Mechanism of Spontaneous Termination of Stable Atrial Flutter in the Canine Sterile Pericarditis Model

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Background. We tested the hypotheses that spontaneous termination of stable atrial flutter is directly related to spontaneous beat-to-beat cycle length oscillations and that block of the circulating reentrant wave front occurs in an area of slow conduction.

Methods and Results. We studied 30 episodes of spontaneous termination of stable atrial flutter induced by atrial stimulation in 11 conscious, nonsedated dogs with sterile pericarditis. Additionally, in 5 dogs, 14 episodes of spontaneous termination of stable atrial flutter were studied with a multisite mapping system to record simultaneously from 190 right atrial electrodes. In the conscious-state studies, atrial flutter cycle length oscillations began 6±1 (mean±SEM) beats before termination in 26 episodes, stable atrial flutter evolved into atrial fibrillation in 3 episodes, and no cycle length change occurred before termination in 1 episode. In the open-chest studies, in all instances, spontaneous oscillations began 7±1 beats before termination. The only consistent oscillation pattern occurred for the last two beats: a long cycle length (149±9 milliseconds) followed by a much shorter cycle length (110±6 milliseconds) (P<.01). Activation maps demonstrated that all cycle length oscillations were explained by changes of conduction in an area(s) of slow conduction in the reentrant circuit. In two instances, the last (short) cycle length was associated with disappearance of an area of slow conduction. In all episodes, the last circulating reentrant wave front blocked in an area of slow conduction in the reentrant circuit. Although not tested, during the last beat, the very early arrival of the circulating reentrant wave front at an area of slow conduction suggests an important role for refractoriness, with head and tail interactions, resulting in block.

Conclusions. Spontaneous termination of stable atrial flutter in the sterile pericarditis model (1) is preceded by beat-to-beat cycle length oscillations that result from changes in conduction in areas of slow conduction in the reentrant circuit and (2) results from block of the circulating reentrant wave front in an area of slow conduction. (Circulation. 1993;88[part 1]:1866-1877.)

Key words: reentry • conduction • atrial flutter

We recently described and characterized the atrial flutter sterile pericarditis model.1-4 With this model, sustained stable atrial flutter is readily induced. During those studies, however, we also noted episodes of induced atrial flutter that terminated spontaneously. Previous studies in the tricuspid ring preparation reentry model from the canine heart5,6 have shown that the spontaneous termination of atrial flutter in this model is a result of long-short cycle length oscillations, which result in block of the reentrant wave front because of refractoriness (head-tail interaction) encountered during the short cycle length.5,6 However, the tricuspid ring reentry model is characterized by a reentrant circuit without an area of slow conduction and with an anatomically determined central area of block. The present study characterizes the spontaneous termination of stable atrial flutter in the canine sterile pericarditis model, in which the reentrant circuit is functionally determined and in which one or more areas of slow conduction are present.3,4 We tested the hypothesis that spontaneous termination of stable atrial flutter in the canine pericarditis model is directly related to spontaneous beat-to-beat cycle length oscillations. Furthermore, because previous studies have shown that termination of atrial flutter with rapid pacing4 or antiarrhythmic drug administration7-10 results from block of the circulating reentrant wave front in an area of slow conduction in the reentrant circuit, we tested the hypothesis that this would be true for spontaneous termination as well.

Methods

Spontaneous termination of induced stable atrial flutter was studied 2 to 4 days after creation of sterile pericarditis1 in a total of 14 adult mongrel dogs weighing 18 to 25 kg. In all these dogs, atrial flutter lasting longer than 5 minutes was also induced. Thirty episodes of spontaneous termination of stable atrial flutter were studied in 11 dogs in the conscious, nonsedated state, and 14 episodes were studied in 5 dogs in the anesthetized, open-chest state. Two dogs had spontaneous

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termination recorded in both closed-chest and open-chest studies. All studies were performed in accordance with guidelines specified by our Institutional Animal Care and Use Committee, the American Heart Association Guidelines on Research Animal Use, and the current Public Health Service Policy on Humane Care and Use of Laboratory Animals.

Creation of the Sterile Pericarditis Atrial Flutter Model

The canine sterile pericarditis model was created as previously described. At the time of surgery, three pairs of stainless-steel wire electrodes coated with FEP polymer except at the tip (O Flexon, Davis and Geck) were sutured on the following selected atrial epicardial sites: the interatrial band (known as Bachmann's bundle), the posterior inferior left atrium close to the proximal portion of the coronary sinus, and the right atrial appendage. The distance between each two electrodes of each pair was approximately 5 mm. These wire electrodes were brought out through the chest wall and exteriorized posteriorly in the interscapular region for subsequent use. At the completion of surgery, the dogs were given antibiotics and analgesics and were allowed to recover. Postoperative care included administration of antibiotics and analgesics.

Studies in the Conscious Nonsedated State

Induction of atrial flutter. In all 11 dogs, beginning on day 2 or 3 after surgery, induction of atrial flutter was attempted in the conscious, nonsedated state. By programmed atrial stimulation or rapid atrial pacing techniques described previously, atrial flutter was induced by pacing from one of the electrode sites (Bachmann's bundle, postero-inferior left atrium, or right atrial appendage). All pacing was performed with stimuli of at least twice diastolic threshold and up to 20 mA with a modified Medtronic 5325 programmable, battery-powered stimulator with a pulse width of 1.8 milliseconds. As we have previously shown, there is no difference between the atrial flutters induced with either pacing protocol.

During this induction of atrial flutter, ECG leads I, II, and III were recorded simultaneously with the stimulus artifact from the pacing site and with bipolar electrograms obtained from the other two electrode sites. During induced atrial flutter, the same recordings were made, except that atrial electrograms were then also recorded from the pacing site used to induce the atrial flutter. All electrocardiograms were filtered between a band pass of 0.1 and 500 Hz and the epicardial atrial electrograms between a band pass of 30 and 500 Hz. Data were monitored continuously with an Electronics-for-Medicine VR-16 switched beam oscilloscopic recorder and recorded on photographic paper at a speed of 100 mm/s. All data were also recorded simultaneously on FM tape on a Honeywell 101 FM tape recorder for subsequent playback and analysis.

Characterization of the termination of stable atrial flutter. For purposes of the conscious nonsedated studies, stable induced atrial flutter was defined as lasting longer than 1 minute. All 30 episodes were studied in the absence of cardioactive drugs. After the induction of stable atrial flutter, the rate, cycle length, and duration of the stable period of the atrial flutter were characterized. Stable atrial flutter was documented by the regularity of the beat-to-beat atrial cycle length, polarity, amplitude, and morphology of the recorded atrial electrogram. The duration and type of rhythm that developed before the spontaneous termination of stable atrial flutter were also characterized and further analyzed, along with the associated atrial electrogram morphology, amplitude, polarity, and cycle length oscillations. During these studies, the last of the three epicardial recording sites activated was used to determine cycle length.

Studies in the Open-Chest State

Multipoint mapping. On day 4 after surgery, an open-chest study was performed during 14 episodes of induced stable atrial flutter in five dogs. Each dog was anesthetized with pentobarbital (30 mg/kg IV) and mechanically ventilated with a Harvard respirator (Harvard Apparatus, Natick, Mass). The body temperature of each dog was kept within the normal physiological range throughout the study by a heating pad. The chest was opened and the heart exposed by standard techniques. After the heart was exposed, a previously described electrode array containing 190 unipolar electrodes (Fig 1) arranged in 95 bipolar pairs (Fig 2) was placed on the right atrial free wall and secured with a Velcro belt. The interelectrode distance between each two bipolar electrode pairs in the array was 1.5 mm, and the distance between the centers of bipolar electrode pairs was 4.2 mm diagonally and 6 mm perpendicularly (Fig 1). After placement of the electrode array, the same pacing protocol described above was used to induce atrial flutter.

Data acquisition during open-chest studies. Before, during, and after the induction of stable atrial flutter and during and immediately after its spontaneous termination, unipolar electrograms were recorded simultaneously from all 190 electrodes in the array along with ECG lead II. Data recording and processing were performed with a cardiac mapping system designed at Case Western Reserve University. All signals were individually amplified, filtered between a bandwidth of 1
to 500 Hz, sampled at 1000 Hz, and digitized with a 12-bit analog-to-digital converter. The data were then transferred to a 68020 coprocessor with 4 megabytes of memory via optoisolators. Data collection and processing were performed with this coprocessor, which is resident to a Sperry IT PC host system (IBM AT compatible). A SGT PEPPER (Number Nine Computer Corp, Cambridge, Mass) graphic processor with color monitor was used to display raw and processed data. The system had all processing units (68020, Sperry, SGT PEPPER) designed to operate in parallel. This parallel organization gave the mapping system real-time processing capability. The system was capable of storing and archiving 30 minutes of continuous data from all electrodes. Data were archived on either a floppy disk, hard disk, or tape in their raw, unipolar format.12-14 Two methods were used to record during the period of stable atrial flutter and both during its onset and spontaneous termination. Data either were recorded continuously during the entire episode of atrial flutter and edited later or were recorded continuously into a 4-second circular display buffer that retained only the 4 seconds of data before the manual stopping of data acquisition. The second method required that information from an event of interest (onset, termination) associated with an episode of atrial flutter can be recorded within 4 seconds, and data acquisition can be reinitiated to capture the next event of interest.

Data analysis: Analysis of data consisted of selecting activation times and computation of an isochronous map with a maximum resolution of 1 millisecond. Data in both their raw unipolar format and processed bipolar format (subtracted in the software) were available to assist in the selection. Data were filtered in software with a low cutoff frequency (high-pass filter) of 10 Hz before analysis to avoid baseline drift of the electrograms. A 600-millisecond analysis window was chosen from within 4 seconds of stored data. A time reference signal was selected from one of the electrode sites and was used to depict zero activation time. The electrograms recorded at each site during the time window were displayed on a graphics screen, and selection of activation time was done manually with a cursor. The moment of activation at each site was taken as the peak of the first rapid deflection in a predominant monophasic recording or as the time of the intrinsic deflection in a predominantly biphasic recording. The activation time at sites at which multiple component electrograms were recorded was assigned to the major deflection (highest amplitude for bipolar electrograms or fastest downstroke for unipolar electrograms). Care was taken first to identify all components that were caused by ventricular activation with the QRS complex in the ECG as a marker. If there were two discrete deflections for one atrial complex in the ECG (ie, a so-called double potential), the activation time at these sites was assigned to the deflection with the highest amplitude for bipolar electrograms or the more rapid deflection for unipolar electrograms.15

Because of the differences in size of the right atrium from dog to dog, anatomic landmarks (venae cavae, right atrial appendix, atrioventricular groove) were identified and positioned on the grid (electrode array) by visual inspection. For each atrial beat, activation time at each site was placed on an anatomic grid representing activation at each bipolar recording site, and isochronous lines at 10-millisecond intervals were drawn manually.

Definitions

In this study, slow conduction velocity <0.2 m/s.3,4,16 Stable atrial flutter and atrial fibrillation were defined by a modification of the criteria of Wells et al,11,17 which are based on a single bipolar atrial electrogram recording, with criteria based on sequence of activation mapping. Stable atrial flutter was defined as a rapid atrial rhythm (rate, >240 beats per minute) characterized by a constant beat-to-beat cycle length, polarity, morphology, and amplitude of the recorded bipolar electrograms. Stable atrial flutter was further defined by the presence of a single, constant reentrant circuit with a constant atrial activation sequence. Atrial flutter with cycle length oscillations was defined by the presence of a single, constant reentrant circuit with a constant activation sequence but with cycle lengths that changed by at least 3 milliseconds per beat. Atrial fibrillation was defined as a rapid atrial rhythm (rate, >260 beats per minute) characterized by variability of the beat-to-beat cycle length, polarity, morphology, and/or amplitude of recorded bipolar atrial electrograms. Atrial fibrillation was further defined by the presence of an unstable reentrant circuit (ie, one continuously changing in location and/or length of the central area of block around which the reentrant circuit circulated); more than one reentrant circuit; and/or multiple, simultaneously circulating activation wave fronts. Spontaneous termination of stable atrial flutter was defined as the cessation of atrial flutter and return to sinus rhythm without any drug, pacing, or mechanical intervention.

Statistics

Data are expressed as mean±SEM. Basic comparative statistics were performed with Student’s t test for paired or unpaired data when appropriate. A confidence level of 99% was considered statistically significant.
Results

Studies of Spontaneous Termination of Stable Atrial Flutter in the Conscious, Nonsedated State

Thirty episodes of spontaneous termination of stable atrial flutter in 11 dogs were analyzed. Atrial flutter lasted a mean of 227±28 seconds (range, 69 to 360 seconds) before termination. In all instances, the atrial flutter cycle length (mean, 123±3 milliseconds; range, 105 to 155 milliseconds) was constant during the period of stable atrial flutter.

Recognizing the limitation inherent in recording bipolar electrograms from only three widely separated sites, none of which may be near the site of block in the reentrant circuit, three patterns were observed in the period preceding the spontaneous termination of stable atrial flutter (Fig 3):

1. In 26 of the 30 episodes (86.6%), after the period of stable atrial flutter cycle length, oscillations in cycle length began, unassociated with changes in morphology, polarity, or amplitude of the recorded electrograms. A change in atrial cycle length was first noticed in the electrograms recorded from the Bachmann’s bundle site in 60% of the episodes, from the posteroinferior left atrial site in 28% of the episodes, and from the right atrial appendage site in the remaining 12%. The mean number of oscillatory cycles before termination of atrial flutter was 6.4±0.6 (range, 3 to 13). The rhythm spontaneously terminated with a long-short cycle length sequence for the last two cycles in 18 episodes (Fig 3A).

For these two last cycles, the mean long cycle length was 126±6 milliseconds (range, 90 to 180 milliseconds), and the mean short cycle length was 99±4 milliseconds (range, 80 to 140 milliseconds) (P<.01). The relatively wide range of dispersion of these long and short cycle lengths was because in 7 of these 18 episodes, the duration of the next to the last cycle length was actually longer than the previous stable atrial flutter cycle length. In 10 of the 18 episodes, the duration of the last cycle length was actually shorter than that of the previous stable atrial flutter, and in one episode it was the same as the previous stable atrial flutter cycle length. The rhythm spontaneously terminated with a short-long cycle length sequence for the last two cycles in 7 episodes or with no change in cycle length for the last two beats in one episode. However, as will be seen from the subsequent open-chest multisite mapping studies, within the reentrant circuit itself, the last two cycles before termination were always long-short.

2. In 3 of the 30 episodes (10%), atrial fibrillation evolved from stable atrial flutter, once after 5 minutes 25 seconds, once after 5 minutes, and once after 3 minutes 20 seconds of stable atrial flutter (Fig 3B). The atrial fibrillation that evolved lasted 21 seconds, 1600 milliseconds, and 850 milliseconds, respectively, before spontaneous termination (Fig 3C).

3. In 1 of the 30 episodes (3.4%), no oscillation in atrial flutter cycle length was recorded before spontaneous termination of the induced stable atrial flutter and return to sinus rhythm (Fig 3D). Again, because of the limited number of recording sites during this episode, it was impossible to determine whether there may have been cycle length oscillations elsewhere, eg, from sites within the stable atrial flutter reentrant circuit.

Multisite Mapping Studies of the Spontaneous Termination of Stable Atrial Flutter in the Open-Chest State

Fourteen episodes of spontaneous termination of induced stable atrial flutter in five dogs were analyzed. Atrial flutter lasted a mean of 162±36 seconds (range, 60 to 360 seconds) before spontaneous termination. The reentrant wave front of the induced stable atrial flutter circulated in a clockwise direction around a central area of apparent functional block in 8 episodes and in a counter-clockwise direction in 6 episodes. The mean cycle length of induced stable atrial flutter was 143±7 milliseconds (range, 112 to 192 milliseconds). In all instances, during the period of stable atrial flutter, the beat-to-beat cycle length was constant, the mean beat-to-beat cycle length variability being ±2 milliseconds (Fig 4). Spontaneous oscillations began a mean of 7±1 beats (range, 2 to 14 beats) before spontaneous termination of stable atrial flutter (Fig 5). The first oscillation was an increase in cycle length in 7 episodes and a decrease in cycle length in 7 episodes. There was no consistent pattern of beat-to-beat oscillations except for the last two cycles, which were always a long cycle length (mean, 149±9 milliseconds; range, 106 to 200 milliseconds) followed by a short cycle length (mean, 110±6 milliseconds; range, 78 to 142 milliseconds) (P<.01). A plot of the cycle length oscillations of four representative episodes is shown in Fig 6.

Fig 7 shows the isochronous map of the right atrial free wall during stable atrial flutter in the same representative example as shown in Fig 4. In this case, the atrial flutter was sustained for 6 minutes before spontaneous cycle length oscillations occurred. Note that the reentrant excitation wave front circulates in a counterclockwise direction around an area of apparent functional block, represented by dashed lines in the center of the reentrant circuit. As evident by the crowding of isochronous lines, regions of relatively slow conduction were present in the atrial flutter reentrant circuit that anatomically correspond to the upper portion of the sulcus terminalis (electrode site G), the lower portion of the sulcus terminalis (electrode site B), and in the pectinate muscle area (electrode site D). It was in these regions that the most important changes associated with cycle length oscillations were observed (Fig 8).

The first atrial flutter cycle length oscillation, a decrease in cycle length from 191 to 187 milliseconds, occurred at site B (Fig 5). However, note that the cycle length at five selected sites in the reentrant circuit increased and at one site was unchanged (site C, Fig 5). Note that with the next and subsequent beats during continued cycle length oscillations, there was no consistent pattern at all sites, ie, the cycle length increased at some sites but decreased at other sites for the same reentrant beat (Fig 5). For all studies, however, there were two consistent findings: at the site just proximal to the block, the last cycle length was always relatively quite short, and the electrogram recorded at that site was always clearly different in morphology than during both stable atrial flutter and the immediately preceding period of cycle length oscillations. All these changes are explained by analysis of the activation maps of these beats (see Fig 8).
FIG 3. This page and facing page. Tracings showing three representative examples of spontaneous termination of stable atrial flutter in the conscious nonsedated state. Each example shows recordings of ECG leads I, II, and III recorded simultaneously with bipolar electrograms from the right atrial appendage (RAA), the Bachmann's bundle region (BB), and the posteroinferior left atrium (PLA) at the termination of atrial flutter. A. After 230 seconds of stable atrial flutter, cycle length 125 milliseconds, spontaneous atrial flutter cycle length oscillations developed (denoted by *) and continued for nine beats until the atrial flutter terminated. The last two cycles in the PLA electrogram were 120 and 95 milliseconds, respectively. B and C. After 5 minutes 25 seconds of stable atrial flutter, atrial fibrillation developed spontaneously (B) and lasted for 21 seconds, until it finally terminated with return to sinus rhythm (C). D. After 4 minutes of stable atrial flutter, cycle length 125 milliseconds, atrial flutter spontaneously terminated without any cycle length oscillations. A indicates atrial complex; V, ventricular complex.
Fig 8A through 8G shows the sequence of activation maps for the last six beats before spontaneous termination of induced stable atrial flutter and the map of the first spontaneous sinus beat. Fig 8A shows the activation map of the last stable atrial flutter cycle length. This figure is basically similar to Fig 7. Note the reentrant circuit and the areas of relatively slow conduction, characterized by the crowding of isochronous lines. In these areas, the activation wave front propagates perpendicularly to the longitudinal orientation of the muscle fibers. The regions of slow conduction are located in the upper and lower portion of the sulcus terminalis (which are also pivot points) and the pectinate muscle area. When the activation wave front passes through the lower portion of the sulcus terminalis, the conduction velocity decreases (crowding of isochrones between sites A and B), then the activation wave front accelerates and then decelerates again (crowding of isochrones at site D). This phenomenon can be seen again at site G, where the activation wave front crosses the upper portion of the sulcus terminalis.
The first cycle length oscillation noted in the atrial electrogram corresponding to electrode site B in Fig 5 is not evident in map 8B because the increment in cycle length at that site was <10 milliseconds, the interval of each isochrone. However, the earlier arrival of the wave front at site B led to earlier arrival of the activation wave front at electrode site D. This was associated with an increase in isochrones from three (map 8A) to four (map 8B) at that site (D), which represents the increase in cycle length from 191 to 202 milliseconds shown in Fig 5 (site D). There were no major modifications in the area of slow conduction located in the upper portion of the sulcus terminalis.

Activation map 8C shows that the decrease in atrial flutter cycle length from 202 to 192 milliseconds is associated with a decrease in one 10-millisecond isochronous line in an area of slow conduction, the lower portion of the sulcus terminalis (site B). The rest of the reentrant circuit showed no change in isochronous lines. Activation map 8D shows the next beat. Even though the change in cycle length is just 4 milliseconds (192 to 196 milliseconds), both areas of slow conduction (lower portion of the sulcus terminalis and pectinate muscle area) showed changes in the number of isochrones. The lower area of slow conduction (which included site B) increased the number of isochrones by one, and the pectinate muscle area of slow conduction (which included site D) decreased by one isochrone, so that the net change in cycle length was 4 milliseconds. Cycle length oscillations continue in map 8E as a result of

![Diagram](http://circ.ahajournals.org/)

**Fig 4.** ECG lead II recorded simultaneously with electrograms from selected electrode sites around the atrial flutter reentrant circuit shown in Fig 6. Activation times are in milliseconds. Arrows show the relative activation sequence, and dashed lines connect bottom and top electrograms to indicate the completion of the reentrant circuit. During stable atrial flutter, the beat-to-beat cycle length (191 milliseconds) was constant at all recording sites. Also note that the electrograms show constant beat-to-beat polarity, morphology, and amplitude typically seen during atrial flutter.

**Fig 5.** Same ECG lead II and atrial electrograms from the same episode as illustrated in Fig 4, showing the spontaneous termination of the previously stable atrial flutter. As seen in the atrial electrograms recorded from site B, the first spontaneous change in atrial flutter cycle length, denoted by a circle, was a decrease in cycle length from 191 to 187 milliseconds. After that first oscillation, a variable sequence of cycle length oscillations followed, until finally the atrial flutter spontaneously terminated with a long-short cycle length sequence for the last two cycles at electrode site D. Arrows show the relative activation sequence, and dashed lines connect bottom and top electrograms to indicate the completion of the reentrant circuit.
changes in the same two areas of slow conduction already noted, until spontaneous termination occurs as a result of block of the circulating reentrant wave front in an area of slow conduction—in this episode, the pectinate muscle region (map 8F). Note also the disappearance of the area of slow conduction in the lower portion of the sulcus terminalis associated with the last circulating reentrant wave front. Importantly, the disappearance of this area of slow conduction led to the relatively early arrival of the wave front at the area of slow conduction in the pectinate muscle region, resulting in block. Map 8G shows the sequence of activation during the first sinus beat after the spontaneous termination. There was no difference between this map and the maps recorded during sinus rhythm before atrial flutter induction in this or in any other episode.

Isochronous maps during the period of atrial flutter with cycle length oscillations demonstrated that all changes in cycle length were explained by similar changes in conduction time in an area or areas of slow conduction of the atrial flutter reentrant circuit. There was no change in the length of the line of functional block in this or any other episode analyzed, as evident from both the sequence of activation maps and the sites from which double potentials were recorded. In all instances, the last circulating wave front blocked in an area of slow conduction in the reentrant circuit, nine in the lower portion of the sulcus terminalis and five in the pectinate muscle region, and was independent of the direction (clockwise or counterclockwise) of the reentrant wave front. In the eight dogs in which more than one episode of spontaneous termination of stable atrial flutter was analyzed, the block of the last circulating wave front occurred in the same location.34 In two episodes, the last reentrant wave front was associated with complete disappearance of a previous area of slow conduction. In the other episodes, the isochrones in the area of slow conduction decreased during the last reentrant atrial flutter beat. Thus, in all episodes, important changes in conduction through an area of slow conduction caused the circulating reentrant wave front to arrive relatively early at the next area of slow conduction, resulting in block.

**Discussion**

From analysis of the data from both the closed-chest and the open-chest studies in this model, several observations can be made. First, the spontaneous termination of stable atrial flutter is always preceded by cycle length oscillations. The cycle length oscillations were not simply organized in a sequential long-short pattern, as previously demonstrated by Simson et al in a canine model of atrioventricular reentry in which the accessory atrioventricular connection was an electric circuit. Furthermore, the sequential cycle length changes did not display a regular pattern until the last two cycles, which always formed a long-short sequence, as previously shown by Frame et al during spontaneous termination of reentrant excitation in the tricuspid ring preparation from the canine heart. Cycle length oscillations were also one of the most important mechanisms found in spontaneous termination of atrioventricular reentrant tachycardia in 24 patients by Ross et al, in which all episodes of block in the reentrant circuit were observed after a short cycle during cycle length alternations.

Second, comparison of the data from several recording sites within the reentrant circuit demonstrates that the cycle length may prolong at some sites and shorten at other sites during the same beat (see Fig 5). Similar behavior was observed by Frame et al,6 despite the fact that the reentrant circuit in the pericarditis model always includes one or more areas of slow conduction, whereas the reentrant circuit in the tricuspid ring model does not. Thus, not having sequences of activation maps
FIG 8: This page and facing page. A through G, Seven consecutive activation maps beginning with the last stable atrial flutter cycle length (CL) (map A). Map B shows the activation map for the first atrial flutter cycle length oscillation. Note that this oscillation is associated with an increase of one isochrone line in the area of slow conduction in the pectinate muscle region (site D). Activation map C shows that the decrease in atrial flutter cycle length is associated with a decrease in a 10-millisecond isochrone line in the lower portion of the sulcus terminalis (site B). Activation map D shows an increase in cycle length, and the prolongation of the cycle length is associated with a prolongation of conduction time in the lower portion of the sulcus terminalis (site B) and also with a decrease of conduction time in the pectinate muscle region (site D). Maps C and D show that even a minor change in cycle length in the atrial flutter reentrant circuit can be associated with important changes in more than one area of slow conduction. Oscillation of cycle length continues (map E) and is associated with changes in isochrones in the same two areas as already noted, until spontaneous termination occurs in a previous area of slow conduction, the pectinate muscle region (map F). Note the disappearance of the area of slow conduction in the lower portion of the sulcus terminalis (map F). Map G shows the first sinus beat. This map was the same as the sinus beat maps recorded before the atrial flutter induction. IVC indicates inferior vena cava; RAA, right atrial appendage; SVC, superior vena cava.

that include the atrial flutter reentrant circuit emphasizes the limitations of recording from a limited number of selected sites, especially when they are distant from the reentrant circuit. In fact, this probably explains why not all the spontaneous terminations of stable atrial flutter in the closed-chest portion of our study manifested a long-short cycle length sequence for the last two cycles.
Third, there was no change in the central area of functional block around which the reentrant wave front circulated during the cycle length oscillations, since its location and length remained unaltered. Also, no new area of functional block appeared. Therefore, occurrence of cycle length oscillations could not be explained by changes in the central area of block. Also, the fact that the reentrant circuit is constant explains the absence of changes in the configuration of atrial electrograms recorded during the cycle length oscillations.

Fourth, the areas of slow conduction in the reentrant circuit play a key role in the generation of cycle length oscillations preceding spontaneous termination of stable atrial flutter in the sterile pericarditis model. This behavior is different from the tricuspid ring model, where an area of slow conduction was not observed. The present study does not elucidate the process of initiation of cycle length oscillation, nor does it demonstrate, per se, the factors that are responsible for the termination of stable atrial flutter. However, it clearly demonstrates that, after initiation of cycle length oscillations, changes in conduction velocity through an area (or areas) of slow conduction critically affect subsequent cycle length oscillations and ultimately lead to block. The only areas of slow conduction in the reentrant circuit that influenced cycle length oscillations were in the lower portion of the sulcus terminalis and in the pectinate muscle region. In all cases analyzed, an area of slow conduction in the region of the upper portion of the sulcus terminalis did not contribute to the oscillations. Why this occurred is uncertain, and it is possible that with more studies, this area, too, would have been involved.

Fifth, it was striking that the interruption of the reentrant wave front always occurred in an area of slow conduction. This is consistent with previous reports from our laboratory that showed that interruption of atrial flutter in this model by rapid pacing occurred when the orthodromic wave front from the pacing impulse blocked in an area of slow conduction. In addition, it has been shown that drug-induced termination of atrial flutter in this model also resulted from block of the circulating reentrant wave front in an area of slow conduction.

Further Analysis of Spontaneous Termination of Stable Atrial Flutter in the Conscious, Nonseated (Closed-Chest) State

These studies clearly demonstrate that spontaneous termination of stable atrial flutter is preceded by cycle length oscillations. However, the three selected atrial electrogram recording sites were all rather distant from
the actual reentrant circuit in the free wall of the right atrium. Thus, the fact that not all episodes of spontaneous termination of stable atrial flutter analyzed in the closed-chest state displayed a long-short cycle length sequence of the last two cycles before resumption of sinus rhythm most likely reflects this limitation of the studies, as does the fact that no cycle length oscillations were observed during one episode of spontaneous termination. Furthermore, during this portion of the studies, transient atrial fibrillation spontaneously evolved from the atrial flutter in 10% of episodes. Since this never happened during an open-chest study, it is difficult to speculate either about the mechanism that underlies this change in rhythm or why the atrial fibrillation subsequently terminated spontaneously.

**Underlying Mechanism of Spontaneous Termination of Stable Atrial Flutter**

As noted above, the last two cycles that preceded spontaneous interruption of atrial flutter always displayed a pattern of a long cycle length followed by a relatively short cycle length. Although refractoriness was not measured in our experiments, it is tempting to suggest, as previously demonstrated by Frame et al.6,8 in the tricuspid ring reentry model, that the circulating reentrant impulse blocked because it encountered refractoriness. In other words, early arrival of the reentrant impulse at a critical site in the reentrant circuit after a previously much longer cycle length caused the impulse to arrive at a time when that site was still refractory. However, as already discussed, the reentrant circuit in the pericarditis model includes one or more areas of slow conduction. It was in these areas where all the changes in conduction occurred during the oscillations, and it was in one of these areas that block occurred.

These consistent findings imply that the areas of slow conduction in the reentry circuit play an important role in the induction of cycle length oscillations and the spontaneous termination of reentry. Termination can result from an enhanced degree of head-tail interaction in one of the areas of slow conduction (ie, an increase in the local wave length resulting from increased local refractoriness). Another possibility is that a low safety factor for conduction in these areas results in failure of propagation. Several factors can contribute to reduced safety, including structural changes such as increased degree of cellular uncoupling at gap junctions,20,21 increased degree of uncoupling between fiber bundles because of edema and cellular inflammatory response, and abrupt changes in load caused by wave front turning (“fanning effect”) relative to fiber direction. In addition, abnormalities of membrane processes can lead to depolarized resting potentials and decrease in sodium current, which also compromise the safety factor. Of course, it is likely that a combination of these factors results in propagation failure in the region of slow conduction. Using a computer model of reentry, Quan and Rudy22 have demonstrated that the presence of inhomogeneities (eg, regions of slow conduction) in the reentry circuit greatly increase the likelihood of conduction block. This theoretical prediction is consistent with the experimental observation of the present study that inhomogeneous regions in the reentrant pathway play an important role in the termination of reentry.

Regarding the observed cycle length oscillations, the theoretical simulations of reentry22,23 demonstrate beat-to-beat alternans in action potential duration during both sustained and nonsustained reentry. The ionic basis for these oscillations is alternating kinetics of the slow calcium channel and of the delayed rectifier potassium channel. Recently, using a newly developed model of the ventricular action potential24 in the theoretical ring model of reentry, Rudy and Quan (unpublished results) demonstrated that spontaneous termination was preceded by cycle length oscillations that typically lasted for 10 beats. At the site of termination, the last two beats displayed a long-short pattern of cycle length oscillations, leading to block. These simulations were conducted in a model of a homogeneous reentrant pathway, suggesting a dominant role of refractoriness in termination of reentry in a homogeneous circuit. As stated above, the reentrant pathway associated with atrial flutter is inhomogeneous and includes several regions of slow conduction. Under these conditions, it is likely that the interplay between refractoriness and conduction properties in the regions of slow conduction brings about cycle length oscillations and spontaneous termination.

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