Vulnerability to Fibrillation and the Ventricular-Excitability Curve

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Previous reports have given a description of the cyclic changes in excitability of both auricle and ventricle of the dog’s heart \((1, 2)\). It was found that the dog’s auricle is 'vulnerable' to fibrillation throughout the major dip area of the excitability-recovery curve \((3)\). A study of ventricular vulnerability has now been made. Cats and turtles were used almost exclusively in this investigation because their smaller hearts could be defibrillated more easily than the ventricle of the dog. The secondary purpose of this study was to determine whether or not the phenomena of the recovery of excitability are similar in the hearts of different vertebrates.

**METHODS**

The methods employed were those adopted in a recent study \((4)\). In the cat as in the dog, silver-silver chloride stimulating and recording electrodes mounted in lucite plaques were attached to the superficial layers of the auricular and ventricular muscle. The exposed knobs of the electrodes consequently came in contact with uninjured tissue. After attachment of the electrodes and inactivation of the sino-auricular node the thorax was closed by approximation of the edges of the sternal incision. Defibrillation of the cat ventricle was accomplished by high voltage alternating current shocks of short duration \((0.5-1.0\) second) administered through padded electrodes placed on either side of the heart. Usually defibrillation was accomplished within 30 seconds. When a single shock failed, repetitive counter shocks were used \((5)\). Testing was not resumed for such time, usually 5 to 10 minutes, as was required for any disturbance in excitability and response to disappear. Turtles were pithed; the plastron removed and electrodes attached to the exposed ventricle. It was possible to drive the ventricle without inactivation of normal pacemakers by further surgical procedures. Defibrillation occurred spontaneously in all cases.

In a few experiments the test stimuli were placed with respect to the time of origin of the intrinsic beat by triggering the oscilloscope sweep and the testing stimulator by means of the major deflection of the electrogram. Generally, however, the heart was driven with one stimulator and its excitability determined by rectangular test shocks from a second stimulator. The strength of test shocks was determined by measurement of milliamperes of current flow. Testing shocks were given every 7th to 9th cycle and the responses recorded on a 12-inch monitoring cathode ray tube.

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The results to be reported were obtained in a series of 12 pithed turtles and 24 cats anesthetized with Nembutal (30 mg/kg.). A number of single tests were made on the ventricles of dogs in a manner to be described below.

RESULTS

Phenomena of the Excitability Cycle. The strength-interval curves and the strength-duration curves taken at many intervals of the cardiac cycle in both auricle and ventricle, demonstrated the breaks and the reversal in the direction of recovery which had been observed previously in the dog (2, 3), (figs. 1 and 2).

The terminal boundary of the total refractory period was practically identical for stimuli of various durations (0.1-15 msec.), but the longer duration shocks showed a much shorter absolute and longer relative refractory period. Longer duration shocks also revealed the dips more clearly. In the cat auricle and turtle ventricle a single dip was usually observed but both an early and a later or major dip were very clearly demonstrated in the cat ventricle. A postrefractory temporary decline of threshold below the normal level was found in 3 of 12 turtles; 7 of the 20 cat ventricles and 3 of the 5 auricles studied. In this supernormal period, lasting 20 to 50 msec. in the mammal the stimulus requirement was 10 to 15 per cent (0.05-0.10 ma.) below the late diastolic threshold requirement. As in the dog, the sequence of two dips and a long lasting shallow supernormality suggested a damped oscillation of the recovery processes.

Test shocks applied during the relative refractory period induced a propagated response only after considerable latency, thus an unresponsive period was again demonstrated in both auricle and ventricle. The response of the ventricle to threshold stimuli could not be advanced beyond the peak of the unipolar T wave and placement of such stimuli earlier and earlier in the refractory period merely increased the latency of the response. In the cat, as in the dog (4), the termination of the total refractory period corresponds with the apex of the monopolar T wave.

The cat's heart also behaves as does the dog's (4) in response to changes in rate. No special study of the problem was made in this species but it was observed in 3 experiments in which tests were made that acceleration of the heart rate moved the excitability-recovery curve to the left and produced a diminution of the absolute refractory period and the period of resting or normal excitability without modification of the relative refractory period.

Fibrillation and the Vulnerable Period. It was impossible under the condition of these experiments to produce true fibrillation in the cat's auricle by means of single shocks of 0.1- to 15-msec. duration and of 0 to 25 ma. in intensity. Although these same auricles could be fibrillated easily by tetanic stimuli of low intensity, procedures normally used did not permit determination of a true fibrillation threshold. Single shocks of high intensity were adequate, however, for the production of multiple systoles and thus thresholds for repetitive firing were obtained. Figure 3A shows a correlation between the dip area and the period during which multiple auricular extrasystoles could be elicited.

In terminating a few experiments performed in the course of other work on the dog's ventricle, it was possible to ascertain that the dog's ventricle like the auricle
is readily fibrillated by the application of a single test shock when this falls within the major dip area of the refractory period. Prior to and following the dip areas shocks of maximal duration (15 msec.) and varying intensity (0–30 ma.) can be applied with impunity. It is more difficult to defibrillate the dog’s ventricle than the cat’s and a prolonged period of fibrillation generally results in a changed duration of the
refractory periods and a marked shift of excitability and fibrillation thresholds. Consequently no serious attempt has thus far been made to delineate in detail the vulnerable period and fibrillation thresholds of the dog's ventricle.

Since the cat's ventricle is very easily brought out of fibrillation by shocks of high intensity (30-40 volts) and since it shows the multiple dip phenomena it appeared to be a favorable test object. Consequently its susceptibility to fibrillation at all intervals of the cycle was determined by progressive increase of test shock strengths until the maximum of the stimulator was reached. As in the case of the dog's auricle (3, 6) most tests were made with shock of 1- to 3-msec. duration because longer duration shocks gave a less clear definition of the most vulnerable period. Shocks applied during the absolute refractory period and following recovery of normal excitability failed to elicit fibrillation regardless of their strength and duration.

In most cases it was possible to fibrillate and defibrillate the heart numerous times without permanent detectable changes in thresholds or vulnerability. Occasionally, however, following fibrillation the refractory periods were prolonged and thresholds in general were raised; the heart also showed a greater susceptibility to fibrillation. It often became impossible to obtain an extrasystole during the vulnerable period and the fibrillation threshold fell to a value below that which had been determined previously as the threshold for extrasystole. Since the susceptibility to multiple firing occurred at the same intervals as vulnerability to fibrillation (3) an attempt was frequently made to find the areas of greatest susceptibility by limiting stimulus strength to that which would produce only multiple extra beats.

In all of this work on susceptibility to fibrillation there was much variation but it was possible to ascertain that during both the early and late or major dip areas, in contrast to other intervals of the cycle, the heart tends to respond by repetitive extrasystoles and/or fibrillation to test shocks of suprathreshold intensity. Figure 4

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Fig. 2. Turtle ventricle. A: Strength-duration curves. Cycle length 1100 msec. showing reversed relationship of curves taken at 625 and 650 msec. B: Strength-interval curve and relationship of vulnerable period to the dip area.
shows the type of response considered to be multiple firing and the response called fibrillation. At least one dip and vulnerable period was always obtained in testing the excitability of the ventricle. In those cases giving an early and a late or major dip, vulnerability was not always detectable in both dip areas—it occurred either at one or the other. In 4 of the 8 experiments on cats giving clear double dips, however, there were two vulnerable periods (fig. 3B). The greatest vulnerability generally occurred within the major dip but occasionally fell slightly later in the cycle.

Strength-interval excitability curves were obtained from the cat's ventricle by both bipolar and monopolar stimulation. As in the dog a change in the recorded complex (2) occurred in the major dip area. The impulse appeared to originate near the anode during the dips as contrasted with a cathode origin at other intervals of the cycle.

A 'disappearance-phenomenon' (6) or failure to respond to suprathreshold stimuli was observed in both the cat auricle and ventricle of cats and turtles early in the relative refractory period. It commonly occurred before the vulnerable period and was obtained occasionally between the two vulnerable periods in those ventricles which exhibited two dips and associated vulnerability (figs. 2 and 3).

**DISCUSSION**

This work and associated experiments (7) indicate that the phenomena described in previous papers are not peculiar to the dog's heart. The fact that vulnerability of the ventricle is associated with both the early and late or major dip supports
the hypothesis that the events or conditions giving rise to these fluctuations of excitability also contribute to the fragmentation of response which results in fibrillation.

Some hypotheses are suggested by comparison of these results with the work of Draper and Weidmann (8) and Woodbury, Hecht and Christopherson (9) recording from single cells. In the latter paper (9) three processes or phases of recovery are hypothesized. It is stated that a reversal of the recovery or the repolarization process may occur for an instant (9, p. 313) between phase 1 and 2. Draper and Weidmann also record a reversal in direction of potential change just after the spike and before establishment of the plateau phase. A similar dip or notch late in the plateau phase of the potential is shown in some of Draper and Weidmann's and Woodbury's records.

Fig. 4. TURTLE ELECTROGRAMS indicating responses to suprathreshold stimuli during vulnerable period. Initial downward deflection in ventricular driving is artifact of driving stimulus. Displacement of base line in tracings of multiple extrasystoles and fibrillation is part of test-shock artifact. QRS of extrasystoles indicated by arrows. One lead was attached to a hook electrode imbedded in ventricular apex and the other to a clip on abdominal muscle. Test-shock duration 12 msec.

The work of these two groups gives some evidence, therefore, that repolarization of the heart muscle is not a smoothly progressive unidirectional process. Their experiments also indicate that there are different phases in the recovery processes of cardiac muscle. It is conceivable that these facts of observation bear relationship to the variations in the recovery process which we have observed in testing the heart's excitability cycle.

SUMMARY

The cat auricle and ventricle and the turtle ventricle resemble the auricle and ventricle of the dog with respect to phenomena of excitability recovery following a normal beat. These chambers are most vulnerable to fibrillation at those intervals of the cycle which show a dip in the excitability-recovery curve. In ventricles showing a clear early and secondary or major dip in the recovery curve there are two corresponding vulnerable periods. These are clearly separated by an interval during which suprathreshold stimuli give either single extrasystoles or no propagated response.
REFERENCES


