Tachycardia- and bradycardia-dependent bundle-branch block after acute myocardial ischaemia

Nabil El-Sherif

From the Cardiology Department, Faculty of Medicine, Cairo University, Cairo, Egypt¹

Critical observation of the onset and course of transient bundle-branch block after acute myocardial ischaemia in 5 patients showed that the block was initially demonstrated both on increasing heart rate (tachycardia-dependent block) and on slowing (bradycardia-dependent block), with normal intraventricular conduction at intermediate heart rates. In some patients normal conduction disappeared within 2 to 12 hours with bundle-branch block present at all heart rates, to reappear again within 24 hours with block occurring at both higher and lower rates. Three patients were followed for 3 to 7 months and showed that the critical rates for both tachycardia- and bradycardia-dependent block altered in such a way that the range of heart rates associated with normal conduction gradually increased until the block could no longer be elicited at the heart rates studied. It is suggested that tachycardia- and bradycardia-dependent bundle-branch block after acute myocardial ischaemia can be explained by characteristic changes in the electrophysiological properties of two groups of Purkinje fibres which may be due to differential localization of metabolites released in the ischaemic zone. Contrary to previous reports our findings suggest the presence of dissociation between enhanced automaticity of the pacemaker cells and bradycardia-dependent conduction disturbances. The various mechanisms that have been previously invoked to explain bradycardia-dependent conduction disturbances are critically reviewed with special reference to cases of bradycardia-dependent paroxysmal atrioventricular block.

The majority of cases of intermittent bundle-branch block are rate dependent, with the conduction disturbance usually associated with either acceleration of the heart rate (tachycardia-dependent block) or slowing of the rate (bradycardia-dependent block) (El-Sherif, 1972). We have recently shown by analysis of clinical records that repetitive block of the impulse in one part of the bundle-branch system (the posterior division of the left bundle) can be explained by the concurrent operation of a tachycardia- and bradycardia-dependent block (El-Sherif, 1973). Study of the onset and course of transient bundle-branch block in patients after acute myocardial ischaemia revealed several examples of rate-dependent bundle-branch block, showing both tachycardia- and bradycardia-dependent block with normal intraventricular conduction at intermediate

heart rates. This report describes these observations and their possible electrophysiological significance.

Patients and observations

Five patients admitted to the hospital with acute myocardial infarction developed bundle-branch block within 12 to 36 hours from the onset of pain. Four patients showed left and one right bundle-branch block. All patients had a history of one or more documented myocardial infarctions in the past; previous records showed no evidence of bundle-branch block in 4, but one case had a transient bundle-branch block during a previous acute episode. Three patients developed varying degrees of AV conduction disturbance. All 5 patients first showed normal intraventricular conduction at intermediate heart rates, with the bundle-branch block appearing both at higher and lower rates. In 4 patients, the beats described as showing 'normal' intraventricular conduction actually revealed a slight degree of intraventricular conduction defect. In 3 patients, the range of heart rates with normal intraventricular conduction was observed to decrease and disappear within 2 to 12 hours, so that bundle-branch block was present at all heart rates. One of these patients died 12 hours later. In the other 2, a range of heart rates with normal intraventricular conduction was again ob-

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¹ Present address: Division of Cardiology, Department of Internal Medicine, Mount Sinai Medical Center of Greater Miami, Miami Beach, and the Department of Internal Medicine, University of Miami School of Medicine, Coral Gables, Florida.

FIG. 1 Case 2, record A illustrates the QRS pattern during 'normal' intraventricular conduction (on the left) and left bundle-branch block (on the right). Record B shows supraventricular tachycardia with left bundle-branch block. Record C demonstrates a tachycardia-dependent left bundle-branch block with a critical cycle length of 880 msec. See text for details. Intervals in Fig. 1-5 are expressed in hundredths of a second.

served within 24 hours, with bundle-branch block occurring both at higher and lower rates. In one of these patients, consistent normal intraventricular conduction was maintained from 48 hours after the acute episode, while in the other tachycardia- and bradycardia-dependent bundle-branch block were still observed in records taken 3 months later. In the remaining 2 patients, normal intraventricular conduction at intermediate heart rates never disappeared, and the bundle-branch block could be elicited by either increasing or slowing the rate. These patients were followed for 4 and 6 months, and the critical rate for tachycardia-dependent block varied from 83 to 110 a minute, and for bradycardia-dependent block from 24 to 61 a minute. Usually, with the passage of time, an increasing critical rate for tachycardia-dependent block and a decreasing critical rate for bradycardia-dependent block resulted in a gradual increase in the range of heart rates associated with normal intraventricular conduction. Details of all the cases are shown in the Table and illustrative examples follow.

Case reports

Case 2

Fig. 1-3 were obtained from a 60-year-old woman who was admitted to the hospital with an 8-hour history of acute chest pain. The patient had had three previous episodes of myocardial infarction. During the first epi-

sode, 8 years before, the electrocardiogram showed evidence of acute anteroapical infarction, but previous records did not show bundle-branch block. The electrocardiogram on the last admission showed sinus rhythm at a rate of 75 a minute, with a PR interval of 0.2 sec and QRS duration of 0.11 sec (Fig. 1 A, left). The presence of small q waves in inferior surface leads with ST-T changes not present in the previous records, together with serial enzyme determinations, suggested a fresh transmural myocardial infarction.

Sixteen hours later the patient developed paroxysmal supraventricular tachycardia at a rate of 150 a minute with an aberrant intraventricular conduction of left bundle-branch block pattern (Fig. 1 B) and went into acute pulmonary oedema. Intravenous administration of 0.4 mg lanatoside-C (Cedilanid) and 120 mg frusemide controlled both the tachycardia and the pulmonary oedema. The electrocardiogram reverted to sinus rhythm and normal intraventricular conduction, suggesting the presence of a tachycardia-dependent left bundle-branch block. Fig. 1 C was obtained 6 hours later. The resting record showed sinus arrhythmia at a rate of 60-75/min. The record illustrates a tachycardia-dependent left bundle-branch block with critical shortening of the RR interval to 880 msec. Bradycardia-dependent left bundle-branch block was demonstrated at the same time. Fig. 2 shows the effect of bradycardia induced by carotid sinus compression. It is seen that after RR intervals up to 1400 msec, normal intraventricular conduction is still

FIG. 2 Case 2, records A to D illustrate a bradycardia-dependent left bundle-branch block with a critical cycle length of 1400–1460 msec. Record E shows a left bundle-branch escape beat marked X. See text for details.

FIG. 3 Case 2, records under A were taken four months after the acute ischaemic episode. (a) shows absence of tachycardia-dependent left bundle-branch block at short cycle length of 620 msec. On the other hand, a bradycardia-dependent block is demonstrated at a critical cycle of 1760–1780 msec (b) to (c). X and X₁ represent left bundle-branch escape and extrasystolic beats, respectively. The record under B was obtained three months later and showed absence of bradycardia-dependent block up to a cycle length of 2720 msec. See text for details.

TABLE Pertinent data in 5 patients showing tachycardia- and bradycardia-dependent bundle-branch block following acute myocardial ischaemia

Case No.	Age and sex	Rhythm	Bundle-branch block	AV conduction disturbance	ECG during normal IV conduction	Initial range of normal IV conduction (RR interval in msec)	Period of observation of intermittent BBB
1	72 M	NSR	RBBB	1st-degree block	Acute infero-lateral MI	600-1040	24 hr
2	60 F	NSR	LBBB	—	Acute inferior MI	880-1460	6 mth
3	68 M	SVT	LBBB	—	Acute inferior MI	720-1560	4 mth
4	64 F	NSR	LBBB	—	Acute infero-lateral MI	840-960	3 mth
5	57 M	NSR	LBBB	1st- & 2nd-degree block	Acute anterior MI	860-1100	6 hr; patient died from pump failure

Abbreviations: NSR, normal sinus rhythm; SVT, supraventricular tachycardia; RBBB and LBBB, right and left bundle-branch block, respectively; MI, myocardial infarction; IV, intraventricular.

observed. Beats following RR intervals of 1460 msec or longer show a left bundle-branch block pattern. Two (sometimes more) consecutive sinus beats with left bundle-branch block were observed (Fig. 2 B and D). The PR interval of conducted sinus beats occurring after long RR intervals was slightly prolonged (from 0.20 to 0.26 sec). Fig. 2 E shows an interval of 2360 msec which is followed by an idioventricular escape beat with a right bundle-branch block pattern suggesting a left ventricular origin. The presence of an rsR' configuration in V₁ may suggest that the beat arises from the left bundle-branch system rather than from the distal left Purkinje system. Analysis of Fig. 1 C and Fig. 2 reveals that there is normal conduction in the left bundle-branch system at RR intervals between 880 and 1460 msec, while left bundle-branch block develops both in shorter and in longer cycles. Bradycardia-dependent block could be demonstrated at RR intervals of 1460 to 2360 msec; in a longer cycle a left bundle-branch escape beat occurs.

The patient was followed for seven months and electrocardiograms revealed gradual shortening of the critical RR interval for tachycardia-dependent block and lengthening of the RR interval for bradycardia-dependent block, with increase in the range of RR intervals with normal intraventricular conduction. The records in Fig. 3 A were obtained four months after the last episode of acute ischaemia. Tachycardia-dependent bundle-branch block was not present at RR intervals of 620 msec (Fig. 3 A, a). On the other hand, bradycardia-dependent bundle-branch block developed at a critical RR interval of 1760-1780 msec. It is interesting to observe that the left bundle-branch escape beats are still seen at a relatively constant escape interval of 2300 msec (marked X). However, early coupled ectopic beats from the same bundle-branch system (marked X₁) and other sites were also observed. Fig. 3 B was obtained 7 months after the last episode. At that time neither tachycardia-dependent

nor bradycardia-dependent block was observed at RR intervals of 560 (not shown in the Figure) and 2720 msec, respectively.

Case 4

Fig. 4 was obtained from a 64-year-old woman who was admitted to hospital with a history of acute chest pain of 6 hours' duration. The patient had had a myocardial infarct 3 years before and her records never showed bundle-branch block. The electrocardiogram on admission showed normal sinus rhythm at a rate of 78 a minute, with a PR interval of 0.17 sec, QRS duration of 0.1 sec, and evidence of acute inferolateral myocardial infarction (Fig. 4, top left).

Twelve hours after admission, the electrocardiogram showed sinus bradycardia at a rate of 50 a minute and a complete left bundle-branch block pattern (Fig. 4, top right). This was associated with a slight fall in blood pressure and the patient was started on isoprenaline infusion to increase both the heart rate and the blood pressure. Close observation of the electrocardiogram during the next few hours showed that the bundle-branch block was intermittent and occurred both on acceleration and slowing of the heart, with normal intraventricular conduction at a narrow range of intermediate heart rates. Records A to C in Fig. 4 are consecutive with only a few beats omitted. The first half of record A shows sinus tachycardia at a rate of 105 a minute and left bundle-branch block during isoprenaline infusion. When the infusion was stopped, the heart rate slowed gradually and at a critical RR interval of 840 msec, normal intraventricular conduction was observed, illustrating the presence of a tachycardia-dependent left bundle-branch block (Fig. 4 B). Further slowing of the heart rate by carotid sinus compression (CSC) (Fig. 4 C)

FIG. 4 Case 4, the top record illustrates the QRS pattern during normal intraventricular conduction (on the left) and left bundle-branch block (on the right). Records A to C show a tachycardia- and bradycardia-dependent left bundle-branch block with a narrow range of normal intraventricular conduction at cycle lengths between 840 and 960 msec. See text for details.

revealed the presence of a bradycardia-dependent left bundle-branch block that reverted to normal intraventricular conduction at critical shortening of RR interval to 960 msec (the last beat in record C). These observations could be demonstrated repeatedly; the changes in the heart rate were not associated with any significant change in the blood pressure. Critical analysis of records A to C in Fig. 4 reveals that normal conduction in the left bundle-branch system is only observed at a relatively narrow range of RR intervals of 840 to 960 msec, corresponding to a heart rate of 62 to 71 beats a minute. Both at higher and lower rates left bundle-branch block develops.

Electrocardiograms obtained 6 hours later showed disappearance of the narrow range of heart rates with normal intraventricular conduction, with left bundle-branch block observed at all heart rates. Three days after admission, normal intraventricular conduction was again observed with left bundle-branch block occurring at RR intervals shorter than 620 and longer than 1280 msec. The electrocardiograms 3 months after the last ischaemic episode failed to show a tachycardia-dependent bundle-branch block at RR intervals of 580 msec, but still revealed bradycardia-dependent left bundle-branch block at a critical RR interval of 1620 msec.

Case 5

Fig. 5 was obtained from a 57-year-old man who was admitted to the hospital with a history of acute chest pain of 4 hours' duration. The patient had had two previous episodes of myocardial infarction, 2 and 5 years before the last admission. During the second episode, the electrocardiograms showed transient left bundle-branch block. At the last admission evidence of acute anterior myocardial infarction and varying degrees of AV conduction disturbance were seen.

Fig. 5 A was obtained 6 hours after admission. The first half of the upper strip shows sinus rhythm at a rate of 91 a minute with prolongation of the PR interval (grade I AV block) and a left bundle-branch block pattern; following a blocked sinus impulse the conducted beat reveals normal intraventricular conduction. The next part of the strip shows a higher degree of AV block followed by an escape beat (E) showing the left bundle-branch block pattern. Examination of subsequent records suggests that the escape beat may be of supraventricular origin (AV junctional or from the bundle of His) with the aberrant intraventricular conduction explained by the presence of bradycardia-dependent left bundle-branch block. The second strip of Fig. 5 A shows periods of 3:2 AV Wenckebach conduction. The opening

FIG. 5 Case 5, record A shows varying degrees of AV conduction disturbances and a tachycardia-dependent left bundle-branch block. Record B obtained one hour later shows bradycardia-dependent left bundle-branch block. See text for details. E, escape beat, X late coupled extra-systolic beat, CSC, carotid sinus compression.

beat of the Wenckebach period shows normal intraventricular conduction while the second beat occurring after a shorter RR interval has a left bundle-branch block pattern. The last part of the strip shows 2:1 AV block with normal intraventricular conduction. Note the presence of late-coupled ectopic beats marked X. Critical analysis of Fig. 5 A reveals the presence of tachycardia-dependent left bundle-branch block.

Record B was obtained 1 hour later. Sinus bradycardia with respiratory sinus arrhythmia and consistent 1:1 AV conduction was observed. A bradycardia-dependent left bundle-branch block could be seen during the slow phase of the arrhythmia at critical lengthening of the RR interval to 1100–1120 msec (the upper strip of Fig. 5 B). Carotid sinus compression (CSC) resulted in pronounced sinus bradycardia and consistent left bundle-branch block (the lower strip of Fig. 5 B). In records obtained 4 hours later, the left bundle-branch block was constantly observed at all heart rates. The patient died 12 hours later from pump failure.

Discussion

The demonstration of the concurrent development of tachycardia-dependent and bradycardia-dependent block, with normal intraventricular conduction at intermediate heart rates, during the course of transient bundle-branch block after acute myocardial ischaemia has not been previously reported.

In a recent experimental study (El-Sherif *et al.*, 1973a, b) the onset and course of transient bundle-branch blocks after ligation of the anterior septal artery in dogs were analysed. Bundle-branch block during both rapid and slow heart rates with normal conduction at intermediate rates was constantly observed both at the onset and before the termination of the transient conduction abnormality. The bundle of His usually behaved in a similar fashion to the bundle-branches, showing both tachycardia- and bradycardia-dependent blocks. The lack of reports of similar findings in humans can only be partially attributed to infrequent close scanning of transient bundle-branch blocks in the course of acute myocardial ischaemia. A more plausible explanation is that rate-dependent AV conduction and/or bundle-branch blocks are not actively sought, because the induction of changes in the heart rate necessary to reveal them is frequently not feasible in critically ill patients. Another factor may be the brief duration of the characteristic changes (El-Sherif *et al.*, 1973a). However, the demonstration of tachycardia- and bradycardia-dependent block in some patients several months after the acute episode suggests that this may not be only an acute phenomenon, but may be related to the electrophysiological disturbances underlying intermittent bundle-

FIG. 6 Schematic representation of the electrophysiological mechanisms underlying tachycardia- and bradycardia-dependent bundle-branch block. Transmembrane potential of two Purkinje fibres from a proximal and a more distal portion of the bundle-branch system (1 and 3) and two electrograms (2 and 4) are depicted (see the sketch in panel A). The proximal fibre has a low resting potential and depressed phase-4 depolarization while the distal fibre shows slight reduction of resting potential and normal slope of phase-4. Panels B to D show the response of the two fibres to slow (CL (cycle length) 1600 msec), intermediate (CL 1000 msec), and rapid (CL 600 msec) driving frequencies. Note reduction of amplitude and upstroke velocity of action potential of the proximal fibre at the rapid driving rate and of the distal fibre at the slow driving rate. This is illustrated in the corresponding electrograms by delay of the Purkinje spike marked by arrow. Note that the distal electrogram (4) shows delay of the Purkinje spike both at the rapid and slow driving frequencies as compared to the intermediate rate. Delay of the Purkinje spike will be reflected in the surface electrogram by the inscription of a bundle-branch block pattern. See text for details. S, stimulus; M, muscle potential.

branch block in general. The latter tends to occur both at rapid and slow rates with normal conduction at an intermittent range of heart rates. The recent demonstration of a tachycardia- and bradycardia-dependent left anterior hemiblock in a young man with severe muscular dystrophy (Elizari, Lazzari, and Rosenbaum, 1972) shows that this is not necessarily related to acute ischaemic injury of the bundle-branch system. Our preliminary analysis of the course of ischaemic intermittent bundle-branch block in humans suggests that the critical rates for both tachycardia- and bradycardia-dependent block change in such a way that the range of heart rates with normal intraventricular conduction increases

as ischaemia becomes less, as shown by improvement in the ST-T changes in the conventional leads. However, the prognostic significance of this observation should await further studies.

The temporary nature of bundle-branch block in many cases where this complicates acute myocardial ischaemia (Julian, Valentine, and Miller, 1964; Bauer, Julian, and Valentine, 1965) is consistent with pathological studies that suggest relative immunity of the conducting tissue to ischaemia at least in a morphological sense (Sutton and Davies, 1968; Hackel *et al.*, 1972). The relative sparing of the conduction fibres suggests that factors other than hypoxia *per se* may be responsible for the

transient conduction disturbance (Udelnov, 1961; Harris, 1966; Hackel *et al.*, 1972). These factors, released by the injured myocardial cells and other inflammatory cells, may accumulate and alter the ionic environment surrounding the conduction tissue and hence its electrophysiological properties. These factors may be dissipated or washed out later on with the development of effective collateral circulation resulting in reversal of the conduction disturbance.

Electrophysiological significance

Tachycardia-dependent bundle-branch block developing at very short cardiac cycles as exemplified by early coupled supraventricular premature beats and rapid supraventricular tachyarrhythmias is consistent with known electrophysiological characteristics of the conduction system, and is readily explained in terms of impulse spread through incompletely repolarized fibres. Tachycardia-dependent bundle-branch block at relatively long RR intervals is pathological and is conventionally ascribed to abnormal prolongation of the functional refractory period of the conduction system (El-Sherif, 1972). However, the underlying electrophysiological mechanisms have not been precisely delineated. On the other hand, bradycardia-dependent bundle-branch block is the subject of a good deal of speculation (Massumi, 1968; El-Sherif, 1972). Several mechanisms have been proposed, and recently bradycardia-dependent block was explained on the basis of enhanced phase 4 depolarization of the bundle-branch system (Massumi, 1968; Sarachek, 1970; El-Sherif, 1972). This explanation represents an extrapolation of the observation of Singer, Lazzara, and Hoffman (1967) on the behaviour of isolated Purkinje fibres which have been subjected to a variety of pathophysiological interventions.

The finding of concurrent tachycardia- and bradycardia-dependent bundle-branch block after acute myocardial ischaemia can be explained by characteristic changes in the electrophysiological properties of different groups of Purkinje fibres which may be caused by differential localization of metabolites released in the ischaemic zone (El-Sherif *et al.*, 1973a). The presence of two groups of cells arranged in series and responding differently to changes in the cardiac cycle length can explain why conduction across the entire bundle-branch system is impaired both by increasing or decreasing the heart rate. Ischaemia leads to leak of a large amount of K^+ from the intracellular to the extracellular space (Harris, 1966). Local increase in the extracellular K^+ concentration results in reduction of the resting potential, slowing of the upstroke velocity, decrease of the electrotonic spread, and increase of the thresh-

old of Purkinje fibres (Crane-field, Klein, and Hoffman, 1971). All these factors can contribute to the reduction of conduction velocity. The electrical excitability and refractoriness of partially depolarized fibres differs from the excitability and refractoriness of normal Purkinje fibres, and complete recovery of excitability usually takes longer than the duration of the action potential (Crane-field *et al.*, 1971; Crane-field, Wit, and Hoffman, 1972). The fibres thus show a 'time-dependent' rather than a 'voltage-dependent' response to cycle length changes, which is somewhat similar to the normal response of some cells in the sinoatrial and atrioventricular nodes (Hoffman and Crane-field, 1960). Thus the initial phase of tachycardia-dependent bundle-branch block can be explained by the characteristic response to shortening of the cardiac cycle of Purkinje fibres partially depolarized by high extracellular K^+ (El-Sherif *et al.*, 1973a).

The simultaneous occurrence of bradycardia-dependent block is particularly interesting since increased extracellular K^+ is known to depress phase 4 depolarization. Two of our clinical observations are particularly pertinent. Firstly, the finding that long bradycardic intervals are usually necessary to reveal bradycardia-dependent bundle-branch block suggests the presence of a normal or slowly rising rather than an enhanced slope of phase 4 depolarization. Secondly, the observation of long bradycardic intervals without pacemaker escape can be explained by shift of the threshold potential towards zero. In a recent experimental study of transient bundle-branch block after ligation of the anterior septal artery in dogs (El-Sherif *et al.*, 1973a, b), bradycardia-dependent bundle-branch block was demonstrated in the first few hours after ligation and usually after long bradycardic intervals. At this stage automaticity was depressed as shown by the long bradycardic intervals without pacemaker escape. Later in the experiment, and with the development of enhanced automaticity, it was usually possible to illustrate that bradycardia-dependent block did not occur at rates significantly slower than the escape rate. These experimental findings are consistent with our clinical observations and suggest dissociation between enhanced automaticity and bradycardia-dependent conduction disturbances which may be related to the difference in behaviour of the threshold potential. Thus the shift of the threshold potential rather than enhanced phase 4 depolarization may be the crucial factor in the display of bradycardia-dependent block. The former permits gradual reduction of the membrane potential to levels at which significant reduction of conduction is likely to occur. This effect will be accentuated if there is an initial slight to moderate

reduction in the resting potential. Another factor which can contribute to bradycardia-dependent block without pronounced enhancement of phase 4 depolarization is decrease of the membrane responsiveness (Singer and Ten Eick, 1971). It is suggested that in another segment of the bundle-branch system in which there is much less increase of extracellular K^+ , a bradycardia-dependent bundle-branch block can develop as a result of a combination of factors. These include slight to moderate decrease of resting potential, a normal slope of phase 4 depolarization, and reduction of membrane responsiveness associated with shift of the threshold potential toward zero. The clinical observation of bradycardia-dependent bundle-branch block several months after the ischaemic episode associated with significant depression of the escape rhythm suggests that shift of the threshold potential may not be only an acute phenomenon. A schematic representation of the electrophysiological mechanisms of tachycardia- and bradycardia-dependent bundle-branch block is shown in Fig. 6.

Strong evidence for the view that a varying degree of partial depolarization with or without impairment of membrane responsiveness is pertinent for both tachycardia- and bradycardia-dependent block, is our observation that in several clinical examples of rate-dependent bundle-branch block, the beats usually described as showing 'normal' intraventricular conduction actually represented an incomplete degree of bundle-branch block. This may suggest the presence of a large population of Purkinje fibres with partially depolarized action potentials.

The observation that in some patients the initial phase of tachycardia- and bradycardia-dependent bundle-branch block with normal intraventricular conduction at intermediate heart rates progresses to a constant bundle-branch block can be explained by further deterioration of the electrophysiological properties of the group of partially depolarized Purkinje fibres probably related to further increase of extracellular K^+ . At a critical degree of conduction delay in the bundle-branch system (relative to conduction in the other branch), a pattern of complete bundle-branch block will be constantly present in the electrocardiogram. The reappearance of normal intraventricular conduction at intermediate heart rates can be attributed to the development of collateral circulation with the washout of offending metabolites, so that recovery proceeds in the affected bundle-branch.

Critique of bradycardia-dependent block in the proximal His-Purkinje system

Bradycardia-dependent block in the proximal His-

Purkinje system can manifest as bradycardia-dependent bundle-branch block, atrioventricular block, or aberrancy of the QRS configuration of supraventricular escape beats. Bradycardia-dependent bundle-branch block was described as early as 1915 by Wilson, and in the past 50 years various mechanisms have been invoked. In several early reports the effect of vagal impulses and/or transient changes in coronary perfusion have received much attention. Since in many cases the abnormality usually develops in response to vagally mediated slowing of the sinus rate, the phenomenon was attributed to the effect of vagal impulses on conduction in the His-Purkinje system (Comeau, Hamilton, and White, 1938). In spite of much evidence that vagal impulses do not significantly affect the conduction in the infranodal specialized conducting tissue, controversy still prevails not only with respect to clinical observations (Wilson, 1915; Holzmänn, 1943; Katz and Pick, 1956; Scherf, Blumenfeld, and Yildiz, 1961) but also to experimental and anatomical studies (Mitchell, Brown, and Cookson, 1953; Crane-field, Hoffman, and Paes de Carvalho, 1959; Eliakim *et al.*, 1961; Truex, 1961). The effect of transient change in coronary perfusion is even more controversial. Acute reduction of the blood supply to the bundle-branch system was thought to act through local metabolic and physicochemical changes altering the transmembrane ionic gradient, with secondary prolongation of the refractory period (Vesell and Lowen, 1963). Though a possible role of acute reduction of the mean blood pressure especially after long bradycardiac intervals cannot be completely ruled out, we have repeatedly shown, both in clinical and experimental observations (El-Sherif *et al.*, 1973a, b), that the change from normal intraventricular conduction to bradycardia-dependent bundle-branch block can occur with minimal critical slowing of the heart rate unaccompanied by any appreciable change in the blood pressure.

Two other mechanisms have been suggested to explain bradycardia-dependent aberrancy of the QRS complex, especially of late supraventricular escape beats. Anomalous ventricular excitation due to impulse spread along paraspecific fibres of Mahaim (Pick, 1956) and preferential longitudinal dissociation of conduction in the AV junctional tissue with desynchronization of the normal sequence of depolarization in the AV junctional area and its distal bundle-branches (Scherf and James, 1972) have been suggested. Though it is possible that one or the other mechanism can operate under certain circumstances, most of the clinical examples of QRS aberrancy of late 'supraventricular' escape beats can be explained by the electrophysiological mechanisms for bradycardia-dependent bundle-

branch block suggested in this report. Recently it has been suggested that so-called aberrant junctional escape beats arise from the proximal part of the intraventricular conduction system (Massumi, Ertem, and Vera, 1972). These beats usually show a QRS configuration different from conducted supraventricular beats but are not sufficiently wide and bizarre to suggest ventricular origin. We have recently shown in an experimental study (El-Sherif *et al.*, 1973a) that in the presence of bradycardia-dependent conduction delay in one of the bundle-branches, late impulses whether arising from above the bundle of His, at the bundle of His, or from the proximal portion of the bundle-branch system, can show exactly the same aberrant QRS configuration. Thus, in the presence of bradycardia-dependent conduction disturbance in the bundle-branch system, the QRS configuration of late aberrant beats can give no clue as to the site of origin of the impulse.

Supernormal conduction has been repeatedly invoked to explain clinical examples of unexpected improvement of either atrioventricular or intraventricular conduction of beats terminating short RR cycles, while impaired conduction is present at relatively longer cycle lengths (Von Hoesslin, 1923; Lewis and Master, 1924; Ashman and Herrmann, 1925; Burchell, 1942; Simon and Langendorf, 1944; Scherf and Scharf, 1948; Pick, Langendorf, and Katz, 1962). Recently a complex explanation implicating both Wedensky phenomena have been suggested for similar observations (Schamroth and Friedberg, 1969; Friedberg, 1971, 1972). A bradycardia-dependent conduction disturbance provides in our opinion a more plausible explanation for most of the previously cited examples. Of particular interest are cases of bradycardia-dependent paroxysmal AV block in which the onset of block coincides with critical slowing of the cardiac cycle (Schwartz and Schwartz, 1961; Dressler, 1966; Slama *et al.*, 1969; Coumel *et al.*, 1971). In a recently reported example (Coumel *et al.*, 1971) a 'zone of opportunity' for conduction was described which corresponds to the range of intermediate heart rates for normal conduction with block at both higher and lower rates in our study. Our demonstration of the frequent occurrence of bradycardia-dependent block in the proximal His-Purkinje system, including the bundle of His (El-Sherif *et al.*, 1973a, b), provides the electrophysiological explanation of this type of paroxysmal AV block. Furthermore, our illustration that bradycardia-dependent block is frequently associated with depressed automaticity provides an explanation for a puzzling *sine qua non* requirement for paroxysmal AV block, i.e. failure of escape of a subsidiary pacemaker.

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Requests for reprints to Dr. Nabil El-Sherif, Department of Internal Medicine, Mount Sinai Medical Center, 4300 Alton Road, Miami Beach, Florida 33140, U.S.A.