The mechanisms of atrial fibrillation and flutter have been subjects of continuous controversy. Fibrillation is a more complicated arrhythmia than flutter, and many previous analyses of flutter have been extended to fibrillation. Since the similarity of the mechanisms underlying these two arrhythmias has not been demonstrated, many current theories on the mechanism of fibrillation are therefore not necessarily reliable. Another weakness in the various theories concerning the origin of fibrillation and flutter stems from the possibility that the mechanisms initiating these conditions may be different from the mechanisms maintaining them, so that initiation and maintenance should be considered separately. For instance, proponents of the multiple re-entry and multifocal theories of fibrillation have encountered considerable difficulty in attempting to explain how fibrillation or flutter can spontaneously terminate.

In a previous study of ventricular fibrillation, unmistakable differences in the firing time of adjacent cells were revealed by recording with intracellular electrodes. In spite of this, no such information was obtained with extracellular electrodes, and activity recorded extracellularly did not appear an adequate indication of intracellular events. However, because the electrical activity during the initial and recovery stages of fibrillation was relatively regular, it appeared possible to study propagation of excitation during these stages with extracellular electrodes. Consequently, electrical activity during electrically induced atrial fibrillation has been simultaneously recorded from as many atrial points as possible through closely spaced bipolar direct leads. Even though the complexity of the sequence of activity during maintained fibrillation does not permit a description of this stage from our experiments, the relative simplicity of the initial and recovery phases may furnish a key to understanding both these periods and maintained fibrillation.

**Methods**

Adult mongrel dogs were anesthetized with pentobarbital sodium (36 mg/kg) and artificial respiration was instituted. The chest was opened widely and the heart exposed. Efforts were made to expose all parts of the atrium. In some experiments, the heart was perfused using a modified Langendorff technique in order to explore more thoroughly excitation of the posterior wall of the atrium, the posterior caval orifices, etc.

Atrial fibrillation was induced by stimulating various points in the atrium through two conventional tungsten electrodes, insulated except at the tip and separated by 1 mm to 3 mm. Occasionally, two pairs of stimulating electrodes were used to facilitate induction of fibrillation. Single square wave pulses were used so that the shock artifact would not be present during early fibrillation. Repetitive stimulation was occasionally required. When single shocks were used, the stimulus was triggered by hand. The pulses were delivered as the atria reached the peak of contraction. This technique was found to deliver the stimulus just before electrical repolarization terminated, i.e., in the "vulnerable period." Repetitive stimulation was usually triggered by hand, also. Several shocks were delivered in rapid sequence. Pulse duration was usually 10 msec, but was increased in hearts in which fibrillation was produced with difficulty. Stimulating voltage was usually about 1.5 times the threshold, but was gradually increased when fibrillation was difficult to induce. In one experiment, the stimulating current was gradually raised from below to above the threshold to exclude the possibility of severe
The shocks were generated by a Grass stimulator or by a stimulator assembled from Tektronix waveform generators and Tektronix pulse generators with a separate mixer amplifier and radio-frequency isolation unit.

The recording electrodes were multipolar electrodes of a type described previously. They consisted of fine insulated (0.003 inches) tungsten wires, laid side by side, with their tips 1 mm to 2 mm apart. They were inserted vertically, obliquely or horizontally into the atrial wall. The recording was so arranged that one bipolar lead was recorded from each point on the atrium. The number of analyzable recordings varied from 12 to 20 in each experiment. Some electrodes were dislodged during fibrillation, and records from these were not used.

A Rycom 12-channel cathode ray oscilloscope and an Offner 8-channel direct-writing oscilloscope recorded the data simultaneously; at times up to six channels of a 16-channel oscilloscope were also used. Each channel was connected to two adjacent terminals on a multipolar electrode to make a 1-mm bipolar connection. The standard lead II electrocardiogram was usually fed to one channel of both the Rycom oscilloscope and the Offner oscillograph for two purposes: a) it served as a time reference potential, and b) it permitted identification of (and exclusion from the analysis of) ventricular electrical activity. Leads close to the ventricle at times were influenced by its activity. The paper speed of the Offner oscillograph was usually 500 mm/sec. The film speed used on the Rycom and 16-channel oscilloscopes was usually 100 mm/sec, which provided as good time resolution as the higher paper speed on the oscillograph. Timing signals from a single oscillator were fed into one channel of each recorder. Timing signals consisted of single pulses at 50-msec intervals, with every tenth pulse omitted.

In analyzing the records, the timing signals, the stimulus artifacts, and the standard lead II electrocardiogram were used to correlate the records obtained from the different recorders. A very small correction (about 2.5 msec) was necessitated by the pen lag of the oscillograph. The peak of the main deflection of the atrial depolarization complex was regarded as the instant of local activity in each lead. Sixteen experiments were subjected to detailed analysis; in most of these there were many episodes of fibrillation and recovery.

**Results**

**INITIATION OF ATRIAL FIBRILLATION**

Despite the completely chaotic appearance of the ordinary body surface electrocardiograms during atrial fibrillation, some regular phenomena were noted within the atrium during the initial stage. For example, when simultaneous records from different leads, often widely separated geographically, were compared with each other, the pulse intervals separating the beats tended to be the same. This indicated that excitation was probably being conducted through most of the atrium. Also, the interval between beats at each recording point tended to be constant. The rate of firing at most atrial points ranged from about 530 to 1000 beats per minute during this period. The pulse interval ranged from 60 msec to 112 msec. All recording points tended to fire closely together in time and then to be silent, so that there were coordinated periods of activity and rest. It therefore often seemed that the frequency and pattern of activation were relatively constant for most of the atrium during the initial stage of fibrillation.

Extremely rapid firing was observed in the region near and around the stimulating electrodes in most experiments (in all experiments where records from this area were available). During this period of local firing, depolarization rates ranging from 1000 to 3000 beats per minute, with pulse intervals from 20 msec to 60 msec, were noted (fig. 1, channel S-2). When several leads near the stimulating electrodes were simultaneously monitored, it was found that many points near the site of stimulation tended to fire simultaneously and at the same intervals during the period of rapid firing. Some slight irregularity was, however, noted. For instance, discharge at one point might at one instant precede that at a second point, and slightly thereafter the sequence might be reversed (fig. 1, channels S-2 to 5). Very frequently, the firing rate at one point in the region of rapid firing differed by a factor of two or three from that at another point. In most instances, a series of lines could be drawn to connect the corresponding firing instants in most of the leads; these lines joined every second, third, or fourth spike in the leads showing very rapid firing. These lines produced a "propagation pattern" initially similar to the extrasystolic pattern caused by the electric shock which
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initiated fibrillation. The pattern changed gradually. Furthermore, by correlating this pattern with the anatomical position of each recording point, it was possible to plot the pathway of excitation at the beginning of fibrillation. Similar plots were made during the termination of fibrillation. In some experiments, records from some locations did not fit into the propagation pattern plotted for the majority of points, but when the same plotting procedure was followed for these locations as a group, there were indications of the existence of a second propagation pattern which was partly independent of the first. This situation was particularly common during the termination of fibrillation (see below).

An example of a single propagation pattern is shown in figure 2. In this experiment, the stimulating electrodes were placed in the right lateral side of the right atrial appendage. At the beginning of atrial fibrillation, which started between lines 34 and 35, rapid firing was seen at point O6, midanterior to the stimulated point. Rapid firing was also seen occasionally at point Ru on the right of and anterior to the orifice of the inferior vena cava. As is shown in figure 2A, we can draw a series of successive propagation patterns which are similar in shape to one another. The earliest points excited during each beat were

FIGURE 1
Rapid local firing during the initiation of atrial fibrillation. Ordinate: Designation of recording leads. S: Records taken by the 16-channel oscilloscope with electrodes close to and around the stimulating electrodes. R: Records taken by Rycom oscilloscope with electrodes at atrial points more distant from the stimulating electrodes. II: A standard lead II body surface electrocardiogram. Abscissa: Measurement was started from an arbitrary time before fibrillation.

Rapid local firing is most visible in lead S2, but can be seen in the other S leads. Compare with the propagated activity in the "R" leads, for example, R6, R7, or R8. Deflections corresponding to the QRS deflections in II, more clearly seen in R1 and R3, should be excluded from the analysis. Stimulus artifacts appear between vertical lines 2 and 4, 7 and 10, 11 and 13, and 14 and 16. Broken line at R and curved marks at bottom indicate 50-msec time intervals.
Initiation of atrial fibrillation. A: Analytic diagram of depolarization time at each lead. Ordinate: Designation of recording leads. R: Records taken by Rycom cathode ray oscilloscope. O: Records taken by Offner direct writing oscillograph. Abscissa: Time from an arbitrary moment before fibrillation; interval is 50 msec (100 msec from 30 to 32). Hatched area: Period of single shock stimulation. Dots indicate the depolarization time at each explored site; solid lines joining dots show each depolarization pattern. Broken lines indicate that the propagation occurred only locally, that the discharges at two points did not clearly belong to the same pattern, or that the corresponding discharges at some leads were not observed definitely because of artifacts or local block. B: Diagram of the atria showing depolarization at explored sites at times between lines 34 and 36 in A above. Solid circles: superior or outside sites; open circles: inferior or inside sites; letters and numerals in parentheses correspond to designation of leads in A. Numerals indicate time of depolarization in milliseconds measured from the depolarization time of the site Rn. In drawing this diagram, the atria were "spread out." Therefore, the distance between Rn and O0, for instance, is much smaller than is shown in this figure.

No numerals are shown when corresponding depolarization time is not certain. Stim.: The site of stimulation. SVC: Superior vena cava. IVC: Inferior vena cava. PV: Pulmonary veins.

During many of the experiments, the fibrillation produced by a stimulus was tran-
sient, and the complete course of a fibrillatory episode was recorded. As indicated earlier, the pattern of activation during "established" fibrillation was so complicated that it could not be analyzed. However, as the atrium began to recover from fibrillation, the time relationship became fairly clear, and propagation patterns could usually be drawn for the last few "beats" of the fibrillation. The interval between pulses during these beats tended to be fairly constant, as it did during the onset of fibrillation. The intervals between successive discharges in each lead and at different places also tended to be constant. Local rapid firing sometimes continued until shortly before the last fibrillatory beat, but frequently it was not observed in the last stage. Several different forms of termination of fibrillation were observed as follows:

1. In many experiments, the last few beats before the return of sinus rhythm showed a pattern of activity which indicated that the beats probably originated from a single focus (fig. 4). Specifically, a) the intervals between instants of depolarization were similar at various points (although in a few leads the interval was about twice as long as it was in other leads, indicating conduction block; b) in such a beat one point depolarized earliest, and this was frequently the same as the earliest point in the initial stage. Occasionally, the point of earliest activity shifted to another point, usually close to the site of the original stimulation; c) the interval between the beats was usually sizeable, implying that there was no continuous (or circus) movement. However, as seen in figure 4, conduction was often delayed in one or more regions (R₁₀, R₁₀), so that propagation of excitation is difficult to describe.

2. In about one-third of the recovery phases analyzed, the propagation pattern for the last beat of an episode of atrial fibrillation was different from the patterns for previous beats, which had been similar to each other. Activity started at a point somewhat removed from the site of original stimulation. Frequently, the wave appeared to depolarize all the recording sites and then to be conducted back to the initial site one or more times to produce a large "circus movement" or "re-entry." This pattern is shown in figure 5, which depicts the recovery phase of the episode of fibrillation illustrated in figure 2. In all but one of the last three beats (intervals 82 to 88) the earliest activity was at O₆, R₇, R₆ etc., and the shape of the propagation pattern was similar to that seen in the initial phase. However, the last beat was quite different (lines 89 to 91). It seemed to start at O₂, which lay at about the midpoint of the left posterior side between the orifices of the superior and inferior venae cavae. For some unknown reason, activity seemed to be conducted only to the left atrium (O₆, O₃, R₁₁). Note that in these leads the pulse interval between this and the preceding beat was nearly the same as the preceding interval, whereas in other leads, which seemed to be independent, the last pulse interval was much longer than the preceding one. This finding suggests that the last beat in the latter leads occurred through conduction of the excitation wave from O₂ to
Propagation of a last fibrillatory beat including a circus movement. These patterns show end of the episode of atrial fibrillation from which initial patterns in figure 2 were derived. A: Analytic diagram of depolarization time at each lead. Ordinate: Arbitrary time measurement from a point during fully developed fibrillation. Broken lines are hypothetical propagation. Other notations are the same as in figure 2A. Atrial fibrillation ends at between lines 89 and 91. Beat between lines 95 and 96 is an atrial premature beat, and beat between lines 103 and 105 is a sinus beat. Note that pattern for premature beat immediately after fibrillation shows "straightening" or "shortening" in comparison to the sinus beat. B: Diagram of the atria showing depolarization at explored sites at times between lines 88 and 91 in A. Other notations as in figure 2B.

O₂, O₁, and R₁₁. Between time intervals 89 and 91 activity seemed to move around some circular pathway in the left atrium. The details of this pathway are a matter of conjecture. However, it can at least be said that the propagation to the right occurred thereafter, and that the excitation wave moved from O₂, eventually reached the anterior-inferior part of the line between the orifices of the superior and inferior venae cavae (R₆, R₇, R₈), and again returned to point O₂. Other parts of the excitation wave seemed to have proceeded to the right atrium, crossing the line R₆, R₇, and R₈ without any such circuitous path. Furthermore, since the next to last firing interval at O₂ (87 to 89) was similar to the preceding interval (85 to 87), it is not likely that point O₂ suddenly became spontaneously rhythmic, but more likely that this beat (89) at O₂ was conducted from some other point, possibly R₆, so that there was actually a more extensive circus movement with R₆ and O₂ being excited twice.

It is also noteworthy that a point which was considered to be the starting point for the previous beats was quite inactive during this last instant. Point Oᵦ, which had the most rapid rate of local firing in the initial phase, showed no activity for a fairly long interval (86 to 89). Similar phenomena were observed in other experiments. This indicates the possibility that some mechanism may perpetuate abnormal depolarization after the cessation of local firing.

3. In some experiments, the propagation pattern for the last beat before recovery was of shorter duration than the control sinus beat. Before this beat of short duration occurred, two different types of activity were observed, neither of which seemed to be an incidental finding. a) The activity preceding this beat was sometimes similar to a possible circus movement described above, except that the last beat had a short duration. An illustration is seen in figure 6. b) Sometimes the...
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activity before the beat consisted of independent firing of two or more groups of atrial cells. Each of these cell groups had its own firing interval and was excited at a regular rate. Surprisingly, the "short beat" occurred without any sudden change of the pulse interval. That is, the propagation pattern had gradually become increasingly shorter in duration. It is significant that the last pulse interval was usually longer than (a above) or equal to (b above) the preceding intervals. A few exceptions, in which the final interval was shorter than the preceding ones, were noted, especially when there might have been a circus movement or re-entry. In passing, it may be noted that the premature beat which immediately followed atrial fibrillation occasionally showed a similar short duration (fig. 5A, lines 95 to 96).

4. Uncommonly, one group of atrial recording points was excited between the "beats" of another group or groups of points, even during the last stages of atrial fibrillation. Such firing occurred when the exceptional group had the same pulse interval as the other groups and when it had a different pulse interval.

Discussion

NATURE OF THE ARRHYTHMIA DESCRIBED

Since most of our experiments showed recovery originating through a series of relatively regular phenomena, it is pertinent to state why we regard the arrhythmia induced as fibrillation and not flutter. Although recovery appears to have been a "regular" phenomenon, extremely irregular patterns of activity were recorded at all sites shortly before recovery. This activity was irregular with respect to both the frequency of firing at each point and the relationship between firing rates at various points. Furthermore, the firing rate in the majority of cells was about 600 per minute, which is well above the rates commonly called flutter. The peripheral electrocardiogram at this time was characteristic of fibrillation.

A number of pieces of evidence from these experiments support the concept that fibrillation induced by electrical stimulation originates at a single focus. Events during the initial phase pointing to unifocal origin include: a) rapid local firing at the stimulated point, b) origination of the propagation pattern at the site of local firing, c) similar pulse intervals from beat to beat at each of many leads, and d) the presence of a time gap between two successive beats, which tends to rule out a continuous circulating wave. Additional evidence from the recovery phase indicates that recovery involves a similar pattern. This includes: a) the relatively constant propagation pattern, indicating conduction from an area near the initial focus to the rest of the atrium, and b) reappearance of time intervals between two successive beats, as in the initial phase. Probably the single focus continues its rapid activity throughout transient atrial fibrillation as induced in these experiments. However, for the reasons discussed earlier, the validity of this assumption cannot be clearly demonstrated from our records.

From the observations concerning the initiation and termination of fibrillation in these experiments, we have derived the following theory of the origin and perpetuation of fibrillation. This type of fibrillation seemingly requires a single, rapidly firing focus, which may consist of a single pacemaker cell or a group of cells. (Alternatively, the pacemaker may consist of a small "circus wave" of activity which includes a number of cells in a localized region.) This rapid focus appears to be a necessity for atrial fibrillation in our experiments. In the initial phase, the firing at this focus is so rapid that not all discharges can spread because adjacent cells are at times refractory. Waves of excitation either follow a tortuous pathway or are conducted extremely slowly from the site of the origin of the local firing. Some waves travel only a short distance before being blocked by a wall of refractory cells. Others propagate farther, and approximately half the impulses from the rapid firing zone are conducted to the entire atrium. While these waves spread at submultiples of the maximal frequency, one or more circulating pathways of activity, termed either "circus movement" or "re-entry," may occasionally develop. Owing to the initial rapid firing and...
possibly to a circus-like movement, impulses may restimulate cells just at the end of repolarization, leading to a shortening of the action potential and a slowing of conduction velocity, as shown by Trautwein and Dudel, and this activity may perpetuate the arrhythmia.

As we have indicated, the events during established fibrillation do not permit a simple description by our recording technique. Indeed, they may be too complicated to permit description by any technique. The situation during fibrillation is a completely chaotic one in which all of the mechanisms seen in the initial and terminal states probably participate. During maintained fibrillation, there are probably some areas of the heart where the impulse is being transmitted by conventional cell-to-cell conduction; there is probably a large number of cells firing spontaneously; also there are probably circus movements. The closest description of the arrhythmia might be to call it multifocal or even "omni-focal." It is our belief that our description of the origin and termination of the arrhythmia leads to this conclusion, and that the mechanisms we have been able to demonstrate are active in established fibrillation. We realize that others may not accept this interpretation.

From these experiments we cannot definitely rule out a multifocal theory of the origin of fibrillation, but the relatively short fibrillation that ends spontaneously does not appear to involve multiple separated foci. In the analysis of the initial and recovery phases, the similarity of the pulse interval at different sites over a period of time was stressed. Of course, even when the excitation wave is conducted from one point to another, the pulse intervals need not be always the same at the two points. However, when each of several recording points shows a constant pulse interval, but the intervals at the various points differ, the atria can be thought to have divided into "isolated" regions, activated by different pacemakers. Even where records from these experiments could be interpreted as indicating such separation, the atrium was usually beating as a unit just before recovery, or if there were isolated "units," their number was at most two or three. Shortening or "straightening" of the propagation pattern in the last beats of fibrillation appears to duplicate what is usually assumed to happen when electric shock terminates fibrillation. Probably when fibrillation terminated spontaneously in this fashion, all of the cells were active within a very short interval; there was then a period when all cells were refractory. This led to a pause in the rapid activity and allowed a normal sinus beat to control the atrium. Where the terminal shortening of the propagation pattern was preceded by activity suggesting circus movement, it is possible that the atria were being excited by two waves of activity which tended to fuse. Alternatively, the number of recording points in these experiments may have been too few to display the total duration of depolarization. As the atria do not appear to have any rapidly-conducting, specialized conduction system, the shorter-than-normal duration of a particular beat, if it is a true finding, can be explained if one or more central pacemakers excite the atria over shorter-than-normal conduction pathways. Alternatively, we may attribute the events to random activity.

Scherf and co-workers and Prinzmetal et al. showed that flutter and fibrillation produced by aconitine originated at a single focus in the dog atrium. Lewis' circus movement theory was supported by experiments conducted by Rosenblueth et al., who found that atrial flutter could be easily induced if the muscular bridge between the orifices of the venae cavae was occluded. After confirming both these groups of observations, Kimura et al. and Takayasu et al. concluded that electrically produced atrial flutter differs from that produced by aconitine. In unpublished experiments, we also observed a unifocal arrhythmia with aconitine. The present experiments differ from those of Rosenblueth, Kimura, Takayasu and their co-workers, since our arrhythmia was apparently not flutter. Although circus movements apparently occurred in some of our experiments, this type of activity did not appear to be the cause of the arrhythmia. A block between the venae cavae was not required. It is entirely possible, how-

Circulation Research, Volume XIV, February 1964
ever, that a more "classical" type of circus movement than we observed may develop in fibrillation or flutter.

Summary

1. Atrial fibrillation was induced in dogs by single electrical shocks. Close bipolar direct electrograms were taken from various parts of the atrium; as many as 22 electrograms and a standard lead II electrocardiogram were recorded simultaneously. Initial phase and recovery phase of fibrillation were analyzed.

2. In the initial phase of atrial fibrillation, local firing consisting of rapid tachysystole of 996 to 3000 per minute was observed near the stimulating point in most experiments. Except for the leads showing local firing, the interval between beats at each recording point tended to be constant, and a time gap between two successive beats was observed. A propagation pattern could be plotted which seemed to start from the origin of local firing; some beats were conducted only locally, and others (every second, third or fourth discharge) were conducted widely. The cause of atrial fibrillation was considered to be local firing of one small area of the atrium, i.e., the unifocal theory of the origin of atrial fibrillation was supported.

3. During recovery from atrial fibrillation, features similar to those seen in the initial phase often appeared, although local firing disappeared. In some experiments, the atrium was separated electrically into a few groups of cells beating independently, and in others a "circus pathway" appeared to exist in the last beat. It seems that electrical separation of the atrium into many parts and circus movements, or multiple re-entry, may develop during the course of fibrillation, and that these phenomena perpetuate atrial fibrillation.

4. During the last beat of atrial fibrillation, the time required for all cells to depolarize was occasionally less than the duration of the normal sinus beat. A similar phenomenon was sometimes observed in the premature beats following atrial fibrillation.

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Multiple Recording During Electrically Induced Atrial Fibrillation
TOYOMI SANO, ALLEN M. SCHER and With the technical assistance of O. F. Brown
With the technical assistance of O. F. Brown

Circ Res. 1964;14:117-125
doi: 10.1161/01.RES.14.2.117

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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