ABSTRACT

The main ventricular conducting fascicles were slightly injured in anesthetized dogs by gently scratching them with a blunt needle introduced through the ventricular wall. Initially the bundle branch block that resulted was rate independent (stage 1). When conduction returned to normal, both premature atrial and vagal stimulation reproduced the bundle branch block (stage 2). During stage 2 (5–15 minutes), three conduction ranges were documented: an early (phase 3) block range, a late (phase 4) block range, and an intermediate normal conduction range. The normal conduction range was narrow at the beginning but widened progressively, mostly at the expense of the phase 4 block range. Another period during which only phase 4 bundle branch block occurred (stage 3) preceded total normalization (stage 4). The escape beats that arose from the injured fascicle were most abundant and had the shortest coupling during stage 1, they were less common and their coupling became longer during stages 2 and 3, and they disappeared in stage 4. The tachycardia-dependent or phase 3 bundle branch block was related to a prolongation of refractoriness; the bradycardia-dependent or phase 4 bundle branch block was attributed to slight hypopolarization, enhanced spontaneous diastolic depolarization, and a shift in the threshold potential toward zero. These abnormalities were assumed to be secondary to the hypopolarization, which was probably the basic derangement. This hypothesis satisfactorily accounts for the observation that phase 3 and phase 4 bundle branch block commonly coexist in the same injured fascicle.

KEY WORDS

fascicular injury prolonged refractoriness phase 3 block threshold potential vagal stimulation phase 4 block escape beats hypopolarization spontaneous diastolic depolarization

Two types of rate-dependent bundle branch block are known to exist. In one type bundle branch block occurs when the heart rate is accelerated (1); in the other type bundle branch block appears after long diastolic intervals or when the heart rate is slow (2–16). The former type, tachycardia-dependent bundle branch block, is attributed to prolonged refractoriness (1). The latter type, bradycardia-dependent bundle branch block (15, 16), is uncommon, and different mechanisms such as vagal effects (3, 4, 6–8, 10), supernormality (1, 9), concealed conduction (13), and hypoxia (12, 13) or stretching (2) of the conducting tissue during the long diastolic intervals are thought to be involved. Recently, this form of rate-dependent bundle branch block has been related to spontaneous diastolic depolarization (15, 16). Although the mechanism of tachycardia- and bradycardia-dependent bundle branch block is obscure as is their relationship to each other, in both types of bundle branch block conduction in the diseased fascicle is partially affected, block is intermittent (17, 18), and only incomplete interruption of conduction occurs.

Recently, it has been demonstrated that bradycardia-dependent bundle branch block is much more common than it was previously assumed to be and that, in most cases of intermittent bundle branch block, tachycardia- and bradycardia-dependent bundle branch block coexist in the same affected fascicle (17–21). Thus, intermittent bundle branch block tends to occur at both rapid and slow rates with an intermediate normal conduction range. The tachycardia-dependent bundle branch block, which has been related to a prolongation of recovery, is termed phase 3 block, assuming that block occurs when an impulse reaches the diseased fascicle during phase 3 of the preceding action potential. The bradycardia-dependent bundle branch block, which has been related to subnormal polarization (hypopolarization) plus enhanced spontaneous diastolic depolarization, is termed phase 4 block. Two critical rates have been identified: one rate separates the phase 3...
block range from the normal conduction range and the other rate separates the normal conduction range from the phase 4 block range. An accordion effect has been described (17-21): the phase 3 and phase 4 block ranges seem to compress the normal conduction range. Similar behavior has been documented and correlated with fibrosis and partial interruption of the left bundle branch in a dog with spontaneously occurring intermittent bundle branch block (21).

The present study attempted to determine whether phase 3 and phase 4 bundle branch block could be reproduced in the conduction system of the intact canine heart. A technique was developed to slightly injure any of the ventricular conducting fascicles and thus to produce transient bundle branch block. When conduction returned to normal, the same bundle branch block was evoked by either increasing or decreasing the heart rate. The three conduction ranges were documented, and the conduction changes and the occurrence of escape beats that arose from the injured fascicle were correlated with the degree of injury.

Methods

MATERIALS

Mongrel dogs weighing 12-20 kg were anesthetized with sodium pentobarbital (30 mg/kg, iv) and placed under controlled respiration. The chest was opened through a midsternal thoracotomy, and the pericardium was incised at the level of the apex, the right atrium, and the base of the right ventricle. Electrodes for recording conventional electrocardiograms (ECG) were placed, and a unipolar lead similar to lead V1 was connected to the right ventricle. In most experiments, the electrical activity of the His bundle and the left bundle branch was recorded via fine Teflon-coated wires inserted into the area of the His bundle and the left bundle branch. The technique of Scherlag et al. (22) was used for recording from the His bundle. The technique for recording from the left bundle branch consisted of hooking the left bundle branch just below the junction of the noncoronary cusp with the right coronary aortic cusp; the needle transporting the wires was impaled through the middle third of the right ventricular wall and directed toward the area just below the membranous septum. After piercing the ventricular septum, the needle was pulled back until the hooked tip of the wires remained on the left septal surface.

A pulse generator (Medtronic 5837) was used to stimulate or drive the heart via a bipolar catheter placed against the lateral wall of the right atrium. The vagi were exposed and left intact in the neck. Faradic current was used for vagal stimulation. Bipolar leads from the His bundle and the left bundle branch were led into high-gain preamplifiers (Sanborn 350-2700C), filters between 15 and 5,000 cycles/sec were used. The ECG was recorded using standard electrocardiographic preamplifiers (Sanborn 350-3200A). All of the records were displayed on a six-channel photographic recorder (Sanborn 4560 series recorder), and paper speeds between 50 and 200 mm/sec were used. Control recordings were obtained to determine the configuration of the atrial and the ventricular deflections and normal conduction times, including the atrium–His bundle (A-H), the His bundle–ventricle (H-V), the atrium–left bundle branch (A–LB), and the left bundle branch–ventricle (LB–V) intervals. Control studies included determination of the effects of premature atrial stimulation, atrial overdrive at different rates, and vagal stimulation at different intensities and durations of the faradic current.

RESULTS

Table 1 summarizes the results of 23 experiments in which rate-dependent bundle branch block was provoked. Phase 4 bundle branch block occurred in 21 experiments, and phase 3 and phase 4 bundle branch block occurred at the same time in 18 experiments; phase 3 bundle branch block alone was not observed. Of these 23 experiments, left bundle branch block was provoked in 6, right bundle branch block was provoked in 10, and left anterior hemiblock was provoked in 7. Ventricular escapes occurred in 15 experiments.

CONDUCTION CHANGES PRODUCED BY TRANSIENT FASCICULAR INJURY

Since it was impossible to always produce the same degree of mechanical injury, there was a certain degree of variation in the individual experiments. However, the following general sequence of events was consistently documented (Table 1). Immediately after injury, complete bundle branch block was present at all diastolic
The injured region was inexcitable or unable to transmit impulses. After 5-10 minutes (the duration of stage 1), bundle branch block occurred after both short and long diastolic intervals with normal conduction between these intervals (stage 2). At the transition between stages 1 and 2, incomplete bundle branch block was commonly observed; however, the turning point that separated stage 1 from stage 2 was the moment when rate-independent bundle branch block changed into rate-dependent bundle branch block. Stage 2 was characterized by three conduction ranges: an early (phase 3) block range, a late (phase 4) block range, and an intermediate normal conduction range. After the three ranges were identified, a progressive widening of the normal conduction range was observed; this progressive widening was at the expense of both the phase 3 block range and the phase 4 block range, but particularly and necessarily at the expense of the phase 4 block range. Accordingly, the normal conduction range was always narrow at the beginning and much wider toward the end of stage 2, which commonly lasted between 5 and 15 minutes.

Approximately 10-20 minutes after the initial injury, phase 4 bundle branch block occurred only after extremely long diastolic intervals, and phase 3 bundle branch block could not be obtained; this period was designated stage 3. Stage 4 was signaled by the disappearance of phase 4 bundle branch block, indicating normalization of conduction for any rate of stimulation. The disappearance of escapes from the injured region was an additional indication that normalization had occurred. The entire sequence from stage 1 to stage 4 lasted between 15 and 30 minutes.

Figures 1-4 illustrate the sequence of a typical experiment. Figure 1 shows the occurrence of slight ventricular aberration after premature stimulation (A) and normal conduction after a pause of 11.26 seconds provoked by vagal stimulation (B) in the control study. Figure 2 shows tracings before (A) and after (B) injury of

---

**TABLE 1**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Conduction disturbance</th>
<th>Stages</th>
<th>Escapes</th>
<th>Incomplete BBB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Si</td>
<td>S2</td>
<td>S3</td>
<td>S4</td>
</tr>
<tr>
<td>1</td>
<td>LBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>2</td>
<td>LBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>3</td>
<td>LBBB</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>LBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>5</td>
<td>LBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>6</td>
<td>LBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>7</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>8</td>
<td>RBBB</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>9</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>10</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>11</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>12</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>13</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>14</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>15</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>16</td>
<td>RBBB</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>17</td>
<td>LAH</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>18</td>
<td>LAH</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>19</td>
<td>LAH</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>20</td>
<td>LAH</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>21</td>
<td>LAH</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>22</td>
<td>LAH</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>23</td>
<td>LAH</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

S1 = stage 1, S2 = stage 2, S3 = stage 3, S4 = stage 4; EIF = escapes of the injured fascicle; BBB = bundle branch block; LBBB = left bundle branch block; RBBB = right bundle branch block; and LAH = left anterior hemiblock.

---

**Circulation Research, Vol. XXXIV, May 1974**
the left bundle branch; these tracings illustrate the development of left bundle branch block. Tracings A and B in Figure 3 were recorded during a 5-minute period following injury. During this interval, the left bundle branch block was rate independent (stage 1). However, 5–7 minutes after the initial injury, the left bundle branch block pattern disappeared at the spontaneous rate (110–120 beats/min). At that moment tracings C–G were recorded in rapid sequence. In tracing C, left bundle branch block occurred after premature stimulation with R–R intervals of 0.26–0.28 seconds, and normal conduction occurred after R–R intervals of 0.46–0.51 seconds. In the control study in Figure 1A, a much shorter interval of 0.20 seconds that was preceded by a longer cycle of 0.33 seconds was followed by practically normal ventricular conduction. In tracing D, the left bundle branch block was elicited by an overdrive rate of 193 beats/min (R–R intervals of 0.31 seconds), and, after the overdrive was stopped, normal conduction occurred after R–R intervals of 0.53–0.66 seconds. In tracings E and F, all long pauses provoked by vagal stimulation (arrows) were terminated by a sinoatrial beat with the same left bundle branch block. In tracing G, the beat following a 2.10-second interval was probably a junctional escape that also showed left bundle branch block. Tracings C–G are representative of stage 2. During this interval, left bundle branch block was present at R–R intervals shorter than approximately 0.36 seconds; normal conduction occurred between 0.36 and 1.00 seconds, and left bundle branch block occurred again after diastolic intervals longer than 1.00 second. Tracing A in Figure 4 was recorded 4 minutes after tracing G in Figure 3; it also showed left bundle branch block after premature stimulation. Tracing B was recorded 3 minutes later; the atria were paced at the same rate as they were in Figure 3D, but left bundle branch

---

Control tracings. A: Lead 1. Premature atrial stimulation caused slight ventricular aberration after coupling intervals of 0.20 seconds. S = stimulus artifact. B: Continuous recording from lead 1 during vagal stimulation (arrow). A pause of 11.26 seconds was terminated by a sinoatrial beat that showed normal intraventricular conduction. Figures 2–4 are from this experiment also.

---

A: Leads I, II, III, and V1 simultaneously recorded (control tracing). B: Same leads as in A after injury of the left bundle branch. These tracings showed the development of left bundle branch block. The QRS complex widened from 0.04 to 0.08 seconds.
Rate-independent and rate-dependent bundle branch block. All records are lead I electrocardiograms. A and B: Recordings during a 5-minute period following injury of the left bundle branch. The left bundle branch block pattern remained unchanged regardless of the diastolic intervals (stage 1). The longer intervals were obtained by vagal stimulation (arrows). At the end of tracing B atrial overdrive occurred. C: Beats 1, 5, 7, 9, and 11 showed normal intraventricular conduction, and left bundle branch block occurred during atrial stimulation in beats 2, 3, 4, 6, 8, and 10. D, E, and F are continuous. D: Left bundle branch block provoked by rapid atrial pacing (phase 3 block); normal conduction occurred when pacing was discontinued. E and F: Long pauses provoked by vagal stimulation (arrows) were terminated by sinoatrial beats with left bundle branch block pattern (phase 4 block). G: Beat following a diastolic interval of 2.10 seconds was a junctional escape. The R-R interval of 1.06 seconds indicates that the critical diastolic interval for phase 4 left bundle branch block was around 1.00 second. Tracings C-G were representative of stage 2. Intervals are expressed in seconds.

A: Recording made 4 minutes after tracing G in Figure 3; it still shows left bundle branch block after premature stimulation (stage 2). B and C: Left bundle branch block occurred after a pause of 2.76 seconds but did not occur during rapid atrial pacing or premature atrial stimulation (stage 3). D: Recording made 20 minutes after injury that shows total normalization (stage 4).
rate-dependent bundle branch block did not occur. In tracing C, which was recorded after termination of the overdrive, left bundle branch block occurred after a pause of 2.76 seconds but did not occur after a single premature stimulation (R-R intervals of 0.26 seconds). From tracing A onward, shorter and shorter R-R intervals were needed to cause phase 3 left bundle branch block, and longer and longer pauses were required to provoke phase 4 left bundle branch block. In tracing D, 20 minutes after initial injury, left bundle branch block did not occur after either the shortest or the longest diastolic intervals.

Figure 5 shows the control tracing of another experiment. The QRS complex and the A-H, the H-V, the A-LB, and the LB-V intervals were normal. A single premature atrial stimulation with an R-R interval of 270 msec caused a slight prolongation of the A-H interval, but the H-V and the LB-V intervals and the QRS complex remained normal. Figure 6 exhibits the right bundle branch block pattern provoked after the right bundle branch was injured. During the next 8 minutes, right bundle branch block was rate independent (stage 1); then the tracing in Figure 7 was recorded. At that moment, ventricular conduction was normal for the spontaneous rate, as shown in the first two beats separated by an R-R interval of 370 msec. Following these two beats, four different degrees of right bundle branch block that were due to different diastolic intervals provoked by short vagal stimulations (arrows) could be recognized. A small degree of right bundle branch block was seen in the beats following pauses of...
Different degrees of right bundle branch block occurred and were proportional to the length of the R-R interval (see text for details).

420 and 440 msec (beats no. 4, 5, and 8). A greater degree of right bundle branch block occurred in the beats following pauses of 460 and 480 msec (beats 7 and 10), and a still greater degree of right bundle branch block was seen in beat 3 following a pause of 550 msec. Complete or high-grade right bundle branch block occurred in beats 6 and 9 following pauses of 880 and 800 msec, respectively. Thus, the aberration was proportional to the coupling of each beat and was practically unrelated to the preceding cycle length. Greater degrees of right bundle branch block were best indicated by a taller and more notched R wave in V1, a smaller S wave in the same lead, and a deeper S wave in leads II and III. H-V and LB-V intervals remained normal, indicating that the conduction disturbance occurred in the injured right bundle branch only. Figure 8 was recorded a couple of minutes later. The first two beats in Figure 8A are the termination of an atrial overdrive at a rate of 170 beats/min (R-R intervals of 350 msec), and they show complete right bundle branch block. The three following beats originated in the sinoatrial node and showed progressively decreasing degrees of right bundle branch block. In Figure 8B two single premature stimulations were followed by complete right bundle branch block. Figures 7 and 8 are representative of stage 2. During this part of the study, the critical R-R interval for phase 3 right bundle branch block was around 340 msec, and the critical interval for phase 4 right bundle branch block was around 400-420 msec. The intermediate normal conduction range was extremely narrow (Fig. 9).

Accordion Effect.—Figure 9 illustrates the three conduction ranges recorded from the ex-
Three conduction ranges and accordion effect during stage 2 of experiments illustrated in Figures 1–4 (A) and Figures 5–8 (B). The normal conduction range was much wider in experiment A (see text for details). The arrows in B indicate the direction in which the degree of bundle branch block progressively increased or decreased.

Incomplete Bundle Branch Block.—In the experiment illustrated in Figure 9B (arrows), several decreasing degrees of right bundle branch block occurred at the transition between phase 3 block and normal conduction (Fig. 8), and a wider range of increasing degrees of right bundle branch block was documented at the beginning of phase 4 block (Fig. 7). Conversely, in Figure 9A, the change from phase 3 block to normal conduction and from normal conduction to phase 4 block was abrupt, and incomplete bundle branch block did not occur. Gradual transitions from phase 3 bundle branch block to normal conduction occurred in only 3 experiments, but gradual transitions from normal conduction to phase 4 block were observed in 14 experiments.

Effects of Fascicular Injury on the Occurrence of Escapes

Junctional Escapes.—In the control study, junctional or His bundle escapes commonly occurred after vagal stimulation and were characterized by independent His bundle and left bundle branch deflections followed by a normal or narrow QRS complex after a normal H–V interval (Fig. 10A). These escapes were unaffected by the experimental procedure and occurred in all stages as well as in the control study. However, the junctional escapes were conducted to the ventricles according to the condition of the injured fascicle. Thus, in stage 1, the junctional escapes showed the same bundle branch block pattern of the sinoatrial beats (Fig. 11A). During stage 2, the junctional escapes often fell on the phase 4 block range and showed the expected bundle branch block pattern (Fig. 11B). During stage 3 the escapes fell on either the normal conduction range or the phase 4 block range and were conducted accordingly. During stage 4 all of the junctional escapes were again normally conducted. During stages 1–3, the His bundle and left bundle branch recordings were essential to determine the site of origin of the junctional escapes; otherwise, the escapes could have been considered to arise from the ventricle opposite to the injured bundle branch.

Escapes Arising from the Injured Fascicle.—After injury of the ventricular conducting fascicles and during stages 1–3, a new type of escape occurred with the following characteristics. (1) The QRS complex was wide, was not preceded by His bundle or left bundle branch deflections, and showed a bundle branch block pattern opposite to the provoked bundle branch block pattern (Fig. 10B). (2) The escape interval was remarkably short, particularly compared with that of the junctional escapes (Fig. 10A and B). (3) The escapes appeared immediately after injury was produced, were most abundant during stage 1, became progressively less common during stages 2 and 3, and disappeared in stage 4. The escape interval was shorter during stage 1 and became longer during stages 2 and 3, particularly prior to disappearance (Fig. 10B and C). (4) Commonly, the escapes fell slightly beyond the beginning of the phase 4 block range (Fig. 12). Since these escapes showed a bundle branch block pattern opposite to the pattern that was provoked, followed pari passu the effects on conduction, were present when bundle branch block was present, and disappeared when bundle branch block totally disappeared, it is reasonable to assume that they arose from the injured region and to attribute them to increased automaticity or enhanced spontaneous diastolic depolarization in or around the injured segment.
FIGURE 10
Ventricular escapes arising from the injured fascicle. A: In the control, a strong vagal stimulation provoked a pause of 12,400 msec, which was terminated by a His bundle escape that was normally conducted. No ventricular escapes were present. B: After injury of the right bundle branch and during stage 1, right bundle branch block occurred in the first and the last two beats. A vagal stimulation similar to that in A caused a pause which was interrupted by two ventricular escapes (E) with coupling intervals of 1,720 and 1,800 msec. These escapes showed a left bundle branch block pattern, were not preceded by His bundle deflections, and supposedly arose from the injured right bundle branch. C: During stage 3 of the same experiment (note that the first two beats show normal ventricular conduction) and after a similar vagal stimulation, the same ventricular escape appeared after a much longer coupling interval (4,700 msec). This condition preceded total disappearance of the ventricular escapes during stage 4.

Discussion

PHASE 4 BUNDLE BRANCH BLOCK
These studies showed that phase 4 bundle branch block can be produced practically at will in any ventricular conducting fascicle of the intact canine heart. Since phase 4 bundle branch block has also been demonstrated in many individuals (17-20), we can assume that phase 4 block is a common physiological response to some types of fascicular injury. However, in the past, this variety of rate-dependent bundle branch block was considered to be rare. This misunderstanding arose from the fact that in individuals it is difficult to produce the long pauses necessary to unveil phase 4 bundle branch block and from the absence of appropriate experimental studies. One exception is the study by Drury and Mackenzie (24), who reported similar observations in 1934. However, although phase 4 block is common, it becomes apparent only when it is properly investigated, and it seldom occurs spontaneously.

The present study is an extension of the work performed by Singer et al. (25) on isolated strands of Purkinje fibers. These authors provoked conduction delay or block by applying stimuli late in diastole after causing an enhancement of spontaneous diastolic depolarization by stretching, hypoxia, low potassium, etc.; their results may be correlated with our observations on the conducting fascicles of the intact dog. In addition, although the enhancement of spontaneous diastolic depolarization could not be directly proved in our studies, it was supported by the occurrence of escapes arising from the injured fascicle. Thus, the phase 4 bundle branch block that we were able to provoke following fascicular injury and after vagal stimulation was related to the development or the enhancement of spon-
Rate-dependent bundle branch block

A: Junctional escapes during stage 1 shortly after injury of the right bundle branch. The pause of 1,100 msec was terminated by an independent His bundle deflection that was not preceded by a P wave (His bundle escape) but was followed by a complete right bundle branch block pattern after a normal H-V interval similar to that of all the other sinoatrial conducted beats. B: In the same experiment during stage 2 right bundle branch block became rate dependent. Right bundle branch block occurred during a short run of atrial tachycardia (phase 3 bundle branch block), and the His bundle escape terminated the pause of 1,020 msec (phase 4 bundle branch block); however, the other beats showed normal intraventricular conduction. Vertical arrows indicate short vagal stimulation. His bundle deflections are indicated by oblique arrows.

The practically constant association of phase 4 bundle branch block with phase 3 bundle branch block that was not reported by Singer et al. (25) indicated a more complex mechanism with participation of other factors.

**Physiological Basis of Rate-Dependent Bundle Branch Block**

According to the results of studies performed on Purkinje fibers in a bath preparation with microelectrode techniques (25-30), the following hypothesis may be proposed. Phase 4 bundle branch block is related to a small degree of hypopolarization, which probably causes both an enhancement of spontaneous diastolic depolarization and a shift in the threshold potential toward zero. In the present experiments, the assumption that slight or moderate mechanical injury of the conducting fascicles causes hypopolarization is reasonable, because most forms of injury of any excitable tissue cause partial or total depolarization (1). However, the hypopolarization is only slight or moderate, because severe hypopolarization would cause complete block and even total unresponsiveness of the involved fibers, i.e., rate-independent bundle branch block as found in stage 1 of our experiments, but not phase 3 and phase 4 block. Also, slight hypopolarization is compatible with normal conduction (28, 31, 32); this finding is essential to explain the occurrence of the intermediate normal conduction range that separates phase 4 block from phase 3 block.

Singer et al. (25) have attributed phase 4 block essentially to an enhancement of spontaneous diastolic depolarization. However, in normal Purkinje fibers, spontaneous diastolic depolarization is not likely to be accompanied by a significant conduction delay, and, in all of the control dogs, the longest possible diastolic intervals...
FIGURE 12

Tracing during stage 2 recorded 15 minutes after the right bundle branch was injured. The pause of 1,190 msec caused by vagal stimulation (left top arrow) was terminated by a sinoatrial beat showing a small degree of right bundle branch block, indicating the beginning of the phase 4 block range. A slightly stronger vagal stimulation (second top arrow) caused a longer pause, which was interrupted by a ventricular escape showing a left bundle branch block pattern with a coupling interval of 1,320 msec. The escape interval was slightly longer than the critical diastolic interval for phase 4 block. It was assumed that both the conduction disturbance and the escape were related to enhanced diastolic depolarization in the injured fascicle.

(up to 28 seconds) did not cause any degree of bundle branch block. This observation agrees with the fact that drugs or other factors which can provoke a marked enhancement of spontaneous diastolic depolarization, e.g., digitalis, isoproterenol, or low potassium, do not cause intraventricular block in the intact animal. The same phenomenon was true in isolated strands of Purkinje fibers, and, as emphasized by Singer et al. (25), an important impairment of conduction did not occur unless spontaneous diastolic depolarization was accompanied by generalized diastolic depolarization. This finding shifts the weight of the importance of determining phase 4 block from enhanced spontaneous diastolic depolarization, which may be secondary, to hypopolarization, which may be primary or more essential. Enhanced spontaneous diastolic depolarization alone cannot cause bundle branch block, because the normal threshold potential of Purkinje fibers is around −70 mv (27), and up to this reduction in membrane potential conduction is not severely affected (25, 28). This finding also explains why a shift in the threshold potential toward zero is an essential requirement for spontaneous diastolic depolarization to produce a conduction defect (25). Since hypopolarization may cause or be accompanied by an enhancement of spontaneous diastolic depolarization and a shift in the threshold potential toward zero (25, 29), the hypothesis that hypopolarization is or may be the basic physiological derangement underlying phase 4 bundle branch block becomes more reasonable.

Since hypopolarization causes a prolongation of refractoriness (29), phase 3 bundle branch block can also be readily explained. Moreover, the fact that a single initiating factor can create the conditions for both phase 3 and phase 4 block makes this hypothesis more probable, because none of the other proposed explanations accounts so readily for the fact that phase 3 and phase 4 block coexist in the same injured fascicle. Membrane responsiveness (33, 34) that is also directly reduced by the mechanical injury could operate as an additional factor favoring or increasing the degree of block (shifting the phase 3 block range to the right and the phase 4 block range to the left and thus shortening the normal conduction range); however, rate dependence makes reduced membrane responsiveness per se an unlikely cause of the conduction disturbances.

Role of Vagal Stimulation. —Since phase 4 bundle branch block was uncovered during vagal stimulation, the question of whether a direct
vagal effect might have participated arises. Although the possibility of direct vagal influence on the ventricles has been indicated by different studies (35–37), an increase in vagal tone does not affect intraventricular conduction (38), and ventricular and Purkinje fibers are insensitive to the action of acetylcholine (27). Moreover, recent electrophysiological evidence (39) has indicated that acetylcholine does not impair bundle branch conduction and that, under certain circumstances, by depressing the slope of spontaneous diastolic depolarization, conduction velocity may even improve. Accordingly, the bundle branch block precipitated by vagal stimulation was attributed to the indirect effect of depressing sinoatrial activity.

**TERMINOLOGY**

Phase 4 bundle branch block has been considered paradoxical (2), because it is an exception to the rule that rate-dependent bundle branch block is provoked only by an increase in rate. Recently, this variety of rate-dependent bundle branch block has been termed bradycardia-dependent bundle branch block (15, 16). Although bundle branch block is most often provoked by a decrease in heart rate, it depends on the critical rate for phase 4 bundle branch block, which, under certain conditions, may be more toward the tachycardic side than it is toward the bradycardic side. For example, in Figure 7, phase 4 bundle branch block appears after R–R intervals of 400–420 msec, corresponding to a rate around 150 beats/min. It would be unrealistic to designate this effect bradycardia-dependent bundle branch block; we prefer to call this process phase 4 block (17–21) because, although some of the mechanisms may still be obscure, there is no doubt that the bundle branch block occurs during phase 4 of the preceding activation process.

Since hypopolarization can be accompanied by a tendency for refractoriness to extend beyond the end of the action potential (29), the early block does not necessarily mean that impulses fall on phase 3 of the preceding action potential; this assumption would indicate an improper use of the term phase 3 block (17–21). Although it is impossible to prove or disprove whether action potentials are prolonged under the conditions in which this form of rate-dependent bundle branch block can occur, the term phase 3 block, used side by side with phase 4 block, is a simple way of individualizing and at the same time interrelating these two varieties of rate-dependent bundle branch block. In general, phase 3 bundle branch block refers to an abnormal condition in which recovery is prolonged due to injury. The aberrant conduction that occurs during premature supraventricular stimulation in the control dogs may be considered a physiological variety of phase 3 bundle branch block; the limit between phase 3 block and its physiological variation may be difficult to determine in borderline situations. However, in the present study in which refractoriness was substantially prolonged after injury, this problem was unimportant.

**References**


*Circulation Research, Vol. XXXIV, May 1974*
Experimental Production of Rate-Dependent Bundle Branch Block in the Canine Heart
MARCELO V. ELIZARI, GERARDO J. NAU, RAÚL J. LEVI, JULIO O. LÁZZARI, M. SUSANA HALPERN and MAURICIO B. ROSENBAUM

Circ Res. 1974;34:730-742
doi: 10.1161/01.RES.34.5.730
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1974 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/34/5/730

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org//subscriptions/