary circuit of the induction coil is first closed and the secondary shock absorbed, then the secondary circuit is opened ready for the experiment. When the arm falls, the primary circuit is first opened, producing an induction shock at the stimulating electrodes, and the secondary coil is shunted.

Thus all mechanical operations are performed by merely raising the falling arm. The trip switch is set and the induction-coil-battery circuit closed. The hook is pushed back and automatically sets the escapement on the armature. Observations can thus be made in rapid succession.

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EXPLANATION OF PLATE 8

FIG. 1. Curves recorded from the point of stimulation; (a) during control observation, and (b) during vagal stimulation. The stimulus appears as a thickening on the rising limb of the wave.

FIG. 2. Fibrillation of the auricles following a single induction shock during stimulation of the vagus. Stimulation begun at A and ended at B.

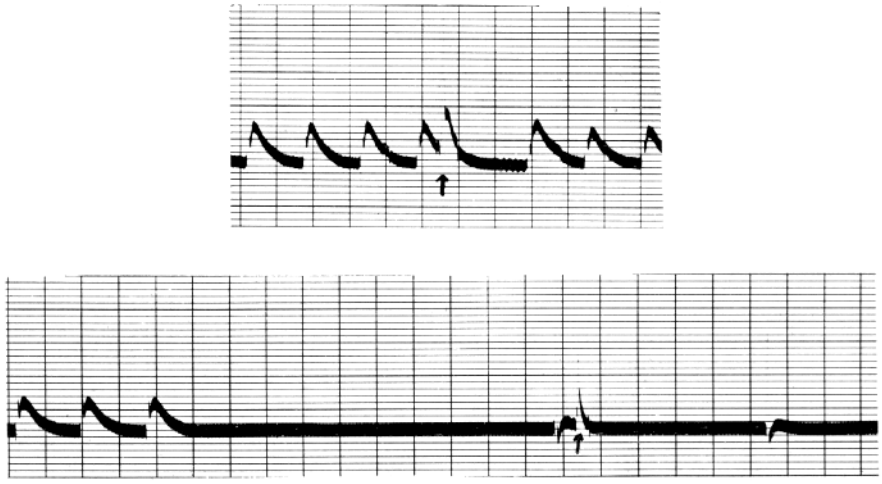

FIG. 1

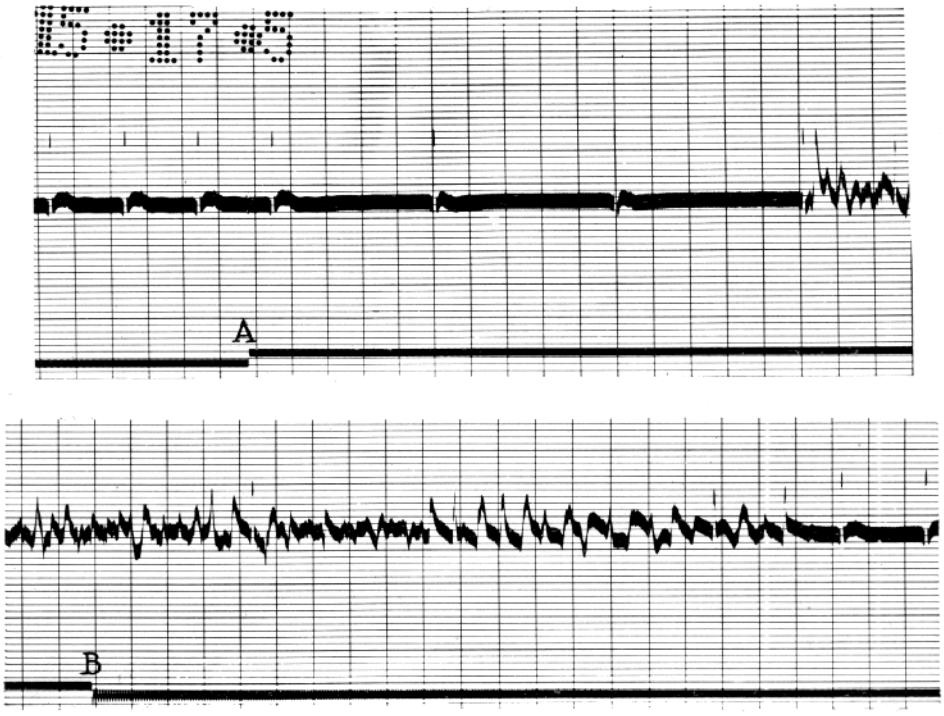

FIG. 2

(Andrus and Carter: Refractory period of normal dog's auricle)