Electrophysiological studies in patients with rate-related intermittent left bundle-branch block¹

David S. Cannom,² Daniel J. Goodman, and Donald C. Harrison

From The Cardiology Division, Stanford University School of Medicine, Stanford, California 94305, U.S.A.

Two patients who developed left bundle-branch block with increase in heart rate are presented. Atrial pacing during His bundle recording studies showed differing responses in the ventricular specialized conduction system of the two patients. In one, the onset of left bundle-branch block was associated with no change in the previously normal HV interval (50 msec), while in the second the HV interval doubled to 80 msec during the development of left bundle-branch block. These two responses are discussed in the light of the electrophysiology of the ventricular specialized conduction system, and suggest that certain patients with rate-related left bundle-branch block have trifascicular disease.

The appearance of intermittent left bundle-branch block on the surface electrocardiogram is seen with both slow and accelerated heart rates (Massumi, 1968; Bauer, 1964; Sarachek, 1970; El-Sherif, 1972). Though speculative, most authors have related bradycardia-dependent left bundle-branch block to spontaneous phase four diastolic depolarization of portions of the ventricular specialized conduction system. Consequently, that portion of the conduction system would be refractory to the next anterograde sinus impulse and would result in a bundle-branch block pattern on the electrocardiogram (Massumi, 1968).

Little attention, however, has been paid to the mechanisms underlying left bundle-branch block seen in association with accelerated heart rates. Using the His bundle technique, we have recently studied two patients who present contrasting electrophysiological phenomena during the development of their tachycardia-dependent left bundle-branch block. It is our purpose to describe these patients clinically, to outline the electrophysiological studies done, and to speculate upon the causes of the contrasting conduction abnormalities noted during the His bundle study.

Subjects and methods

Case reports

Case 1 A 45-year-old man had a 4-year history of exertional substernal chest pain typical of angina pec-

toris. In 1971 he underwent a Master's test which showed transient left bundle-branch block associated with an acceleration in heart rate. In March 1973, he had substernal chest pain and was admitted to another hospital to rule out myocardial infarction. An electrocardiogram on admission showed left bundle-branch block but infarction was not documented by serial serum enzymes. The chest pain continued to increase in frequency and severity, and in April 1973 he was admitted to Stanford University Hospital for further diagnostic studies.

The patient's past medical history and physical examination were unremarkable. His electrocardiogram at admission is shown in Fig. 1.

The patient underwent a diagnostic left and right heart catheterization using standard techniques. The only abnormality noted was a resting left ventricular end-diastolic pressure of 15 mmHg, which rose to 20 mmHg with exercise. During the period of exercise, the patient's heart rate increased to 109 beats a minute, at which time a left bundle-branch block pattern was present on the electrocardiogram. There were no other abnormalities in the haemodynamic study.

Coronary arteriography was performed by the Judkins technique. Multiple lesions resulting in 75 per cent narrowing were noted in the midportion of the left anterior descending artery, and there was a 90 per cent stenosis at the proximal portion of the circumflex coronary artery. The right coronary artery was dominant with only minimal plaques present. Left ventricular contractility as assessed by angiography was considered normal.

On the following day, the patient underwent a His bundle study. Standard techniques were employed (Scherlag *et al.*, 1969). A No. 7 French quadripolar catheter was inserted into the median basilic vein and advanced to a position in the right atrium abutting the sinus node. A No. 7 French tripolar catheter was

Received 15 January 1974.

¹ This work was supported in part by NIH grants.

² Present address: Section of Cardiology, Yale University School of Medicine, New Haven, Connecticut, U.S.A.

FIG. 1 Standard 12-lead electrocardiogram of Case 1 taken at the time of his admission to Stanford University Hospital. Note normal PR interval and QRS duration.

inserted into the right femoral vein and advanced to a position across the tricuspid valve in the region of the bundle of His. The proximal two poles of the right atrial catheter and the three bipolar electrodes from the His bundle catheter were inserted into the AC input of an Electronics for Medicine electrocardiograph pre-amplifier through a bypass filter between 40 and 500 Hz. An electrocardiographic lead II was displayed simultaneously. The distal two poles of the right atrial catheter were attached to a pacemaker (Medtronic 5837) to enable right atrial pacing. Careful attention was paid to the grounding of all equipment. Measurements made from the tracings included the AH interval (from the onset of atrial depolarization recorded in the His catheter to the onset of the His bundle depolarization) and the HV interval (from the onset of the His bundle deflection to the onset of ventricular depolarization).

The patient was not considered a candidate for coronary artery bypass surgery and was discharged on propranolol and nitroglycerin.

Case 2 A 62-year-old man was referred to Stanford University Hospital in December 1972 for evaluation of recurrent palpitations. He had a 15-year history of essential hypertension treated with reserpine and was in good health until 18 months before admission, when he noted the onset of intermittent palpitations. An electrocardiogram taken six months before admission showed sinus bradycardia, and he was treated with procainamide and propantheline bromide.

The episodes of palpitations continued to occur two or three times a week and lasted from 30 minutes to one hour. They were associated with diaphoresis but not with nausea, dizziness, dyspnoea, or chest pain. During one attack, an electrocardiogram was taken and he was noted to be in atrial fibrillation.

The patient's past medical history was noncontributory. On referral to Stanford University Hospital, he

was noted to be slightly obese. His blood pressure was 190/90 mmHg; pulse 55 and regular. The remainder of his physical examination was unremarkable.

The clinical impression at the time of admission was that the patient had a form of the sick sinus syndrome with associated tachycardias. He underwent a His bundle study using the same technique as described for Case 1. The 12-lead electrocardiogram taken at the time of admission at Stanford is shown in Fig. 2.

FIG. 2 Standard 12-lead electrocardiogram of Case 2 taken at the time of admission to Stanford University Hospital. The PR interval and QRS duration are normal.

Results

Fig. 3 represents a baseline tracing from Case 1 during the His bundle study. The patient's right atrium is being paced at 80 beats a minute, and at this rate the HV interval is 50 msec.

With an increase in the heart rate to 112 beats a minute, left bundle-branch block developed, as shown in Fig. 4. The patient's AH interval has increased slightly, but there has been no change in the HV interval, which remains constant at 50 msec. It was found on numerous occasions that the critical rate at which the patient developed left bundle-branch block on the surface electrocardiogram was 92 beats a minute. At no time during the study did the patient's HV interval fluctuate.

Fig. 5 shows the patient's response to the termination of right atrial pacing at a rate of 150 beats a minute. The first two beats after right atrial pacing are of a complete left bundle-branch configuration, but a careful comparison with the QRS complexes in Fig. 3 shows that even the fourth complex in Fig. 5 has not returned completely to the control configuration.

FIG. 3 His bundle electrogram of Case 1, with the patient in control state at a paced rate of 80 beats a minute. Shown are electrographic lead II (L_2), a high atrial electrogram (AE), and two His bundle electrograms (HBE). The atrial electrogram is labelled A, the His bundle deflection is labelled H, and the ventricular electrogram is labelled V. The stimulus artefact is labelled S. The time lines are 100 msec at a paper speed of 100 mm/sec. In the control state, the patient's AH interval is 70 msec and the HV interval 50 msec.

FIG. 4 At a paced rate of 112 beats a minute, Case 1 has developed left bundle-branch block with a QRS duration of 120 msec. The labels are the same as those noted in Fig. 3. The AH interval is 80 msec and the HV interval 50 msec.

FIG. 5 During rapid atrial pacing at 150 beats a minute, as shown in the first two beats in this illustration, the QRS complex demonstrates a complete left bundle-branch block configuration (Case 1). Even after the pacemaker is abruptly turned off (after the second QRS configuration), the third and fourth beats still show a complete left bundle-branch block configuration, while in beats 5 and 6 the QRS complex is gradually resuming the control configuration (Fig. 3). The HV interval remains constant at 50 msec. The AH interval has returned to its control level of 70 msec after the pacemaker has been turned off. The labels are the same as in Fig. 3.

FIG. 6 His bundle recording for Case 2 in the control state is shown, with the patient in a regular sinus rhythm. The sinus rate is 77 beats a minute, the AH interval is 80 msec, and the HV interval 50 msec. The QRS complex is of normal configuration and duration. Labels are the same as in Fig. 3.

The electrophysiological data from Case 1 contrast with those obtained during the His bundle study in Case 2. This patient had an abnormal sinus node recovery time of 1,600 msec, which was compatible with the clinical impression of sick sinus syndrome.

Fig. 6 shows the resting tracing of Case 2. The heart rate is 77 beats a minute, the QRS is of normal morphology, and the HV interval is 40 msec.

Fig. 7 illustrates that with right atrial pacing a critical heart rate of 91 beats a minute is reached, at which the patient develops left bundle-branch block.

While the AH interval has increased by 70 msec, the HV interval, which was 40 msec when the QRS was of normal morphology, has increased to 80 msec with the development of left bundle-branch block. This represents an increase of 40 msec over the patient's baseline HV interval.

Because of the clinical and electrophysiological diagnosis of the sick sinus syndrome, a permanent right endocardial demand pacemaker was inserted and the patient was treated with quinidine to control the recurrent atrial arrhythmias. He is currently doing well.

FIG. 7 The rate of atrial pacing has been increased from 89 beats a minute (first two stimuli) to 91 beats a minute in the subsequent three complexes. At the critical rate of 91, the patient develops left bundle-branch block. The HV interval is seen to increase from 40 msec (in beats 1 and 2) to 80 msec (in beats 3 through 5). The AH interval, which is 150 msec, is constant, but the overall PR interval is increased by 40 msec. Labels same as in Fig. 3.

Discussion

These two patients are of interest because of the contrasting electrophysiological phenomena associated with the development of tachycardia-related left bundle-branch block. These phenomena must be understood in the context of normal ventricular activation. Durrer *et al.* (1970), in their study of the activation sequence in the isolated human heart, showed that the right endocardial surface is normally activated at the anterior papillary muscle some 5 to 10 msec after the onset of left ventricular cavity activation. Studies *in vivo* using catheter recordings of left and right bundle-branch potentials have verified these results and have shown that the left and right bundles are activated nearly simultaneously (Rosen *et al.*, 1971). In patients having a QRS of normal morphology, it would be expected that the right and left aspects of the ventricular septum would be activated almost in synchrony.

While an extensive literature exists regarding conduction in *stable* left bundle-branch block, there has been no previous appraisal of conduction in the ventricular specialized conduction system during *intermittent* left bundle-branch block. Rosen *et al.* (1971) have presented three cases of intermittent left bundle-branch block in which the HV interval did not change when left bundle-branch block appeared with increased heart rates induced by pacing. Castellanos (1973) cites one case of intermittent left bundle-branch block artificially induced by an atrial premature depolarization, in which the HV interval increased by 20 msec. However, it is unclear from his Fig. 1 whether the HV interval has been properly measured.

The normal HV intervals in Rosen's cases above

are in contrast to those patients having stable, fixed left bundle-branch block. In nearly all these patients, the HV interval has been found by earlier investigators to be prolonged (Haft *et al.*, 1971; Ranganathan *et al.*, 1972). As has been emphasized, the HV interval represents the shortest temporal conduction pathway between the His bundle and the ventricular myocardium and, thus, if the right bundle or either of the two divisions of the left bundle are conducting at normal velocities, the HV interval should be normal (Cannom, Goldreyer, and Damato, 1972). Thus, when the HV interval is prolonged in stable bundle-branch block, it must be concluded that there are abnormalities in conduction in all three fascicles of the specialized conduction system resulting in reduced conduction velocities and an increase in the HV interval.

Experimental animal models comparable to the fixed left bundle-branch block in humans do not exist. Amer *et al.* (1960), when producing experimental left bundle-branch block in dogs by incising the left bundle beneath the aortic valve, found that while the activation of the entire *left* septal surface was delayed by an average of 35 msec, there was *no* effect on the sequence of activation of the right septal surface (with one experimental exception noted). This would be the same as stating that the HV interval would not vary by more than 5 to 10 msec from normal, as explained above by the work of Durrer *et al.* (1970), if left bundle-branch block is produced by a process analogous to surgical interruption of the main bundle itself (Amer *et al.*, 1960). This is because the right bundle conducts normally. However, as stated, this is not the typical finding in fixed bundle-branch block in humans.

These concepts are pertinent to the electro-

physiological data in the two patients studied (see Results section). In Case 1, in whom the HV interval did not alter during the development of left bundle-branch block with pacing, we conclude that his right bundle-branch was functioning normally. With an acceleration in heart rate, his right bundle did not become more refractory, comparable to results in normal patients without conduction abnormalities (Hoffman and Cranefield, 1960). It could be argued that the presence of coronary artery disease involving both his left anterior descending and circumflex coronary arteries has compromised the blood supply to his main left bundle. In a fashion analogous to the surgically-induced bundle-branch block of Amer *et al.* in canines (1960), when a critical rate is reached, the blood supply to the main left bundle becomes inadequate, and left bundle-branch block develops. However, the HV interval remains normal, as the blood supply to the right bundle is not compromised. Alternatively, the diseased left bundle-branch can conduct normally at lower heart rates, but with the stress of a fast heart rate, the number of impulses that can be conducted is exceeded.

In contrast, in Case 2 when a critical heart rate is reached and left bundle-branch block develops, the HV interval increases from 40 to 80 msec. The doubling of the HV interval, with associated increase in the PR interval on the surface electrocardiogram as well, is beyond experimental variation. It suggests that when left bundle-branch block develops, not only is the left bundle abnormally refractory, but the right bundle has become abnormally refractory as well, resulting in the increased HV interval. This response is in contrast to normals in whom the ventricular specialized conduction system becomes less refractory with increased heart rates (Hoffman and Cranefield, 1960). It would be expected that while the right bundle-branch has become increasingly refractory and has resulted in an increased HV time, it is still less refractory than either fascicle of the left bundle-branch itself (Cannom *et al.*, 1972). In the absence of any evidence in this patient for coronary artery disease, it is probable that Case 2 has primary degenerative disease of his conduction system.

The electrophysiological data presented in these two patients with rate-dependent left bundle-branch block show that differing phenomena may exist at the time of development of left bundle-branch block. Whether the HV interval increases or remains the same with the development of left bundle-branch block depends upon the refractoriness of the remaining fascicle, namely, the right bundle. If it is 'normal' or only minimally diseased, it will respond to increased rates without increasing the HV in-

terval when left bundle-branch block appears. On the other hand, if the right bundle is involved in the process, causing the intermittent left bundle-branch block, it would be expected that the HV interval would increase with the development of left bundle-branch block, as is noted in Case 2.

These observations have both conceptual and clinical importance. Case 2, in whom the HV interval increased with the appearance of left bundle-branch block had associated disease of the sinus node, as well as the right bundle-branch. It can be argued that more clinical concern should be registered for the patient who develops an increased HV interval with rate-dependent left bundle-branch block. In such a patient, there is direct electrophysiological evidence for trifascicular disease at faster rates, and this phenomenon, over a period of time should theoretically increase the likelihood of third-degree heart block developing below the His bundle. However, the precise clinical implications of this electrophysiological observation await the prospective analysis of the subsequent clinical course in patients showing increased HV intervals with rate-dependent bundle-branch block.

References

- Amer, N. S., Stuckey, J. H., Hoffman, B. F., Cappelletti, R. R., and Domingo, R. T. (1960). Activation of the interventricular septal myocardium studied during cardiopulmonary bypass. *American Heart Journal*, **59**, 224.
- Bauer, G. E. (1964). Transient bundle-branch block. *Circulation*, **29**, 730.
- Cannom, D. S., Goldreyer, B. N., and Damato, A. N. (1972). Atrioventricular conduction system in left bundle-branch block with normal QRS axis. *Circulation*, **46**, 129.
- Castellanos, A., Jr. (1973). H-V intervals in left bundle-branch block. A letter to the Editor. *Circulation*, **47**, 1133.
- Durrer, D., Van Dam, R. T., Freud, G. E., Janse, M. J., Meijler, F. L., and Arzbaecher, R. C. (1970). Total excitation of the isolated human heart. *Circulation*, **41**, 899.
- El-Sherif, N. (1972). Tachycardia-dependent versus bradycardia-dependent intermittent bundle-branch block. *British Heart Journal*, **34**, 167.
- Haft, J. I., Weinstock, M., DeGuia, R., Gupta, P. K., and Fano, A. (1971). Assessment of atrioventricular conduction in left and right bundle branch block using His bundle electrograms and atrial pacing. *American Journal of Cardiology*, **27**, 474.
- Hoffmann, B. F., and Cranefield, P. F. (1960). *Electrophysiology of the Heart*. McGraw-Hill, New York.
- Massumi, R. A. (1968). Bradycardia-dependent bundle-branch block: a critique and proposed criteria. *Circulation*, **38**, 1066.
- Ranganathan, N., Dhurandhar, R., Phillips, J. H., and Wigle, E. D. (1972). His bundle electrogram in bundle-branch block. *Circulation*, **45**, 282.
- Rosen, K. M., Rahimtoola, S. H., Sinno, M. Z., and Gunnar, R. M. (1971). Bundle-branch and ventricular activation in man: a study using catheter recordings of left and right bundle-branch potentials. *Circulation*, **43**, 193.

Sarachek, N. S. (1970). Bradycardia-dependent bundle-branch block: relation to supernormal conduction and phase 4 depolarization. *American Journal of Cardiology*, **25**, 727.

Scherlag, B. J., Lau, S. H., Helfant, R. H., Berkowitz, W. D., Stein, E., and Damato, A. N. (1969). Catheter technique

for recording His bundle activity in man. *Circulation*, **39**, 13.

Requests for reprints to Dr. Donald C. Harrison, Cardiology Division, Stanford University School of Medicine, Stanford, California 94305, U.S.A.