Aberrant A-V Impulse Propagation in the Dog Heart: A Study of Functional Bundle Branch Block

By Gordon K. Moe, M.D., Ph.D., Carlos Mendez, M.D., and Jaek Han, M.D., Ph.D.

A dual transmission system was postulated in 1956 to explain certain features of A-V impulse propagation: unexpected delay in the ventricular arrival of early premature atrial impulses; changes in the electrical configuration of the delayed ventricular complexes; and atrial or ventricular echoes. A similar hypothesis was proposed by Rosenblueth, and certain complex A-V dysrhythmias in the human subject have also been interpreted in terms of a "longitudinal" dissociation of the A-V transmission system. Additional experimental observations have been explained in terms of a dual pathway, and a possible anatomic basis has been described, but the validity of the hypothesis has not been fully substantiated. For example, Hoffman et al. have shown that the phenomena of delay and configurational aberration of ventricular responses can be explained without postulating a dual transmission system.

In the hypothesis as originally presented it was proposed that two pathways, differing with respect to conduction velocity and refractory period, communicate between atrium and ventricle. Shortly following that publication, some additional vagaries of A-V impulse propagation were observed which indicated that the hypothesis was inadequate or, at best, over-simplified. In the present study we describe some of these phenomena together with additional evidence which indicates, in confirmation of Hoffman et al., that some of the features previously ascribed to a dual conduction pathway can be explained by conduction disturbances within the specialized conduction system of the ventricle. Under certain conditions, this system can be forced to exhibit longitudinal dissociation with generation of echoes which are propagated back to the atrium. In other words, an intraventricular "dual system" can be exposed which is independent of the properties of the A-V node. In the course of these studies, additional features of intranodal dissociation were also discovered. These, which support and extend the concept of a dual transmission system within the A-V node, will be described in detail in a subsequent study.

Methods

Two series of acute experiments were conducted on mongrel dogs of both sexes. In the first group the animals were anesthetized by intravenous injection of thiopental, 20 mg/kg, followed immediately by sodium barbital, 200 mg/kg. Under artificial respiration, the chest was opened in the mid-line, the heart was cradled in the opened pericardium, and bipolar stimulating and recording electrodes were clipped to the epicardial surface of the right atrial appendage and the anterior septal margin of the right ventricle. Electrical responses of atrium and ventricle were displayed on a dual beam cathode ray oscilloscope and photographed on 35 mm paper moving at a speed of 100 mm per second. The vagus nerves were cut; the thoracic sympathetic ganglia were removed when necessary.
to reduce the spontaneous frequency of the heart.

The second group of experiments was conducted on dogs prepared in a manner similar to the technique described by Alanis et al., in which the heart of a recipient animal is perfused from a donor animal. Both animals were anesthetized by intravenous injection of pentobarbital, 30 mg/kg. The chest of the recipient animal was opened, ligatures were loosely placed around the brachiocephalic artery, the left subclavian artery, and the aorta just distal to the subclavian. Ligatures were also placed around the hilus of each lung. An arterial perfusion line was attached through cannulae inserted into a common carotid artery of the donor animal and the left subclavian artery of the recipient. A tube for the collection of venous blood was inserted through a stab wound between the ribs at the most dependent point in the right thorax.

After heparinization of both animals, the arterial perfusion line was opened and the aorta and brachiocephalic arteries of the recipient animal were ligated, except in some experiments in which the right vertebral artery was left patent to provide for survival of the vagus nerves. The superior and inferior venae cavae were cut open to permit the free drainage of venous blood into the thoracic cavity; the pulmonary hilar ligatures were tied; and the right lung was excised. The venous blood, draining from the chest by gravity, was filtered through silicone treated glass wool in an open funnel and returned to the donor animal through a cannula inserted in the right external jugular vein. To obviate the need of a pump, the donor animal was placed about 20 cm below the recipient, and the height of the collecting funnel was adjusted so that the venous pressure of the donor maintained a safe level of blood in the funnel. The arterial pressure of the donor animal was observed by means of a mercury manometer attached to the arterial perfusion line. The pressure at the level of the perfused heart was 80 mm Hg or more in all experiments. Additional doses of heparin and pentobarbital were administered to the donor animal as needed.

After the perfusion was established, a window was opened in the free wall of the right atrium, parallel to the A-V groove, to expose the septal surface in the region of the A-V node and the bundle of His. A bipolar electrode consisting of a pair of sharp steel needles separated by 0.5 mm and insulated, except at the points, was suspended from loosely coiled wires and attached to the endocardial surface of the atrium at the atrial margin of the A-V node. A similar electrode pair was placed on the His bundle just above the insertion of the septal leaflet of the tricuspid valve. The position was adjusted to provide sharp "H" action potentials of adequate amplitude. An additional pair was placed on the His bundle for stimulating purposes; its position was adjusted until it was possible to excite the common bundle without simultaneously activating the adjacent atrial or ventricular muscle. Other recording electrodes were attached to the epicardial surfaces of the right and left ventricles. Records of electrical activity were obtained photographically by means of an Electronics for Medicine D-8 recorder at a paper speed of 100 mm/sec. The hearts, being isolated, were neurally "decentralized."

In both series of experiments, the heart was driven by rhythmic stimuli obtained from Grass stimulators or Tektronix pulse generators and passed through isolation units. After a series of from 6 to 16 driving stimuli, one or more test stimuli were delivered, either through the driving electrodes or through a different pair of electrodes. The driving and test pulses in the first series were obtained from two or more serially connected Grass stimulators: the intervals between pulses were determined by delay of the trigger pulses. In the open-heart experiments the sequence of stimuli was set up by push-button delay units and the intervals were counted from a 100 kc crystal oscillator. The instrument was designed by W. J. Mueller and constructed in the Bioelectronics Laboratory at the State University of New York, Upstate Medical Center.

Because the properties of the A-V transmission system were known to be frequency-dependent, the S-A node was usually crushed to permit observations at lower heart rates. In those experiments in which the effects of vagal stimulation were studied, the S-A node was preserved in order to avoid traumatic interruption of vagal fibers. Additional procedural details are described in the section on results.

The following abbreviations are used: RP, refractory period; FRP, functional refractory period (i.e., the shortest attainable interval between two responses of a tissue at the recording site); RBB and LBB, right and left bundle branches, respectively.

**Results and Discussion**

**TEMPORAL DELAY AND CONFIGURATIONAL CHANGE OF VENTRICULAR RESPONSES TO PREMATURE ATRIAL EXCITATION**

It was occasionally observed in the earlier study that, as the interval between driven and premature atrial responses (A1A2) was gradually reduced, the interval between the corresponding ventricular responses (V1V2) underwent a sudden increase of about 30 to 50 msec, i.e., the A2V2 conduction time abrupt-
ABERRANT A-V IMPULSE PROPAGATION

ly assumed an increased value. This was commonly, but not always, accompanied by atrial echoes, and by an alteration of the configuration of the electrogram recorded at the right ventricular surface. It was assumed that the delay and configurational change indicated a vertical dissociation which extended out to the specialized conduction system of the ventricle. The experiments as conducted provided records of responses at the epicardial surface of atrium and ventricle, but not at intermediate levels of the A-V transmission system. Attempts were made, however, to define the circumstances under which the peripheral "aberrant" conduction disturbance appeared.

Two of many experiments in which abrupt delay and change of configuration of the right ventricular electrical response occurred are illustrated in figures 1 and 2. Figure 1 indicates the temporal relationship between responses evoked in the atrium and the corresponding responses recorded at the epicardial surface of the right ventricle in an experiment in which the effect of the basic driving frequency was studied. The heart was driven by rhythmic stimuli applied to the right atrial appendage at the basic cycle lengths (A1A2) indicated in each segment of the figure. After each sixth driving stimulus, a test response was initiated in the atrium through the same stimulating electrodes, at the intervals indicated on the abscissae as A1A2. The corresponding ventricular intervals V1V2 are represented on the ordinate scales. At the longest basic cycle length studied it was found that a sharply defined break in the curve occurred at an A1A2 interval slightly less than 250 msec (fig. 1F). Ventricular responses to more premature impulses occurred with an extra delay of about 35 msec, and exhibited an altered electrical configuration (indicated by the open circles). At higher basic driving frequencies, the margin between "normal" and "aberrant" conduction ranges was shifted progressively to the left. At a basic cycle length of 433 msec, no range of aberrantly conducted impulses was apparent; all of the A2 responses, including the earliest which could be elicited in the atrium (A1A2 = 160), were propagated to the ventricles without the extra increment in propagation time, and with normal configuration (fig. 1A). The over-all functional refractory period of the A-V transmission system, defined as the shortest possible interval between two ventricular responses both propagated from the atrium, diminished with acceleration of the basic driving frequency: from a minimum V1V2 interval of 280 msec at a basic cycle of 801 to 235 msec at the basic cycle of 433 msec.

In terms of the hypothesis presented ear-
Effects of vagal stimulation and driving frequency. Expt. 10-12-56. Dog, 29 kg, thiopental-barbital anesthesia. Stimulating electrodes applied to right vagus nerve below point of section. Abscissae and ordinate scales as in figure 1. Inset records A and B taken at points indicated by arrows A and B. Right ventricular electrogram above, right atrial electrogram below in each record. Vertical arrows indicate time of premature atrial responses which failed to propagate to ventricles during scanning sequence of control curve.

Her, the results obtained in this experiment could be explained by assuming that acceleration of the basic driving frequency shortened the refractory period of the "fast" conduction pathway more than that of the auxiliary "slow" route, thus eliminating or inverting the discrepancy between them at higher frequencies. Consonant with this interpretation, it was found that "echo" responses of the atrium could not usually be demonstrated at higher basic frequencies.

It will have been noted in figure 1 that several ventricular responses were recorded without undue delay and without "abnormal" configuration at the briefest A1A2 intervals when the basic cycle length was 470 msec (fig. 1B). These unexpected "fast" responses alternated irregularly with "slow" responses when the A1A2 interval was kept constant for repeated trials of the test stimulus. A similar and very stable pattern was observed also in the experiment recorded in figure 2. The "control" situation, at a basic cycle length of 515 msec, is indicated by the solid black circles. As in figure 1, the parent A1A2 intervals are plotted along the abscissae; the resulting V1V2 responses are plotted as ordinates. At A1A2 intervals between 175 and 200 msec, an extra delay of the V2 response was recorded at the right ventricular surface. The polarity of the delayed V2 responses was inverted, as indicated in the inset record, A. At briefer A1A2 intervals, the V1V2 interval abruptly fell by about 38 msec, and the configuration of the V2 response returned to normal. A further peculiarity of this experiment was the occurrence of "gaps" in A-V transmission, i.e., failure of ventricular responses as indi-
ABERRANT A-V IMPULSE PROPAGATION

...cated by the vertical arrows at several A1A2 intervals between 175 and 195 msec. The temporal position of the gaps was not stable, but repeated scans with the A2 test stimulus regularly revealed their existence.

As in the experiment of figure 1, the effect of frequency upon the delay and configurational change of the V2 responses was tested. The points indicated by the squares in figure 2 were recorded when the basic cycle length was reduced to 372 msec. The A-V functional refractory period (FRP) was reduced by the acceleration (from 230 msec to 210) but the phenomena of extra delay, polarity change, and intermittent failure of transmission disappeared. All V2 responses for this series of scans had the same configuration as those of the inset record B in the figure.

A more puzzling feature of the system was observed during mild stimulation of the right vagus nerve (open circles in fig. 2). The minimal V1V2 interval was not significantly altered, the atrial refractory period (minimal A1A2 interval) was not appreciably diminished, but the range of abnormal delay and aberrant configuration of the V2 responses was completely and reproducibly eliminated by vagal stimulation. The V2 response pictured in the inset record B was identical in timing and configuration with control responses recorded at a briefer A1A2 interval (170 msec) and at the longer A1A2 interval of 205 msec. No gaps in A-V transmission occurred. Similar effects of moderate vagal stimulation were observed in three additional experiments.

In terms of the original hypothesis, it is difficult to explain how vagal stimulation, which would be expected to depress rather than facilitate A-V transmission, could yield this striking transformation of the recorded pattern.

At this stage in the investigation, it appeared possible that the response patterns illustrated in figures 1 and 2 might be the manifestations of aberrant transmission, not in the A-V node itself, but in more peripheral extensions of the specialized conduction system. Although vagal stimulation does not appear to exert any influence upon the refractory period or conduction velocity of the bundle of His, of the peripheral ramifications of the Purkinje system, or of the ventricles, it may be expected to delay the time of arrival of premature supraventricular impulses at the common bundle. Similarly, acceleration of the basic driving frequency, although accompanied by abbreviation of the atrial, A-V and ventricular FRP, must also alter the arrival time of premature impulses at the His bundle. It seemed likely, in short, that the conduction delay and abnormal configuration of V2 responses in experiments of the type illustrated in figures 1 and 2 resulted when premature impulses arrived at the His bundle early enough to expose partial refractoriness in the intraventricular distribution system. As we had recorded the V2 responses in such experiments at a point on the right ventricular surface near the septum (near the point of earliest electrical activity at the ventricular surface for normal unencumbered A-V transmission), we attempted to determine whether the aberrant phenomena resulted from functional block in the right bundle branch.

In a series of experiments, one of which is illustrated in figure 3, and another of which was previously reported, we first sought to elicit the abrupt delay and configurational changes as portrayed in figure 2. When this pattern was demonstrable, recording electrodes were attached to the right ventricular surface and to the left ventricle, near the apex. Scans of the interval following the last of a series of atrial responses to the basic driving stimuli were conducted as in the experiments of figures 1 and 2. The A2V2 conduction intervals were plotted against the parent A1A2 intervals; A2V2 intervals recorded from the right ventricular electrodes are plotted in figure 3A, and those recorded in the left ventricle for the same A1A2 intervals appear as the ordinates in figure 3B. The solid circles indicate the responses recorded during the control periods. A sharp break representing an abrupt increase of 22 msec in the A2V2 conduction time to the right ventricle occurred as the A1A2 interval was...
reduced to about 235 msec. No such break was apparent in the control curve for the left ventricle. At the longest $A_1A_2$ intervals studied, the $V_2$ response was recorded about 5 msec earlier at the right than at the left ventricular electrodes. At $A_1A_2$ intervals of less than 235 msec, activation of the left ventricle preceded that of the right, and the polarity of the right ventricular electrograms was inverted.

After these scans were recorded, a sharp stylus was inserted through the free wall of the right ventricle and drawn across the surface of the interventricular septum to sever the right bundle branch. After interruption of the right bundle, the $A_1A_2$ scans were repeated; the recorded values are indicated by the open circles. It is obvious that all of the right ventricular responses were delayed, while no change was recorded in the $A_2V_2$ intervals on the left. The configuration of even the $V_1$ electrograms on the right was altered to the "abnormal" polarity of the premature responses recorded during the control period, but the left ventricular electrograms were unchanged. No further alteration of the right ventricular electrograms occurred with early premature responses. Corresponding results were obtained in three experiments, including the one previously described, and it is obvious that block of impulse transmission at some level in the right bundle branch or its ramifications could account for two of the features previously attributed to a "dual" A-V transmission system.

**OPEN HEART EXPERIMENTS; DEMONSTRATION OF RIGHT BUNDLE BRANCH BLOCK**

Experiments of the type just described could not be reproduced at will. The features of "abnormal" delay and of configuration change occurred commonly enough, but not predictably. A premature response of the atrium, attended as it must be by a considerable delay in propagation through the A-V node, cannot regularly be expected to result in activation of the His bundle sufficiently early to find one of the bundle branches excitable while the other is still refractory. Premature excitation of the His bundle by direct stimulation, limited only by the duration of refractoriness in the bundle itself and not by the A-V node, would be more likely to expose such dissociation, even if the disparity in refractory periods of the two branches were very slight. Accordingly, we resorted to the technique described for the second series of experiments, in which the right heart was opened to ex-
pose the right septal surface for direct application of electrodes to the His bundle.

In open heart preparations, recording electrodes were attached to the interatrial septum near the margin of the A-V node, to the bundle of His, and to the epicardial surface of the right ventricle near its septal margin and to the surface of the intact left ventricle near its apex. Stimulating electrodes were attached at another site in the right atrium and on the bundle of His, so that temporal relationships of responses initiated in the atrium could be compared with those elicited by direct stimulation of the bundle. Stimulus parameters and electrode positions which resulted in activation of the common bundle without simultaneous excitation of the adjacent atrial and ventricular septum were readily identified.

Records obtained from such a preparation are illustrated in figure 4. The upper trace in each part of the figure was recorded from the juxtanodal atrial electrodes; the next trace, which also shows activity of adjacent atrial and ventricular muscle, is the record obtained from electrodes on the His bundle. Below these are the records from right and left ventricles, and a record obtained from one each of the pairs of right and left ventricular electrodes. The records of figure 4A display the response to premature excitation of the atrium at a time which yielded an H1H2 interval of 290 msec; the H2 response was not early enough to expose any abnormality of intraventricular conduction, as indicated by the unchanged polarity of the lowermost trace.

In the record of figure 4B, the H2 response was initiated 20 msec earlier. The resulting H1H2 interval was reduced to 275 msec, and the H2 response was now early enough to encounter refractoriness in the right bundle branch. The corresponding response intervals as recorded by the right and left ventricular electrodes were 305 and 275 msec, respectively, i.e., the premature response was propagated at full speed from His bundle to left ventricular surface, but was delayed an extra 30 msec at the right. The altered order of activation is indicated by the inverted polarity of the R-L tracing. In segments C and D of

---

**FIGURE 4**

Block of right bundle branch induced by premature stimulation of atrium (B) and of His bundle (D). Expt. 12-10-63, open heart preparation perfused from donor dog; pentobarbital anesthesia. Electrograms recorded from septal surface of right atrium (A), bundle of His (H), right ventricle (RV), left ventricle (LV), and from one each of left and right ventricular electrode pairs (R-L). Basic cycle length 600 msec. In A and B, driving and premature stimuli applied to atrium; H1H2 intervals 290 and 275 msec, respectively. In C and D, driving and premature stimuli applied to His bundle at S1S2 intervals of 290 and 275 msec. Vertical time lines, 100 msec.

_Circulation Research, Vol. XVI, March 1965_
figure 4, driving and premature stimuli were applied directly to the His bundle, yielding $H_1H_2$ intervals exactly equal to those observed in segments A and B, respectively. The ventricular response patterns were identical to those recorded in A and B. In other words, the aberration of conduction apparent in figures 4B and D was clearly a property of the intraventricular distribution network, and not of the A-V node itself.

The temporal relationships between input and output for a complete range of premature responses induced in the bundle of His are compared with those accompanying atrial stimulation in figure 5. In figure 5A the responses $H_1H_2$, $RV_1RV_2$, and $LV_1LV_2$ are related to the $S_1S_2$ intervals of stimuli applied to the His bundle. The “functional” RP of the His bundle was recorded as the minimal $H_1H_2$ interval (233 msec). At $S_1S_2$ (and $H_1H_2$) intervals just below 270 msec, impairment of conduction in the left bundle (or its peripheral ramifications) is indicated by the plateau in the $LV_1LV_2$ interval curve; propagation of the response to $S_2$ in the right ventricle was only slightly impaired at this time. At $S_1S_2$ intervals below 250 msec, however, there was an abrupt increase in the $RV_1RV_2$ interval, indicating that earlier premature $H_2$ responses found the right bundle (or its peripheral rami) inexcitable. All responses of the right ventricle to earlier stimulation of the His bundle remained “elevated.” The horizontal dotted line indicates the critical $H_1H_2$ interval below which the disparity between the bundle branches was exposed.

The results of a similar scan with premature stimuli applied to the right atrium in the same experiment and at the same basic driving frequency are shown in figure 5B. Here the $H_1H_2$, $RV_1RV_2$, and $LV_1LV_2$ intervals are related to $A_1A_2$. At an $A_1A_2$ interval of 245 msec, ventricular intervals were conspicuously greater than the interval recorded in the His bundle, i.e., propagation of the premature impulse was delayed below the common bundle in both branches. As $A_1A_2$ was reduced below 230 msec, an abrupt increase in $RV_1RV_2$ occurred, while the interval recorded in the left ventricle increased only slightly and $H_1H_2$ continued to decrease. The similarity with figure 5A at this level is obvious. The ventricular intervals remained relatively stable until $A_1A_2$ was decreased to less than 175

![Figure 5](image)

**FIGURE 5**

Right bundle branch block as related to $H_1H_2$ intervals. Expt. 7-30-63. Open heart preparation. In A, driving and premature stimuli applied to His bundle at $S_1S_2$ intervals indicated by abscissae; corresponding response intervals as recorded at right ventricular surface ($RV_1RV_2$), left ventricular surface ($LV_1LV_2$) and in His bundle ($H_1H_2$) are plotted on ordinate scale. In B, driving and premature stimuli applied to right atrium; ventricular response intervals plotted against $A_1A_2$ response intervals. Basic cycle length, 750 msec in both A and B. Horizontal dotted line defines apparent RP of right bundle branch, i.e., $H_1H_2$ interval below which block occurs in the branch.
msec, at which time \( t_{12} \) had increased to more than 255 msec, and the \( RV_1RV_2 \) interval dropped, again abruptly, to a level less than \( LV_1LV_2 \).

All of the \( RV \) intervals corresponding to \( A_1A_2 \) in the range of 175 to 225 msec were accompanied by a configurational change. No change of significant degree was recorded at the left ventricular surface, but the change in the order of activation at the two electrode pairs was indicated by a reversal of polarity in the electrogram recorded between right and left ventricular electrodes.

Several features of A-V transmission are illustrated in figure 5. (1) The minimal \( t_{12} \) interval obtained by supraventricular excitation (fig. 5B) was considerably in excess of the minimal interval obtained by direct stimulation of the bundle, i.e., the His bundle did not appose the principal limitation to premature impulse propagation in this experiment. (2) Progressively earlier premature excitation of the atrium evoked responses which were propagated through the A-V node with progressively increasing delay. (3) The earliest \( A_2 \) responses were sufficiently delayed in nodal passage to arrive at the His bundle later than later \( A_2 \) responses (fig. 5B). (4) When the His bundle was excited at an \( t_{12} \) interval of less than about 255 msec, whether the result of direct or indirect excitation, the right bundle branch (or some peripheral component of it) was refractory, while the left remained excitable.

The resemblance between the \( RV_1RV_2 \) curve of figure 5B and the control curve of figure 2 is striking, and it is surely not coincidental. Whenever a premature atrial response reaches the His bundle early enough to find the two bundle branches unequally excitable, a configurational change and a temporal dissociation at right and left ventricular recording sites must occur. Conversely, any agency which either increases the functional RP of the A-V node, or depresses the conductivity of the node for premature responses, or both, without causing comparable changes in the RP or conductivity of the specialized conduction system in the ventricles, must reduce the chance of exposing the aberrations described above. This conclusion provides a possible explanation of the effects of vagal stimulation and of increased driving frequency.

**EFFECT OF VAGAL STIMULATION**

An experiment designed to test the effect of vagal stimulation on A-V transmission is illustrated in figure 6. The heart was perfused, and electrodes were placed as in the experiment of figure 5. The heart was driven at a basic cycle length of 600 msec by stimuli applied to the atrium. When premature responses of the atrium were induced at \( A_1A_2 \) intervals longer than 260 msec, \( RV_2 \) preceded \( LV_2 \), and the R-L response retained the “normal” polarity. When \( A_1A_2 \) was reduced to less than 260 msec, the \( RV_2 \) response was abruptly shifted by about 30 msec; it now followed \( LV_2 \) by 20 msec, and the polarity of R-L was inverted (fig. 6A and inset record A). (It should be noted that the relative positions of the curves \( RV_1RV_2 \) and \( LV_1LV_2 \) on such a plot do not indicate the sequence of activation. The points for \( RV_1RV_2 \) at \( A_1A_2 \) intervals slightly longer than 260 msec merely indicate that \( RV_2 \) was delayed more than \( LV_2 \); \( RV_2 \) nevertheless still preceded \( LV_2 \).) When the His bundle was stimulated directly, similar results were obtained (fig. 6C), the critical \( t_{12} \) interval below which right bundle block occurred was 275 msec.

Similar scans at the same basic driving frequency were repeated during stimulation of the right vagus nerve at a frequency and intensity sufficient to increase the \( A_1V_1 \) conduction interval by about 10%. The premature atrial responses were now delayed in passage through the node; the briefest \( t_{12} \) interval recorded was 279 msec, and no evidence of configurational change or right bundle branch block was obtained (fig. 6B and inset record B). When the driving and premature stimuli were applied directly to the His bundle, however, the pattern of ventricular responses was exactly the same as that obtained during the control period; the data fit the same curves in figure 6C and are not separately plotted. The reason no intraventric-
ular aberration of conduction time of premature atrial responses occurred during vagal stimulation in this experiment, as in the earlier experiment of figure 2, is thus apparent. By increasing the intranodal conduction time of the premature responses, even a moderate intensity of vagal stimulation delayed the activation of the common bundle until recovery of the branches from the basic response was nearly complete. Similar results were obtained in two additional experiments.

**EFFECT OF FREQUENCY**

The effect of frequency upon intraventricular propagation was studied in several experiments, and is illustrated in figure 7. Apparent block of the RBB in this experiment was recorded at all basic cycle lengths in excess of 420 msec. At the cycle length of 435 msec, premature atrial responses at A1A2 intervals less than 210 msec arrived at the common bundle before recovery of the right bundle occurred (fig. 7A); the horizontal dotted line at 246 msec indicates the H1H2 interval below which failure of the right bundle branch occurred. When the basic cycle was slightly reduced, to 420 msec, premature atrial responses failed to reach the common bundle early enough to expose refractoriness in the right bundle (fig. 7B); but when the common bundle was stimulated directly at the same basic cycle length, premature responses at H1H2 intervals briefer than 240

*Figure 6* Effect of vagal stimulation. Expt. 12-10-63. Open heart preparation. In A, ventricular and His bundle response intervals plotted as ordinates against A1A2 intervals. Inset record A taken at point indicated by arrow. Basic cycle length 600 msec. B: same during stimulation of right vagus nerve. Inset record B taken at arrow. C: ventricular and His bundle response intervals plotted against S1S2 intervals of stimuli applied to His bundle. Same curves fit data from control period and during vagal stimulation. Horizontal dotted line indicates H1H2 interval below which right bundle branch block occurred.

*Figure 7* Effect of frequency. A: 435 msec, premature atrial responses at A1A2 intervals less than 210 msec arrived at the common bundle before recovery of the right bundle occurred (fig. 7A); the horizontal dotted line at 246 msec indicates the H1H2 interval below which failure of the right bundle branch occurred. When the basic cycle was slightly reduced, to 420 msec, premature atrial responses failed to reach the common bundle early enough to expose refractoriness in the right bundle (fig. 7B); but when the common bundle was stimulated directly at the same basic cycle length, premature responses at H1H2 intervals briefer than 240
msec again yielded the temporal and configurational features of right bundle branch block (fig. 7C).

The effect of increased frequency may be interpreted in the same way as the effect of vagal stimulation; in both cases the minimal H₁H₂ interval achieved by premature atrial stimulation was longer than the apparent RP of the right bundle.

In order to determine whether the apparent RP of the right bundle remained longer than that of the common bundle at even higher driving frequencies, the His bundle was driven at progressively increasing rates, and premature H₂ responses were initiated at each driving frequency. Right bundle branch block could be elicited at each frequency until the basic cycle length was reduced to 270 msec. At this frequency the RP of the common bundle was reduced to 177 msec, but no evidence of bundle branch block occurred (fig. 7D). The horizontal dotted line indicates that the apparent RP of the right bundle could not have been greater than 176 msec.

The experiment just described suggests that while the refractory periods of all of the cardiac tissues involved in the conduction pathway between atrium and ventricle are abbreviated by acceleration of the driving

*Figure 7*

Effect of driving frequency. Same preparation as figure 6. A and B, atrial stimulation at basic cycle lengths indicated. C and D, stimuli applied to His bundle. Inset records obtained at arrows.
frequency, the relationship between cycle length and RP is not identical at all levels. A description of this relationship as estimated for the A-V node, the bundle of His, and the right bundle branch in another experiment is displayed in figure 8. The values for the RP of the three tissues as plotted on the ordinate scale are not refractory periods in the usual sense. For the A-V node the value inscribed is the minimal interval between two responses of the His bundle both propagated from the atrium. This minimal H₁H₂ interval was obtained, for each of the four basic frequencies represented, from A₂ scans similar to those plotted in figure 7. It includes the actual RP of that element of the conduction pathway between atrium and His bundle which has the longest or limiting RP, plus an unknown increment in conduction time. The refractory period of the His bundle was determined by direct stimulation; it is the minimal interval between two successive responses of the bundle recorded about 3 mm from the stimulated site. The values for the right bundle represent the shortest H₁H₂ interval at which the H₂ response was propagated over the normal route in the right bundle (i.e., without the excessive delay indicated by the break in the curve of fig. 7C). The ordinate values of the horizontal dotted lines in figure 7 represent the RP of the right bundle as estimated at three basic frequencies.

In the experiment illustrated in figure 8, acceleration of the basic driving frequency reduced the apparent refractory periods of all three tissues, but that of the right bundle was the most profoundly influenced. At the slowest frequency studied (basic cycle = 700 msec), premature atrial responses reached the bundle of His as early as 232 msec after the primary H₁ response; this was 17 msec earlier than an H₂ response could be accepted by the right bundle. At basic cycle lengths of 500 msec or less, no premature atrial response could reach the bundle of His early enough to find the right bundle refractory. Premature responses elicited by direct stimulation of the common bundle still exposed the phenomena of right bundle block, down to a basic cycle length of 200 msec, at which point the apparent refractory periods of the common and right bundles converged. There are, then, three phases of interaction illustrated in the figure: a phase at low driving frequencies within which the RP of the right bundle branch was longer than that of either the A-V node or the common bundle; a phase at intermediate frequencies within which the RP of the RBB lay between the values for A-V node and His bundle; and a phase at high frequencies within which the apparent RP of the RBB was no longer than that of the His bundle. In this latter phase, it is probable that the refractory periods of the His bundle and its right branch were nearly equal, for in this range the earliest possible H₂ response occasionally failed to enter the right bundle when repeated tests were made at a fixed H₁H₂ interval.

The effects of vagal stimulation at various driving frequencies can be readily understood in terms of these relationships. Vagal stimulation does not alter the RP of the common bundle or its branches, but it has a marked action upon the A-V node. Accordingly, vagal stimulation should be expected to raise the A-V node curve without displacing the H or RBB curves; the range of cycle lengths

![Diagram](http://circres.ahajournals.org/)
which block of the right bundle can be elicited by premature atrial excitation will therefore be shifted to the right. This, of course, is exactly the result observed.

**EFFECT OF EPINEPHRINE**

The relationships plotted in figure 8 permit a prediction of the effects of adrenergic stimulation. Epinephrine reduces the RP of all three tissues, but its effect upon the A-V node is considerably greater than that upon the His bundle or its branches. According to this, epinephrine should be expected to lower the A-V node curve more than the RBB curve, resulting in a shift to the left of the phase within which block of the RBB can be exposed by premature atrial responses. This result was in fact observed. In some animals, prior to epinephrine, no evidence of right bundle block was observed following premature atrial responses even at the slowest frequencies studied, although such evidence could be readily demonstrated with direct stimulation of the His bundle. Continuous infusion of epinephrine at rates of 0.4 to 2.0 \( \mu \)g/min, by accelerating the transmission of premature atrial responses, reduced the RP of the A-V node to a value less than that of the RBB and permitted the exposure of intraventricular conduction aberration. In a few experiments, previously reported, the FRP of the A-V node was abbreviated so much by epinephrine that the RP of the His bundle itself imposed the limit to A-V impulse propagation.

Epinephrine, of course, also accelerates the spontaneous frequency of the heart; at the higher driving frequencies necessary to maintain control, the longest basic cycle length that could be studied during epinephrine infusion was often too short to permit demonstration of bundle branch block by atrial stimulation. In addition, epinephrine was found to abbreviate the apparent refractory period of the RBB proportionately more than that of the His bundle, thereby reducing the range within which RBB block could be exposed by premature stimulation of the His bundle. This relationship is illustrated in figure 9. The values recorded during the control period at driving frequencies between 2 and 4/sec are indicated by the open symbols; the curves for the His bundle and its right branch converge at the basic cycle of 250 msec, but bundle branch block could be demonstrated at all lower driving frequencies. During the infusion of epinephrine (2.0 \( \mu \)g/min), the values indicated by the solid symbols were recorded. The apparent refractory period of the RBB was reduced by nearly 25 msec at the longest cycle length studied, while that of the His bundle was reduced by less than 10 msec; the curves converged at a cycle length of 350 msec, and the range of frequencies within which bundle branch block could be demonstrated was correspondingly reduced.

**SITE OF BUNDLE BRANCH BLOCK**

In the experiments described so far, we have applied the term "right bundle branch block" to those situations in which a discontinuity occurred in the curve relating RV intervals to H1H2 intervals, accompanied by an inversion of polarity of the electrogram between right and left ventricular electrodes. We have not specified the presumed site of the block, but it is clear that the same polarity change could be observed whether the conduction failure occurred in the main bundle branch or in a small ramus supplying the
particular site at which the right ventricular electrodes were attached.

A priori it seems unlikely that an abrupt break in the curve relating $H_1H_2$ and $RV_1RV_2$ intervals would occur if the block were limited to the peripheral rami. One might expect a gradual or stepwise prolongation of the $H_0RV_2$ conduction time as, accompanying abbreviation of $H_1H_2$, more and more of the peripheral branches fail to conduct. In some experiments there was indeed a gradual transition: as $H_1H_2$ was diminished, $RV_1RV_2$ was progressively delayed until it followed $LV_2$, thereby inverting the R-L electrogram. In such cases, although impulse propagation was depressed more severely on the right side than on the left, there was no evidence of complete failure of transmission in the RBB. It does not follow that a break in the curve recorded at a single point must indicate block of the main bundle branch, for if the sequence of regional or fractional failure were appropriate, a break could still occur. If regional failure occurred, however, one should expect that the sequence of activation of a number of points on the right ventricle should vary as first one and then another of the peripheral rami drop out.

To test this possibility, experiments were done to determine the sequence of activation at several sites on the right ventricular surface. Figure 10 illustrates one of these experiments in which, at a relatively slow basic driving frequency, premature atrial responses evoked the evidences of apparent RBB block. The location of the electrodes, including four sites in the right ventricle, is indicated in the accompanying sketch, and the sequence of activation for normal ($H_1V_1$) and premature responses ($H_2V_2$) is indicated in the table. In figure 10A, the last basic atrial driving stimulus was followed by a premature stimulus, yielding an $H_1H_2$ interval (indicated by arrows) of 290 msec. The primary response, $H_1V_1$, was recorded earliest at the $RV_a$, and latest at the $LV$ electrodes. The premature response was delayed by an extra 10 to 12 msec ($AHV$) at the right ventricular recording sites, but was propagated without additional delay to the $LV$ site. The delay was essentially equal at all four right ventricular sites; the normal sequence of activation at these sites was therefore retained. When the premature stimulus was slightly earlier, yielding an $H_1H_2$ interval of 280 msec, the pattern of activation was abruptly changed (fig. 10B). While little delay occurred at $LV$, the delay recorded at the right ventricular points was increased by 19 to 37 msec. There were no intermediate values between those recorded in figure 10A and B. In this experiment, briefer $H_1H_2$ intervals could not be obtained by atrial stimulation, but $H_1H_2$ was reduced to 240 msec by stimulation of the His bundle directly. The $H_2V_2$ conduction intervals, including the $LV$ site, were still further increased, but the sequence remained...
unchanged. These values are not shown in figure 10.

If the sequence shown in figure 10B was indeed the result of block in the main bundle branch, then section of the branch should not further alter the distribution. Figure 10C displays the pattern of activation after section of the RBB. The basic driving frequency was the same as in figure 10A and B. The sequence, as listed in column C of the table, was almost exactly the same as that recorded for the premature response in column B.

It is unlikely that the results obtained in this experiment could have been due to regional failure of small peripheral rami of the RBB. The conduction failure must have occurred in a portion of the conduction system common to all four of the right ventricular recording sites. Analogous results were obtained in seven additional experiments, and it seems likely that in all the experiments in which a sharply defined break occurred in the RV curve (17 of 24 experiments) the site of propagation failure was within or at the termination of the main trunk of the right bundle, or in a major branch supplying all of the right ventricular points sampled.

In the experiments just described, the abrupt break in the curve relating H₂ RV₂ conduction time to H₁H₂ occurred at precisely the same H₁H₂ interval for all of the right ventricular points sampled. The magnitude of the abrupt shift in conduction time was not equal at all points, for the sequence of activation no longer followed the normal pattern. In the experiment of figure 10, for example, the “jump” in the curve which occurred when H₁H₂ was reduced from 290 to 280 msec ranged from 9 msec for RVb to 26 msec for RVd. In seven experiments, conducted in the same manner as that just described, the results obtained were more indicative of partial failure. As the H₁H₂ interval was diminished progressively, the sequence of activation changed gradually, until activation of the right ventricle followed that of the left. Breaks in the conduction time curves did not occur regularly, and the results were consistent with depressed conduction rather than complete block in the distribution of the RBB.

**SERIAL BLOCK IN THE RIGHT BUNDLE**

If transmission failure of a premature response can occur at a relatively proximal level in the right bundle, the activation of the right ventricle must of course be achieved by propagation from the left, either through anastomosis within the specialized conduction system or in part through muscle. If the additional delay incurred in the circuitous peripheral route allows time for recovery of the RBB from the primary response, then retrograde excitation of the RBB should occur. If we designate the site of block in the RBB as “x,” and the time of arrival of the premature response (H₂) at x as t, then the time of arrival of the retrograde response at this point will be t plus the additional time ∆t, required for propagation of H₂ through the left bundle, the transseptal communication, and back up the distal portion of the RBB to x. In other words, the tissue just proximal to x, and the tissue just distal to it will be thrown out of phase by a period of time equal to the conduction time through the aberrant circuit. If this be true, the recovery of excitability of the elements on either side of x should also be thrown out of phase, and there should therefore be a period of time following H₂ during which a third response of the His bundle must also be blocked at x. This period of time, barring frequency-related changes in RP, should be roughly equal to ∆t.

The hypothesis is schematically represented in figure 11A; a corollary is illustrated in figure 11B. According to these concepts, the more distal the position of x, the briefest should be the interval ∆t within which H₃ would encounter refractory tissue.

The hypothesis illustrated in figure 11 was tested in eight experiments, in which failure of transmission in the distribution of the right bundle could be demonstrated. In five of these experiments, the functional block appeared to be relatively proximal in the right bundle; that is, the blocked H₂ was followed by a period of greater duration during which H₃ also resulted in the pattern of RBB block.
FIGURE 11
Schematic representation of retrograde activation of right bundle branch after block at proximal level (A) and at distal level (B). Level of assumed block indicated by $\times$-$\times$; time of arrival of $H_2$ at blocked site indicated by $t$, and arrival of retrograde impulse by $t + \Delta t$. Period during which a subsequent $H_3$ response should be blocked at the same site is represented as $\Delta t$.

One of these experiments is illustrated in detail in figures 12 and 13.

The experiment was performed in an open heart preparation with an array of electrodes similar to that represented in figure 10. Block in the RBB occurred at $H_1H_2$ intervals between 255 and 290 msec, as illustrated in figure 12A. The ordinates represent the conduction time of the premature response from the His bundle to one of the right ventricular recording sites (solid circles) and to the left ventricular site (open circles). Following the scan represented in figure 12A, the position of $H_2$ was fixed at 272 msec, i.e., at an $H_1H_2$ interval which repeatedly reproduced the pattern of RBB block. The interval following $H_2$ was then scanned with a third stimulus applied to the His bundle (fig. 12C). There was a period of about 5 msec during which $H_3$ responses could be evoked without propagation to either ventricle, i.e., both branches were still refractory from the $H_2$ response. Following this, there was an additional period of 80 msec during which activation of the left ventricular site preceded that of the right. When the right bundle finally recovered, the $H_3V_2$ interval recorded at the RV site shifted abruptly from 85 msec to 50 msec, a value little greater than the $H_3V_1$ interval.

This experiment may be interpreted to indicate that the $H_2$ response had been blocked, as predicted, at a relatively proximal level in the RBB, and that the peripheral segment was activated retrogradely up to that point. A schematic analysis of this interpretation is presented in figure 13A and B, based on the relationships of figure 12A and C. The refractory period of the His bundle is defined as the densely shaded area at the upper margin of the diagram; the apparent RP of the RBB, indicated by the lighter shading, is represented to be about 30 msec longer than that of the His bundle for the $H_1$ response. Propagation of $H_2$ to the left site ($L_2$) is assumed to take the normal pathway through the left bundle; activation of the right ($R_2$) is indicated by the broken line arising from an arbitrarily defined junctional point, and retrograde

FIGURE 12
Sequential block of RBB. Expt. 6-3-64. Open heart. In A, conduction time of premature response from His bundle to left (open circles) and right ventricular electrode sites (solid circles) plotted as a function of $H_1H_2$ interval. Driving and premature stimuli applied to His bundle. In B, propagation of $H_2V_2$ response. $H_2$ fixed at 292 msec. In C, propagation of $H_3V_2$, when $H_1H_2$ interval reduced to 272 msec. Basic cycle, 700 msec for all three series.

Circulation Research, Vol. XVI, March 1965
ABERRANT A-V IMPULSE PROPAGATION

Activation of the right bundle is projected from the same point (arrow). The earliest propagated H₂ response, and the latest H₃ which still encountered a refractory RBB, are represented by H₃ and H₃', corresponding to H₂H₃ intervals of 195 and 275 msec, respectively. In figure 13B, with H₂ in the same position, H₃ was placed just 5 msec later than H₃' of figure 13A. The pattern of activation of the ventricles abruptly assumed the normal sequence. There were no intermediate values between those diagrammed for parts A and B of the figure.

The analysis constructed in figure 13 is arbitrary in the sense that the level at which block of RBB is assumed to occur, and the level of the junction at which re-entry of the bundle from below is postulated, are schematic, and are obviously not based on direct observation. If only the evidence presented in figure 12C were available, the reconstruction might be a plausible explanation of the observed events, but not a convincing proof that retrograde activation of the RBB had occurred. For example, one might assume that the disparity between the refractory periods of the left and right bundle following the basic cycle (as defined in fig. 12A) was merely increased following the premature H₂, i.e., that the RP of the His bundle, and, presumably its left branch, was abbreviated more than that of the RBB. Such an assumption differs from the relationship already described, and illustrated in figure 8, but a more direct test was applied.

As described above, the period of time during which a premature response of the His bundle encounters a refractory right bundle is diminished as the basic driving frequency is accelerated (fig. 8), i.e., the RP of the RBB was more greatly reduced than that of the left by abbreviation of the cycle length. In order to determine whether this relationship applies also to premature responses, the position of H₂ in the experiment of figure 12 was delayed by 20 msec, and the scan with H₂ was repeated. Under this condition, as shown in figure 12B, there was no break in the curve relating the H₂RV₃ conduction time to the H₂H₃ interval. In other words, when the preceding cycle length was 292 msec, the refractory period of the RBB was at least as short as that of the left. It is therefore exceedingly unlikely that it could have been 80 msec longer in the right than in the left when the preceding cycle was 272 msec. These events are diagrammed in figure 13C.

With this additional evidence at hand, the assumption of retrograde activation of some portion of the right bundle (fig. 13A and B) is more adequately justified. We can be sure that the duration of refractoriness in the RBB following the H₂ response did not exceed that of the left bundle, and that the RBB was unavailable to H₃ only because it had been silently activated from below by H₂. The period during which block of the RBB was demonstrable (the span enclosed by H₃ and H₃' in fig. 13A) then represents the sum of the conduction times for H₂ down the left bundle,
through an intervening bridge of muscle and/or Purkinje tissue, and back up the right bundle.

The actual dimensions of the parallelogram representing the refractory period of the RBB following its retrograde activation in figure 13 are, of course, not known. We can safely assume that the RP terminates just after the line describing the propagation of \( H' \) in figure 13A, and just before the propagation of \( H_3 \) in figure 13B. If we assume that the duration of the RP does not exceed that of the left bundle for the reasons outlined above, and if we further assume that retrograde velocity was the same as antegrade velocity, then the arrow represents a reasonable approximation of the time course of that retrograde activation. Slightly different estimates of conduction time, path length, or RP duration change merely the position of the parallelogram in the schema; they do not alter the basic conclusions.

It should be emphasized at this point that the evidence for block of the main right bundle rather than one of its major branches in the experiment just described is not conclusive. The right ventricular electrodes were attached to points on the anterior surface, and it is possible that some other sites continued to be activated over a normal route not involving propagation from the left bundle. If this were true, then the delay in propagation of \( H_2 \) and \( H_3 \) to the sites sampled in this experiment could be due to activation from some other right ventricular site. This possibility does not, however, change the basic constructs illustrated in figure 13. The source of retrograde activation of that portion of the right bundle under consideration would be another branch of the right bundle, rather than the left, but the basic interpretation would remain the same.

When the two bundle branches are “dephased” by retrograde activation of the RBB, the phenomenon diagrammed in figure 13A should be expected to repeat itself. When \( H_3 \) is denied access to the right bundle because of its retrograde activation by \( H_2 \), then \( H_3 \) in turn should take a course similar to \( H_2 \). Once block in the RBB is established, an appropriate frequency of stimulation should perpetuate it. This prediction was fulfilled in each of several experiments in which it was tried. Whenever a period existed within which \( H_2 \) encountered a refractory right bundle, followed by a longer period during which \( H_3 \) was blocked, the same situation could be demonstrated for \( H_4 \), \( H_5 \), etc. (fig. 14). Once an appropriate frequency was established, the heart could be driven, apparently indefinitely, without resumption of the normal pattern of activation.

**PROXIMAL BLOCK IN THE RIGHT BUNDLE**

In the analyses presented above we have referred to “proximal” block in the RBB. It should be apparent that proximal is used in a temporal rather than a spatial sense, and that even the temporal relationships are only approximated in, for example, the experiment of figure 13. An attempt to define the time more precisely was undertaken in the experiment illustrated in figure 15. The preparation was similar to those just described, except that stimulating electrodes were placed on the right ventricular surface in order to permit induced retrograde excitation of the conduction system. When the heart was driven from the His bundle at a cycle length of

![Figure 14](https://example.com/fig14.png)

**Sequential block of five successive His responses in RBB. Expt. 7-2-64. Open heart. Electrograms from His bundle near site of stimulus (H), from two points on right ventricular surface (RVa and RVb), from left ventricle (LV) and from one each of RV and LV electrodes (R-L). Basic cycle \( S,S_1, S_2 \), 500 msec; \( S_3S_5, 220; S_6S_7, 200; S_8S_9, 190 \) msec.**
ABERRANT A-V IMPULSE PROPAGATION

FIGURE 15

Location of site of block in RBB. Expt. 6-15-64. Assumed level of block indicated by horizontal broken line. Densely scored area indicates refractory period of that portion of His bundle and RBB activated from $H_1$; lightly scored area, activated from stimulus applied to right ventricular surface ($RV_1$). Time scale: msec before and after time of primary His response. In A, $RV_1$ precedes $H_1$ by 18 msec. Effective RP of RBB indicated by broken lines in presence ($RV_1$) and in absence ($<RV_1$) of ventricular stimulus. Double arrow indicates range of time during which $H_2$ encountered refractory RBB, with or without $RV_1$. In B, $RV_1$ precedes $H_1$ by 28 msec; latest $H_2$ indicated by solid line, propagated normally over RBB. In C, $RV_1$ allowed to propagate to His bundle.

800 msec, the $H_1RV_1$ conduction time was 42 msec; when driving stimuli were delivered to the RV site from which $RV_1$ had been recorded, the retrograde conduction interval, $RV_1H_1$, was 40 msec. These measurements were taken to indicate the slope of the corresponding conduction lines in the figure. The heart was then driven by regular stimuli applied to the His bundle, and a premature stimulus was used to define the limits of the $H_1H_2$ interval within which RBB block was apparent. There was a clearly defined period of 27 msec within which $H_2$ encountered a refractory RBB. Following this scan, the right ventricular site was pre-excited by a stimulus delivered at the same time as the last regular driven response of the His bundle, $H_1$. The normograde and retrograde responses should have collided 20 msec after their simultaneous origin, i.e., at some place within the distribution of the right bundle. If this point of collision were below the point at which $H_2$ dies, then the conditions of refractoriness which cause the extinction of $H_2$ should not be altered. If, however, the point of collision were above the site of block, then the more distal tissue, having been pre-excited, should recover earlier and should be available for the passage of $H_2$. In other words, the longest $H_1H_2$ interval at which block occurs should be diminished. Repeated scans of the pertinent boundary intervals were taken while the position of the RV stimulus, relative to $H_1$, was altered. The RV stimulus had no effect when it preceded $H_1$ by as much as 18 msec (fig. 15A), but when it preceded $H_1$ by 28 msec, the expected shift occurred (fig. 15B). The stability of the preparation was checked by recording repeatedly the response to $H_2$ with and without the RV stimulus. The results indicated that the site of block for $H_2$ in the RBB lay between 6 and 11 msec "distal" to the His bundle, a temporal position which must be within the main bundle branch and not in its peripheral rami. The level denoted by the horizontal broken line in figure 15 was drawn at the midway point between the two collision points represented in figure 15A and B.

Confirmation of this conclusion was obtained in the same preparation. When the heart was driven from the His bundle, RBB block was present at $H_1H_2$ intervals of 300 to 327 msec, as indicated in figure 15A. After the range was defined by repeated scans with $H_2$, a similar $H_2$ scan was performed following a retrograde response which was initiated at the right ventricular surface ($RV_1H_2$ of fig. 15C). The interval between the last driven $H_1$ response and the $H_R$ response was the
same as the basic $H_3H_1$ cycle. The RP of the His bundle following its retrograde activation was the same as it was following $H_1$, namely 300 msec. The earliest $H_2$ response which was able to propagate normally through the right bundle occurred at 310 msec after $H_n$. In other words, the $H_1H_2$ interval which defined the end of refractoriness at the limiting level in the RBB was reduced from 327 msec (fig. 15A) to 310 msec (fig. 15C), a difference of 17 msec. This difference, as can be seen by comparing the two parts of the figure, should be twice the conduction time from the His bundle to the point of block. This independent assessment of the level of block, 8.5 msec “distal” to the His bundle, falls within the limits of 6 to 11 msec defined in figure 15A and B, and confirms again the conclusion that block may, and often does, occur within the main bundle branch.

**EFFECT OF SECTION OF THE LEFT BUNDLE**

In the experiments described by Hoffman et al., it was suggested that local delays could account for the discontinuity in what they refer to as a “type 3” curve. Although this may indeed account for breaks at various recording sites, it is unlikely that similar local delays would be widespread throughout the Purkinje system at precisely the same critical $H_1H_2$ interval. If, however, this were the mechanism, it follows that propagation, though markedly delayed, would not be blocked. The indirect evidence described in detail in the preceding pages is sufficiently cohesive to compel the conclusion that the breaks result from block at a relatively proximal level and not merely from conduction delay; but since the left bundle remained “patent” when the right was presumably blocked, the right ventricle was, of course, eventually engaged. If the break in the $H_2RV_2$ curve of figure 12A resulted from complete failure of transmission in the main RBB, then at $H_1H_2$ intervals up to 290 msec activation of the RV point must have been accomplished from the left, and section of the left bundle should, accordingly, produce complete block of $H_2$ responses in this range. Furthermore, the prolonged period, during which block of the RBB was apparent for $H_3$ response in figure 12C, should no longer exist, for retrograde activation of its peripheral portion would then be impossible.

This direct test was applied in an experiment in which, as in the experiment of figure 12, there was indirect evidence of block at a proximal level in the RBB, and of retrograde activation of its peripheral portion. Prior to section of the LBB, the temporal relationships plotted in figure 16A (solid symbols) were recorded. At $H_1H_2$ intervals between 218 msec (the earliest possible $H_3$ response) and 245 msec, the RBB was apparently inexcitable. When $H_2$ was delayed by an additional 2 msec, the $H_2RV_2$ interval abruptly decreased from 63 to 45 msec. When $H_2$ was fixed at 225 msec, within the range at which only the left bundle was excitable, and the succeeding interval was scanned with $H_3$, there was a period of 15 msec during which neither bundle was available, followed by a period of 60 msec during which only the RBB was blocked (fig. 16B). After these events were recorded, the left bundle was severed by means of a needle inserted through the free wall of the left ventricle, and the $H_2$ and $H_3$ scans were repeated. The earliest $H_2$ which activated the ventricles was now recorded at 251 msec after $H_1$, and was clearly propagated over the right bundle (fig. 16A, open symbols). Prior $H_2$ responses, had they merely been delayed rather than blocked,
should obviously have reached the ventricle in spite of section of the left bundle. As a confirmation of the indirect conclusions derived in the preceding sections, the scan indicated by the open symbols in figure 16B was recorded. The H₂ response, placed in the same position as before, was of course not propagated. Under these conditions, the earliest H₃ response of which the His bundle was capable was now propagated to the ventricles over the RBB. After these events were recorded, the RBB was severed in order to prove that the previous section of the left bundle had been complete. Total block between His bundle and ventricles resulted.

These results confirm in every detail the indirect evidence accumulated in the previous experiments. Had the long period of RBB block displayed by the H₃RV₂ curve of figure 16B been the result of refractoriness left by the slow passage of H₂ through the right bundle, then the propagation of H₃ to the right ventricle should have been unchanged by section of the LBB. It follows that the barrier to the propagation of H₃ in the control scan of 16B must have been opposed by retrograde activation from the left. It also follows that if H₂ entered the proximal portion of the RBB, the refractory period left by its entry was no longer than that in the common bundle, for the earliest H₃ response after section was able to traverse the right bundle with scarcely any impedance.

ECHO RESPONSES OF THE HIS BUNDLE

The diagrams of figure 13 suggest that retrograde activation of the right bundle could, under certain conditions, lead to re-entry of the His bundle. If the propagation of H₂ in its course through the ventricular loop were sufficiently slow, and if the RP of the common bundle were sufficiently brief, a recurrent response of the His bundle might occur. This would be likely only when the H₁H₂ interval is as brief as possible, for under these conditions H₂ will be maximally delayed by relatively refractory tissue in its intraventricular passage, and the RP of the His bundle following H₂ will be minimal.

In three experiments, these conditions appeared to be met. Recurrent responses of the His bundle were recorded which could be interpreted as echoes. One of these events is pictured in figure 17. In this experiment the heart was driven by stimuli applied to the His bundle (S₁). A premature stimulus, S₃ (fig. 17A) yielding an H₁H₂ interval of 250 msec, evoked the criteria of bundle branch block just described. The H₂V₂ interval for the right ventricular recording site was 76 msec, and for the left it was 58 msec, as compared with H₁V₁ intervals of 45 and 54 msec, respectively. The H₂ response was not propagated back to the atrium. When H₂ was applied 20 msec earlier (fig. 17B), the H₂V₂ interval increased to 100 and 87 msec at the right and left sites; a recurrent response of the His bundle (H * * ) occurred, and was propagated back to the atrium (A * * ). The interval between H₂ and H * * was 160 msec, barely more than the refractory period of the bundle following the H₂ response. The timing was critical; only the earliest possible H₂ re-

---

**FIGURE 17**

Echo response of His bundle following premature H₂. Expt. 10-25-63. Open heart. In A, H₁H₂ interval 250 msec; in B, H₁H₂ interval 230 msec; echo response in His bundle (H * ) was opposite in polarity to response propagated from atrium; H * * was propagated back to atrium (A * * ) but did not re-engage ventricles. Basic cycle 500 msec.
response was accompanied by the echo. The polarity of the $H^{**}$ response was the same as that resulting from $S_2$, because the recording electrodes were placed proximal to the stimulating electrodes on the His bundle. The polarity was, however, opposite to that observed with atrial stimulation; the recurrent response was presumably propagated over a retrograde pathway from the periphery.

The temporal course and pathway of the $H_2$ response resulting in the recurrent $H^{**}$ cannot, of course, be determined from these records. It is, therefore, not possible to say whether the re-excitation occurred as a result of slow and continuous passage through a ventricular loop, or whether an action potential arriving at a still refractory site endured long enough to activate that site after an appreciable latency. Whichever mechanism was responsible for re-excitation in this experiment, it is likely that the site of failure of $H_2$ in the RBB was relatively high, for if the $H_2$ impulse traveled an appreciable distance (and slowly) into the peripheral branches, it is unlikely that they would have recovered from the refractory state in time to receive the re-entrant response.

An alternative to the interpretation of $H^{**}$ as an echo must also be considered. Since only the earliest possible $H_2$ was followed by recurrent activation of the His bundle, it is possible that $H^{**}$ resulted as a repetitive response to the premature stimulus. Collateral evidence opposes this interpretation. When $H_2$ was placed in a position which yielded the pattern of RBB block, but without an "echo," the ensuing interval was scanned with $H_3$. There was a brief period of time during which the His bundle could be excited without transmission to the ventricles; no recurrent $H$ response occurred. When $H_3$ was placed slightly later it was sometimes propagated and sometimes not. When it was propagated, it evoked the pattern of block in the RBB, and was invariably followed by a recurrent activation. When propagation did not occur, there was no $H^{**}$ response. It is probable, therefore, that the recurrent activation was in fact an echo propagated over an interventricular loop.

**Left Bundle Branch Block**

The evidence presented above conforms with the clinical impression of greater "vulnerability" of the RBB to transmission failure. In 17 of 24 experiments in which the RP of the His bundle and its branches was assessed, the RBB was preferentially blocked; in six experiments delayed propagation without clear-cut evidence of block was recorded, and in one experiment the left bundle was blocked. In the one exception, the results were analogous to those pictured in figures 12 and 13, and 16, but opposite in "polarity." At an $H_1H_2$ interval of 275 msec, a sharply defined break in the curve relating the $H_2LV_2$ conduction interval to the $H_1H_2$ interval, and a still wider period of block of the $H_3$ response was demonstrated (fig. 18). In the records of figure 18, $H_2$ was placed 260 msec after $H_1$; activation of the left ventricle was delayed by about 30 msec, as indicated in the R-L tracing. At $H_2H_3$ intervals up to and including 332 msec, $H_3$ was also blocked in the left bundle (fig. 18A). When $H_3$ was delayed by 10 msec more, propagation over the left bundle was again possible (fig. 18B). On the basis of these results it was concluded that $H_2$ had been blocked at a relatively proximal level in the left bundle and that the distal portion of the LBB had been activated retrogradely from below. If this conclusion were correct, it would be expected that cutting the right bundle should now cause complete failure of transmission for $H_1H_2$ intervals briefer than 275 msec. This was indeed the case. The tracings of figure 18C were recorded after section of the right bundle. The premature response to $S_2$, placed at the same time as in figure 18A and B, now failed to propagate. Following the nonpropagated $H_2$, the earliest possible $H_3$ response ($H_2H_3 = 156$ msec) was now propagated to the ventricles over the left branch. Had the propagation of $H_2$ been progressing slowly through refractory tissue on the left, section of the right bundle might have delayed ventricular activation, but would not have pre-
ABERRANT A-V IMPULSE PROPAGATION

FIGURE 18

Functional block of left bundle branch. Ext. 8-18-64. Open heart preparation. Records from His bundle (H), right and left ventricles (RV and LV) and combined leads (R-L). Stimuli S1, S2, and S3 applied to His bundle. In A and B, S1 evokes pattern of left bundle branch block. S2S3 interval, 260 msec. In A, S3 in latest position which repeats pattern of LBB block (S2S3, 332 msec). In B, S3, placed 10 msec later, is normally propagated. Between B and C, right bundle sectioned (note configuration change in RV and R-L). S3, at same position as in A and B, is completely blocked. The earliest possible response of the His bundle to S1 is now propagated over the LBB.

vented it completely; and, had the left bundle not been activated retrogradely from the right, section of the right bundle should not have altered the propagation of Hs. The results are thus comparable with those illustrated for the opposite situation in figure 16.

Comment

PREFERENTIAL FAILURE OF THE RIGHT BUNDLE BRANCH

The results described and discussed above indicate that, at least under the conditions of these experiments, the right bundle is "weaker" than the left. The results conform therefore with the major portion of previous experimental and clinical experience. The single experiment in which the reverse situation appeared may very well have been the expression of a pathologic change, as is commonly believed to be true of left bundle branch block in human subjects. With few exceptions, however, some depression of conductivity on the left side was present at HiH2 intervals at which failure appeared on the right (the experiment of fig. 4 is one of the exceptions), and in some experiments both bundles failed at the same time. In no case was refractoriness in the ventricular myocardium itself the limiting factor. In all experiments there were conditions under which the His bundle could be excited without transmission to either branch. Whether there may also have been conditions when the bundle branches recovered excitability before the common bundle was not ascertained, but it appears improbable.

The reason for the common occurrence of block at a proximal level in the right bundle is not clear. The duration of the action potential in cells of the specialized conduction system increases progressively from the bundle of His to the peripheral Purkinje fibers,12 and the duration of the RP presumably undergoes a parallel change. One might therefore expect that failure of propagation of premature responses should occur distally, in the tissue with the longest RP, with failure developing at more and more proximal levels as the H1H2 interval is abbreviated. A possible explanation, however, can be offered.

Unless the RP of the peripheral Purkinje tissue is considerably greater than that of the main bundle branch, it is safe to assume that a premature response early enough to encounter relatively refractory tissue in the peripheral distribution will be propagated at less than full speed proximally. If the response is initiated still earlier, increased proximal delay may prevent its arrival appreciably earlier at

Circulation Research, Vol. XVI, March 1965
the distal level. It may therefore be that an early premature response is blocked at the highest level at which an increased RP duration is encountered, rather than at the level which has the longest RP. The system may behave in this respect like the A-V node itself. There is evidence that the earliest premature response which can be initiated in either the atrium or the His bundle will enter the node, even though it fails to traverse it,\textsuperscript{18} that is, the "true" RP of the His bundle may be longer than that of any nodal element. Nevertheless, a premature atrial response will usually be delayed so long in traversing the node that full recovery of the intraventricular conduction system has occurred by the time it arrives; exceptions to this rule have been considered in detail above.

The reasons for the apparently longer effective refractory period of the RBB as compared with the left, and for its greater sensitivity to frequency and to epinephrine (figs. 8 and 9) are less readily explained. The difference is probably not an artefact due to the experimental conditions. Although the right heart was opened for electrode placement, the window was small and was cut through the atrial wall. The septal surface was bathed in the blood draining from the coronary sinus and Thebesian channels, and was not measurably cooler than blood in the left ventricular cavity. In order to avoid artefacts due to injury, electrodes were not attached to the right bundle itself. Finally, the behavior of the open hearts was in every way analogous to that of many preparations in which the heart was not incised.

Perhaps the major difference between the two bundles is their size; the left is considerably larger than the right. If summation is an important feature of conduction in relatively refractory tissue, one would expect a larger trunk to exhibit a greater margin of safety than a smaller one. For example, if a bundle contains \( n \) fibers having "true" refractory periods uniformly distributed between \( t \) and \( t + \tau \), and if \( n/2 \) fibers must have recovered from the refractory state before a response can be propagated, then the effective RP of the bundle will be \( t + \tau/2 \). In a bundle of \( 2n \) fibers having refractory periods distributed between the same limits, the effective refractory period would be only \( t + \tau/4 \). One may also speculate upon the influence of frequency in such a system. The RP of the fibers is greater at lower frequencies, and the absolute range of values (i.e., \( \tau \)) must also be greater. It follows that the discrepancy between the effective refractory periods of two cables of different size should be increased at lower frequencies. In fact, any agency which produces increased temporal dispersion of refractory periods should be expected to exert differential effects upon conducting bundles of different size, even though their qualitative composition be the same. Conversely, an agency which, like epinephrine, reduces the refractory period duration (thereby reducing the dispersion, \( \tau \)) might be expected to have a relatively greater effect upon the effective refractory period of the smaller cable. These suppositions are no more than a speculative explanation of the results displayed in figures 8 and 9, but they may be subject to direct test in model systems.

One further difference between the right and left branches may be important. If the subendocardial portions of the distribution system derive any significant part of their nutrition from the intraventricular blood, then the difference in oxygen tension between right and left may be a factor. This possibility was not tested.

**Conditions Necessary for Demonstrating Functional Bundle Branch Block**

Although clearly defined block of the RBB was demonstrated in a large majority of the experiments in this study, it is obvious that the necessary conditions would occur much less commonly in intact animals, or in animals prepared with chronically implanted intracardiac electrodes as in the experiments reported by Hoffman et al.\textsuperscript{8} Functional block was demonstrable only at lower heart rates, achieved in many of the present experiments only after sympathetic denervation and destruction of the S-A node. These conditions were not, of course, imposed in the chronic
preparations, and it is therefore apparent why the "type 3" curve, representative of RBB block, was only uncommonly observed in Hoffman's studies. It is also apparent that conversion to the pattern of block in the RBB would not be expected to follow the administration of large doses of catecholamines, for the resulting increased spontaneous frequency and the diminution of the RP of the RBB would greatly reduce the chance of inducing block, even with stimulation of the His bundle.

Sufficiently slow heart rates induced by vagal stimulation would, of course, prevent the appearance of functional block following atrial premature beats, but would permit its demonstration by stimuli applied to the His bundle. This was apparently not attempted in Hoffman's study.

It is evident from the relationships represented in figure 8 that the minimal interval between two successive ventricular responses propagated from the atrium cannot always be used as an approximation of the FRP of the A-V node, unless it can be established that delay of the premature response is not imposed by the intraventricular conduction system. At low driving rates the right bundle may often be the cardiac tissue with the longest effective RP.

Aberrant intraventricular conduction might be expected to occur most frequently when A-V transmission is stressed, as by high driving frequencies. In the present experiments it was shown that functional block of the RBB is not usually demonstrable except at low driving rates. This observation confirms the statement, based on clinical studies, that aberrant conduction is more likely with longer preceding cycles and shorter coupling, i.e., as a result of an early premature beat following a long cycle. Once the necessary conditions are generated, however, the pattern of block may be sustained through many cycles of a tachysystolic rhythm, as in a paroxysm of A-V nodal or reciprocal tachycardia, just as in the experiment of figure 14.

RELATIONSHIP TO A DUAL A-V CONDUCTION SYSTEM

As already demonstrated by Hoffman et al., two of the features of A-V transmission previously attributed to an intranodal dissociation are clearly the result of delay or block within the His-Purkinje system. In the earlier study, results which were interpreted as evidence for communicating branches between two pathways were, without any doubt, due to dissociation below the bundle of His. The "communicating branch" which was assumed to accomplish the silent retrograde activation of the faster pathway, thus throwing the two routes out of phase, can now be located in the ventricles. The analysis of the present results which leads to the assumption of retrograde activation of the right bundle branch (figs. 12 and 13) is the counterpart of one of the experiments analyzed in detail in the 1956 paper.

The remaining evidence for a dual system within the A-V node is the occurrence of echoes. The echo responses recorded in the present study were uncommon; it is possible but unlikely that premature atrial excitation could ever reach the His bundle sufficiently early to permit an intraventricular circuit like that illustrated in figure 17. In most of the experiments comprising the present study, however, there was a period of time during which a premature H2 could be propagated to the atria and return as a reciprocal response of the His bundle. In many experiments, in fact, it was necessary to stimulate the atrium simultaneously with the His bundle in order to prevent the interference of echo responses. The temporal relationships of these responses have been studied in detail and will be described in a subsequent publication.

Summary

Excessive delay and configurational change of ventricular responses to atrial premature beats, previously attributed to dissociation within the A-V node, were shown to be due to functional block of the right bundle branch. It was found that the refractory period (RP) of the right bundle branch often exceeded the functional refractory period (FRP) of the A-V node at slow heart rates, permitting an early premature atrial response to reach the
ventricles before recovery of the right bundle. Vagal stimulation and rapid driving frequencies, by delaying the intranodal transit of the premature response, prevented the exposure of bundle branch block. Epinephrine in low doses sometimes facilitated its occurrence.

Premature responses initiated in the His bundle in open heart preparations were commonly blocked in the right bundle under conditions in which atrial premature responses were normally propagated to the ventricles. Evidence was obtained in such preparations that the portion of the right bundle system beyond the site of the block was activated retrogradely from the left side. Under certain conditions the retrograde activation process returned to the His bundle and the atrium as an echo.

References
Aberrant A-V Impulse Propagation in the Dog Heart: A Study of Functional Bundle Branch Block

GORDON K. MOE, CARLOS MENDEZ and JAOK HAN

Circ Res. 1965;16:261-286
doi: 10.1161/01.RES.16.3.261

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1965 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/16/3/261

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/