Longitudinal Dissociation in the His Bundle

Bundle Branch Block due to Asynchronous Conduction within the His Bundle in Man

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SUMMARY This report presents electrophysiological data in 27 patients (out of a series of 110) which suggest longitudinal dissociation in the His bundle (BH). Twenty-five patients showed left bundle branch block (LBBB) which was rate related in three and two had isolated left axis deviation (LAD) with narrow QRS complexes. BH recordings were performed via the right heart, and in each patient the same electrode catheter was used for stimulation of the BH at different sites. The H-V time was prolonged (range 50–70 msec, mean 59) in all 22 patients with constant LBBB, in one of the three of the rate related LBBB, and in one of the two with isolated LAD; and remained unchanged throughout. In all 25 patients with LBBB proximal BH stimulation exhibited QRS complexes identical to those with normal sinus rhythm with a PI-R interval equal to the H-V time. BH stimulation at a constant cycle length, but at a slightly distal site, abolished the LBBB (constant or rate related) and resulted in narrow QRS complexes (≤ 95 msec) with a PI-R interval shorter than the H-V time by 5 to 20 msec. In the two patients with isolated LAD, BH stimulation abolished LAD with a PI-R interval identical to the H-V time. These findings suggest that a bundle branch block pattern and/or axis deviation may result from a focal lesion or an area of altered refractoriness within the BH. The duration of the QRS complexes and/or a shift in QRS axis was normalized by BH stimulation distal to the lesion due to synchronous impulse conduction to both the bundle branches.

ON THE BASIS of their extensive histological studies, James and Sher have recently reported that the longitudinal separation of Purkinje strands by collagen along with specialized nature of intercellular junctions within each strand form an anatomic basis for longitudinal separation of conduction within the normal His bundle. These investigators have proposed the concept of “sinoventricular conduction” which implies that the individual components of the activation wavefront leaving the sinus node, atrium and A-V node are predisposed for specific areas of ventricular myocardium. It was further postulated that the propagation wavefront may be altered in the His bundle (BH) by physiological influences or by focal disease and result in any form of bundle branch block, ventricular aberration and preexcitation. They do admit that their observations provide an anatomic substrate for the concept of longitudinal dissociation of conduction within the His bundle, under both normal and pathologic circumstances, but do not prove the concept. Others have attempted to reproduce the physiological counterpart of these anatomical findings in isolated tissue and animal experiments.

The purpose of this report is to present our data in 27 patients (left bundle branch block in 25 and isolated left axis deviation in two) which suggest longitudinal dissociation in the His bundle. Stimulation from the proximal BH showed

wide QRS complexes and/or axis deviation identical to that seen during normal sinus rhythm (NSR) with a pacing impulse (PI) to QRS (PI-R) interval identical to the control H-V time. Distal BH stimulation resulted in a narrow QRS complex (≤ 95 msec) and/or abolition of left axis deviation (LAD) with a PI-R interval slightly shorter than the H-V time.

Materials and Methods

Data in 25 patients with left bundle branch block (LBBB) and in two with isolated LAD and a narrow QRS complex (out of a total series of 80 patients with LBBB and 30 with LAD) who were studied during right heart catheterization are presented. Patients ranged in age from 36–88 years (mean 62.4) with 11 males and 16 females. Of the patients with LBBB the ECG pattern of LBBB was constant in 22 and was rate related in three. In the 22 patients with constant LBBB, the mean QRS axis was normal in eight and shifted to the left (≥ −30°) in 14; and the QRS duration ranged from 120–160 msec (mean 142). In the three patients (cases 23–25) with rate dependent LBBB the wide QRS complexes ranged from 140–155 msec in duration and the axis was normal in one and shifted to the left in the other two. During NSR, the 27 patients in this study showed normal and prolonged P-R intervals in 23 and four patients, respectively (table 1).

The ECG abnormalities were associated with arteriosclerotic heart disease in 13, diabetes in four, cardiomyopathy in one and hypertension in three patients. There was no clinical evidence of heart disease in 12 patients except for an abnormal ECG pattern. None of the patients had had a recent myocardial infarction in the 8–10 weeks prior to the study, nor were there any in the immediate postoperative period. The patients were not receiving any cardioactive drugs at the time of study. All patients were studied in the postabsorptive state and were premedicated with 100 mg Nembutal, administered intramuscularly a half-hour before the study. The procedure was explained and an informed consent was obtained.

Under fluoroscopic control and intracardiac electrographic monitoring, a bipolar electrode catheter, 5 French in size with ring electrodes (1 mm wide) 10 mm apart, was introduced percutaneously from a femoral vein and placed in the region of the septal leaflet of the tricuspid valve and His bundle electrogrograms were recorded as described previously. The catheter used for BH recordings had a straight and not a preformed curved catheter tip. In the majority of our studies, the catheter tip points upwards in the direction of the outflow tract of the right ventricle and is occasionally horizontally directed. A second bipolar or quadripolar pacing catheter was introduced into the right atrium through an antecubital vein either by cutdown or percutaneously via a 14 gauge medicut needle. The latter pacing catheter was used both for purposes of atrial stimulation and recording of atrial electromgrams.

All recordings were made on a multichannel oscilloscopic photographic recorder at paper speeds of 100 and 200 mm/sec. Three standard ECG leads (I, aVF and V3) were recorded simultaneously with intracardiac recordings. The standard ECG leads and the bipolar electrograms were displayed at frequency settings of 0–20 Hz and 40–500 Hz, respectively. Atrophicventricular conduction was analyzed during NSR, regular atrial pacing (AP) at progressively increasing rates and during induced premature atrial beats (PABs) with increasing prematurity. Atrial stimulation studies were performed at double the diastolic threshold with stimuli 2 msec in duration.

| Table 1. Results in 27 Patients with Distal His Bundle Pacing |

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* = CL at which 2° type I A-H block was manifested.
I = Rate dependent, narrow QRS complexes at slow rates and wide at faster rates.
ASHD = arteriosclerotic heart disease; Diab. = diabetes mellitus; Hyper = hypertension; CL = cycle length; BH = bundle of His; PI-R = pacing impulse to QRS interval; LAD = left axis deviation; N = normal.
The same bipolar catheter as used for BH recordings was utilized for bipolar BH stimulation as described previously.BH stimulation was performed with stimuli 2 msec in duration and at variable stimulus intensity in each patient up to 10 Ma. Initially proximal BH pacing was attempted by using a higher stimulus intensity so as to eliminate inadequate stimulus intensity as a variable for failure to stimulate the BH, rather than a poor catheter position. This approach was used to save time while attempting to stimulate the BH so that efforts could be solely directed toward proper positioning of the catheter tip in the BH region. Once proximal BH stimulation was accomplished the stimulus strength usually could be lowered to 3-4 Ma without the loss of BH pacing or an alteration of QRS morphology in the paced beats. The catheter was then slightly advanced for distal BH stimulation. During BH pacing bipolar right atrial electrograms were recorded simultaneously with the multiple standard ECG leads.

During BH pacing the effect of the following parameters: a) stimulus intensity, b) polarity of the pacing impulse, c) pacing cycle length (two or more) and d) proximal or distal site of BH stimulation by either slight withdrawal from or advancement of the catheter toward the ventricle, was assessed on the PI-R interval, QRS complex (shape and duration) and QRS axis. In each patient following BH stimulation studies, recordings of BH electrograms were repeated to assess any effect of BH stimulation on the H-V conduction.

No arrhythmias or complications requiring therapy occurred in any patient either during or following the stimulation studies. These studies were not associated with the production of A-V block, H-V prolongation or ventricular tachycardia in even a single case. All equipment was completely grounded.

Definition of Terms

The A-H time was measured from the first rapid deflection of the A wave to the onset of the BH deflection. The H-V time was measured from the onset of the BH deflection to the earliest ventricular depolarization recorded on any of the intracardiac electrograms or the standard ECG leads. The PI-R interval was measured from the onset of the pacemaker impulse to the earliest onset of the QRS complex seen on any of the three standard ECG leads. Normal limits of A-H and H-V times in our laboratory are 50-120 and 35-45 msec, respectively. The term "QRS normalization" simply implies normalization of the QRS duration (to within the normal range) and not necessarily a normal ventricular depolarization. Similarly, distal BH stimulation does not necessarily indicate stimulation of the BH at its bifurcation but implies stimulation of the BH at a site relatively distal to the site of proximal BH stimulation or the proximal end of the BH.

Results

The P-R, P-A and A-H times were abnormal in four, two and two of the 27 patients, respectively. The H-V time was prolonged (range 50-70, mean 59) in all 22 patients with constant LBBB. In the three patients with rate dependent LBBB the H-V time remained constant with or without a pattern of LBBB and was prolonged in one. In the two patients with isolated LAD, the H-V time was 45 and 50 msec. In all patients the H-V time remained unchanged during AP at progressively increasing rates until 2° A-V block (Type I) was manifested or up to a rate of 180/minute. During AP the occurrence of 2° A-V block was always localized between A and the BH deflections.

The scanning of the entire sinus cycle with induced PABs did not result in a shortening of the H-V interval nor of QRS duration in any of the patients. None of the patients exhibited any electrophysiological evidence of antegrade conduction via either the Mahaim or Kent type of bypass fibers. Neither stimulation from high or low right atrium nor the rate of AP (with or without the occurrence of 2° Type I A-V block) had any effect on the duration, morphology or the axis of the QRS complex.

During BH stimulation at a constant rate, in each of the 25 patients with LBBB, the duration and morphology of the QRS complex depended upon the site of stimulation, i.e., proximal or distal BH. Stimulation of the BH from its proximal portion exhibited QRST complexes with LBBB pattern identical to that seen during NSR with a PI-R interval similar to the H-V time. Advancement of the catheter by a few millimeters toward the ventricle and a slightly distal BH stimulation (as compared to the previous site) abolished LBBB pattern, resulting in narrow QRS complexes (≤ 95 msec) usually with a normal Q wave in leads I, aV L and a normal r wave in V s; also the PI-R interval was slightly shorter than that noted during proximal BH pacing or the control H-V time. With distal BH pacing and narrow QRS complexes, the PI-R intervals ranged between 40-50 msec and were shorter by 5-20 msec than the control H-V time (fig. 1).

The changes from LBBB to narrow QRS complexes or vice versa were independent of: a) the pacing cycle length, b) the stimulus intensity and c) the polarity of the pacing impulse. The change from wide to narrow QRS complexes was solely related to the site of stimulation in the BH, i.e., proximal or distal, respectively. During distal BH pacing, narrow QRS complexes were usually seen at low stimulus intensity (3-4 Ma). This was generally necessary to accomplish narrow QRS complexes. In most of the patients, pacing at higher intensity (10 Ma) resulted in septal stimulation and wide QRS complexes with a LBBB pattern, different in QRS morphology from that of sinus rhythm. Both the proximal and distal BH stimulation were usually accomplished when the distal or the tip electrode was cathode and in a few cases when it was anode. However, in no case was the abolition of LBBB or distal versus proximal BH pacing dependent on a change in polarity.

1. Abolition of LBBB Pattern

In all eight patients with LBBB and a normal mean QRS axis, proximal BH pacing resulted in QRST complexes and axis identical to those of NSR; and a PI-R interval equal to the H-V time. In these patients distal BH pacing normalized QRS duration (≤ 95 msec) with a PI-R interval shorter by 10–20 msec than the H-V time and the QRS axis remained normal. A representative example is shown by case 6, a 49-year-old male with LBBB (QRS 150 msec) who showed a control H-V time of 50 msec during sinus rhythm (fig. 2).
With induced premature atrial beats or atrial pacing at faster rates the A-H and the PI-R intervals lengthened whereas the H-V interval remained constant. The possibility of antegrade conduction via the Kent bundle was excluded by stimulation studies. Distal BH pacing resulted in narrow QRS complexes (85 msec) in all 12 standard ECG leads with a PI-R interval (40 msec) shorter by 10 msec than the control H-V time (fig. 3). For purposes of better visual conception ECG recordings are shown at a regular paper speed (25 mm/sec) although recordings were also obtained at faster paper speeds to enable precise measurements of the PI-R and QRS intervals.

**Figure 1.** (Case 15) Normalization of the QRS duration with distal His bundle (BH) pacing is shown in a patient with constant left bundle branch block (LBBB). A) Simultaneous recordings of the three standard ECG leads (L-1, aVf and V6) and bipolar electrograms (BE) from the right atrium (RA) and the BH region. The QRS duration (150 msec) and the H-V time (70 msec) are prolonged during NSR. B) Simultaneous recordings of the three ECG leads and the BE (RA). Proximal BH pacing results in QRS complexes with LBBB identical to the sinus beats and a PI-R (70 msec) similar to the H-V time (left half). Distal BH pacing, without a change in stimulus intensity, normalizes the QRS duration to 90 msec with a PI-R interval (50 msec) shorter by 20 msec than the control H-V time. A = atrial electrogram, V = ventricular electrogram, PI = pacing impulse, PI-R = pacing impulse to QRS interval. Time lines in this and subsequent figures are at one second intervals.

**Figure 2.** (Case 6) His bundle recordings in a patient with LBBB and a normal mean QRS axis show an H-V interval of 50 msec. During an induced premature atrial beat (PAB) the A-H interval lengthened (from 50 to 70 msec); the H-V time and the QRS duration remained unchanged and exclude the possibility of antegrade conduction via the Kent type bypass fibers. Spontaneous variations in the morphology of the P wave are also noted.
2. Abolition of LBBB and LAD

In all 14 patients with constant LBBB and a mean LAD, proximal BH pacing resulted in QRST complexes and an axis similar to that of NSR with a PI-R interval equal to the H-V time. Distal BH stimulation resulted in a narrow QRS complex in all; however, the QRS axis remained unaltered (LAD) in five (fig. 4) and was normalized in nine patients (fig. 5).

3. Abolition of Rate Dependent LBBB and LAD

Three patients (cases 23–25) in this study showed rate dependent LBBB at heart rates ≥ 80 beats/minute. The H-V times remained constant throughout irrespective of the QRS duration. A typical response to BH pacing is illustrated in figure 6 (case 24). At heart rates (sinus or AP) identical to that necessary for development of LBBB, proximal BH stimulation resulted in beats with LBBB similar in morphology, duration and axis to that of NSR or AP; the PI-R interval was identical to the H-V time. BH stimulation at a constant rate but at a slightly distal site resulted in disappearance of LBBB pattern with normalization of QRS complexes and axis similar to that seen during sinus rhythm at slower rates (fig. 6). BH pacing from the latter site showed a PI-R interval 5 msec shorter than the control H-V time or the PI-R interval during proximal BH stimulation.

4. Demonstration of LBBB, Narrow QRS and RBBB

One patient (case 5) in this study showed some interesting observations. This 82-year-old male constantly showed LBBB (QRS 155 msec) with normal axis and a prolonged P-R interval (245 msec) during NSR. Both the A-H (140 msec) and H-V (60 msec) intervals were prolonged. During atrial pacing at rates up to 135/minute, the H-V time and the QRS complexes remained constant. At a constant pacing rate, four different types of QRS complexes were exhibited by stimulation at four different sites: a) stimulation from the most proximal portion of the BH showed QRS complexes, identical to those of sinus rhythm with a PI-R (60 msec) interval similar to the H-V time (fig. 7); b) stimulation of the BH at a slightly distal site showed narrow (90 msec) QRS complexes with a shorter PI-R (45 msec) interval (fig. 7); c) a further minimally distal stimulation exhibited QRS complexes with a right bundle branch block (RBBB) pattern (QRS 140 msec) and a PI-R interval of 40 msec (fig. 8, beats 2 and 3); d) additional slight distal advancement of the catheter into the right ventricle resulted in septal stimulation with a LBBB pattern (QRS complex 170 msec) different in morphology; and the PI was immediately followed by a QRS complex with a PI-R interval not measurable (fig. 8, beat 1).

5. Abolition of Isolated Left Axis Deviation

In the two patients (cases 26, 27) with a narrow QRS complex and isolated left axis deviation BH stimulation normalized the QRS axis without a change in QRS duration; and the PI-R interval was similar to the H-V time (fig. 9).

Discussion

Clinically, the ECG patterns of bundle branch block are generally attributed to a corresponding anatomical lesion(s) in the bundle branches. Contrary to these usual considerations the data in the present study suggest that asynchronous conduction within the His bundle due to either an altered refractoriness or a discrete intra-His lesion, may also result in similar ECG patterns of partial or complete bundle branch block. This study shows that in patients with LBBB or isolated LAD, the ECG pattern could be either reproduced or abolished resulting in normalization of QRS duration or axis by stimulation of different portions of the BH.

The findings in this study can be explained best on the basis of longitudinal dissociation and asynchronous conduction within the BH. Stimulation of the BH proximal to the hypothetical intra-His lesion resulted in ventricular depolarization similar to that seen during sinus rhythm. BH stimulation at a site distal to the lesion resulted in narrow QRS complexes due to synchronous impulse conduction to both the bundle branches (fig. 10). Distal BH stimulation implies stimulation of the BH at a site relatively distal to the
proximal portion of the BH, and may be by as little as \(\leq 1-2\) mm.

James and Sherf have reported that the His bundle is partitioned into narrow cords by collagen running in its long axis and with relatively little cross connections between the compartments. The entire conduction is compartmented as various cords are insulated from each other by the collagen which provides the anatomical setting necessary for asynchronous conduction or longitudinal dissociation in the His bundle. The present findings provide the electrophysiological counterpart to the detailed anatomical and histological studies on the fine structure of the His bundle.

The concept of longitudinal dissociation within the BH, due to a lack or scarcity of side to side intercellular low resistance junctions, has been investigated in several experimental studies and indirectly suggested on the basis of standard ECG recordings. To the best of my knowledge, I have not found a published case with proper documentation of an anatomical lesion showing a bundle branch block pattern due to longitudinal dissociation in the His bundle. Recently longitudinal dissociation has also been demonstrated in the canine right bundle following mechanical pressure. Others have reported that the transverse interconnections and thereby the transverse conduction may be less effective in fibers during phase 3 of repolarization. The latter possibility may explain the demonstration of longitudinal dissociation in vitro in Purkinje strands intoxicated by ouabain and depolarized by

**Figure 4.** (Case 9). Shows that distal BH pacing normalizes the QRS duration (from 150 to 95 msec) but the left axis duration (LAD) persists. A) The H-V interval during NSR is 50 msec. B) Shows continuous recordings of the three standard ECG leads and RA electrograms. Distal and proximal BH pacing are shown at a constant stimulus intensity and cycle length (CL). With distal BH pacing and QRS normalization (first 4 beats) the PI-R interval (40 msec) is shorter by 10 msec than that seen during proximal BH pacing (last three beats). The QRS complexes and the PI-R interval with proximal BH pacing are identical to the QRS complexes and the H-V interval during NSR (panel A).

**Figure 5.** (Case 12). Shows abolition of LBBB and LAD with distal BH stimulation. Both the QRS duration and the axis are normalized. A) The H-V time during NSR is 55 msec. B) Shows continuous recordings during distal and proximal BH pacing at a constant CL (680 msec) and stimulus intensity. Both the QRS duration and axis are normalized with distal BH pacing; and the PI-R interval (40 msec) is shorter than the H-V time by 15 msec (first four beats). During proximal BH pacing the QRS complexes are identical to those of sinus beats and the PI-R interval (55 msec) is similar to the H-V time (last three beats).
potassium chloride. This condition involves some degree of depolarization of all fibers and may selectively affect the function of the transverse interconnections. A recent anatomical study has reported that in five of 32 hearts (16%) the His bundle traversed to the right of the crest of the muscular intraventricular septum. The left bundle (LB) in these hearts originated as a narrow stem crossing from right to left through the base of the membranous sep-

**Figure 6.** (Case 24). Shows that aberrancy may occur due to asynchronous conduction within the BH in a patient with rate related LBBB. The rhythm strip (on top) shows a rate related LBBB during NSR. The 12 standard ECG leads show narrow QRS complexes and a normal axis. A) Atrial pacing (AP) shows beats with LBBB (first three beats) and narrow QRS complexes are seen with NSR (last two beats). The H-V time (45 msec) remains constant throughout. B) Shows continuous recordings at a constant CL (500 msec) and stimulus intensity. Distal BH pacing results in narrow QRS complexes (first two beats) similar to those of NSR, despite a faster rate. The PI-R interval (40 msec) during distal BH pacing is slightly shorter than the H-V time. Proximal BH pacing (beats 3 and 4) show QRS complexes and a LBBB pattern similar to that of atrial pacing (beats 5-7) with a PI-R interval (45 msec) identical to the H-V time.

**Figure 7.** (Case 5). Shows a patient with LBBB in whom BH stimulation at different sites resulted in several types of QRS complexes. A) During NSR the H-V time and the QRS complexes are 60 and 155 msec in duration, respectively. B) Shows continuous recordings at a constant CL and stimulus intensity. With distal BH pacing (first three beats) the QRS duration is normalized to 90 msec and the PI-R interval (45 msec) is shorter than the H-V time. Proximal BH pacing (last four beats) shows QRS complexes identical to those of NSR with a PI-R interval (60 msec) similar to the H-V time.
The minimal interval in the proximal bundle was bypassed by discrete stimulation of the right bundle. Therefore, in our series, a pattern of ventricular pacing was seen in a majority of the cases (80%) with distal BH stimulation, and in all during stimulation of either bundle branch.[20] In view of these facts, discrete stimulation of the LB, distal to the lesion in its proximal portion, via an electrode catheter (with electrodes 10 mm apart) is highly unlikely. A high intensity stimulus may bypass a small lesion at the origin of the LB, but this would be associated with simultaneous depolarization of the muscular septum and a wide QRS complex. 3) Narrow QRS complexes may result from simultaneous stimulation of both bundle branches if the distal segment is normal. The PI-R interval resulting from simultaneous stimulation of the proximal portions of the normal bundle branches should be similar to the normal range of RB-V or LB-V time (25–30 msec).[21] During narrow QRS complexes, in none of our cases was the PI-R interval 25–30 msec. Instead it usually ranged between 40–50 msec suggesting stimulation of a site proximal to the origin of the bundle branches, i.e., the BH. 4) The range of normal conduction time through the BH is 15–20 msec. Therefore, the cases with LBBB in which the normalization of the QRS duration was accompanied by a shortening of PI-R interval of less than 15–20 msec (as compared to the H-V time), and especially a shortening of 5–10 msec, cannot be explained by stimulation of proximal portions of bundle branches. 5) The abolition of LAD in the two patients (cases 26, 27) with narrow QRS complexes and PI-R intervals identical to the control H-V time indicates stimulation of the proximal BH and not at its bifurcation. Therefore, it must be concluded that the narrowing of the QRS complex or normalization of the QRS axis could not have resulted from stimulation of either the LB alone or of both the bundle branches simultaneously. 6) In our series of 80 patients with LBBB, BH stimulation normalized the QRS duration in 30%. Therefore, at least half of these cases must be explained on a basis other than...
anatomical variations as the LB originates from a right sided BH in 16%.19

These data did not result from the use of a high stimulus intensity as: 1) The narrowing of the QRS complexes was independent of stimulus intensity and could be demonstrated at 3–4 Ma. Stimulation studies of the distal BH during open heart surgery have revealed that high Ma always resulted in a pattern of ventricular pacing and BH pacing was seen only at low Ma.20 2) Both the wide and narrow QRS complexes resulted from stimulation at identical Ma and cycle length.

3) In patients with rate related LBBB the normalization of QRS was related to a change in stimulation site only. 4) A shorter PI-R interval during narrow QRS complexes, as compared to that with LBBB beats, indicates that the impulse transmission occurred over a shorter distance. This suggests that the changes in QRS morphology are related to different sites of stimulation in the BH and not the Ma.

In this study, the narrow QRS complexes are also not due to direct stimulation of the muscular intraventricular septum which should result in wide QRS complexes. Stimulation of the septum from the right heart usually shows: 1) beats with a pattern of LBBB different in morphology from that of sinus beats (fig. 8) and 2) that the PI is immediately followed by the onset of the QRS complex without an intervening isoelectric period of 40–50 msec.

In most of the cases, BH stimulation was associated with simultaneous depolarization of the right atrium. This in all probability is the result of stimulation by the electrode catheter with electrodes 10 mm apart. It is not necessarily a result of high intensity stimulus as it was seen even during pacing with 3–4 Ma. Similar observations were noted in another study with BH stimulation during open heart surgery.20 These findings in the present study are consistent with BH stimulation in man as previously reported by us and by others utilizing electrode catheter stimulation in dog studies.10, 18, 22

Artificial stimulation of the BH in man usually results in depolarization of its entire thickness at its site of stimulation. These conclusions are suggested by our previous studies with BH stimulation in hundreds of cases, with normal QRS complexes or with bundle branch block patterns, in whom QRSST complexes identical to the sinus rhythm were reproduced by BH pacing. This would not have occurred if only a partial thickness of the BH had been depolarized. Our present data, by reproducing QRSST complexes identical to those of sinus rhythm in patients with LBBB during proximal BH stimulation, further support the above concept.

It is likely that on a rare occasion, catheter stimulation of the BH may depolarize only a portion of the BH thickness and thereby artificially produce asynchronous conduction in the BH. A possible example of this type is illustrated in figure 8 (case 5) which shows four types of QRS complexes. During BH stimulation the beats (no. 6, 7) with LBBB pattern (similar to those of sinus beats) and narrow QRS complexes (beats 4, 5) are readily explained, and this response is similar to that seen in all others. The beat (no. 1) with a very wide QRS and a LBBB pattern, but with a QRS morphology different from that of sinus beats, is due to stimulation of the septum. The beats (2 and 3) with a RBBB pattern and PI-R interval (40 msec) slightly shorter than that during narrow QRS complexes (45 msec) in all probability are the result of depolarization of a partial thickness of the BH containing fibers destined to the left bundle branch.

Several other possibilities fail to explain the beats with a RBBB pattern in figure 8 (beats 2, 3): 1) Stimulation of the right septum should produce LBBB and not RBBB. In addition, during septal stimulation the PI-R interval should not be 40 msec. 2) The possibility of selective stimulation of LB at low Ma (3 Ma) just distal to the lesion in its upper portion (responsible for LBBB during sinus rhythm) is unlikely from the right side of the heart. As discussed above, even in right sided BH and origin of LB, a stimulus intensity needed to shunt the upper LB lesion would also simultaneously depolarize the septum and/or the RB. Furthermore, even if it were possible, a retrograde block to the BH and upper RB would have to be proposed. A high intensity stimulus which could shunt an upper LB lesion should be high enough to shunt retrograde conduction to distal end of BH. There is only a 5 msec difference in conduction from the site where narrow QRS complexes are produced as opposed to those with RBBB. His bundle studies in patients with fascicular rhythms suggest that asynchrony in conduction with a difference of 5 msec between the two bundle branches should not result in QRS complexes as wide as 140 msec.24, 28

Present data seem to suggest that in our patients, the site of lesion responsible for LBBB or LAD in all probability...
was located in the upper half of the BH. In all of our cases with LBBB, the PI-R interval (40–55 msec) during normalization of QRS duration or axis was longer by at least 10–20 msec than the normal RB-V or LB-V conduction time (25–30 msec). Therefore, a portion of the PI-R interval (10–20 msec) during normalization of QRS duration must be attributed to conduction through tissues other than the bundle branches, i.e., the BH and probably its distal half. A normal range of conduction time of 15–20 msec through the BH suggests that the lesion(s) producing LBBB or LAD in all probability was located in the upper half of the BH especially in those cases with minimal or no shortening (≤ 5 msec) in the PI-R interval during normalization of QRS duration or axis (figs. 6 and 9). The above reasoning is indirectly supported by previous studies in man using electrode catheters pervenously or probes during open heart surgery.9, 20 The latter studies indicate that stimulation of the distal BH results mostly in ventricular pacing and only rarely selective BH pacing is seen.20 Accordingly, in our cases, the normalization of QRS complexes or axis must have occurred due to stimulation of the BH relatively proximal to its distal end.

In all of our cases with constant LBBB the H-V time was prolonged indicating a diseased HPS. In most of these cases, the PI-R intervals, during normalization of the QRS duration with BH pacing, were similar to the normal range of H-V intervals. These observations suggest that: a) the H-V prolongation was probably due to a cross sectional delay in a portion of the BH and b) the longitudinal dissociation resulted from unequal degrees of delay or block in various segments of the cross-section of the BH at the involved site(s). The five cases with a PI-R interval ≥ 50 msec during normalization of the QRS suggest additional delay at a second and distal site in the BH probably of equal magnitude through its cross section.10, 26, 27

Present data suggest that intra-His lesions may not only produce ECG patterns of LBBB or LAD but also may result in patterns of RBBB. These data and those from previous clinical studies further suggest that intra-His lesions may play a significant role in the production of complete heart block.26, 28 In a fair number of patients with RBBB and LAD, a prolonged H-V interval is associated with an intra-His delay as is indicated by a prolonged or “split” BH potential.29 An alternative explanation for the frequent association of RBBB with LAD may be suggested on the basis of present observations. If such a pattern was to result from an intra-His lesion, the fibers destined for both the RB and the anterior left ventricular wall are more likely to be affected, because of their close proximity to each other within the BH, as opposed to the fibers destined for the posterior left ventricular wall. Our findings raise further questions about the validity of using the nomenclature of “fascicular blocks,”29 and suggest that the pattern of LBBB and LAD does not always imply two sites of lesions in the LB. Such an ECG pattern may result from abnormalities within the BH alone, BH and the fibers in the LB destined for anterior left ventricular wall or the LB alone. Our findings also suggest the limitations in correlating histological findings with either an ECG pattern or even with electrophysiological studies.

The patients with rate dependent LBBB (cases 23–25) provided a unique opportunity to compare the QRST complexes normalized by BH pacing (despite faster rates) with the control narrow QRST complexes seen during spontaneous sinus rhythm at slower rates; these were found to be similar (fig. 6). These data suggest that: a) the catheter stimulation of the BH beyond the discrete abnormality not only normalizes the QRS duration but also depolarizes the ventricles in a similar fashion as they would be in the absence of an ECG pattern of LBBB; b) in selected cases of LBBB, BH stimulation studies may be useful to either confirm or rule out the diagnosis of an underlying or associated anterior wall myocardial infarction which is generally difficult to diagnose; and c) aberrant conduction or rate related bundle branch block may at times result from altered refractoriness and asynchronous conduction within the His bundle and not always the bundle branches. In addition, aberrant conduction may be due to a localized phenomenon and at a site more proximal than generally considered.

His bundle stimulation studies also may be clinically useful in localizing the abnormal site responsible for an ECG pattern, to assess the number of abnormal sites involved in the HPS, i.e., the BH and/or the bundle branches, and to determine whether the involved HPS has diffuse disease or only a discrete lesion. The discrete or diffuse nature of the lesion(s) and their location, i.e., proximal versus distal involvement of HPS, may be related to different etiological factors and consequently may have different prognoses.

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The Effect of Mannitol Following Permanent Coronary Occlusion

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With the technical assistance of Ross Raymond and Robert Schouler

SUMMARY

Quantitative comparisons of infaracts 24 hours after ligation of the left anterior descending coronary artery (LAD) via thoracotomy were made in 13 control and 13 dogs treated with i.v. 25% mannitol, 2 ml/min for 4 hours following occlusion. Mannitol increased serum osmolality by 44 ± 4 mOsm/l (mean ± 1 SE) with hemodynamic effects limited to a small increase in left ventricular dP/dt. Nonperfusible tissue measured by planimetry at 24 hours was similar in both groups (46 ± 4% of area defined with dye injected into the distal LAD for control versus 48 ± 5% for mannitol treated dogs, P = NS). Creatine phosphokinase activity in infarcted tissues was also similar in both groups. Myocardial blood flows measured with radioactive microspheres were also similar in both groups. Collateral conductance calculated from retrograde flow and aortic pressure increased within the 24 hour period by 146 ± 23% in the control dogs; in the mannitol treated dogs, collateral increased only 38 ± 14% (P < 0.001). Thus mannitol had no effect on ultimate infarct size. Moreover, mannitol appeared to hinder the development of collateral vessels.

THE OBSERVATION of Sheehan and Davies\(^7\) of failing renal reflow after 3 hours of total ischemia evoked a series of extensive studies directed to elucidate the role of early vascular changes in tissue rendered ischemic. In experimental animal models it has been shown that endothelial cells of the small vessels begin to swell within 20 to 120 minutes following the onset of ischemia in the brain,\(^2\) heart,\(^1\) and kidney.\(^6\),\(^9\) This intracellular edema may, by narrowing of the vascular lumen, hinder the passage of red blood cells, thus causing a further reduction of blood supply to the ischemic tissue.\(^6\),\(^7\) It has been proposed that increasing serum osmolality by infusion of hyperosmotic agents such as mannitol may prevent these circulatory defects.\(^3\) Hyperosmotic mannitol given to increase serum osmolality by approximately 40 mOsm/l has been shown to increase flow to the heart following the release of a prolonged coronary occlusion in anesthetized dogs on right heart bypass\(^8\) and increases in blood flow following ischemia were also found in kidneys from rats\(^8\) and dogs\(^9,10\) as well as in brains from rabbits\(^11\) and baboons\(^12\) when treated with mannitol. Changes in regional coronary blood flow in the ischemic as well as in the normal myocardium after treatment with mannitol were also observed in the conscious dogs during acute and chronic myocardial ischemia.\(^14\)\(^-\)\(^18\) In addition, hyperosmolality was found to improve myocardial performance both in isolated cardiac muscle\(^17\)\(^-\)\(^19\) and in the intact heart with normal coronary perfusion and after regional ischemia.\(^20\)\(^-\)\(^22\)

These results led to the speculation that treatment with hypertonic mannitol might be of value in salvaging ischemic

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