Factors Determining Vulnerability to Ventricular Fibrillation Induced by 60-CPS Alternating Current

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Circ. Res. 1967;21;601-608
Circulation Research is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0009-7330. Online ISSN: 1524-4571

Factors Determining Vulnerability to Ventricular Fibrillation Induced by 60-CPS Alternating Current

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ABSTRACT

Very weak, 60-cps alternating current applied directly to the heart can cause ventricular fibrillation; greater current strength is required to induce ventricular fibrillation with a single shock delivered during the vulnerable period of the cardiac cycle. The present experiments were designed to examine the basis of this difference. The studies were performed in anesthetized open-chest dogs. The current strength required to induce ventricular fibrillation was 0.52 ± 0.16 ma with 60 cps for 5 sec, and 15.0 ± 4.3 ma with a single square-wave pulse of 10 msec. However, when the duration of 60 cps was reduced to produce only 4, 3, 2, or 1 ventricular response, the threshold for ventricular fibrillation after the last response was 0.4, 2, 18, or 24 ma respectively. After any given number of successive premature ventricular responses, the fibrillation threshold was comparable with either 60 cps or a single pulse. We concluded that, if an accelerating ventricular tachycardia that is produced by 60-cps stimulation is of sufficient duration (5 or 6 beats), the VF threshold is reduced progressively after each premature ventricular response, thus making it possible to induce VF with very weak current.

ADDITIONAL KEY WORDS

arrhythmias | electric shock | electrophysiology of the heart | pacemakers | re-entry | ventricular fibrillation threshold | ventricular tachycardia | dog

■ Measurements of the ventricular fibrillation threshold have been used by many investigators in the past to assess the electrophysiological state of the heart. Most of these investigators have determined the fibrillation threshold by applying a single square-wave shock to the heart during the vulnerable phase of the cardiac cycle (1, 2); others applied alternating current (usually 60 cps) (3-5). Although it has been observed that the current strength required to induce fibrillation in the normal heart with a square-wave shock is much greater than that required with 60 cps (6), a systematic evaluation of this difference has not been reported previously. Our experiments were designed to examine the basis for the difference in fibrillation thresholds determind by the two methods of stimulation.

Methods

The experiments were performed on 14 mongrel dogs weighing 12 to 20 kg. The animals were anesthetized with pentobarbital sodium (30 mg/kg iv) and ventilated with a Harvard respirator. The chest was opened through a median sternotomy and the pericardium was used to cradle the heart. The vagus nerves were divided in the neck to stabilize heart rate. The sinoatrial node was then crushed to slow the intrinsic heart rate, and a bipolar pacing electrode was implanted on the epicardial surface of the right atrial appendage. A similar bipolar recording electrode was implanted on the epicardial surface of the right ventricle and a test electrode on the anterior surface of the left ventricle. The test electrode consisted of four 25-

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This work was supported in part by U. S. Public Health Service Research Grants HE-08845, 5-TO1-HE-05369, 1-F2-HE-32,281, and K3-HE-19,949 from the National Heart Institute.

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Accepted for publication September 19, 1967.

gauge needles insulated except at their tips and embedded in a plaque. The needles were 5 mm apart and projected approximately 2 mm beneath the epicardial surface. Two contacts on the test electrode were used to deliver the desired pattern of stimuli to the ventricle and the other two to test ventricular fibrillation threshold (the minimal amount of current required to induce ventricular fibrillation).

Signals from the recording electrode were amplified with a Tektronix 122 preamplifier, displayed on a Tektronix 561 oscilloscope, and recorded on a Hewlett Packard 3971-A tape recorder. A lead II electrocardiogram also was monitored. Records were selected from the tape and reproduced on a Brush 16-2308 oscillograph at a paper speed of 5 inches/sec. The pattern of stimuli applied to the ventricle was recorded on separate channels of the tape system.

Patterns of stimulation were programmed by using a series of coupled Tektronix 160 pulse generators. The outputs of the pulse generators were used to trigger Grass stimulators, and the actual pulses delivered to the heart were isolated from ground. A specially designed stimulator, used to deliver 60-cps current to the heart, also was triggered from a pulse generator, and its output was isolated from ground. The voltage, duration, and time of occurrence of all stimuli to the heart could be individually controlled. The basic pacing stimulus was delivered to the right atrium at a rate of 120/min, and test patterns were delivered to the ventricle either after every sixth basic beat or on demand. This system permitted us to measure the ventricular fibrillation threshold after a basic beat with either a square-wave pulse or 60-cps current. In addition, up to six premature ventricular beats could be induced either with pulses or 60 cps, and the ventricular fibrillation threshold after any one of these premature beats could be measured. The current (milliamperes) delivered to the heart during a test of the fibrillation threshold was measured on a Tektronix 502 dual beam oscilloscope by observing the voltage drop across a 1000-ohm resistor in series with a cathodal electrode. During the time at which a pattern of test stimuli was delivered to the ventricle, the basic pacing stimulus to the atrium was interrupted.

Each value for the ventricular fibrillation threshold in the graphs represents the average of two or three separate observations. This was done to assure reproducibility of the data; if the separate observations did not agree closely the animal was excluded from this report. In addition, the fibrillation threshold after a basic beat was determined at regular intervals throughout each experiment to assure that the preparation was stable during the period of study.

Results

With a single square-wave pulse of 10-msec, the minimal amount of current required to induce a propagated ventricular response at end-diastole, that is, the excitation threshold of ventricle, was $0.10 \pm .05$ ma (mean $\pm$ 1 SD). When the pulse was applied during the vulnerable period of the cardiac cycle, the threshold for ventricular fibrillation was 15.0 ± 4.3 ma. With 60-cps stimulation for 5 sec, the threshold for propagated ventricular responses was $0.21 \pm .06$ ma (peak to peak) and that for fibrillation was 0.52 ± 0.16 ma. Thus, the fibrillation threshold was approximately 30

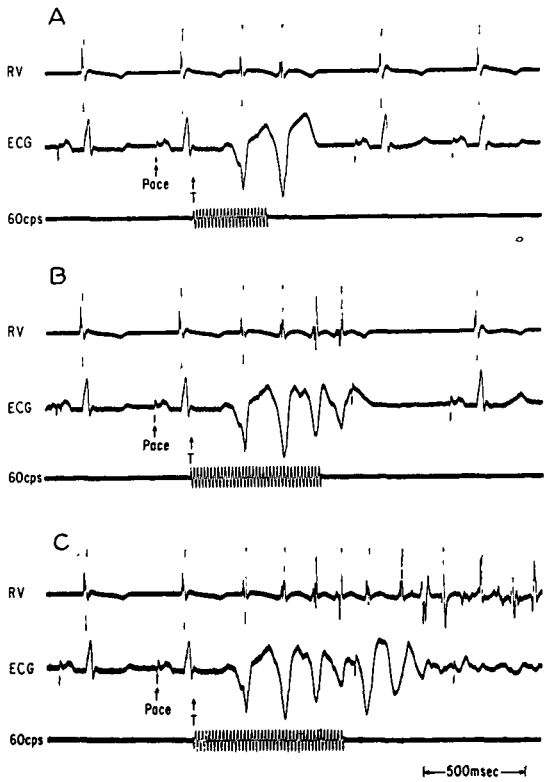

FIGURE 1

Effects of varying the duration of 60 cps on the response of the heart. In panel C, 60 cps of 714 msec and 0.4 ma induced fibrillation. In panel B, the duration of 60 cps was decreased to 635 msec and only 4 responses were produced. In panel A, the duration of 60 cps was decreased to 365 msec and only 2 responses were produced. RV = right ventricle; ECG = lead II electrocardiogram; 60 cps = the pattern of stimuli applied to the ventricle; T = test pulse.

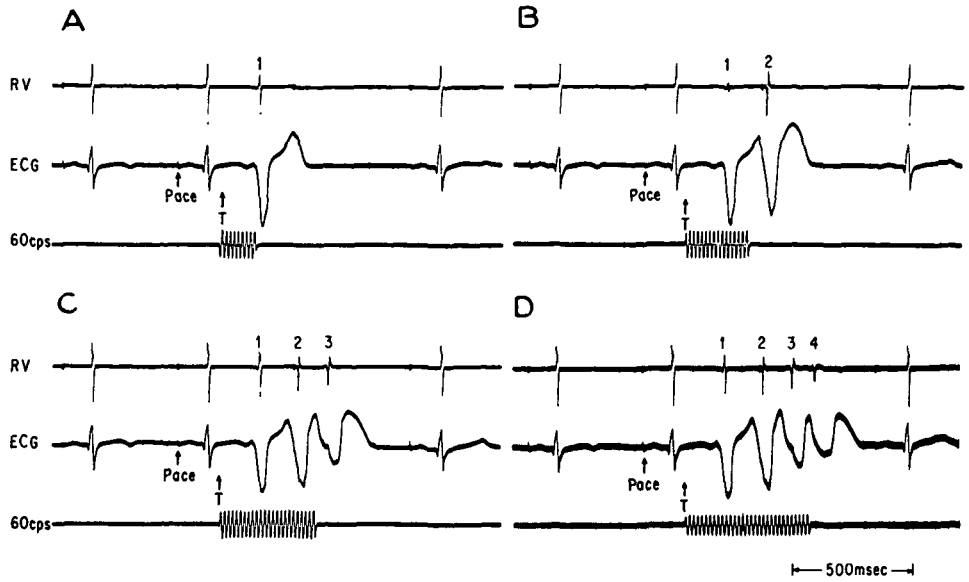

FIGURE 2

The method for testing the effects of changes in the duration of 60 cps on ventricular fibrillation threshold. In panels A-D, the duration of weak 60-cps current was increased stepwise to produce 1, 2, 3 or 4 responses. At each duration, the strength of the current was increased to measure the fibrillation threshold. Abbreviations same as in Figure 1.

times less with 60 cps than with a single shock.

Very weak 60-cps current did not induce fibrillation when applied for shorter periods. This observation is illustrated by the tracings shown in Figure 1. In this experiment, it was first determined that 60 cps for 5 sec and 0.4 ma would induce fibrillation. The duration of 60 cps was then reduced so that the entire period of stimulation fell within the absolute refractory period of the preceding basic beat. The duration was then increased stepwise while the current intensity was maintained at 0.4 ma. The duration of 60-cps stimulation could be adjusted to produce up to 6 responses without inducing fibrillation, but if the duration of stimulation exceeded 800 to 1000 msec, fibrillation was produced.

Although the observations noted above demonstrate that a critical duration (approximately 1 sec) of 60 cps was required to produce fibrillation with weak currents, they did not establish whether there is a relation between the duration of 60 cps and the current intensity required to induce fibrillation. Experiments designed to examine this question are shown in Figures 2 and 3. Figure 2 demonstrates that the duration of weak 60 cps (peak-to-peak current twice the excitation threshold) could be adjusted to produce 1, 2, 3 or 4 ventricular responses without inducing fibrillation. At each duration, the amplitude of 60-cps current was then increased until fibrillation was produced. The results of six such experiments are presented in Figure 3. The amplitude of 60 cps which produced fibrillation is plotted on the vertical axis in milliamperes. When the duration of 60 cps was sufficiently short to produce only 1 ventricular response, the current strength required to induce ventricular fibrillation was approximately 25 ma. In every animal, as the duration of 60 cps was increased to produce 2, 3 or more ventricular responses, the current required to induce fibrillation was reduced. Curves relating the duration of 60 cps to the ventricular fibrillation threshold leveled off between 4 and 6 responses (corresponding to a duration of 60 cps of approximately 1 sec), and further prolongation of the period of stimulation did

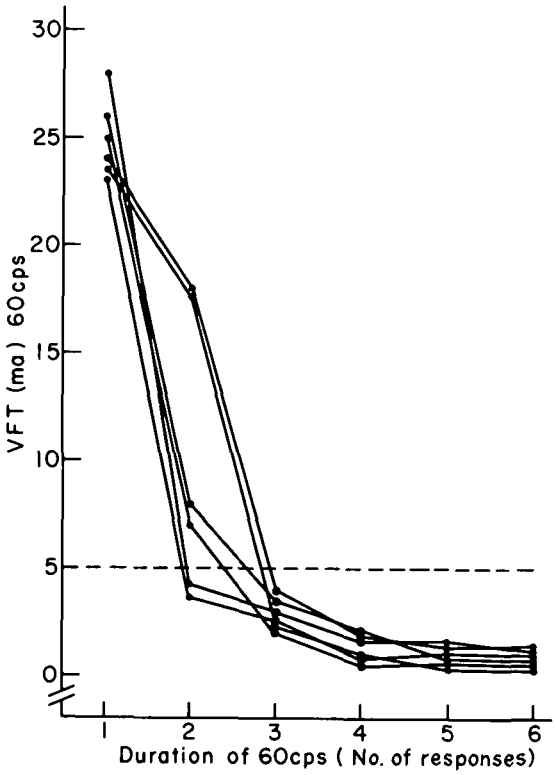

FIGURE 3

The effect of changing the duration of 60 cps on the ventricular fibrillation threshold (VFT). VFT is plotted in milliamperes on the vertical axis, and the duration of stimulation is plotted on the horizontal axis in terms of the number of responses produced at a weak current strength. Data from 6 dogs.

not further reduce the fibrillation threshold.

The data presented above suggested to us that when the ventricle was exposed to 60-cps current for up to 1 sec, each response during the period of stimulation was followed by a reduced fibrillation threshold. To test this hypothesis, two additional types of experiments were performed. In 7 dogs, the ventricular fibrillation threshold was measured with a single pulse applied during the vulnerable period after the basic beat and during the vulnerable periods following each response from the first through the fifth to weak 60 cps. The technique used in this type of experiment is illustrated in Figure 4, panels A-D. In a second group of 9 dogs, the response of the heart to 60 cps was simulated by a train of pulses that produced a pattern of ventricular responses nearly identical to that with 60-cps stimulation. The fibrillation threshold was measured with a single pulse of 10 msec during the vulnerable period after each response. The technique used in this type of experiment is illustrated in Figure 5, panels A-D. The data from one dog in which all three patterns of stimulation were used are presented in Figure 6. The ventricular fibrillation threshold is plotted on the vertical axis and the number of ventricular responses prior to the test is plotted on the horizontal axis. The fibrillation threshold after any given number of responses was comparable whether it was measured with 60 cps or with a single pulse. It also is apparent that the results were comparable regardless of whether the responses prior to the test were induced with 60 cps or with a single pulse; the fibrillation threshold was reduced as the number of responses prior to the test increased.

It can be seen from Figure 1 that when 60 cps was applied to the ventricle, an accelerating tachycardia of several beats in duration preceded the onset of self-sustaining fibrillation. The question whether acceleration per se contributed to the fall in fibrillation threshold during the early period of stimulation was examined in 9 dogs. Ventricular premature beats were induced at varying intervals after every sixth basic beat, and the threshold after the premature response was measured by a single pulse during the vulnerable period. The fibrillation thresholds after premature responses with long and short coupling intervals were compared to those after a basic beat in the same animal. In each dog, the fibrillation threshold after a premature beat with a short coupling interval was lower than that after a basic beat or after a premature beat with a long coupling interval. These data are presented in Figure 7.

Discussion

In 1940 Wiggers and Wégria (7, 8) described the production of ventricular fibrillation by single induction shocks applied at a critical time during ventricular systole. Since

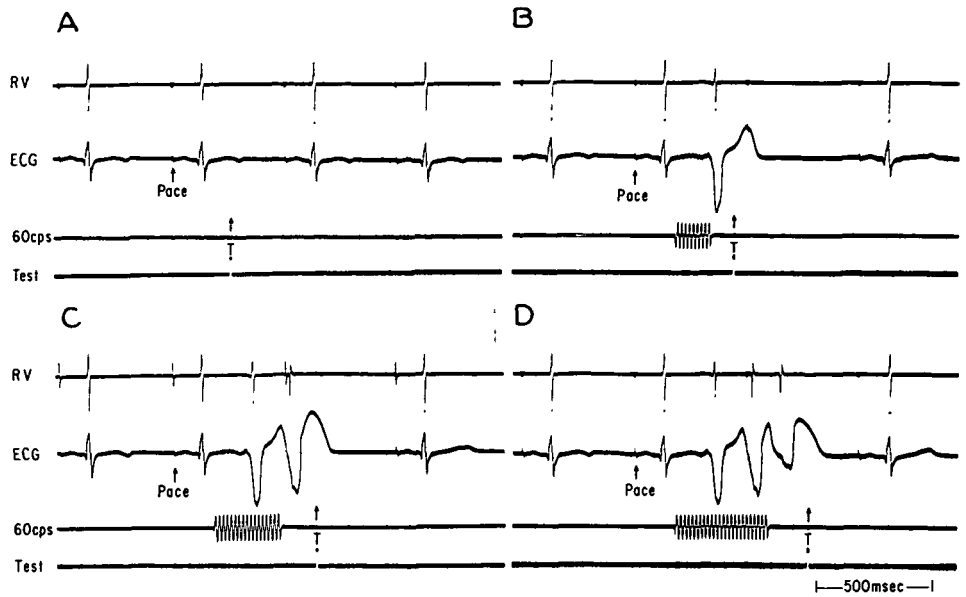

FIGURE 4

The method for testing the ventricular fibrillation threshold with a pulse applied during the vulnerable period after the last of a series of beats in response to 60-cps stimulation. In panels A-D, 0, 1, 2 or 3 responses were induced with 60-cps stimulation and the threshold was measured with a pulse (test) during the vulnerable period after the last beat. See text for details. Abbreviations same as in Figure 1.

shock applied at either an earlier or a later time in the cardiac failed to produce fibrillation, they called this critical period the "vulnerable phase." In subsequent experiments, Wiggers (9) and Moe et al. (10) compared the onset of fibrillation induced by single shocks with that obtained using 60-cps stimulation. Their observations suggested that strong square-wave shocks during the vulnerable period produced a premature ventricular beat and a long-lasting excitatory state at the region of stimulation which was the source of subsequent irregular impulses. They postulated that if one of these spontaneous impulses fell during the vulnerable period after the stimulated beat, fibrillation would result. The observation that fibrillation could be induced by weak 60-cps stimulation applied during diastole was used as evidence to support the above postulate (6). It was reasoned that during the application of 60 cps, an early cycle induced a premature beat and that a later cycle, which fell during the vulnerable period of the premature beat, induced fibrillation. The hypothesis upon which Wégria and Wiggers based their interpretation was that the fibrillation threshold after a premature beat was lower than after a basic beat. In subsequent experiments designed to test this hypothesis, Wégria, Moe and Wiggers (11) were unable to demonstrate that the fibrillation threshold was lower after a premature beat than after a basic beat. They did demonstrate that the vulnerable period was prolonged after a premature response. Han, de Jelon, and Moe (12) observed more recently, however, that the fibrillation threshold was lower after a premature response than after a normally conducted beat, if the threshold was measured at points close to the site of origin of the premature response.

We reasoned that if weak 60-cps current was applied to the ventricle for relatively long periods (1 to 5 sec), a series of premature responses would be produced. If the fibrillation threshold fell after each premature re-

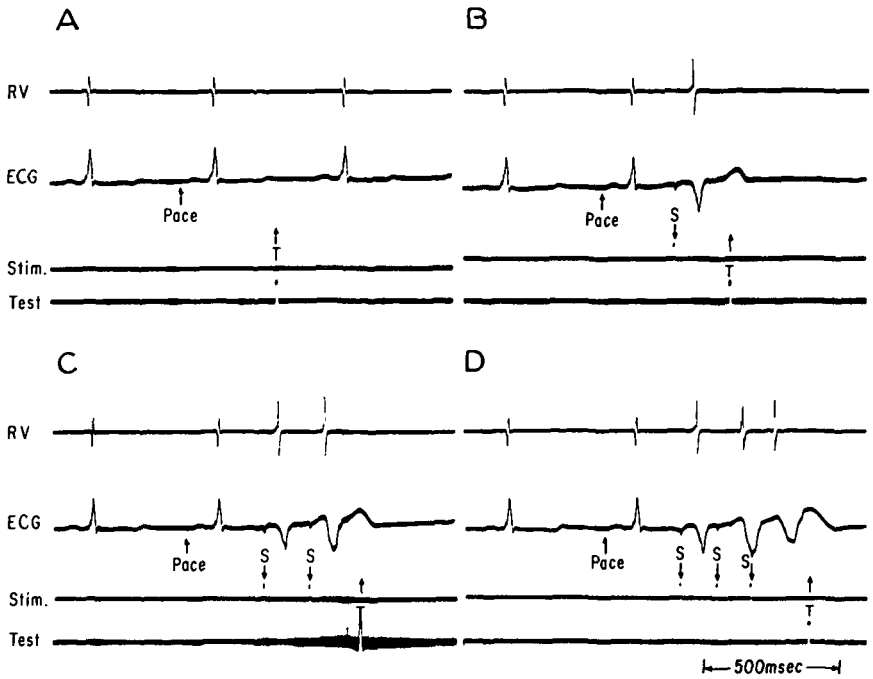

FIGURE 5

The method for testing the ventricular fibrillation threshold with a pulse applied during the vulnerable period after the last of a series of beats induced by a train of pulses. In panels A-D, 0, 1, 2 or 3 responses were induced by pulses (Stim.) and the fibrillation threshold was measured with a pulse (test) after the last beat. See text for details. S = stimulus; other abbreviations same as in Figure 1.

sponse, and if it fell to a level close to the excitation threshold, then at some point during the vulnerable period of one of the responses, the intensity of the stimulation would be adequate to induce fibrillation. If this hypothesis was correct, it should follow that (1) within certain limits the fibrillation threshold measured with 60 cps would be inversely related to the duration of stimulation, and (2) it should be possible to determine that the fibrillation threshold measured with a pulse would decrease not only after one premature beat, as shown by Han et al. (12), but would decrease even further after each of a series of repetitive premature beats.

Our experiments have shown that these predictions were correct. The fibrillation threshold measured with 60 cps was inversely related to the duration of stimulation. This relationship was demonstrated up to a total duration of stimulation of approximately 1 sec (the duration required to produce from 4 to 6 repetitive responses prematurely). When the duration of weak 60 cps was adjusted to produce from 1 to 6 premature beats, the fibrillation threshold measured with a single pulse after the last response was reduced as the number of responses prior to the test increased. After 4 or 5 repetitive premature beats, the fibrillation threshold measured with a pulse or with 60 cps was less than 1 ma and approached the diastolic excitation threshold. These data appear to be sufficient to account for the fact that with 60-cps stimulation lasting for 1 sec or longer, the amount of current required to induce fibrillation is very low. It appears that the basis for this low fibrillation threshold is that 60-cps stimulation induces a short run of premature responses, each of which is accompanied by a substantial fall in the fibrillation threshold during the vulnerable period which follows. The fact that the

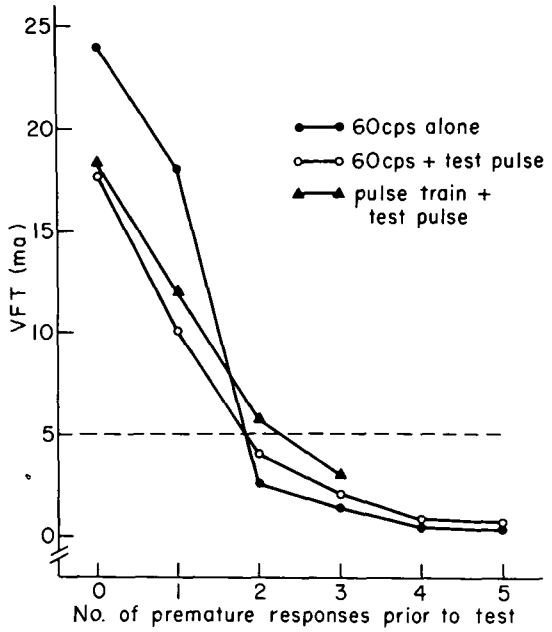

FIGURE 6

The relation between the number of responses prior to the test, and the ventricular fibrillation threshold (VFT), which is plotted on the vertical axis in milliamperes. The number of responses prior to the test is plotted on the horizontal axis. Solid circles = data obtained by varying the duration of 60 cps alone. Open circles = data obtained by inducing 0 to 5 responses with 60-cps stimulation and then testing the fibrillation threshold with a pulse after the last response. Solid triangles = data obtained by producing 0 to 3 responses with a train of pulses and testing the threshold after the last response with a pulse. See text for details.

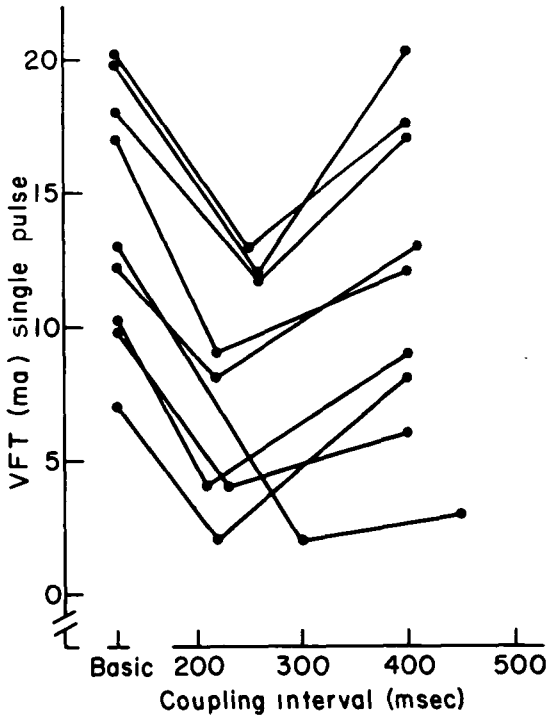

FIGURE 7

The effects of varying the coupling interval between a premature ventricular beat and the last basic beat, on the ventricular fibrillation threshold (VFT) after the premature beat. VFT after a basic beat is plotted on the left. Data from 9 dogs. See text for details.

fibrillation threshold is related to the duration of stimulation is in contrast to the conclusion of Wégria and Wiggers (6).

When the duration of weak 60-cps stimulation was adjusted to produce only one premature response and the strength of the current was then increased until fibrillation was produced, the fibrillation threshold was comparable to that measured with a single pulse during the vulnerable period (approximately 25 ma). Furthermore, the fibrillation thresholds measured with 60 cps or with a pulse were comparable after any given number of premature ventricular beats during a short run. These data, with the considerations noted above, suggest that the basis for the difference between fibrillation thresholds measured with a single pulse and with long-lasting 60 cps is that the single-pulse technique measures the threshold after a normally conducted beat, while 60 cps measures it after the last of a series of premature responses.

It is apparent from the early experiments of Wiggers (13) that the onset of fibrillation induced by a single shock or alternating current is preceded by an accelerating ventricular tachysystole that lasts for several beats. The observation that the fibrillation threshold after a premature ventricular response with a short coupling interval was lower than that after a response with a long coupling interval suggests that acceleration per se may contribute to the fall in fibrillation threshold during an accelerating tachysystole. Han and Moe (14) have demonstrated that temporal dispersion of recovery is greater after premature beats

with short coupling intervals than after premature beats with long coupling intervals. It seems reasonable to assume, therefore, that the degree of nonuniformity of recovery would be enhanced after each response during a period of acceleration; and the resulting nonhomogeneity could contribute to the observed reduction of fibrillation threshold after each response.

Our data demonstrate a possible basis for the observation that a leak of very weak current from improperly grounded equipment may cause ventricular fibrillation in patients (15). These data also are relevant to the observation that stimuli derived from cardiac pacemakers may induce fibrillation. Although the usual output of a cardiac pacemaker is considerably less than that required to induce fibrillation in the normal heart the fibrillation threshold of the diseased heart may be lower than normal. In addition, it is probable that the fibrillation threshold is reduced even further following one or more premature ventricular beats. If the pulse supplied by a pacemaker should fall during the vulnerable period after one or more spontaneous premature ventricular beats, the fibrillation threshold may be lower than the output of the generator, and fibrillation could result (16).

Acknowledgment

The authors express their gratitude to Mr. Philip Talbert for his design of the AC stimulator and to Miss Eleanor Timmerman for constructing the cardiac electrodes. The technical assistance of Mr. James Manley, Mr. William Joyner and Mr. Hubert Barber is also gratefully acknowledged.

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