Atrial Tachycardia, Flutter, and Fibrillation

By R. H. Lyons, M.D., A. Farah, M.D., G. K. Moe, M.D., Ph.D., and J. A. Ahlström, M.D.

DR. RICHARD H. LYONS: Today we are going to discuss abnormal atrial rhythms. It has always seemed strange to me that though the physiologists have described delirium cordis since the beginning of vivisection, abnormal atrial rhythms were not recognized clinically until approximately 1880, when Sir James Mackenzie was able to notice in pulse tracings that the atrial impulse of the venous pulse disappeared in some patients who had irregular heart beats. Fast heart rates had been noticed earlier and William Stokes had described in 1856 a typical example of paroxysmal atrial tachycardia in a patient who was relieved by emetics. It was not until 1906, however, that Cushing and Edmonds were able to relate the phenomenon of atrial fibrillation in man to atrial fibrillation in animals. In 1908 Rotherber of Vienna proposed the theory that atrial dysrhythmias arose from multiple ectopic foci, and in 1920 Sir Thomas Lewis proposed the theory of a circus rhythm. In spite of these conflicting theories, little attention was paid them until recently when a variation of the Rotherber concept was revived as the sole cause of abnormal atrial activity.

Because of time we will not discuss atrial extrasystoles per se except to mention that they may have many potential causes but only occasionally can cause and effect be clearly demonstrated in man. Our discussion will involve primarily three types of abnormal atrial activity: atrial flutter, atrial fibrillation, and paroxysmal atrial tachycardia. Dr. Farah, how do you resolve the conflict between an ectopic focus and a circus rhythm as the cause of these abnormal rhythms?

DR. ALFRED FARAH: In recent years a unitary theory of production of atrial arrhythmias has been proposed that attempts to explain all the atrial arrhythmias on the basis of a rapidly firing ectopic focus. This hypothesis has its main merit in being a relatively simple and easily understandable concept. However, this simplified hypothesis cannot stand up to the experimental test. It has been shown by Rosenblueth and Garcia Ramos that in dogs one can set up a self-perpetuating type of atrial flutter that conforms to a circus movement. The important factors that determine a circus movement are the length of the pathway surrounding an obstacle, the conduction velocity of the impulse, and the refractory period of the tissue. The longer the pathway surrounding an obstacle the more likely it is to produce a circus movement. Everything else being equal, a short pathway will prevent the setting up of a circus movement. Refractory period determines the rate as well as the persistence of a circus movement. Prolongation of the refractory period will decrease the rate and finally will abruptly stop the circus movement. Conduction velocity is also an important factor, any increase in conduction velocity would tend to stop while a

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decrease in conduction velocity will tend to perpetuate the circus movement. It is also possible to produce atrial flutter by injecting a few micrograms of aconitine into the atrium. This type of flutter first described by Sherf, in its simplest form, behaves like an ectopic focus discharging regularly at rates of 400 to 600 beats per minute. The amount of aconitine injected influences the frequency of discharge from such foci. Thus, experimentally at least, one can produce 2 types of atrial flutter: one which conforms to a circus movement, the second conforming to the focal discharge hypothesis. It is not too difficult to demonstrate that both types of flutter can co-exist in the same atrium; thus a third type, namely, a mixed type of flutter can be demonstrated in the dog. There is no reason to believe that the basic types of flutter produced experimentally in the dog cannot also occur in the human heart.

The change of flutter to fibrillation and the change of fibrillation to flutter can also be demonstrated in the dog. Vagal stimulation, either directly or reflexly, readily converts a flutter of either type to atrial fibrillation.

Dr. Lyons: Dr. Moe, I know you agree with Dr. Farah that it is unrealistic to believe that there is a single mechanism of atrial flutter—is this also true as an explanation of atrial fibrillation?

Dr. Gordon K. Moe: According to either hypothesis it is believed that the regular electrical oscillations occurring either in the electrocardiogram or in direct recordings from the atrium are produced when the mechanism of origin has a sufficiently slow rate so that the atrium can be activated as a whole with each successive discharge of the ectopic pacemaker or each successive circuit of the circus movement. Fibrillation is diagnosed when the rate of discharge of an ectopic focus is so rapid that due to the refractoriness of part of the atrium regular excitation cannot occur, or when the circus movement about an obstacle occurs so rapidly that regular activation of the entire atrium cannot occur. The fundamental difficulty with both these notions as an adequate description of atrial fibrillation is that it is hard to believe that either small circus movements or ectopic pacemakers could be endowed with the necessary stability to persist for many years as atrial fibrillation commonly does. It becomes necessary then to construct an explanation for atrial fibrillation that is consistent with this observed behavior, namely, the long persistence of fibrillation.

If one stimulates the atrium, an impulse will be transmitted uniformly and essentially concentrically to all extremities of the atrium, and if the frequency of stimulation of the atrium or the frequency of initiation of impulses from whatever agency is sufficiently slow, orderly excitation of the atra will occur. If, however, an impulse is initiated at a time when recovery is incomplete and the atria are irregularly excitable, the propagation of such an impulse cannot be regular, and disorganized atrial activity must be apparent in the electrocardiogram or in direct electrograms. When an impulse has been propagated through atrial muscle, it would be expected that the recovery wave should follow the excitation pathway with essentially the same concentric form. However, the duration of the refractory period in atrial muscle is not uniform. In various portions of the atrial muscle differences of as much as 40 msec. can be demonstrated in the ordinary preparation of an anesthetized dog with an open chest and much greater differences can be elicited by vagal stimulation. If the atria do not recover in the same sequence as the fibers have been activated, irregular propagation must occur whenever an early premature impulse is initiated in the atrium. If this premature impulse is propagated irregularly, it would be expected that it would move slowly through areas in which the muscle was partially refractory, since conduction velocity is depressed in partially refractory tissue. It would move more rapidly in those areas that had fully recovered, and it becomes apparent then that the wave front of this impulse should conform itself to the retreating edge of the previous excitation wave. In other words, this advancing wave front should be-
come serrated and irregular. If a second premature response is initiated at the same or at a different site immediately following the first premature response, it now falls in tissue that is even more irregularly excitable. It also follows that this advancing wave front must become more serrated and more irregular, with advancing tongues moving around islets of tissue so refractory that they escape excitation entirely. In other words, the wave front for the third or perhaps the fourth of a series of premature beats in the atrium might be expected to become fractionated. If we assume that fractionation of this sort can occur (and this assumption is common to most discussions of the mechanism of atrial fibrillation since the very earliest descriptions 50 or 60 years ago), it becomes apparent that orderly excitation of the atria is no longer possible. The wave front will have broken into isolated independent wavelets that can circulate at random. These wavelets would be changing in number, changing in conduction velocity, and changing in pathway constantly as the disorder persists. Two wavelets meeting about an island of refractory tissue would be expected to fuse and become one. On the other hand, a larger wavelet may split about an island of refractory tissue or a peninsula of such tissue and become divided into 2 independent wavelets.

It now becomes necessary to explain why fibrillation can persist as long as it does. It seems obvious that the greater the number of such independently circulating wavelets the less is the likelihood that these could fuse into a single wavelet which would terminate the dysrhythmia. If there are few such wavelets the statistical probability that they might fuse and fall into phase with all of the muscle becoming refractory or excitable at the same instant is relatively large. If on the other hand the number of wavelets is very large, the statistical probability that they would fall into phase and terminate the dysrhythmia becomes vanishingly small.

We shall now consider those features of atrial behavior that would determine how many of such randomly circulating wavelets could coexist. First in importance is, of course, the size of the atria. A large mass of atrial muscle can certainly support or contain a larger number of wavelets than a small mass of atrial tissue. Furthermore, if the refractory period is short, the total number of such wavelets should be large. If the refractory period is very long, for example, the whole atrium will remain refractory following an excitation process, and fibrillation would be impossible. Conduction velocity must also be an important factor. If conduction velocity were very rapid, any excitation process would be rapidly propagated to the most remote extremes of the atria; all of the fibers would be forced into phase; and the dysrhythmia could not continue. So we have these 3 factors which favor the maintenance of fibrillation, once induced: first, the mass of the atrial muscle; second, the duration of the refractory period; third, the conduction velocity.

Dr. Lyons: Dr. Moe, you have expressed this concept of atrial fibrillation more clearly than I have heard it in the past. What kind of evidence exists to support this concept and how do you relate this to the hypothesis of focal discharge and circus rhythm?

Dr. Moe: Garrey described one of the crucial experiments about 1914 when he showed that if he divided an isolated fibrillating heart into sufficiently small pieces fibrillation was arrested. It was implied by Garrey that when the mass of muscle had been reduced to a sufficiently small magnitude, circus movement of the kind he postulated was no longer possible because no pathway was long enough. It would also follow in terms of the present theory that when the mass has been reduced by cutting, the residual piece of tissue can no longer contain a sufficiently large number of wavelets to sustain fibrillation. When fibrillation is produced in a dog heart by rapid electrical excitation, this fibrillation will be self-sustained provided the vagus nerves are stimulated. Stimulation of the vagus, of course, reduces the mean refractory period of the atrial tissue and would therefore be expected to increase the total number of wavelets. Fibrillation so induced in the dog heart
is always self-limited within seconds after the initiating agency is turned off when the vagi are not stimulated, which implies that the total mass of tissue in the usual dog atrium is not large enough to sustain atrial fibrillation in the absence of some accessory agency. When atrial fibrillation is induced by rapid stimulation of the atrial appendage and is maintained by stimulation of the vagus nerve, clamping of the atrial appendage with a stout surgical hemostat immediately interrupts fibrillation in the appendage from which the dysrhythmia originated while fibrillation continues uninterrupted in the body of the atrium and will continue as long as vagal stimulation is continued.

Another piece of evidence in support of the notion that a large mass is required to support an adequate number of wavelets is a recent observation at the School of Veterinary Medicine at the University of Pennsylvania where fibrillation was produced in unanesthetized cattle weighing about 1000 pounds each. Fibrillation was produced by intra-atrial stimulation with electrodes introduced through a jugular vein catheter. In these cattle fibrillation persisted for days or weeks in the absence of medication and in the absence of vagal stimulation. In fact, fibrillation was not abolished in these animals by the administration of doses of atropine up to 1 mg. per Kg. Under these circumstances one may conclude that the atria of animals of this size are sufficiently large to support an adequate number of randomly wandering wavelets even in the absence of abbreviation of the refractory period through the agency of vagal stimulation.

Dr. Lyons: Dr. Moe, from this description of atrial fibrillation one really wonders how atrial fibrillation ever spontaneously stops, which we know that it does clinically. Certainly your explanation also has many clinical analogies, such as the frequency of atrial fibrillation associated with mitral stenosis or mitral insufficiency where there is enlargement of the atria. Do you have any ideas why we do occasionally see atrial fibrillations spontaneously ceasing?

Dr. Moe: No matter how many such independent wavelets might coexist in the atrium, there is nevertheless a statistical possibility that they may fall in phase and, therefore, the dysrhythmia may be self-limited. One might add that this conforms with the opinion of Dr. Frank Wilson, who often said that when fibrillation stopped it was an accident and that with drug therapy one merely set up the conditions to permit this accident to occur more readily.

Dr. Lyons: Certainly the physician did not do it directly by administering drugs, but we do know that we can administer certain drugs such as quinidine that will be effective in setting up these conditions.

Dr. Farah, can you tell us about the actions of quinidine and digitalis as they relate to the concepts of flutter and fibrillation presented?

Dr. Farah: It is possible to explain some of the effects of some of the important drugs used in the treatment of these arrhythmias. The quinidine-like substances when studied on a circus-movement type of flutter reduce the atrial rate and usually proportionately increase the ventricular rate. Once atrial rate has been reduced to values around 300 to 350 beats per minute one suddenly sees a short period of electrical quiescence followed by a reversion to a sinus rhythm. This effect of quinidine can also be demonstrated in a focal discharge type of flutter and here the atrial rate has to be reduced to much lower values before reversion to a normal rhythm is seen. Furthermore, a circus type of flutter requires smaller amounts of quinidine for reversion than an aconitine (focal discharge) type of flutter. In atrial fibrillation quinidine and quinidine-like substances frequently first convert the fibrillation to a flutter followed by the reversion to a normal rhythm. The effects of quinidine on the electrical properties of cardiac muscle explain to some extent the slowing and reversion to a normal rhythm. The most significant point is the increase in the refractory period produced by quinidine and quinidine-like substances, which is dependent on dosage. The decrease in flutter
ATRIAL ARRHYTHMIAS

rate is due to a decrease in conduction velocity produced by quinidine. Thus, the increase in refractory period tends to stop while the decrease in conduction velocity tends to perpetuate the circus movement. The resultant of these 2 effects of quinidine is quite unpredictable and it is a question of chance or accident that the flutter suddenly reverts to a normal rhythm. With quinidine one can consistently stop a circus type of flutter in the dog provided one uses enough of the drug. This is not always the case with an aconitine (focal discharge type) induced flutter, where one occasionally has to use large amounts of quinidine, which produce severe ventricular disturbances and even ventricular fibrillation.

The effects of quinidine on a focal discharge are due to the ability of quinidine to suppress impulse production. This effect of quinidine can be demonstrated in both normal and abnormal pacemakers. The suppression of impulse production by quinidine is rather poorly understood and it may be related to the effects of quinidine on the rate of entry of sodium ions during activity. Wiedman has shown that local anesthetics and probably quinidine decrease the rate of rise of the action potential and this in turn may be related to the effects of quinidine on the rate of entry of sodium ions. These effects of quinidine on membrane permeability may conceivably explain the reduction in rate of impulse production and the changes in refractory period and conduction velocity. The effects of quinidine on atrial fibrillation are a reduction in the number of recorded impulses at any one point in the atrium and occasionally a change of the fibrillation to flutter. As Dr. Moe has already stated, the changes in refractory period, conduction velocity, and excitability produced by quinidine will tend to reduce the number of wavelets and thus decrease the fibrillation rate. The reversion to a normal rhythm here is a question of chance. Drug administration sets up a state in which the statistical probabilities are more favorable for the simultaneous stoppage of the multiple wavelets.

Digitalis effects on atrial flutter are rather complex and depend on the direct effects of digitalis glycosides on atrial muscle and the indirect effects mediated via the reflex activation of the vagus.

The direct effects which are studied in the vagotomized atrium are increase in refractory period and a decrease in conduction velocity and excitability. These changes cause a decrease in atrial flutter rate and finally a reversion to a normal rhythm. On the other hand, application of digitalis to an innervated heart frequently changes a flutter to a fibrillation. This change is mediated via the vagus, since cutting the vagi abruptly changes the fibrillation to a normal rhythm. The administration of atropine will do the same thing as cutting the vagi. One explanation for these findings is that the direct effects of digitalis, which tend to stop the flutter, are masked by the vagally mediated effects, which cause the fibrillation. If vagal effects are suddenly removed by atropine or vagal cutting, the direct effects come to the fore and tend to slow and finally to convert the flutter to a normal rhythm.

Dr. Lyons: If this is true, and I have no doubt concerning your facts, then the clinician dealing with a patient with a sudden onset of flutter or fibrillation may make the conditions less likely for spontaneous conversion to normal if he uses digitalis. On the other hand, if he does not slow the ventricular rate, he may lose the patient. This clinical dilemma is usually easily resolved in favor of the patient, and digitalis is administered rather than atropine to control the ventricular rate. Quinidine is then used in an attempt to reset the stage for conversion. Certainly the administration of atropine or quinidine without previous digitalization may expose the patient to serious increases in ventricular rate. Can you resolve this dilemma for us, Dr. Farah?

Dr. Farah: No.

Dr. Lyons: One type of atrial activity that is often favorably modified by increased vagal stimuli is paroxysmal atrial tachycardia. How does this differ from atrial flutter and atrial fibrillation, Dr. Abildskov?
Dr. J. A. Abildskov: I will consider paroxysmal atrial and atrioventricular nodal tachycardias together, since they have several characteristics in common. One point that needs emphasis is that these are clinical rather than experimental entities. As Dr. Farah and Dr. Moe have said, atrial fibrillation and flutter can be produced experimentally by a variety of means. In experimental animals these arrhythmias show most of the features of their counterparts in patients. Unlike fibrillation and flutter a disturbance with the characteristics of paroxysmal tachycardia cannot be regularly and reproducibly initiated in experimental animals. Repetitive stimulation electrically or chemically at rates comparable to those of paroxysmal tachycardia does not constitute the experimental counterpart of paroxysmal tachycardia, since it does not provide the opportunity to test vagal effects on the pacemaker. Since experimental paroxysmal tachycardia cannot be initiated at will, we actually have less precise knowledge of its nature than we do that of flutter and fibrillation.

In the absence of all but a few relevant experimental observations, the clinical characteristics are the major basis on which to postulate a basic mechanism. There are 3 such characteristics that seem to me most pertinent to the probable basic nature of these tachycardias. One is the occurrence of frequent supraventricular premature beats before or after the bout of tachycardia. This has been frequently observed and has been widely interpreted to indicate a similarity in the basic mechanism of premature beats and paroxysmal tachycardia. Since it is a widely held view that premature beats represent impulse formation in ectopic sites, it has been an easy step to view paroxysmal tachycardia also as rapid, regular impulse formation in an ectopic center. The point which now requires emphasis is that not all premature beats necessarily represent ectopic focal discharges. Experiments carried out by Dr. Moe and co-workers show that some premature beats actually represent a reciprocal rhythm in which an impulse originating in the atria is transmitted to the ventricles and also back to the atria. This second atrial response to a single stimulus has been termed an "echo." At this time it is not known whether the premature beats exhibited by patients subject to paroxysms of tachycardia are ectopic focal discharges or "echoes" such as those produced in Dr. Moe's experiments. If they should be shown to be the latter, their occurrence would actually constitute strong evidence against the view that paroxysmal tachycardia consists of rapid impulse formation in an ectopic center.

A second feature of paroxysmal supraventricular tachycardias that must be taken into account is a consideration of their basic nature in the absolute regularity of the cardiac rhythm. This characteristic is extremely useful diagnostically and is striking from the standpoint of physiology when it is considered that periodic fluctuations of autonomic tone do not influence the cardiac rate. This is a feature of paroxysmal tachycardia that is extremely difficult to attribute to ectopic focal discharge. The sinoatrial node, which is a site of impulse formation whose properties are reasonably well known, is certainly subject to variation in sympathetic and parasympathetic tone; it responds by altering the rate of impulse formation. While it is true that nerve fibers are more abundant in the sinoatrial node than in other portions of the atria, it would still seem that at least some atrial foci and atrioventricular nodal foci should be so located that variations in nervous tone would result in irregularity of impulse formation. That such irregularity is not a feature of paroxysmal tachycardia does not disprove the ectopic focus theory but does stimulate the search for another mechanism which would seem more likely to result in a regular cardiac rhythm.

A third characteristic of supraventricular tachycardia, which is both interesting physiologically and useful therapeutically, is the response to vagal stimulation. It is well known that such stimulation may have no effect but that when it is effective, the result is abrupt termination of the tachycardia. In those in-
stances where vagal stimulation has no effect on paroxysmal tachycardia, an ectopic focal mechanism is certainly possible. It has been demonstrated that vagal fibers are not uniformly distributed in the atria and an individual focus might well be in an area not subject to a sufficiently high concentration of acetylcholine to alter its performance. It is more difficult to account on the basis of ectopic focal discharge for those tachycardias which are terminated by vagal stimulation. As mentioned previously, the effect of vagal stimulation on the normal cardiac pacemaker is to slow gradually the rate of impulse formation. I know of no reason to believe an ectopic focus subject to vagal influence ought not to operate in a similar fashion with gradual slowing rather than abrupt cessation of pacemaker activity. We have then a second characteristic of paroxysmal supraventricular tachycardia which, while not disproving ectopic focal activity, is difficult to account for on that basis.

The absolute regularity and the response to vagal stimulation of paroxysmal supraventricular tachycardia have led some to postulate a mechanism other than ectopic focal activity. Doctors Barker, Wilson, and Johnston and Dr. Ashman considered these features to be more adequately explained on the basis of circus movement mechanisms. A recirculating wave into and out of the sinus node was postulated for those tachycardias we label atrial in origin and a similar reentry into and out of the atrioventricular node for nodal tachycardia. Such a mechanism accounts nicely for the abrupt termination of paroxysmal tachycardia on vagal stimulation, since the alteration in refractory period so produced might suddenly block the reentry path. A reentry phenomenon also accounts for the regular cardiac rhythm, since the excitation path is fixed.

It must be apparent that in my opinion a reentry phenomenon is the probable mechanism of paroxysmal tachycardia. The likelihood of such a mechanism has recently been enhanced by evidence of a dual transmission system in the atrioventricular node and by experimental findings in 2 animals in which a dysrhythmia with the features of paroxysmal tachycardia happened to occur. I wonder if Dr. Moe will discuss these findings and their relation to clinical paroxysmal tachycardia.

Dr. Moe: Many of the postulated explanations for reciprocal rhythm and for paroxysmal tachycardia have implied the existence of a dual transmission system due either to nonuniform alteration of the properties of the bundle of His, or of the node itself, or perhaps due to the existence of 2 discrete pathways. Experiments which were carried out in our laboratories some 3 to 4 years ago elicited 3 features of atrioventricular transmission which are consistent with the existence of 2 normal pathways in all of the mammalian species that were examined. These features of atrioventricular transmission are, first of all, an unexpected excess temporal delay in the propagation of very early premature atrial stimuli to the ventricles; second, the frequent demonstration of atrial echoes following atrial premature excitation or ventricular echoes following premature ventricular excitation. This latter observation has recently been confirmed by Rosenbleuth. It has been possible to produce atrial or ventricular echoes and even multiple echoes. Finally, there were configurational changes in the ventricular electrical response following very early premature atrial excitation.

As Dr. Abildskov suggested, it is usually impossible to set up a true paroxysmal tachycardia experimentally. In fact, on only 2 or 3 occasions in more than 100 experiments on dog hearts we have observed spontaneous bouts of self-sustained tachycardia that have all of the features of the paroxysmal supraventricular tachycardia observed clinically, namely, the fixed cycle length, the onset following immediately upon a premature atrial systole, and cessation upon the introduction either of premature beats in atrium, or ventricle or upon intense vagal stimulation.

Dr. Lyons: Did you think that in these instances the dual transmission mechanism
from the atrium to the ventricle was involved?

Dr. Moe: This was certainly our interpretation. The notion would be that the premature impulse finds 1 of the 2 alternate pathways in the transmission system excitable while the other is still refractory, makes its first trip to the ventricle over only 1 of the 2 pathways and by the time it reaches there finds the alternate pathway available and excitable for a return trip to the atrium.

Dr. Lyons: Dr. Moe, would you summarize the points that have been covered in this conference?

Dr. Moe: We know on the basis of experimental evidence it is possible to produce rapid atrial activity by means of a circus movement about one of the naturally occurring or an artificially induced obstacle in the atrial muscle. It is probable that the same phenomenon occurs spontaneously. It is also possible to produce rapid atrial activity by means of a rapidly discharging ectopic focus produced either by repetitive electrical stimulation or by the administration of aconitine. Since an ectopic focus can be produced experimentally, it seems reasonable to suppose that nature occasionally performs the same experiment. It is therefore unnecessary, and indeed even unrealistic, to propose that only 1 mechanism can exist to explain all of the atrial tachycardias. It would be my conviction that certain instances of atrial tachycardia, whether regular or irregular, can be due to circus movement activity. It is possible that some instances of atrial tachycardia are due to ectopic focal activity and it is possible, and I believe probable, that self-sustained fibrillation however induced, whether by an ectopic focus or by a circus movement, is maintained by the existence of numerous randomly circulating wavelets. It has been possible to produce paroxysmal tachycardia in a few isolated instances by means of premature atrial excitation under conditions that would favor the exposure of the dual transmission system, and it is possible that the same situation occasionally occurs in atrioventricular nodal tachycardia in the human subject.
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