The Pathophysiology of Tachycardia-dependent Paroxysmal Atrioventricular Block After Acute Myocardial Ischemia

Experimental and Clinical Observations

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SUMMARY

The pathophysiology of paroxysmal A-V block (PAVB) was studied in 20 anesthetized dogs after ligation of the anterior septal artery. Simultaneous recording of leads II and aV_{_{r}}, as well as intracardiac recordings from the His bundle (Hb) and both bundle branches, were monitored. In 18 of 20 experiments, PAVB was localized in the Hb. In all experiments, PAVB occurred subsequent to Mobitz type II A-V block. In eight experiments, PAVB occurred spontaneously during sinus rhythm and was preceded by a period of Wenckebach periodicity superimposed upon a 2:1 A-V block. Vagal-induced slowing of the sinus rate resulted in immediate resumption of 1:1 A-V conduction. In 18 experiments, PAVB was induced by atrial pacing at a critical heart rate in each case (180–300 beats/min). Evidence is presented that A-V conduction was consistently blocked below a critical H-H interval. Slowing the pacing rate, termination of pacing or increasing the pacing rate until physiological A-V nodal block occurred, all could result in a longer H-H interval and immediate resumption of A-V conduction. When the critical heart rate for PAVB was maintained, a slow idioventricular escape rhythm occurred.

Five patients who developed PAVB after acute myocardial ischemia are also reported providing the clinical counterpart for the experimental observations. In all five cases, PAVB occurred on acceleration of the sinoatrial rate (105–140 beats/min) which was spontaneous in two and induced by drugs given for varied therapeutic indications in three (isoprenaline in two and atropine sulfate in one). In all five, PAVB was associated with Mobitz type II and/or 2:1 A-V block. These experimental and clinical observations suggest that PAVB after acute myocardial ischemia appears to be due to a tachycardia-dependent repetitive concealed conduction in the ischemic His-Purkinje system, probably mainly in the Hb. The clinical observations point out potential consequences of a rapid atrial rhythm in patients with acute myocardial ischemia and type II A-V block.

Additional Indexing Words:

Anterior septal artery
Intra-His bundle block
Mobitz type II block
Tachycardia-dependent block
Wenckebach phenomenon
Repetitive concealed conduction
Stokes-Adams syndrome

Paroxysmal A-V Block may be defined as the sudden occurrence of repetitive block of the atrial impulse during 1:1 A-V conduction (or occasionally 2:1 A-V block), resulting in a transient total interruption of A-V conduction. The onset of the arrhythmia is usually associated with a period of ventricular asystole before the return of conduction or the escape of a subsidiary pacemaker. This period of ventricular asystole, often exaggerated by delayed escape rhythms, frequently dramatizes the clinical picture of the arrhythmia. The systematic study of the pathophysiology of paroxysmal A-V block is limited not only by the transient and elusive nature of the rhythm disorder but also by the frequently precarious clinical condition of the patients. We have recently produced an appropriate experimental model for study of the pathophysiology of various A-V conduction disorders following ligation of the anterior septal artery in the dog. In this report we will discuss the pathophysiology of paroxysmal A-V block following acute ischemic injury of the canine heart. In addition,
several clinical examples of paroxysmal A-V block following acute myocardial infarction are reported that provide correlative evidence for the experimental observations.

Experimental Observations — Materials and Methods

Forty-five adult mongrel dogs weighing 10–20 kg were anesthetized with intravenous sodium pentobarbital (30 mg/kg). The animals were intubated and placed on a mechanical respirator. Blood pressure in the femoral artery was monitored through a polyethylene catheter connected to a Statham transducer. A thoracotomy incision was made through the fourth left intercostal space. The bifurcation of the left coronary artery was exposed by retracting the tip of the left atrial appendage and incising the epicardium overlying the proximal portions of the anterior descending and left circumflex arteries. The anterior septal artery was exposed by blunt dissection of the bifurcation and branches of the left coronary artery and a silk ligature was placed around the vessel to be occluded after control records were taken.

To record from the specialized ventricular conducting tissue, electrode catheters (5 French, bipolar rings 1 cm apart) were inserted into peripheral arteries and veins, into the left or right common carotid artery to the aortic root for recording His bundle activation; into the left femoral artery to the left ventricle in order to record from the left bundle branch and into both right and left femoral veins to the right ventricle in order to record the potentials from the His bundle and the right bundle branch. In one half of the experiments, after placing the ligature around the anterior septal artery, the left thoracotomy was closed and the animal turned in order to expose the heart through a right thoracotomy. One or more pairs of plunge wire electrodes (0.003 inches in diameter) were placed in the His bundle to record His bundle activation from proximal and distal portions. In addition to the electrograms, two or more standard electrocardiographic leads were recorded, specifically leads II and a VF. In order to validate each of the catheter electrode recordings, pacing at various intensities, i.e., just above threshold and two to three times threshold was performed at various rates from each of the bipolar electrodes. In experiments that developed an intra-His bundle lesion with the His bundle potential split into two deflections (H1 and H2), validation of both His deflections was carried out as previously reported.

Atrial pacing was obtained via a bipolar plunge wire electrode inserted in the left atrial appendage. Pacing was performed with a Grass S88 stimulator and stimulus isolation unit SIU5. Vagal-induced slowing or cardiac arrest was accomplished by delivery of 0.05 msec square wave pulse of 1 to 10 volts intensity at a frequency of 20 Hz through silver electrodes inserted into the left or right cervical vagosympathetic trunk. All records were obtained on a multichannel oscilloscopic photographic recorder (E for M DR-8) at paper speeds of 25 to 200 mm/sec with the filter frequencies of 0.1–200 Hz for ECG leads and 40–200 Hz for electrogram recordings. Some of the recordings were stored on a magnetic tape recorder (Honeywell 5600) and replayed so that selected sections could be registered on photographic paper for detailed analysis.

Control records during sinus rhythm, vagal-induced cardiac slowing and atrial pacing up to rates that produced atrioventricular Wenckebach conduction were obtained in each experiment before the anterior septal artery was ligated. The recorded electrical activity was then monitored for intervals up to 8 hours after ligation. In all experiments postmortem dissection was performed to verify that the anterior septal artery had been completely ligated.

Experimental Observations — Results

In all animals the control records showed a Wenckebach type second degree A-V block localized between recording sites of the atrial and His bundle deflections at pacing rates between 240–300 beats/min. Critical rates for Wenckebach periodicity proximal to the recording site of the His bundle deflection usually remained constant throughout the experiment. This observation suggested that the A-V node is not critically involved in the ischemia following ligation of the anterior septal artery. Neither the dissection of the anterior septal artery per se nor the placement of plunge wire electrodes was attended with any significant trauma to the A-V conduction system as shown in control experiments.

After abrupt ligation of the anterior septal artery, the majority of animals showed significant ST and T wave changes. Within 4–20 min following ligation all the animals except three showed ventricular premature contractions, ventricular tachycardia, and in some cases, ventricular fibrillation. Vagal-induced slowing of the heart rate was used to prevent ventricular fibrillation until the rhythm stabilized, which occurred invariably after the first 20–30 minutes. In spite of careful attention to the vulnerable arrhythmic period, six dogs succumbed to ventricular fibrillation in the first 30 min after ligation. All but one of the 39 dogs that survived the early arrhythmic period subsequently (within one to 2½ hours of ligation) developed varying degrees of conduction disorders at the level of the His bundle, right and left bundle branches or any combinations of these (table 1). A characteristic pattern for evolution of intra-His bundle lesions was observed. This began with a first degree intra-His bundle block with a split His bundle potential (H1 and H2) and a prolonged H1-V interval

| Table 1 |

| Localization of Conduction Disorders in the Canine Proximal His-Purkinje System Following Ligation of the Anterior Septal Artery in 39 Experiments |
|-----------------|-----------------|-----------------|-----------------|
| Number of experiments | His bundle | Right bundle | Left bundle |
| 10 | + | - | - |
| 12 | + | + | - |
| 4 | + | - | + |
| 2 | + | + | |
| 2 | - | + | - |
| 8 | - | + | + |

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and passed through a second degree block characterized by intermittent block of the atrial impulse between the two His deflections to a complete (third degree) intra-His bundle block.

Paroxysmal A-V block was observed in 20 out of 38 experiments (53%). Table 2 summarizes the findings in these 20 experiments. In 18 experiments (90%), paroxysmal A-V block was localized in the His bundle. In the remaining two experiments, the block was localized distal to the single His bundle deflection but proximal to the bundle branch potential in the presence of a bundle branch block pattern in the electrocardiogram. Although this may suggest that the block is occurring at the proximal bundle branch system (bilateral bundle branch block), the possibility of the presence of a latent His bundle lesion which was not detected by our recordings cannot be excluded.5, 8

Paroxysmal A-V block was observed to develop spontaneously during normal sinus rhythm in eight experiments. Spontaneous paroxysmal A-V block always occurred subsequent to the development of second degree A-V block. A characteristic pattern for the evolution of spontaneous paroxysmal A-V block was noted. Atrioventricular conduction changed from a 1:1 pattern to a short period (a few seconds to 2 min) of 2:1 A-V block before paroxysmal A-V block ensued. The conducted beats during 2:1 A-V block showed a progressive prolongation of the H-V interval before the last conducted beat with the longest H-V interval being followed by complete A-V block. The pattern represented a Wenckebach periodicity superimposed upon a 2:1 A-V block.

A classical example of spontaneous paroxysmal A-V block is shown in figure 1 which was obtained 90 min following ligation of the anterior septal artery. A His bundle deflection was recorded from the left side with a catheter electrode (HbL) whereas a plunge wire electrode inserted on the right side recorded the proximal His bundle potential (HbW). The standard lead electrocardiogram reveals normal sinus rhythm with right bundle branch block. The first half of panel A shows 1:1 A-V conduction. Note the clear splitting of the His bundle potential, in the HbL recording, into two deflections (H1 and H2) with a gradual increase of the H1-V interval from 34 to 45 msec. The delay was localized exclusively between the two His deflections (see the magnified section, encircled). Failure of ventricular depolarization after the fourth atrial impulse occurred with the block localized between the two His deflections. This is followed by a period of 2:1 intra-His bundle block. The H2-V interval of conducted beats gradually increased from 38 to 70 msec before the development of paroxysmal A-V block in the second half of panel B. Note the delayed escape of an idioventricular focus marked X. Although the block occurred between the two His deflections, the initial His potential was diminutive and

<table>
<thead>
<tr>
<th>Expt. no.</th>
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<th>2° A-V block</th>
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<td></td>
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<td>Right bundle</td>
<td>Left bundle</td>
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</tr>
<tr>
<td>20</td>
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</table>

Table 2

Analysis of 20 Experiments Showing Paroxysmal A-V Block Following Ligation of the Anterior Septal Artery in the Dog

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sometimes difficult to detect. On the other hand, the His bundle deflection in the Hb (W) electrogram is simultaneous in timing with the first deflection of the His recording in the Hb (L) electrogram. The Hb (W) electrogram shows clearly that the block is occurring below the site of recording of this His deflection. However, the Hb (L) electrogram might be misinterpreted as showing A-V nodal block because it failed to show clearly the proximal His bundle deflection.

During spontaneous paroxysmal A-V block it was possible to resume A-V conduction immediately by vagal-induced slowing of the sinus rate. When vagal stimulation was stopped and the sinus rate accelerated, after a short period of 2:1 A-V conduction paroxysmal A-V block usually recurred. Figure 2 was obtained from another experiment two hours after ligation. The standard electrocardiographic leads show sinus rhythm and a right bundle branch block pattern. The His bundle recording reveals a markedly prolonged H-V interval. Strips A and B are consecutive, with a few beats of complete heart block omitted. Figure 2, strip A, illustrates the onset of spontaneous paroxysmal A-V block which is preceded by a short period of Wenckebach periodicity superimposed upon a 2:1 A-V block. Note the delayed occurrence of an idioventricular escape beat, marked X. Figure 2, strip B, illustrates that vagal-induced slowing of the sinus rate, applied during spontaneous paroxysmal A-V block, resulted in immediate resumption of 1:1 A-V conduction. This observation strongly suggests that spontaneous paroxysmal A-V block in this particular experimental setting is a rate-dependent (tachycardia-dependent) phenomenon. This experiment was one of two in which a split His bundle deflection was not demonstrated and the block was localized distal to the single His potential in the presence of complete right bundle branch block pattern. Although this may suggest that the paroxysmal A-V block is localized in the left bundle branch system, the possibility that a latent intra-His bundle block, not detected by the catheter electrode recording, exists cannot be excluded. Such a situation is clearly illustrated in figure 1.

In 18 experiments, including six in which spontaneous paroxysmal A-V block was observed, the block could be induced by pacing the atria at a critical rate higher than the sinus rate. This was always possible shortly after second degree A-V block was observed. This is illustrated in figures 3 and 4. Figure 3, panels A to C, shows the evolution of an intra-His bundle block. Note gradual fractionation of the His bundle potential associated with an increase in its duration as well as prolongation of the H-V interval 45 min after ligation of the anterior septal artery (figure 3, panel B). Fifteen minutes later, the His potential has split into two distinct deflections (H1 and H2) with further increase of the H1-V interval (figure 3, panel C). This represents first degree intra-His bundle block. Figure

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

*Recordings of His bundle electrogram by a catheter electrode in the left ventricle (Hb (L)) and a plunge wire electrode (Hb (W)) obtained 90 min after ligation of the anterior septal artery. Panels A and B are continuous and illustrate the spontaneous development of 2:1 intra-His bundle block (panel A) followed by paroxysmal intra-His bundle block (panel B). See text for discussion. X = an idioventricular escape beat. Timelines in this and subsequent records are set at 1 sec intervals.*

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Figure 2
Catheter electrode recording of the His bundle electrogram from the left ventricle (Hb (L)) obtained two hours after ligation of the anterior septal artery. Panel A illustrates the onset of spontaneous paroxysmal A-V block which is preceded by a period of Wenckebach periodicity superimposed upon 2:1 A-V block. Panel B illustrates that vagal-induced slowing of the sinus rate applied during spontaneous paroxysmal A-V block resulted in immediate resumption of 1:1 A-V conduction. See text for discussion.

3, panel D, illustrates the spontaneous occurrence of second degree intra-His bundle block. Notice the slight gradual increase of the H1-H2 interval before the occurrence of an intra-His bundle block. This is an example of Wenckebach periodicity with only a few msec increment of conduction delay. Figure 4 was obtained from the same experiment 2 min following figure 3, panel D. Atrial pacing started

Figure 3
Catheter electrode recording of the His bundle electrogram from the left ventricle (Hb (L)) showing evolution of intra-His bundle block after ligation of the anterior septal artery. See text for details.
at PI with a gradual increase of the pacing rate (shortening of the atrial cycles). Atrial pacing resulted in immediate 2:1 intra-His bundle block. Gradual shortening of the atrial cycles was associated with a slight increase of the H1-H2 interval of the conducted beats. At a critical shortening of the atrial cycle to 305 msec (atrial rate of 195 beats/min) complete intra-His bundle block developed. Although gradual increase of the pacing rate always resulted in a short period of 2:1 A-V block before paroxysmal A-V block developed, the latter could be induced abruptly during sinus rhythm and 1:1 A-V conduction if atrial pacing was started at the critical rate that induced the block or at any higher rate. The Wenckebach increment on top of the 2:1 A-V block that preceded the induced paroxysmal A-V block was always of a lesser degree (5-15 msec) compared to that preceding spontaneous paroxysmal A-V block (25-40 msec) in spite of a slower atrial rate in the latter.

A characteristic finding in induced paroxysmal A-V block was that A-V conduction was consistently blocked at a critical H1-H2 cycle length. On the other hand, A-V conduction immediately resumed once a longer H1-H2 cycle occurred. Lengthening of this cycle length could be produced either by slowing the pacing rate or terminating atrial pacing or by increasing the pacing rate to the rate at which physiological A-V nodal conduction block, and thus a longer H1-H2 interval, occurred. This is shown in figure 5 obtained 90 min following ligature of the anterior septal artery and shortly after second degree intra-His bundle block was observed. Panels A to C represent portions of a continuous record, with only a few beats of complete heart block omitted. Atrial pacing started at PI, with gradual increase of the atrial rate. Gradual shortening of the atrial cycles first resulted in 2:1 intra-His bundle block with a few msec increment of the H1-H2 intervals of conducted beats. At a critical atrial cycle (or H1-H2 cycle) of 295 msec, consistent intra-His bundle block developed. Further shortening of the atrial cycles in panel B resulted in A-V nodal Wenckebach conduction with gradual lengthening of the A-H1 intervals before the occurrence of an A-V nodal block. This resulted in an effective H1-H1 interval of 305 msec and intra-His bundle conduction resumed immediately. Further shortening of the atrial cycles in panel C gave rise to a 2:1 A-V nodal block. However, consistent intra-His bundle block persisted because the effective H1-H1 intervals were shorter than the critical interval of 295 msec. Atrial pacing was stopped in the second half of panel C. This resulted in immediate resumption of 1:1 intra-His bundle conduction after an atrial escape cycle of 455 msec.

During spontaneous paroxysmal A-V block the delayed occurrence of a slow escape rhythm was observed. However, conduction usually resumed within one to a few minutes. In induced paroxysmal A-V block on the other hand, the block remained so long as the critical rate of rapid atrial pacing is main-
tained. A slow, first irregular, later fairly regular escape rhythm developed. This is shown in figure 6 which was obtained from the same experiment in figure 5. The paced atrial rhythm was maintained at a rate slightly higher than the critical rate for paroxysmal intra-His bundle block. This resulted in the escape of a slow idioventricular rhythm at a rate of 21 beats/min (figure 6, panel A). Figure 6, panels B and C, shows that the escape focus is probably located in the left bundle branch system because a left bundle

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**Figure 5**

Catheter electrode recording of the His bundle electrogram from the right ventricle (Hb (R)) obtained 90 min following ligation of the anterior septal artery. Panels A to C represent portions of a continuous record with only a few beats omitted. The record illustrates paroxysmal intra-His bundle block induced by atrial pacing and the interplay of physiological A-V nodal refractoriness. See text for details.

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**Figure 6**

Recordings obtained from the same experiment shown in figure 5. Panel A shows atrial pacing at a rate of 214 beats/min which resulted in persistent intra-His bundle block and the escape of a slow idioventricular rhythm. Panels B and C show catheter electrode recordings of the His bundle electrogram from the right ventricle (Hb (R)) and a left bundle electrogram (Lb). During 2:1 intra-His bundle block in panel B, the Lb-V interval in conducted beats is 18 msec. In panel C, the escape beat is preceded by a left bundle potential with an Lb-V interval of 10 msec. This in addition to the right bundle branch block pattern of the escape QRS suggests an origin in the proximal left bundle branch system.
branch potential preceded the escape beats. Of 18 experiments showing spontaneous or paroxysmal A-V block localized in the His bundle, the escape rhythm was idioventricular in 16 and arose from the distal His bundle in only two experiments (table 2).

As a rule paroxysmal A-V block could be induced relatively early in the experiment during the early stages of second degree A-V block. Later in the experiment either a persistent complete A-V block developed or A-V conduction showed improvement. In the latter situation, atrial pacing usually failed to induce paroxysmal A-V block but frequently resulted in high grade A-V block. Some cases showed evidence that the rapid atrial rate necessary to induce paroxysmal A-V block could not be achieved due to the interference of physiological A-V nodal refractoriness. This is shown in figure 7 which was obtained from the same experiment in figures 5 and 6, three and a half hours after ligation. Figure 7, panel A, shows atrial pacing at a fast rate of 286 beats/min which resulted in a regular 6:1 intra-His bundle block. Note that in figure 5, paroxysmal A-V block was induced at a much slower rate. Further increase of the atrial rate in figure 7, panel B, gave rise to a 2:1 A-V nodal block with successful intra-His bundle conduction of every other beat, which resulted in a 4:1 A-V response. Termination of atrial pacing at the end of figure 7, panel B, resulted in immediate resumption of 1:1 A-V conduction. Critical analysis of the H₁-H₂ intervals in figure 7 reveals that the H₁-H₂ interval of conducted beats in panel A is significantly longer (50 msec) compared to the H₁-H₂ interval of conducted beats in panel B, 30 msec, both during rapid atrial pacing (first part of panel B) and normal sinus rhythm (the last part of panel B). This occurred in spite of the fact that the higher grade intra-His bundle block in panel A resulted at a relatively longer R-R interval. This observation strongly suggests that concealed intra-His bundle conduction is present in panel A due to the shorter H₁-H₂ cycle lengths. The observation may also suggest that paroxysmal intra-His bundle block observed earlier in the experiment may have been due to a higher degree of repetitive concealed conduction in the diseased His bundle. On the other hand, the failure to induce paroxysmal A-V block later in the experiment is probably related to the fact that the critical atrial rate necessary to produce the arrhythmia could not be achieved due to interference of physiological A-V nodal refractoriness.

**Clinical Observations**

Five clinical cases of paroxysmal A-V block after acute myocardial infarction were analyzed (table 3). The diagnosis of acute myocardial infarction was

![Figure 7](https://circ.ahajournals.org/doi/10.1161/01.CIR.50.9.522/figure-7)

Recordings from the same experiment shown in figures 5 and 6, obtained 3½ hours after ligation of the anterior septal artery. Panel A shows atrial pacing at a rate of 286 beats/min giving rise to a 6:1 intra-His bundle block. In panel B, further increase of the atrial rate gave rise to a 2:1 A-V nodal block with intra-His bundle conduction of every other beat resulting in a 4:1 A-V response. Atrial pacing was terminated at the end of panel B with immediate resumption of 1:1 A-V conduction. Note that the H₁-V interval of conducted beats in panel A (90 msec) is longer than the H₁-V interval in panel B (70 msec), reflecting concealed intra-His bundle conduction in panel A. See text for details. The unmarked arrows in panel B point to the H₁ deflection.
Table 3

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<th>Case</th>
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<th>IV conduction disorder</th>
<th>Course</th>
<th>Shock. Heart Failure</th>
<th>Sinus rate of A-V block</th>
<th>Sinus rate of P-A block</th>
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<td>Old antero-septal MI, recent infero-lateral MI</td>
<td>Mobitz type II and 2:1 A-V block</td>
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<td>Spontaneous sinus arrhythmia</td>
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<td>115-125 beats/min</td>
<td>105-115 beats/min</td>
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<td>Spontaneous sinus arrhythmia</td>
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Representative electrocardiograms from case 1 showing paroxysmal A-V block on acceleration of the sino-atrial rate. The top record illustrates the patient 12-lead standard electrocardiogram on admission showing an old antero-septal infarction and recent ST-T changes in infero-lateral surface leads. The rhythm strips in panels A to D are not continuous, however strips C and D represent consecutive records in which a 40 sec long rhythm strip showing complete A-V block was omitted. See text for details.
tracings recorded from case 1. This patient differed from the rest of the group in having a history of transient episodes of dizziness several months before the last observation. Constant ECG monitoring during the last admission correlated these episodes with the abrupt onset of ventricular asystole and complete A-V block. The top tracing in figure 8 illustrates the patient's standard electrocardiogram taken during the last admission. The record shows an old antero-septal myocardial infarction that was present in the patient's previous records together with recently developed ST-T abnormalities in infero-lateral surface leads. Figure 8, strip A, shows 1:1 A-V conduction at an average sinus rate of 87 beats per min and a P-R interval of 0.18 sec. Figure 8, strip B, shows a faster sinus rate of 102–108 beats per min and the sudden failure of A-V conduction without an appreciable change in the sinus rate or the P-R interval (Mobitz type II block). Figure 8, strip C, illustrates the onset of paroxysmal A-V block which was always preceded by an acceleration of the sinus rate to 115–120 beats/min or higher. The record shows a period of ventricular asystole of 2½ sec followed by the escape of an idioventricular rhythm at a rate of 40 beats/min. Note that after the onset of ventricular asystole, spontaneous slowing of the sinus rate and shift of the sinus pacemaker occurred. Figure 8, strip D, represents a tracing recorded 45 sec following the onset of paroxysmal A-V block in strip C and illustrates the re-establishment of 1:1 A-V conduction.

One-to-one A-V conduction was only resumed when the sinus rate fell below 100 beats/min. However, analysis of several episodes showed that there were occasional time intervals lasting seconds up to 2 min during which complete A-V block persisted in spite of the fact that the atrial rate decreased below the rate which induced the paroxysmal A-V block.

In three patients (cases 3 to 5), paroxysmal A-V block occurred when acceleration of the atrial rate was induced by drugs. In cases 3 and 4, increase of the atrial rate was secondary to isoprenaline infusion that was started for correction of hypotension associated with sinus bradycardia in case 3 and with 2:1 A-V block in case 4. In case 5, the increase in atrial rate was secondary to an atropine sulfate injection given for sinus bradycardia associated with ventricular ectopic beats. In all three cases, when the atrial rate increased above 110–130 beats/min, a high grade A-V block developed that was abruptly followed by paroxysmal A-V block. The electrocardiograms reproduced in figure 9 show representative tracings from case 3. The top tracing in figure 9 illustrates the patient standard electrocardiogram taken on admission. The record reveals an acute anterior myocardial infarction with right bundle branch block and left axis deviation. Figure 9, strip A, illustrates the patient's cardiac rhythm on admission and shows sinus bradycardia with an average rate of 48 beats/min. Because of the slow sinus rate associated with a low blood pressure, isoprenaline infusion was initiated. Figure 9, strip B, was obtained shortly after the start of infusion and shows an increase of the sinus rate to 95 beats/min with 1:1 A-V conduction continuing. Further increase in the atrial rate was associated with a sudden development of 2:1 A-V block that rapidly changed to a high grade A-V block and terminated in a paroxysmal A-V block. This is illustrated in figure 9, strip C, which shows a regular 6:1 A-V block that changed to a 7:1 block followed immediately by ventricular asystole for several seconds before an irregular escape beating occurred (not shown in the figure). An interesting observation was the significant lengthening of the P-R interval of conducted beats during the high grade A-V block with very slow ventricular rate (0.26 sec) compared to a P-R interval of 0.16 sec in figure 9, strip B, at a much higher ventricular rate. This observation is comparable to the experimental observation in figure 7 and similarly suggests the occurrence of concealed conduction in the A-V pathway at the high atrial rate. It also suggests that the ventricular asystole that later followed may represent a high degree of repetitive concealed conduction in the A-V pathway.

Figure 9

Representative electrograms from case 3 showing paroxysmal A-V block that followed isoprenaline infusion with marked acceleration of the sinus rate. The top record illustrates the patient 12-lead standard electrocardiogram on admission, showing right bundle branch block, left axis deviation, and acute antero-septal myocardial infarction. Panel A illustrates the patient's cardiac rhythm on admission and reveals sinus bradycardia at a rate of 48 beats/min. The rhythm strip in panel B was obtained shortly after the start of isoprenaline infusion and shows an increase of the sinus rate to 95 beats/min with 1:1 A-V conduction. Panel C illustrates the development of sinus tachycardia (130 beats/min) with a high grade A-V block that terminated in complete A-V block and a prolonged ventricular asystole. Note the lengthening of the P-R interval of conducted beats in panel C (0.26 sec) compared to a P-R interval of 0.16 sec in panel B. This suggests concealed A-V conduction in panel C. See text for details.

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In the presence of an intraventricular conduction abnormality in the present case, it is possible that concealed conduction is occurring in the His-Purkinje system rather than in the A-V node.

Discussion

The experimental observations in the present report illustrate the close association between the early stages of second degree A-V block and the occurrence of paroxysmal A-V block. They also illustrate that both paroxysmal A-V block occurring abruptly during sinus rhythm and that induced by rapid atrial pacing are tachycardia-dependent, meaning that the A-V block occurred at "higher" rather than only at "high" rates. The fact that paroxysmal A-V block was observed only after second degree A-V block has developed, together with the observation that a period of Wenkebach periodicity superimposed upon a 2:1 A-V block usually preceded the onset of paroxysmal A-V block, provides an insight into the possible electrophysiological disturbance underlying the arrhythmia. Recent electrophysiological studies from this laboratory have suggested that both the early stage of second degree intra-His bundle block (the equivalent of the so-called Mobitz type II block) and the later stage (the Wenkebach periodicity) are different stages of the same electrophysiological disturbance. In vitro studies utilizing intracellular recordings have shown that the ischemic His-Purkinje system conducts decrementally during both stages of second degree A-V block with the "Mobitz type II" block representing the initial stages of decrement of conduction. These findings reveal that paroxysmal A-V block develops only when the His-Purkinje system starts to conduct decrementally. The occurrence of a period of Wenkebach periodicity superimposed upon a 2:1 A-V block before the onset of paroxysmal A-V block apparently reflects the development of a higher degree of decremental conduction immediately preceding the onset of the arrhythmia. It also suggests the presence of concealed conduction of the blocked impulses during the 2:1 periodicity. The consistent A-V block that later develops may be thus ascribed to the occurrence of repetitive concealed conduction. Another observation that strongly suggests the presence of concealed conduction in the ischemic His bundle is the development of a longer His bundle conduction time during atrial pacing and high grade intra-His bundle block (fig. 7). Recent in vitro observations utilizing the same experimental model in this study has revealed evidence of a tachycardia-dependent repetitive concealed conduction in the ischemic His bundle. Impaled ischemic His bundle cells showed repetitive decremented action potentials at a critical rate of rapid stimulation resulting in consistent failure of conduction. Thus both the experimental observations in this report and the recent in vitro studies strongly suggest that paroxysmal A-V block following acute myocardial ischemia is due to a tachycardia-dependent, repetitive, concealed conduction at the site of lesion in the ischemic His-Purkinje system, mainly in the His bundle.

Repetitive concealed conduction has been suggested as the mechanism of prolonged ventricular asystole in cases of second degree A-V block. Both clinical reports and electrophysiologic studies utilizing the microelectrode technique have demonstrated repetitive concealed conduction in the A-V node. It is generally agreed, however, that both paroxysmal A-V block and the closely associated Mobitz type II A-V block represent forms of sub-A-V nodal block. On the other hand, concealed conduction has been shown to occur in the His-Purkinje system and rate-dependent repetitive decremental conduction was demonstrated in excised bundles of canine Purkinje fibers subjected to a high potassium concentration. The phenomenon of Wenkebach periodicity on top of a 2:1 A-V conduction has also been recently reported in association with the Stokes-Adams syndrome. However, the clear transition from a period of Wenkebach periodicity superimposed upon 2:1 A-V block to paroxysmal A-V block has not been shown before.

Our experimental observations suggest that the His bundle is a critical site in the development of paroxysmal A-V block. Direct extrapolation of this observation to humans should be guarded because of species difference in the distribution of the coronary vascular tree. However, it is worth noting that several of our experimental observations have shown that the His bundle was the site of paroxysmal A-V block in spite of the presence of a bundle branch block pattern in the electrocardiogram (table 2) which is frequently taken to indicate bilateral bundle branch block in clinical records. On the other hand, some cases of intra-His bundle block may be misinterpreted as A-V nodal block if the proximal His bundle deflection (H1) is not recorded (fig. 1). This may explain not only some of the occasional reports of Mobitz type II block in the A-V node but also the rare finding of paroxysmal A-V block localized above the recording site of the His bundle deflection. Recent histopathological correlations of the His bundle electrogram may help to assess the value of His bundle recording in humans for precise localization of the site of A-V conduction disorder; however, there is some doubt as to how far pathological alterations can reflect electrophysiologic disorders.

The clinical observations in this report provide several correlative evidences to the experimental find-
ings. First, although the exact site of A-V block in the clinical cases cannot be ascertained in the absence of a His bundle recording, the presence of right bundle branch block and left axis deviation in four of five cases suggest that the block may have occurred in the His-Purkinje system. The fifth patient showing normal intraventricular conduction may have had an intra-His bundle lesion. Second, all cases illustrated the close association of Mobitz type II A-V block and/or 2:1 A-V block with paroxysmal A-V block. Third, evidence of repetitive concealed conduction in the His-Purkinje system has been demonstrated in case 3. Lastly, all cases have shown that paroxysmal A-V block was related to acceleration of the atrial rate. However, the occasional observation that 1:1 A-V conduction was not immediately resumed when the atrial rate slowed down (fig. 8) represents a point of departure between the clinical and experimental observations. This finding raises the possibility that other electrophysiological mechanisms may be involved in clinical examples of tachycardia-dependent paroxysmal A-V block. A fatigue phenomenon following repetitive concealed conduction in the ischemic His-Purkinje system may be operative in these clinical cases.

Increase in atrial rate was postulated as a possible cause of intermittent complete A-V block and Stokes-Adams attacks as early as 1905. Wenckebach and Winterberg and Gilchrist have discussed the role of atrial rate in the change to higher degrees of block in patients showing type II block. Tachycardia-dependent paroxysmal A-V block following acute myocardial ischemia has not been reported although critical analysis of several published figures showed an associated sinus tachycardia. On the other hand, few cases of tachycardia-dependent paroxysmal A-V block have been described in patients with Stokes-Adams syndrome not suffering from acute myocardial ischemia. McHenry and Knoebel reported a case of paroxysmal A-V block associated with acceleration of the sinoatrial rate which was very similar to cases 1 and 2 in the present report. Schwartz and Schwartz reported a few cases in which isuprel given to treat transient heart block in patients with Stokes-Adams syndrome resulted in marked sinus tachycardia and paroxysmal A-V block closely simulating the observations in cases 3 and 4 in this report. In two recent papers by Cheng and Cheng, two patients with right bundle branch block, left axis deviation, and 1:1 A-V conduction during sinus rhythm were described. Atrial pacing resulted in the development of complete A-V block in the His-Purkinje system. Critical analysis of one of the figures (figure 3) reveals that atrial pacing at a rate of 85 beats/min induced a Wenckebach periodicity below the site of recording of the His bundle deflection. On further increase of the atrial pacing rate to 88 beats/min, 2:1 A-V block in the His-Purkinje system developed with slight but distinct increase of the H-V interval of conducted beats, followed by the occurrence of complete A-V block: i.e., tachycardia-dependent paroxysmal A-V block.

Although the present report investigates the pathophysiology of paroxysmal A-V block following acute myocardial ischemia, there is some evidence that a similar electrophysiological mechanism may be operative in patients with Stokes-Adams syndrome and paroxysmal A-V block not suffering from acute myocardial ischemia. In these patients there is also the close association of Mobitz type II block and paroxysmal A-V block. Several patients show what has been described as "labile" A-V conduction which, at least in some cases, represented a tachycardia-dependent 2:1 A-V block. In most of these cases, paroxysmal A-V block occurred spontaneously during sinus rhythm and more closely resembled examples of spontaneous paroxysmal A-V block in the experimental study. Although we have demonstrated that experimental examples of spontaneous paroxysmal A-V block represented in fact a rate-dependent phenomenon, no such observations have been documented in the clinical setting. Our experimental observations, however, suggest that in paroxysmal A-V block the two variables that may be involved are the degree of pathophysiological disturbance in the His-Purkinje system and the atrial driving frequency. There is evidence to suggest that the greater the degree of pathophysiological disturbance, the more chance for paroxysmal A-V block to occur at a relatively slower atrial rate. It is thus possible that in some clinical examples of Stokes-Adams syndrome with a "labile" A-V conduction state, some variation in the degree of the electrophysiological disturbance in the A-V conduction system may be brought about by such factors as slight changes in the coronary perfusion and/or the level of circulating catecholamine. The latter may act through greater decrement of conduction in already depressed Purkinje fibers. These factors — rather than a change in the heart rate — may explain the episodes of paroxysmal A-V block that may develop abruptly during normal sinus rhythm while at other times conduction may be sustained during a relatively higher atrial rate.

It is important to comment, however, on the fact that most clinical examples with chronic "stable" lesions in the His-Purkinje system respond to rapid atrial pacing by either A-V nodal block, 2:1 or a higher degree of block in the His-Purkinje system, but not by paroxysmal A-V block. One explanation is to assume that chronic stable lesions in the His-Purkinje system do not carry the propensity for repetitive con-
cealed conduction necessary for paroxysmal block. Our experimental observations, however, may provide an electrophysiological explanation for some of these cases. We have demonstrated that later in the experiment following ligation of the anterior septal artery, rapid atrial pacing failed to induce paroxysmal A-V block while resulting in a higher degree of A-V block. In some of these cases, evidence for concealed conduction in the A-V pathway could still be demonstrated (fig. 7). On further increase of the atrial rate, physiological A-V nodal refractoriness came into play with resultant decrease in the input to the His-Purkinje system. It is thus possible that in some clinical examples with established His-Purkinje lesions, the atrial input to the His-Purkinje system necessary for the development of repetitive concealed conduction is relatively high and cannot be achieved due to the interference of physiological (or sometimes pathological) A-V nodal refractoriness. In these cases, the A-V node plays a protective role against repetitive concealed conduction in the diseased His-Purkinje system.

The electrophysiological mechanism for paroxysmal A-V block described in this study does not necessarily apply to all cases of paroxysmal A-V block. Several examples of bradycardia-dependent paroxysmal A-V block have been described and the phenomenon was ascribed to spontaneous diastolic depolarization in the His-Purkinje system. However, as recently pointed out, this phenomenon cannot be responsible for the majority of cases of paroxysmal A-V block which are closely associated with type II A-V block.

Our understanding of the pathophysiology of A-V conduction disorders is far from complete. Further experimental and clinical observations are necessary to provide more insight into the mechanism of paroxysmal A-V block. However, the experimental and clinical observations in this report point out potential clinical consequences of rapid atrial rate, whether spontaneous or induced by drugs, in patients with acute myocardial ischemia and type II A-V block.

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