Electrophysiologic Studies on Mobitz Type II Second-Degree Heart Block

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SUMMARY
Experimental studies were carried out in animals with intracellular and extracellular electrodes used to record simultaneously from the atrium, atrioventricular (A-V) node, bundle of His, bundle branches, Purkinje fibers, and ventricles to determine the site of conduction delay and block in Mobitz type II second-degree heart block. Type II block with block occurring within the His-Purkinje system was observed only rarely in normal animals; however, Mobitz type II block could be induced in normal hearts by slight but undetectable variations in the P-P interval. Sudden conduction failure was usually due to block within the His-Purkinje system. Type II block also resulted from failure of conduction within the A-V node during depressed A-V conduction due to rapid atrial pacing, vagal stimulation, or ouabain infusion. The classification of second-degree heart block according to Mobitz type I (increasing P-R interval) and Mobitz type II (constant P-R interval) block should take into account that the site of block in both cases can occur either in or below the A-V node. Admittedly, in man Mobitz type I block is most often intranodal while type II block is usually infranodal following myocardial infarction. His bundle electrocardiography may therefore be indicated to determine the site of block in patients with Mobitz type II block, particularly in those with prolonged P-R intervals.

Additional Indexing Words:
Cardiac arrhythmias  Atrioventricular block  Bundle of His Purkinje system
Conduction delay  P-R interval  P-P interval  Electrocardiogram

Second-degree heart block was classified by Mobitz into type I and type II block.1 Mobitz type I atrioventricular (A-V) block is characterized by a gradual prolongation of the P-R interval until failure of a ventricular response occurs (Wenekebach periods), while type II block is characterized by sudden dropped beats without antecedent lengthening of the P-R interval in the electrocardiogram (ECG). Type I block is easily produced experimentally in normal mammalian hearts, including in man, by rapid atrial pacing, and is considered a normal functional property of the heart. Progressive prolongation of the P-R interval until complete A-V block occurs has been demonstrated to result from delays and block within the A-V node. Rare exceptions have been reported.2,3

Except for the observations of Watanabe and Dreifus,4 recorded during digitalis toxici-

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ty, it has not been possible to produce type II Mobitz block in the normal mammalian heart. The difficulty of experimentally producing type II block correlates with the clinical observation in man that there is usually pathologic involvement of the infranodal system in type II block, and that block of the nonconducted beat results from block below the bundle of His within the diseased ventricular specialized conduction system (VSCS).

The present studies were undertaken to investigate possible experimental methods of producing type II Mobitz block. Also, since the sudden dropped beat in the presence of a constant P-R interval in type II block is usually associated with block below the bundle of His in man, it was of interest to determine if the sudden blocked beat could be demonstrated to result from conduction failure above the His bundle under some circumstances. The need to distinguish between type II block above or below the bundle of His may be important from a clinical standpoint in man. Sudden dropped beats occurring within the A-V node would probably not carry as serious a clinical prognosis as would block within the VSCS; clinical experience has repeatedly demonstrated that infranodal block is associated with a high mortality rate and requires a pacemaker to prevent Stokes-Adams attacks.

These studies demonstrate that it is possible to produce type II A-V block in normal hearts with block occurring above the bundle of His during small changes in the P-P interval. Type II block within the VSCS can only rarely be produced in the normal animal. Critical examination of published examples of spontaneously occurring type II block in man has also found variations in the P-P interval associated with sudden dropped beats. We propose, therefore, that in some cases of Mobitz type II A-V block the dropped beat may be associated with small variations in the P-P intervals.

Methods

Isolated Heart Preparation

Hearts were rapidly excised from rabbits weighing 1.5 to 3.0 kg and anesthetized with sodium pentobarbital (30 mg/kg). The hearts were dissected in Tyrode’s solution and the right atrial and ventricular septal endocardial surface was exposed to enable microelectrode impalement of various regions of the A-V conduction system. The preparations were bathed at 37°C by Tyrode’s solution equilibrated with 95% oxygen and 5% carbon dioxide.

Transmembrane microelectrodes and bipolar surface electrodes were used to record simultaneously from atrium, A-V node, His bundle, right bundle branch, Purkinje fibers, and ventricular muscle. The recordings were displayed on a cathode-ray oscilloscope and stored on analog tape; they were later photographed on 35-mm film. The preparations were electrically driven by stimuli delivered through isolation units using a digitally programmed stimulator.

Whole Animal Preparation

Animals were anesthetized by intravenous sodium pentobarbital (30 mg/kg) and maintained on controlled positive ventilation. The hearts were exposed by right (fifth intercostal space) or midsternal thoracotomy. Bipolar recordings were made from atrium, His bundle, left and right bundle branches, and ventricular muscle using either electrode plaques sutured to the heart4 or plunge electrodes.5 The electrograms were displayed on an eight-channel Electronics for Medicine recorder and photographed on paper or 35-mm film. Electrical stimuli were delivered through isolation units using a programmable stimulator. These methods have been described in detail previously.2

Results

Mobitz type II second-degree A-V block is characterized by a constant P-R interval with sudden dropped beats. In man this type of second-degree block is usually associated with a bundle-branch block pattern. In clinical cases of type II block in man in which bundle of His electrograms were obtained, the site of conduction failure has usually been reported to be below the bundle of His within the ventricular specialized conduction system. Figure 1 is one of the few examples of type II block with block below the bundle of His that we were able to record in a normal experimental animal. The record was obtained from an experiment on a calf in which bilateral bundle-branch block below the bundle of His routinely occurred when small variations were made in the P-P interval. The QRS pattern in
Mobitz type II heart block occurring in the His-Purkinje system of the open-chest calf. Bipolar electrograms were recorded from the right atrium (RA), bundle of His (BH), left bundle branch (LB), and right ventricle (RV) together with lead II of the electrocardiogram (II). In the bundle of His electrogram a indicates the atrial response, h the His potential, and s the ventricular response. In the left bundle-branch electrogram b indicates the left-bundle potential. The third atrial response is blocked below the bundle of His recording site in the presence of a constant P-R interval. The time line denotes 40 msec. The time lines at the left of the figure are inaccurate; the electrograms are correct, as shown by constant RA-RV conduction times for the first two beats.

Figure 1

Mobitz type II block occurring in the His-Purkinje system of the open-chest calf. Bipolar electrograms were recorded from the right atrium (RA), bundle of His (BH), left bundle branch (LB), and right ventricle (RV) together with lead II of the electrocardiogram (II). In the bundle of His electrogram a indicates the atrial response, h the His potential, and s the ventricular response. In the left bundle-branch electrogram b indicates the left-bundle potential. The third atrial response is blocked below the bundle of His recording site in the presence of a constant P-R interval. The time line denotes 40 msec. The time lines at the left of the figure are inaccurate; the electrograms are correct, as shown by constant RA-RV conduction times for the first two beats.

In figure 1 the calf heart was paced from the atrium with a basic cycle length of 420 msec. The third atrial response was made 90 msec more premature (or 2 mm shorter in a normal ECG tracing) than the basic cycle length; this might be considered within the range of sinus arrhythmias. Electrograms were recorded from the right atrium (RA), bundle of His (BH), left bundle branch (LB), and right ventricle (RV) simultaneously with a lead II electrocardiogram (II). Time lines denote 40-msec intervals. The first two atrial responses in the right atrial electrogram (RA) were conducted through the A-V node and excited both the bundle of His (h potential) and the left bundle branch (b potential). The third atrial response was blocked before it reached the ventricles, as demonstrated in the ECG. The His electrogram (h) accompanying the blocked atrial response indicates that block must have occurred below the bundle of His and above the site of recording from the left bundle branch. The right atrium-to-right ventricular electrogram interval (RA-RV) remained constant at 124 msec preceding the dropped beat, and the right atrial-to-His electrogram interval, which approximates A-V nodal conduction time, was increased by only 5 msec accompanying the dropped beat. Although in some cases of type II block there is a variation in the P-R interval following the
dropped beat, in this instance the P-R interval remained constant.

Figure 2 demonstrates type II Mobitz block in the isolated rabbit heart. In this experiment the heart was paced from the atrium at a constant rate of 99/min; this rate caused some beats to be dropped abruptly. Electrograms were recorded from the right atrium (RA) and right ventricle (RV) simultaneously with transmembrane action potentials recorded from a bundle of His fiber (BH) and right bundle-branch fiber (RBB). Time marks (T) denote 100-msec and 1-sec intervals. Notice that each right atrial electrogram was accompanied by an action potential recorded from the bundle of His, and that the atrial-to-His bundle conduction time (RA-BH) and His-to-right ventricle conduction time (BH-RV) remained constant. The bundle of His action potential was not accompanied by a right bundle-branch action potential when the atrial impulse failed to be conducted to the ventricles (fourth, eighth, and tenth RA responses). Therefore, in this example of Mobitz type II block, conduction failure occurred below the bundle of His somewhere above the impaled bundle-branch fiber. Figures 1 and 2 confirm studies completed in man where the sudden dropped beat in type II second-degree block results from block within the ventricular specialized conduction system.

In some preparations it was possible to demonstrate complete A-V block preceded by a constant P-R interval (type II block) which resulted from conduction failure above the bundle of His. Figure 3 shows data from an in vivo dog preparation in which electrograms were recorded from the right atrium (RA), bundle of His (H), and left endocardial Purkinje fiber (LPF) simultaneously with the lead II electrocardiogram (II). Time marks denote 100-msec intervals. The right atrium was paced at a basic cycle length of 258 msec (heart rate of 234/min). At this rapid rate conduction time through the A-V node was increased by 12 msec, but the P-R interval of 0.14 sec is still within the normal range in the dog (0.06 to 0.15 sec). Every fourth atrial beat was made premature by 20 msec. In the standard electrocardiographic tracing this
would mean that every fourth response would have a variation in the P-P interval of 0.5 mm; that is, a sinus arrhythmia was present which would be barely perceptible in the routine ECG tracing. This small variation in the P-P interval resulted in 4:3 second-degree block, and it can be observed in the lead II ECG that the fourth atrial response is blocked. As so commonly occurs in clinical cases of type II block in man, the P-R interval following the blocked response was slightly shorter than that for the responses preceding the blocked response.

The fact that bundle of His and left Purkinje electrograms were not recorded during the dropped response demonstrates that in this instance of type II Mobitz second-degree block conduction failure occurred above the bundle of His, rather than within the VSCS as is the usual case in man. This finding is important since it points out that type II block can occur above the bundle of His as well as within the VSCS, and that small variations in cycle lengths can determine whether an atrial response is or is not conducted to the ventricles. Similar findings of type II block above the His bundle occurred when A-V conduction was depressed by vagal stimulation and slight variations were made in the P-P intervals.

Figure 4 shows another example of Mobitz type II block that occurred spontaneously in an in vivo dog experiment in which a toxic dose of ouabain (3 mg/kg) was administered.

**Figure 3**

Mobitz type II block due to conduction failure within the A-V node of the open-chest dog. Bipolar electrograms were recorded from the right atrium (RA), the bundle of His (H), and the left endocardial Purkinje fiber (LPF), together with lead II of the electrocardiogram (II). The His potential in the bundle of His electrogram is denoted by h, and the Purkinje spike by p. The timing marks denote 100 msec. The fourth atrial response was blocked above the bundle of His without previous lengthening of the P-R interval.

**Figure 4**

Mobitz type II block with conduction failure occurring within the A-V node following a toxic dose of ouabain (3 mg/kg) in the open-chest dog. Bipolar electrograms were recorded from the right atrium (RA), the bundle of His (BH), and the right ventricle (RV), together with a lead II ECG (II). The timing signal (T) denotes 100 msec. A 2:1 second-degree A-V block develops with a constant P-R interval for all conducted beats.
The atria were not electrically paced. Electrograms were recorded from the right atrium (RA), bundle of His (BH), and right ventricle (RV), along with a lead II ECG (II). In the BH electrogram, the first smaller biphasic complex is the His bundle potential, and the second larger complex records ventricular septal activity. In figure 4 normal sinus rhythm spontaneously progresses to 2:1 second-degree A-V block. Although all 2:1 A-V block has been classified as type II block by some investigators, this concept has been seriously questioned by Langendorf and Pick. Classification of 2:1 A-V block into type I or type II block depends upon the ability to find a transition to or from a lesser degree of A-V block. If a variation in P-R interval occurs during lesser degrees of A-V block, then the 2:1 block is of type I, while a constant P-R interval during lesser degrees of A-V block is type II. Since there is a constant P-R interval (constant atrial-to-His bundle depolarization interval and His bundle-to-right ventricular excitation) preceding the occurrence of 2:1 second-degree block, and the P-R interval during the conducted beat with 2:1 block is the same as during 1:1 conduction, there can be no question that this is an example of type II Mobitz block. The important point to note is that unlike the clinical cases studied to date in man, conduction failure in this instance of type II block results from complete A-V block above the bundle of His recording site, and not within the ventricular specialized conduction system. Therefore, this is a second example of type II Mobitz second-degree block with block occurring above the His bundle recording site.

Type II Mobitz block was also demonstrated in the isolated rabbit heart preparation, with the abruptly dropped beat being due to block within the A-V node, as shown in figure 5. Right atrial and right ventricular electrograms and transmembrane action potentials from an A-V nodal and right bundle-branch cell were recorded simultaneously. Time marks indicate 100-msec intervals. Notice that after the first conducted atrial response the second and third atrial responses were blocked below the A-V node but above the impaled right bundle-branch fiber. The fourth atrial response was conducted to the ventricle, and the fifth atrial response was blocked within the A-V node. In all cases the atrial pacing interval and the atrial-to-A-V nodal conduction time remained constant. Figure 5 therefore

![Figure 5](http://circ.ahajournals.org/)  

**Figure 5**  
Mobitz type II block occurred within both the A-V node (fifth beat) and the His-Purkinje system (second, third, seventh, ninth, tenth beats) in this isolated rabbit heart preparation. Bipolar electrograms were recorded from the right atrium (RA) and the right ventricle (RV), together with transmembrane potentials from the N region of the A-V node (N) and the right bundle branch (RBB). The timing signal (T) denotes 100 msec. Thus, the sudden dropped beat in Mobitz type II block may sometimes result from conduction failure within either the A-V node or the infranodal system.
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demonstrates Mobitz type II block resulting from conduction failure within the A-V node as well as within the ventricular specialized conduction system (His-Purkinje system).

Recent studies indicate that concealed His bundle extrasystoles or echo beats can cause pseudo-type II block.4, 8, 9 Such findings have been dependent upon the chance occurrence of an extrasystole or echo beat blocking a regularly conducted beat. In our experiments we were able to demonstrate pseudo-type II block consistently by evoking extrasystoles in the bundle of His using a technique for intracellularly stimulating and recording through the same microelectrode.10 This technique allows precise localization of the site of stimulation as well as direct verification of activation of the same cell.

In figure 6 are shown simultaneous atrial and ventricular electrograms and a transmembrane potential recording from the bundle of His in an isolated rabbit heart. The ladder diagram is included below the analog tracings as an orientation to the sequence of conduction. Notice that after the third conducted beat a premature action potential is evoked in the bundle of His by stimulation through the recording microelectrode. The premature action potential is concealed both antegrade and retrogradely, but has the effect of blocking conduction of the subsequent atrial activation (fourth atrial response). The electrocardiographic pattern that this intervention produces is "pseudo" Mobitz type II block with the site of block occurring within the A-V node.

Figure 6
Pseudo Mobitz type II A-V block due to premature concealed impulses arising in the bundle of His. Bipolar electrograms were recorded from the right atrium (RA) and right ventricle (RV), together with the transmembrane potential from the His bundle (H). The fourth His bundle action potential was prematurely evoked by stimulating the impaled cell through the recording microelectrode and was not conducted either antegrade or retrograde. This premature H response did enter the A-V node and prevent the fourth atrial response from being conducted. The timing signal denotes 100 msec. Below the experimental record is the corresponding ladder diagram showing the conduction pattern through the right atrium, A-V node (AVN), His bundle, and right ventricle.
Mobitz type II block occurring within the ventricular specialized conduction system is associated clinically in man with disease status of the heart and is indicative of impending bilateral bundle-branch block. Most clinical cases of Mobitz II show bundle-branch block patterns in the ECG. As might be expected, it is difficult to demonstrate this type of A-V block experimentally in the normal heart. In the calf (fig. 1) bilateral bundle-branch block could be induced following slight changes in the P-P interval. Only right bundle-branch block could be shown in the normal dog heart during variations in the P-P interval. The ability to produce block in the VSCS by premature atrial beats has been reported before.\(^2\)\(^,\)\(^11\)\(^,\)\(^12\) At relatively slow driving rates the functional refractory period (shortest interval between two propagated beats) of the Purkinje system can exceed that of the A-V node, and premature beats may fail to traverse the Purkinje system for this reason. The basis for the difference between the calf and dog hearts regarding the ability of the former to exhibit bilateral bundle-branch block is not known. This may reflect a species difference in the characteristics of A-V node or VSCS conduction, or it may be due to differences between the newborn heart and the adult heart.\(^2\)\(^,\)\(^13\)

Type II block developing above the bundle of His is easily demonstrated in both the in vivo animal preparation and the isolated heart preparation. If the normal heart is paced at a rapid enough rate to embarrass A-V conduction but not rapid enough to cause Wenckebach periods, beats can be dropped at will by eliciting occasional slightly premature atrial stimuli (5 to 20 msec premature). The slightly premature atrial responses fail to conduct through the already depressed A-V node since they fall within the A-V nodal functional refractory period. The conducted beats show a constant atrial-to-ventricular conduction time since they occur consistently at the beginning of the relative refractory period of the A-V node (fig. 3). In these instances the slight variations in the P-P interval cause the beats to be blocked within the A-V node rather than the VSCS. This results from the differential effects of cycle lengths upon the A-V node and the VSCS tissues, whereby at rapid rates of drive the functional refractory period of the Purkinje system shortens while the nodal refractory period lengthens. The A-V node therefore offers the greater barrier to conduction during rapid driving rates. Spontaneous dropped beats within the A-V node accompanied by constant A-V conduction times were also demonstrated in the open-chest dog in experiments in which A-V nodal transmission was stressed by toxic doses of ouabain or by vagal stimulation (fig. 4). Sudden dropped beats within the node without antecedent changes in A-V conduction time were also seen in the isolated rabbit heart (fig. 5).

The present studies emphasize that Mobitz type II second-degree block can be experimentally produced in normal animal hearts with block occurring within either the A-V node or the VSCS during slight variations in P-P intervals. The region of the conduction system where block will occur is determined not only by the pathophysiologic state of the conducting tissue but also by the rate and rhythm of impulse arrival at these sites. It follows that in the diseased human heart, where conduction is already depressed, slight variations in P-P interval may sometimes be the precipitator of the sudden dropped beats that are seen clinically. The sinus arrhythmia seen in some of the reported clinical records of type II block lends support to this hypothesis.\(^3\) Furthermore, irregular activation of the VSCS is a necessary consequence of first- or second-degree block within the A-V node. Dropped beats may occur within the VSCS because of this irregular activation. Therefore, occasional dropped beats due to block within the VSCS accompanying second-degree heart block within the A-V node should not alone be considered an indication of pathology involving the infranodal system.

Experience in patients with Mobitz II block has shown that: (1) type II block is not as common as type I; (2) type II A-V block is usually associated with bundle-branch block;
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(3) 2:1 A-V block, when it is associated with a normal QRS pattern, is usually due to block within the A-V node; and (4) if 2:1 A-V block is associated with a bundle-branch block pattern the site of block can be either nodal or within the VSCS.

Our experiments show that the region of A-V block cannot be predicted solely on the basis of the behavior of the P-R interval preceding the blocked beat. However, when the P-R interval preceding the dropped beat is constant but prolonged and associated with a normal QRS, block within the node should be considered. Accurate localization of the site of the block in these experimental preparations was made possible by direct recordings from the various sites in the A-V conduction system. This study points out the value of clinical procedures such as His bundle recordings to supplement the ECG in establishing the site of second-degree heart block to facilitate diagnosis and treatment in certain complex cardiac dysrhythmias.

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