Repetitive Ventricular Arrhythmia Resulting from Artificial Internal Pacemaker

By Morton E. Tavel, M.D., and Charles Fisch, M.D.

The use in clinical medicine of internally implanted artificial pacemakers for the treatment of Stokes-Adams disease is gaining rapidly in popularity. Complications arising from this mode of therapy are said to be confined largely to the occurrence of infection around the implanted foreign body and technical difficulties with the presently used apparatuses and their electrodes.1,2 In recent publications, certain investigators1,3,4 have given serious consideration to the theoretical possibility that electrical stimulation of the heart during the vulnerable phase of the relative refractory period might result in repetitive ventricular firing or ventricular fibrillation. These investigators have not, however, during extensive clinical experience, observed such a phenomenon despite the fact that the artificial stimulus very often was seen to fall within T waves.

Wiggers and Wégria5 generally are given credit for establishing and characterizing the presence of the vulnerable period, during which short electrical shocks delivered to the ventricular muscle will result in repetitive ventricular arrhythmias, including fibrillation. This period occurs near the end of systole, at the time when the T wave in the electrocardiogram is being inscribed. In their studies,6 however, the electrical current necessary to produce fibrillation in the normal animal was several hundred times the threshold required to produce a single beat in diastole, a strength far exceeding that of the present-day artificial pacemakers.

We wish to present a case in which a patient’s heart manifested repetitive ventricular firing which at times was indistinguishable from ventricular fibrillation. The ventricular firing followed artificial stimulation during the T wave by a commonly used internal pacemaker designed to deliver a relatively small current.

Case Report

A 26-year-old Caucasian man was admitted to the hospital on February 28, 1963, for evaluation of heart disease. His difficulties had begun 1 year previously, shortly after a chest injury resulting from an automobile accident, and his symptoms were characterized by dyspnea on exertion, easy fatigability, and a 20-pound gain in weight. Because of the discovery of unexplained cardiac enlargement, he was referred to this institution for evaluation. Following numerous studies, which included right and left heart catheterization, it was determined that the patient had severe isolated tricuspid insufficiency, almost certainly posttraumatic in origin. His electrocardiogram showed regular sinus rhythm with right bundle-branch block and a QRS duration of 0.12 second.

On March 20, 1963, the patient was operated upon and, after unsuccessful attempts were made to repair a leaflet of the tricuspid valve which had torn free from the papillary muscle, a prosthetic Starr-Edwards valve was implanted. A right atrial approach was employed throughout the operation. Competent valve function was restored, as measured at the time of surgery, and a cardiopulmonary bypass procedure was utilized for a total of 101 minutes. The patient tolerated the procedure well with a continuously satisfactory blood pressure.

Shortly after the operation was completed, complete heart block developed with atrioventricular nodal rhythm at a rate of 63 beats per minute. During the ensuing 2 days, several grand mal convulsive seizures occurred, each begin-

From the Department of Medicine (Division of Cardiology) and the Heart Research Center, Indiana University School of Medicine; the Krannert Heart Research Institute, Marion County General Hospital, Indianapolis, Indiana.

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ning on the left side of the body. On March 22, it was clear that left hemiparesis was present; this condition persisted with slight improvement throughout the patient’s subsequent 2-month hospital stay. Numerous electrocardiograms indicated that the rhythm was changing from complete heart block, to second-degree heart block with 2:1 atrioventricular conduction, to periods of completely normal atrioventricular conduction.

On April 19, the patient again was operated upon, and an artificial pacemaker (General Electric Model A-2065A) was implanted. This was accomplished with an anterior thoracotomy through which the apex was exposed, and an avascular site was selected for insertion of the electrodes ½ cm. apart. The pacemaker was implanted beneath the left upper abdominal skin, and a subcutaneous tunnel was made for the connecting wires. The pacemaker was set initially to run at a fixed rate of 64 impulses per minute, delivering a biphasic impulse of 5-msec. duration with a potential of 3.7 millivolts and a maximum current energy of 65 microjoules. This stimulus strength is estimated to be 4 to 10 times the threshold required to cause ventricular contraction, and it decreases as the rate is increased, so that a rate of 120 will carry a stimulus of about half-strength. At the time of implantation, the ventricles were observed to be responding well to the artificial stimulus.

On the day after the implantation procedure, the patient manifested two syncopal episodes, characterized by loss of consciousness, respiratory arrest, generalized muscular rigidity, and cyanosis. Preceding and during one of these attacks, a ventricular tachycardia was observed, which spontaneously reverted to the previous rhythm. The electrocardiogram taken at that time showed several such episodes of varying lengths, all of which followed artificial stimulation during the T wave (fig. 1 A-F). A third syncopal episode with repetitive ventricular arrhythmia occurred, which was quite persistent and which necessitated termination by external countershock. At that time, the artificial stimulus rate was 58 impulses per minute. Shortly afterward an induction coil was procured and applied externally over the pacemaker in order to increase the stimulus rate. When the artificial rate was set at 75 impulses per minute or more, no arrhythmia was noted (fig. 1 G). When the rate was slower, however, bizarre ventricular conduction occurred periodically and only when the artificial stimuli fell on the T waves (figs. 1 and 2). At other times in the cycle, effective stimuli were followed by "normal" responses.

![Figure 1](http://circ.ahajournals.org/)

Standard electrocardiographic lead III. Row A-F: Periods of repetitive ventricular firing following artificial stimulation during the vulnerable period. Row G: After the artificial stimulus rate has been increased, the implanted pacemaker gains control of the ventricular response, thus preventing artificial stimulation during the T waves.
During the next 2 weeks, the hospital course was uneventful except for the development of infection in the left pleural cavity, which responded to appropriate antibiotic therapy. The patient continued to manifest varying atrioventricular block. Only occasional isolated bizarre ventricular conduction was noted. On May 5 it was evident that the artificial pacemaker activity had ceased entirely.

The patient was discharged on May 27, 1963, in relatively good condition, with residual left hemiparesis and varying atrioventricular block.

Discussion

One readily can see that when the artificial stimulus fell within a very narrow range during the T wave (approximately 0.34 second after the beginning of the Q wave of the antecedent cycle), paroxysms of repetitive ventricular arrhythmia frequently would result (figs. 1 and 3). Stimuli applied earlier in the refractory period failed to initiate a ventricular response. If the pacemaker stimulus appeared later in the cycle, only single ventricular complexes would result. The conduction of these ventricular complexes was aberrant, as compared with the complexes evoked by the pacemaker during diastole, if their onset appeared early enough to interrupt the T wave. As artificial stimuli fall earlier in the terminal portion of the electrical systole, there is an increasing latent period between stimulus and the ultimately resulting ventricular excitation, which ranges from 0.01 to 0.08 second. The degree of aberration of these ventricular complexes varies with the prematurity of their appearance. The earliest effective stimuli evoked the earliest ventricular complexes that had the greatest degree of aberration and that were often followed by repetitive ventricular firing. Table 1 summarizes the relation of the artificial stimulus to the type of response evoked when applied at different times during the cycle.

In all the figures above, there is present a sinus tachycardia with a predominant atrioventricular conduction ratio of 2:1 and superimposition of P waves onto T waves. Thus, it is difficult to delineate the exact termination of the T waves of conducted beats. Careful study of other leads and of electrocardiograms taken on other days, showing a similar ventricular rate and conduction pattern, revealed that the Q-T interval for conducted beats (from the sinoatrial node) was
about 0.44 second. The P waves are not responsible for the repetitive firing, since the latent period to the first complex of the series is too short, and there is a persistent predictable relation between only the artificial stimuli and the ventricular arrhythmia. As can be

![Figure 3](image)

**Figure 3**

Closer view of figures 1 and 2, showing the exact relation between preceding cycle, electrical stimulus, and type of ventricular response. Time intervals summarized in table 1.

**Table 1**

<table>
<thead>
<tr>
<th>Period between preceding Q wave and artificial stimulation (seconds)</th>
<th>Latent period between the stimulus and the ventricular response (seconds)</th>
<th>Ventricular response</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 - 0.33</td>
<td>0.08</td>
<td>None</td>
</tr>
<tr>
<td>0.34</td>
<td></td>
<td>Repetitive ventricular firing or isolated premature ventricular contraction with aberrant conduction</td>
</tr>
<tr>
<td>0.34 - 0.43</td>
<td>0.08 – 0.01</td>
<td>Isolated premature ventricular contraction with aberrant conduction</td>
</tr>
<tr>
<td>0.44 or more</td>
<td>0.00</td>
<td>Premature ventricular contraction with “normal” conduction</td>
</tr>
</tbody>
</table>
noted in figure 1, row G, when the artificial pacemaker rate was increased, a loss of atrioventricular conduction resulted, due to retrograde discharge of the atroventricular node, so that sinoatrial impulses no longer reached the ventricles, and there remained only one pacemaker for the ventricles, the artificial one. Thus, further stimulation during the vulnerable period and runs of repetitive ventricular firing were eliminated.

The evidence for such a vulnerable period, during which a stimulus can evoke repetitive ventricular firing and fibrillation, has been well worked out in several animal species. Fortuitously, we were able, in a more direct fashion, to confirm the existence of such a period in man and to relate it fairly accurately to the time of artificial stimulation of the ventricles.

Why such a small electrical stimulus can produce such a serious ventricular arrhythmia is both of academic and clinical importance. Although, as previously cited, the stimulus strength required to produce this effect under normal circumstances is several hundred times the threshold necessary to produce a single ventricular contraction during diastole, there are several means by which this can be modified. Hoffman et al. showed that accurate application of the stimulus during the period of relatively enhanced excitability could reduce the stimulus required for repetitive firing to approximately 20 times diastolic threshold. Palmer has shown that a stimulus strength of about 10 times diastolic threshold could evoke repetitive firing if the area of stimulation were placed in such a fashion that earlier repolarizing tissue is stimulated at the same time that the adjacent myocardium is still partially refractory. When Palmer obtained such a result, there was a close relation between QRS interruption of a T wave, aberrant ventricular conduction, and repetitive firing. The fact that the artificially evoked ventricular response interrupted the T wave is taken as evidence for the development of excitation during which some of the myocardial tissue has not yet completely repolarized. This sets the stage for fragmentation of response and probably re-entry, which will lead ultimately to fibrillation. Thus, Palmer apparently was able to obtain T-wave interruption and fibrillation with small stimuli by taking advantage of the asynchronous repolarization of myocardial tissue under certain conditions. Those conditions were stimulation of earlier depolarizing areas of the heart (the septum), stimulation at the site of origin of a preceding ectopic ventricular complex, and stimulation of an ischemic area of ventricular myocardium after the passage of a conducted supraventricular complex. It is well recognized that ischemia causes shortening of the action potential and earlier recovery and a lower fibrillation threshold.

Palmer also showed that prolongation of ventricular conduction through hypokalemia also fostered more pronounced T-wave interruption and a greater incidence of fibrillation.

Under usual experimental circumstances, graded strengths of stimuli, when applied during the vulnerable period, produce first single extrasystoles, then multiple repetitive extrasystoles, and finally repetitive extrasystoles culminating in fibrillation. Repetitive responses cannot be evoked when the stimulus—no matter what its strength—is applied outside of the vulnerable period. When one applies a threshold stimulus to the ventricle during the relative refractory period, a latent period develops before this stimulus is translated into a detectable wave of depolarization. The earlier one stimulates prior to total cardiac recovery, the longer will be the latent period. Thus, all propagated complexes tend to fall just outside of the T wave of the preceding cycle, no matter when the stimulus was administered. This changing latent period phenomenon was well exemplified in our case, although it appears here that the resulting premature complexes began before
the T wave had finished. Higher-than-threshold stimuli may cause earlier responses in the relative refractory period; however, the early ventricular response in our case may be more apparent than real, since total recovery may have occurred in the stimulated myocardial area despite continued inscription of the T wave caused by later repolarization of more remote areas.

Available clinical observations also have bearing on the current problem. Smirk and Palmer showed that in certain situations premature ventricular extrasystoles would interrupt preceding T waves, thus producing a high incidence of repetitive ventricular arrhythmias and sudden death. Serious myocardial disease existed in almost all of these patients (with ischemic heart disease high on the list), and one easily can appreciate the likelihood that asynchronous repolarization probably was present in these patients. It also is interesting that these authors found one young patient in this category with the Wolff-Parkinson-White syndrome, and they cited other work in which T-wave interruption, ventricular tachycardia, and sudden death have been observed in conjunction with this condition. Again, one notes that asynchrony of ventricular excitation occurs in the Wolff-Parkinson-White syndrome.

We were able to find two cases previously recorded wherein repetitive ventricular firing was seen in association with artificial pacemaker stimulation during the T wave, and the circumstances surrounding its occurrence were most interesting. Dittmar and associates, in reporting three patients with long-term pacemakers and electrode implantation, observed one patient in whom artificial stimuli fell on T waves and induced repetitive ventricular extrasystoles. The patient later died suddenly. The stimulus strength and stimulus duration were not mentioned in this specific case. Moreover, in their electrocardiographic examples, some of the pacemaker stimuli in one tracing failed to evoke ventricular responses during diastole, while in a lower strip showing repetitive firing, all the stimuli were effective. This raises some question concerning the artificial pacemaker's function. The patient was a 26-year-old man who had predominant second-degree heart block and 2:1 atrioventricular conduction. In addition, there was a short P-R interval and prolongation and aberration of the QRS complex of conducted beats, closely resembling the Wolff-Parkinson-White syndrome. At necropsy, chronic rheumatic myocarditis and cardiac hypertrophy were found; in addition, there was inflammatory reaction in the myocardium around the electrodes and fibrinous pericarditis. Elmqvist and associates, in a study of 18 cases, observed one instance of repetitive firing in a 74-year-old man. In this instance, there was slow idioventricular rhythm with a prolonged QRS deflection. The artificial stimulus was set at twice the threshold required for a single diastolic response and its duration was 2.5 msec. When the pacemaker rate was slowed to 27 impulses per minute, occasional dominance of the heart by the slightly faster autonomous ventricular pacemaker allowed the artificial impulses to fall in the T waves and to induce repetitive firing of the ventricles. These were completely abolished by an increase in the rate of artificial stimulation, allowing it to regain dominance of the ventricle.

In all cases reported thus far, the first ventricular complex initiating the chain of repetitive firing has had a bizarre prolonged configuration with respect to the impulses evoked artificially during diastole, and this initial bizarre complex has caused interruption of the terminal portions of the preceding T waves. This early timing and aberration of response appear to be prerequisites for the initiation of repetitive firing. However, such complexes do not necessarily augur a serious arrhythmia in man, for they have been described as occurring frequently without repetitive firing in patients with implanted artificial pacemakers.

Because of the limited time span of pacemaker use, the incidence of repetitive ventricular tachycardias in response to small artificial stimuli is not clearly defined. Since it is possible that sudden death may result from
these arrhythmias, the exact incidence of this phenomenon may never be established.

There are several possible explanations for the occurrence in our case of the arrhythmia in response to a small stimulus. Firstly, the fibrillation threshold may be lower in man than in experimental animals. This explanation appears inadequate since, at the present time, this complication has been rare in association with external \(^1\) and internal \(^3\) \(4\) artificial pacemaker stimulation. A second possible explanation is that the actual stimulus delivered was of a great enough magnitude to reach the fibrillation threshold; the stimulus then was applied during the narrow time interval when it could be effective. This is a possibility that cannot be discounted, inasmuch as the actual stimulus delivered may have exceeded diastolic threshold by as high as 10-fold. Our stimulus duration (5 msec.) was also somewhat longer than those used by other investigators, \(^1\) \(3\) \(4\) who generally used stimuli of shorter than 3 msec. Increasing the stimulus duration has been shown to lower both the fibrillation threshold and the threshold required to induce isolated beats in diastole. \(^7\) \(8\) The margin of safety (the difference between threshold stimulus strength required for a single diastolic response and that required to produce fibrillation) is also reduced as the stimulus duration lengthens. \(^10\) Hence our relatively long stimulus duration per se could have been instrumental in the result produced. Another possibility is that an inherent condition within the ventricles predisposed to a lower fibrillation threshold value. A possible enhancing factor in this case would be the pre-existing right bundle-branch block, which may have imparted to the ventricles an asynchrony of repolarization. Such an explanation is attractive, particularly inasmuch as the other two reported cases also had prolonged aberrant ventricular conduction in the beats preceding the repetitive arrhythmia. To a limited extent, the previously cited work of Palmer \(^10\) also supports this hypothesis. Lastly, the rate of stimulation may be of importance. It has been demonstrated that runs of spontaneous ventricular tachycardia and fibrillation can be suppressed by electrical stimulation of the ventricles faster than a critical rate that varies widely from patient to patient. \(^20\) In all three reported cases of repetitive firing the corresponding ventricular cycles preceding the T waves on which stimuli produced repetitive ventricular arrhythmias were 0.9 second or longer. No satisfactory explanation has been offered for enhanced propensity for fibrillation at slower rates. The refractory period is prolonged as the cycle length is increased, and this might allow for exaggerated asynchrony of repolarization, thus laying the groundwork for fragmentation of a premature ventricular complex propagated during partial recovery.

Because of the small number of cases reported thus far, we can only speculate about means whereby one can prevent the occurrence of repetitive ventricular arrhythmias resulting from implanted pacemakers. In order to prevent both ventricular irritability and the dominance of the heart by an intrinsic cardiac pacemaker, the artificially induced impulses should be set at the fastest rate compatible with good mechanical function of the heart; a tentative minimum rate of 70 beats per minute seems reasonable. \(^1\) Based on experimental data, \(^10\) \(21\) implantation site for the electrodes is also of theoretical importance, since placement in portions of the ventricle last depolarized (the base of the heart) is less likely to be associated with repetitive ventricular complexes, these areas having a higher fibrillation threshold. It might follow that, in situations where serious arrhythmias are most likely to develop, implantation into the region of the pulmonary conus might be considered. This consideration must be weighed against the possibility that mechanical efficiency of the heart may be less if the right ventricle is the site of electrode implantation. \(^22\) It is also obvious that artificial pacemaker stimulus strength should be maintained at as near a threshold value for stimulation as possible. Stimulus duration probably should be less than 3 msec.
Summary

We have presented a case summary of a patient in whom several periods of repetitive ventricular arrhythmia—at times indistinguishable from fibrillation—were induced by artificial internal pacemaker stimuli falling in the T wave of a preceding cycle (the vulnerable period). Ours is the third such case to be reported and, although this repetitive response is said to be rare, the exact incidence remains to be determined. The theoretical and clinical implications are discussed and possible explanations are given for why such small artificial stimuli are capable of evoking such serious arrhythmias in certain patients. We also have suggested measures that might reduce the likelihood for this complication to arise.

References

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MORTON E. TAVEL and CHARLES FISCH

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