Supernormal Conduction and Excitability or supernormal excitability conduction

http://cardiolatina.com/wp-content/uploads/2017/09/Normality-that-is-Abnormal.pdf

Fernandes-Cardoso A1, Dutra-Kreling GA1, Grindler J1, Pérez-Riera AR2. Normality that is abnormal. J Electrocardiol. 2016 Nov - Dec;49(6):980-982. doi: 10.1016/j.jelectrocard.2016.07.029. Epub 2016 Jul 28.

Normality that is abnormal.

Author information

1. Electrocardiology Sector, Central Institute of Clínicas Hospital, Faculty of Medicine, University of São Paulo (HCFMUSP), Brazil.
2. Design of Studies and Scientific Writing Laboratory in the ABC School of Medicine, Santo André, São Paulo, Brazil. Electronic address: riera@uol.com.br

Abstract

Supernormal conduction is defined as better-than-expected conduction in patients with depressed conduction during a short interval in the ventricular cycle. It is mainly observed in long-duration electrocardiogram (ECG) assessments. Its occurrence during 12-lead ECG is uncommon and its interpretation demands knowledge on electrophysiological alterations that are hard to understand. By reporting this case we aim to propose a rationale sequence that should be considered when facing an ECG with these same features, which would enable a greater accuracy to make a definitive diagnosis.

KEYWORDS: Atrial premature beat; Bundle branch block; Linking phenomenon; Supernormal conduction

Supernormal excitability and conduction imply conduction that is better than anticipated or conduction that occurs when block is expected. It is a phenomenon where intermittent narrow QRS complexes can occur despite underlying bundle branch block (BBB) at a slower rate. The phenomenon is much more common than previously thought, particularly in the presence of certain clinical conditions (**Elizari MV 2014**). Cellularly, this occurs if the ventricular rate is just beyond the effective refractory period of the septal myocardium, while at the same time, the above phase 4 voltage allows for supernormal conduction without the aid of the bundle branches or Purkinje system.

It should be emphasized that most of the cases of so-called supernormal excitability conduction described in humans have been associated with baseline disturbance of A-V conduction.

Thereforem the term supernormal has been referred to improved conduction but not to conduction that is better than normal

Historical aspects: The earliest observation of "supernormal' conduction in a patient with complete heart block was Sir Thomas Lewis (1881-1945). The great master wrote: “There is a case recently reported from my laboratory, in which an auricular rhythm and a much slower ventricular rhythm interplay and produce almost accurate coupling.... In the whole series of curves, response of the ventricle is invariably to any auricular systole which falls between the summit of T and its end-point, there is no response to an auricular systole falling in any other part of the ventricular cycle. ... In other words, over this phase there has been an overswing in the recovery curve of responsiveness, reminiscent of or identical with the "supernormal" phase of recovery described by Adrian and Lucas” (Lewis T 1911;1913). (**Lewis T, 1924**.)

Sir James Mackenzie (12 April 1853 (Scone, Scotland) – 26 January 1925 (London, England) published tracings that were recorded in 1913 in a patient with right bundle branch block and paroxysmal AV block. Resumption of the sinus rhythm was possibly due to "supernormal" conduction induced by the retrograde conduction of the escape impulse. The relatively frequent clinical reports of purported AV nodal "supernormality" that followed the original description by Lewis contrasted with the relative paucity of observations of "supernormality" of the His-Purkinje tissue. In the clinical setting, "supernormality" of conduction is manifested by better than expected, but not more rapid than normal, conduction, thus, the term relative supenormality or "supernormality" is

more appropriate when applied to the ECG. In man, "supernormal" conduction is recorded only in abnormally functioning cardiac tissue. It has been demonstrated in the His-Purkinje fibers, but not in the AV node, the His bundle, or the atrial or ventricular myocardium. In fact, its existence in tissue other than the His-Purkinje is denied by most investigators. The paradox of unexpected improved AV conduction ascribed to "supernormal" AV nodal conduction can be explained by a number of alternate mechanisms such as the "gap" phenomenon, "peeling," or dual AV nodal conduction.etc

In man, “supernormal” excitability and “conduction” is recorded only in abnormal functioning cardiac tissue.

Effects of Membrane Potential on Supernormal Excitability and Conduction.

In 1955, Weidmann first demonstrated a period of supernormal excitability in sheep Purkinje fibers. He demonstrated the relationship between the amplitude and voltage time course of Purkinje fiber APs evoked at different levels of membrane potential by means of premature stimulation (**Weidmann 1955**).

Impulses resulting from premature stimulation were thought to propagate at reduced velocity until they encountered fully repolarized tissue, at which time conduction velocity was thought to return to normal

Impulses elicited by stimuli applied immediately after the end of repolarization, a thus at the maximum level of membrane potential, display a greater rate of rise and amplitude of AP.

Propagate more rapidly than those initiated later at a somewhat lower level of membrane potential.

Premature beats evoked early during the repolarization phase of the AP often reached the more distant electrode earlier than did later response evoked at membrane potentials closer to maximum resting potentials.

The apparent conduction time between two recording electrodes often decreased with increasing prematurity.

Purkinje fibers exhibit supernormal conduction and supernormal excitability while His-bundle and ventricular muscle fibers do not. In an experiment where 3 microelectrodes

were simultaneously implanted along a canine Purkinje fiber Weidman found that the period supernormal excitability was due to the rapid recovery of excitability

The time course of two simultaneous recorder Purkinje transmembrane AP are displayed together with the threshold current required to evoke a conducted response.

The graph of the transmembrane potentials displays the threshold current required to evoke conducted responses during the repolarization phase.

It can be noted that there is a decreased current requirement associated with repolarization in Purkinje fibers.

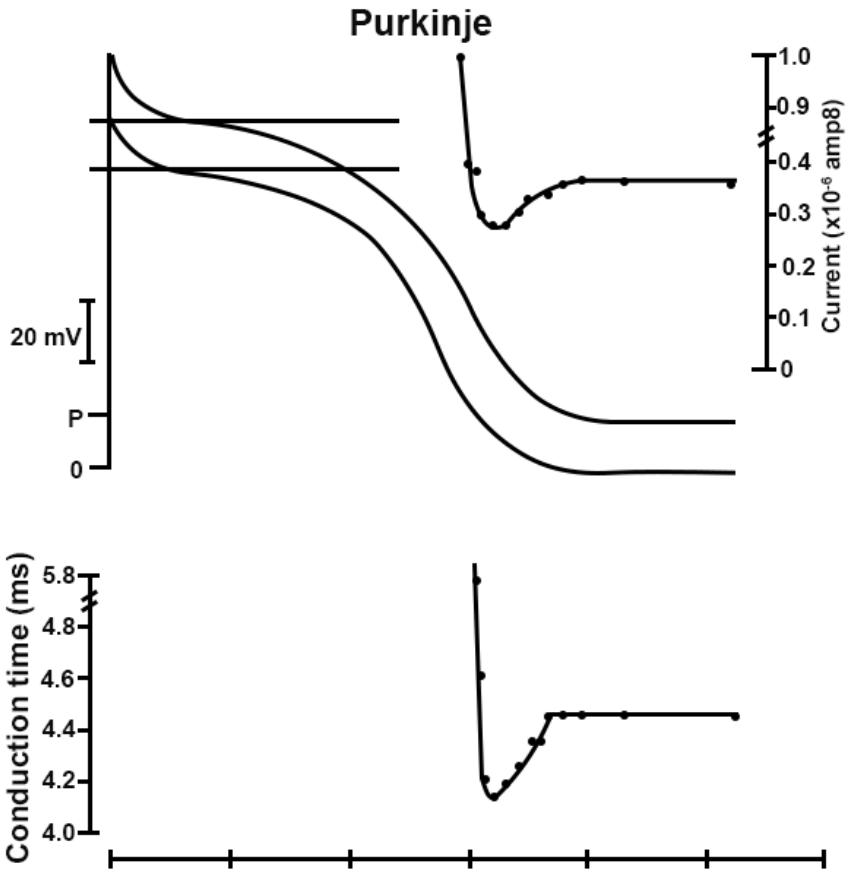
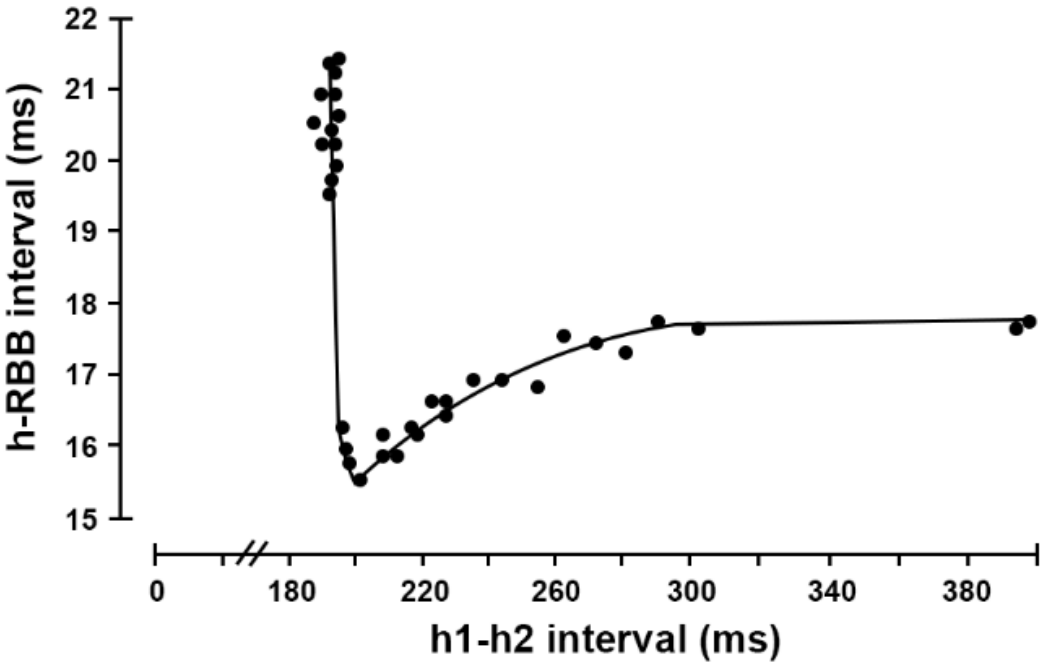


Figure above: the action potentials were recorded in isolated Purkinje fiber 4 mm apart. P corresponds to the AP recorded near the stimulating intracellular microelectrode and D indicates the distal AP. The graph at the top indicates the minimal depolarizing currents with the excitability curve. Bottom: the graph plotted on the same time course as the APs show the conduction times between P and D recording sites. All data are plotted on the common).

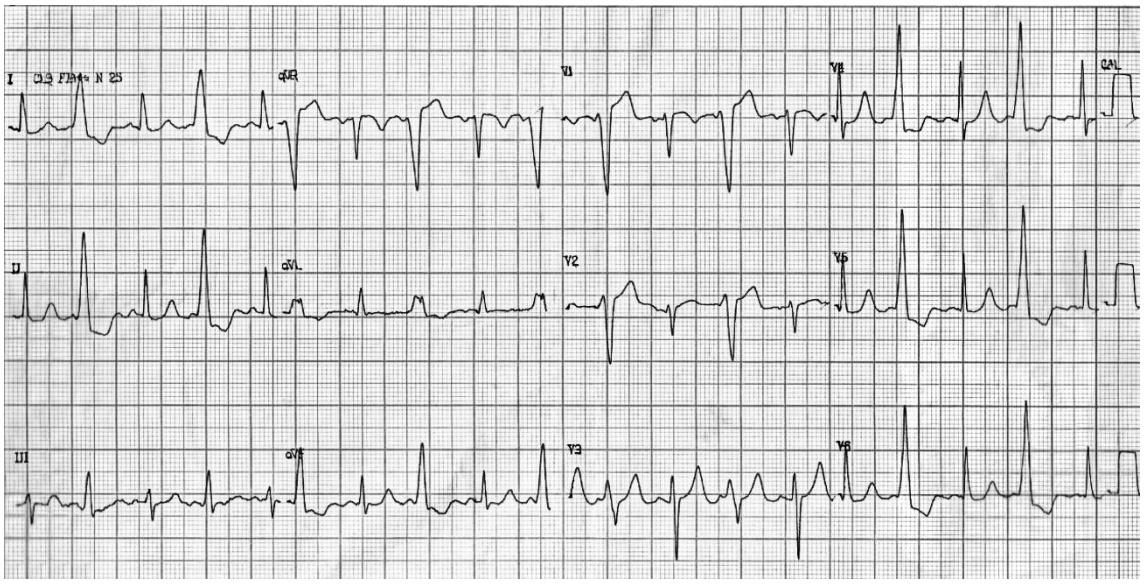


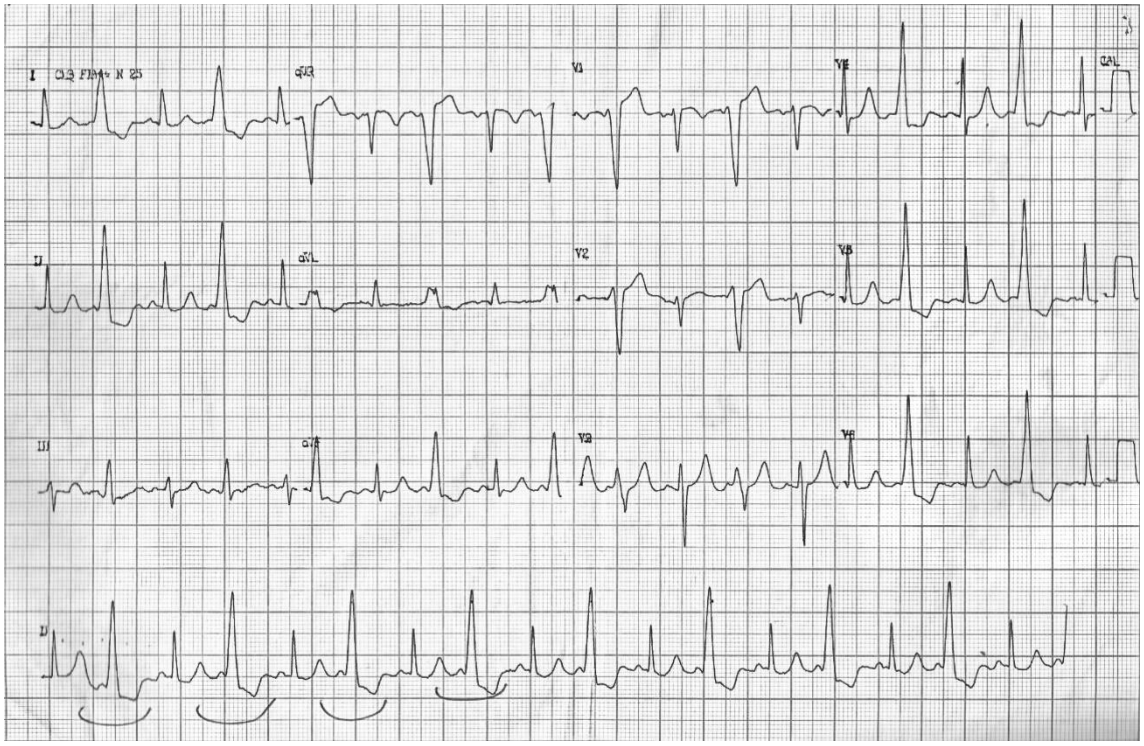
Supernormal conduction in the His-Purkinje system of the intact canine heart. The ordinate indicates the conduction times between the electrograms from the His bundle and the distal RBB. The premature beats (h1-h2 intervals) are plotted on the abscissa. The supernormal phase with the increase in conduction of 2,2 ms (12,4%) occurred at h1-h2 intervals between 195 and 290 ms. (Elizari MV 2014)

The supernormal phase of conduction has several outstanding features:

A prolonged refractory period, either in the His-Purkinje system or AV accessory pathways, (**Przybylski J, 1987**.) appears to be one of the prerequisite requirements for its occurrence. The 3 following ECGs are examples of supernormal phase of conduction in accessory pathways

Example of supernormal phase of conduction in accessory pathways


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6


I
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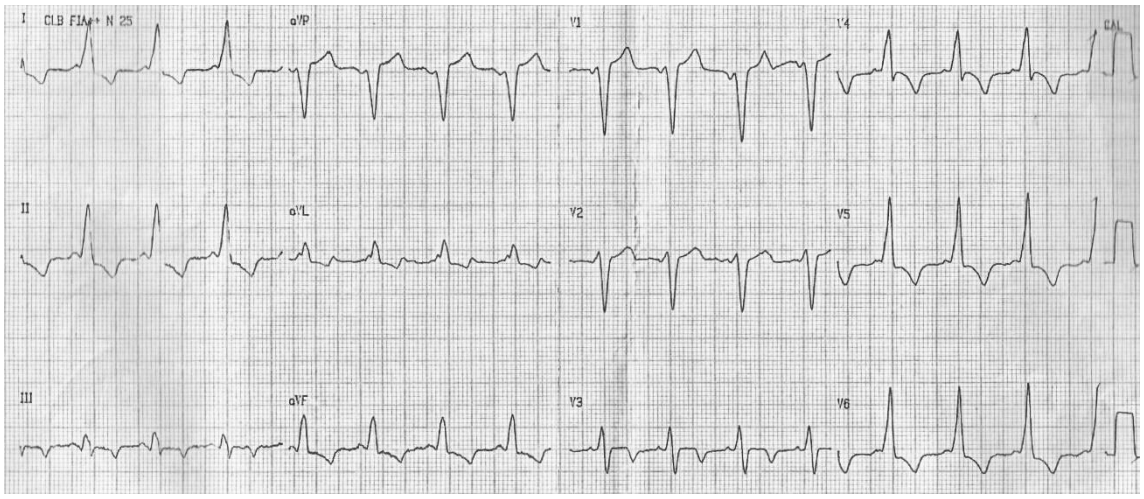


It is an exceptional case of 2:1 supernormal conduction in a patient with accessory pathway (AP). For supernormal conduction to exist, the fascicle where the phenomenon occurs should be “sick” and additionally it is necessary and extended refractory period. In this case, this may be perfectly documented as, with a given rate, there is a permanent block of the AP and both PR and intraventricular conduction are normal (permanent block in the AP). In another tracing, with a heart rate only a little lower, the AP conducts all the time. In APs, conduction and the block through the pathway, in relation to the rate, are very random and frequently overlap at equal rates, and it is difficult to delimit exactly the duration of the prolonged refractory period. With regard to the tracing with the 2:1 block, the images are opposite to those observed when this occurs in the His bundle branches. In pre-excitation, the AP block manifests with normal QRS; while when QRS conducts is aberrant. About the mechanism, it is 2:1 supernormal conduction in the AP.
2:1 supernormal conduction always occurs in specialized conduction tissue and never in the common myocardium. In this case necessarily the AP is constituted by specific tissue (Purkinje-like tissue). During conduction through the AP with 2:1 block, concealed retrograde activation of the AP occurs, in such a way that the following beat will present a normal QRS by the block of the pathway in the refractory period, since the range for supernormal conduction has shifted to the right due to concealed activation and the impulse falls outside the period of supernormal conduction.

Supernormal Conduction

Other denominations: relative supernormality or "supernormality".

Electrocardiographic manifestation of "supernormal" conduction is defined as conduction that is more rapid than expected or presence of conduction when block is anticipated. It is not supernormal in the sense or being more rapid than normal. Therefore, the term relative supernormality or "supernormality" is more appropriate. The mechanism of "supernormal" conduction is conduction during a period of supernormal excitability and conduction associated with altered membrane potential. Some of the more common

phenomena that are not dependent on conduction during the supernormal period but manifest better than expected conduction, thus simulating

"supernormal" conduction, include:

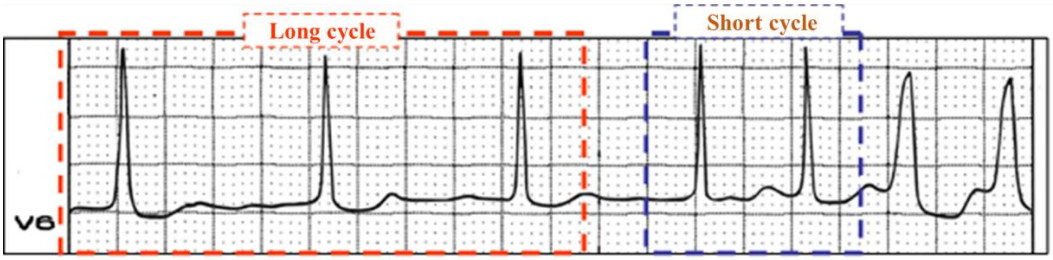
1) Supernormal excitability in phase 3,
2) Diastolic phase 4 depolarization**,**
3) The "gap" phenomenon,
4) dual AV nodal conduction,
5) Peeling back refractoriness, the shortening of refractoriness by changing the preceding cycle,
6) The Wenckebach phenomenon in the bundle branches, summation of subthreshold responses. Summation propagation disturbances in the nerve and in the muscle was described by the first time by Adrian and Lucas. (**Adrian ED, 1912**)
7) Wendensky facilitation, and
8) Bradycardia-dependent conduction blocks.

Physiologic mechanisms explaining apparent supernormal conduction include:

- Supernormal conduction mechanisms
- Resolution of bradycardia-dependent block (phase 4 block)
- Tachycardia-dependent right bundle-branch block (RBBB) associated with supernormal conduction (SNC) and atrial flutter: When an impulse is conducted to the ventricles beyond 720ms after a QRS complex of RBBB pattern, the impulse falls after the abnormally long effective refractor period of the RBB and passes through the RBB. When the conducted impulse occurs within 720ms after a QRS complex of RBB configuration, the impulse usually falls in the refractory period and is blocked in the RBB; however, only when the impulse occurs 480 or 490ms after that does it fall in the supernormal period and passes through the RBB. The findings shows that the presence of supernormal conduction plays an important role in the initiation of reentrant ventricular tachycardia(**Katoh T2000**.). The phenomenon of a 2:1 bundle branch block was reported during atrioventricular (AV) nodal reentrant tachycardia, sinus tachycardia, atrial fibrillation, and atrial flutter. A 2:1 bundle branch block is attributed to first- and

second-degree bundle branch block, linking, electrical alternans, aberrancy (Figure), or supernormal conduction.

Figure Example of atrial fibrillation with aberrancy



In this long strip of V6 with the patient in AF, aberrancy occurs when a short cycle follows a long one. The two last QRS complexes are aberrant with left bundle branch block pattern: Gouaux-Ashman or Ashman phenomenon. Clearly, the last two beats are not premature ventricular contractions.

Gouaux-Ashman or Ashman phenomenon (**Gouaux JL 1947**) is an intraventricular conduction disorder that occurs in the His-Purkinje system, caused by a change in HR. This depends on the effects of HR on the electrophysiological properties of the heart and may be modulated by metabolic, electrolytic and drug-caused alterations. The conditions that alter the duration of the refractory period of the branches are responsible for the Ashman phenomenon. These conditions are commonly observed in:

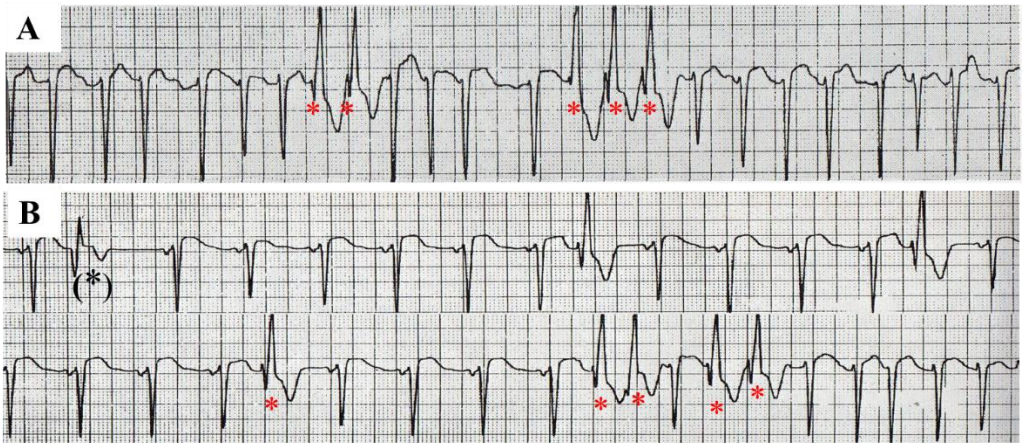
1) Atrial fibrillation (AF);

2) Atrial tachycardia;

3) PACs.

In these cases, aberrant conduction occurs when a short cycle follows a long one. Aberrant conduction follows a long/short sequence during AF. The last 2 complexes are aberrant and with the pattern of left bundle branch block: Gouaux-Ashman or Ashman phenomenon.

** Because the premature contraction in a retrograde manner, penetrates into the AV node increasing its refractoriness and thus, it delays the anterograde transmission of the subsequent atrial impulse.

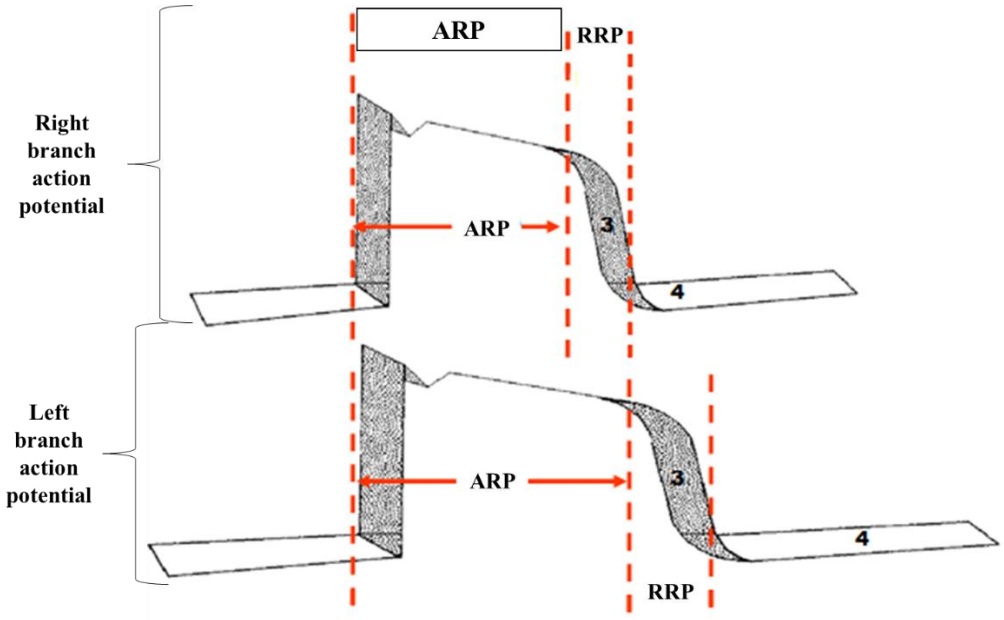


In the upper panel (**A**) the rhythm is of AF with a high ventricular response rate because no atrial activity is observed and QRS complexes are of irregular presentation with marked variation in time occurrence. The QRS complexes indicated by asterisks*, show triphasic rsR' pattern of the RBBB type, the first r deflection has the same direction as that of the base beats and there is no compensating pause. These 3 elements make the diagnosis of aberrant conduction.

Panel **B** shows the same tracing in sinus rhythm. The second beat **(***) is a premature ventricular contraction because the first deflection (Q) presents an opposite direction to the base complex (r) and because there is complete compensating pause. Additionally, repolarization reveals lesion current and subepicardial ischemia (primary ST/T). The beats indicated by red asterisks are supraventricular extrasystoles with aberrant conduction, because they have triphasic pattern of RBBB with QRS complexes of variable widths.

RBBB is more frequent than LBBB because the absolute refractory period of RBBB is shorter related LBBB (Figure).

Figure Normal differences between action potentials of the right and left branches



ARP– Absolute refractory period; RRP – Relative refractory period

- Worsening in conduction in the unaffected branch, leading to conduction times' equalization in both branches;
- Fusion beat (**Gomes JA1975**);
- Linking phenomenon (Luzza 2015a,b)
- SNC window (Lehmann 1985)

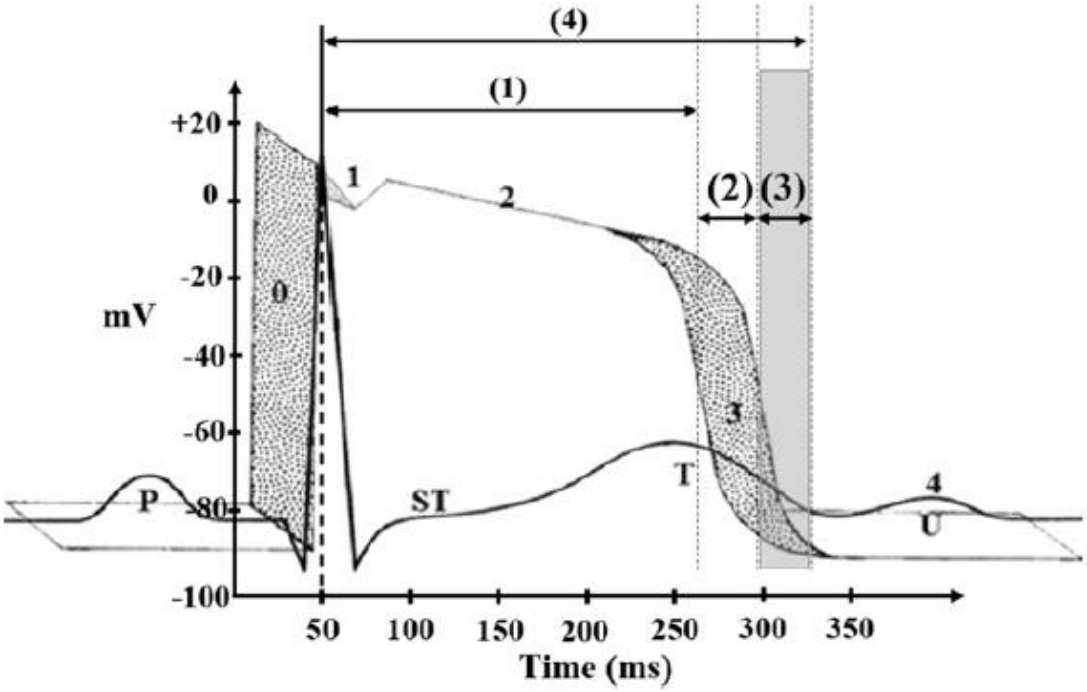
Alternative mechanisms were found to explain several different electrocardiographic examples of apparent supernormal atrioventricular (A-V) conduction in man: **"pseudo supernormal conduction"**

- Wedensky effect (Oreto 1892)
- Gap phenomenon (**Wu D 1974**) (**Moe GK, 1968**) (**Gallagher JJ,1973A**) , (**Gallagher JJ. 19873 B**) (Damato AN, Wit AL, Lau SH. Observations on the mechanism of one type of so-called supernormal AV conduction. Am Heart J. 1971;82:725–30.)(Wu D, Denes P, Dhingra R, Rosen K. Nature of gap phenomenon in man. Circ Res. 1974; 34:682–92.)
- Sudden shortening of the PR interval during A-V nodal Wenckebach phenomenon by concealed reentry within the A-V node (**Gallagher JJ,1973A**).
- The Wenckebach phenomenon in the bundle branches permitting normalization of aberrant intraventricular conduction (Gallagher 1973)
- Summation of sub threshold impulses (Lukas 1989)

- Dual atrioventricular nodal pathways causing longitudinal dissociation of the AV node (Moe 1968: Denes 1975)
- Longitudinal dissociation in the RBB (Walston 1976)
- Peeling back refractoriness (Suzuki 1989)
- The shortening of refractoriness by changing the preceding cycle length (Denker 1984)
- Pulsatile changes in vagal discharge (Moe 1968; Jedlicka 1987)
- Facilitation of conduction by ectopic beats (Gallagher 1973)
- Bilateral bundle branch block (Childers 1978)
- Ventriculophasic (vagal) depression of nodal conductivity (**Moe GK, 1968**); (Childers 1978)
- Occult 2:1 A-V block, in which an idioventricular beat "retracts" an otherwise refractory barrier within the A-V node (**Moe GK, 1968**).
- Alternation between dissociated intranodal transmission pathways (**Moe GK, 1968**).

1) **Supernormal excitability in phase 3**

Supernormal excitability is defined as the ability of the myocardium to respond at the end of phase 3 of the cardiac AP to a stimulus that would be ineffective at other times. During the supernormal period excitation is possible in otherwise subthreshold stimulus. Possible explanations are: a) availability of fast Na^+ channels and b) Proximity of membrane potential to threshold potential



Relationship between action potential phases (0 (QRS), 1 (J-point), 2(ST-segment), 3 (T-wave), 4 (U-wave)), surface ECG and changes in myocardial excitability: (1) Absolute refractory period; (2) Relative refractory period; (3) Supernormal period. It is coincident with the end of T wave*; (4) Period of complete restoration of normal excitability. In automatic cells phase 4 diastolic depolarization has spontaneous ascension called or automatism

*Supernormal conduction occurs at relatively constant period within the cardiac cycle close to the end of the T wave and is related with the presence of a supernormal excitability phase, experimentally demonstrated in the late phase of repolarization of cardiomyocytes. Several other similar electrophysiological mechanisms, such as Wedensky effect, the gap junction phenomenon, peelingback refractoriness, and other miscellaneous, must be considered during its interpretation to help us clarify this intriguing phenomenon.

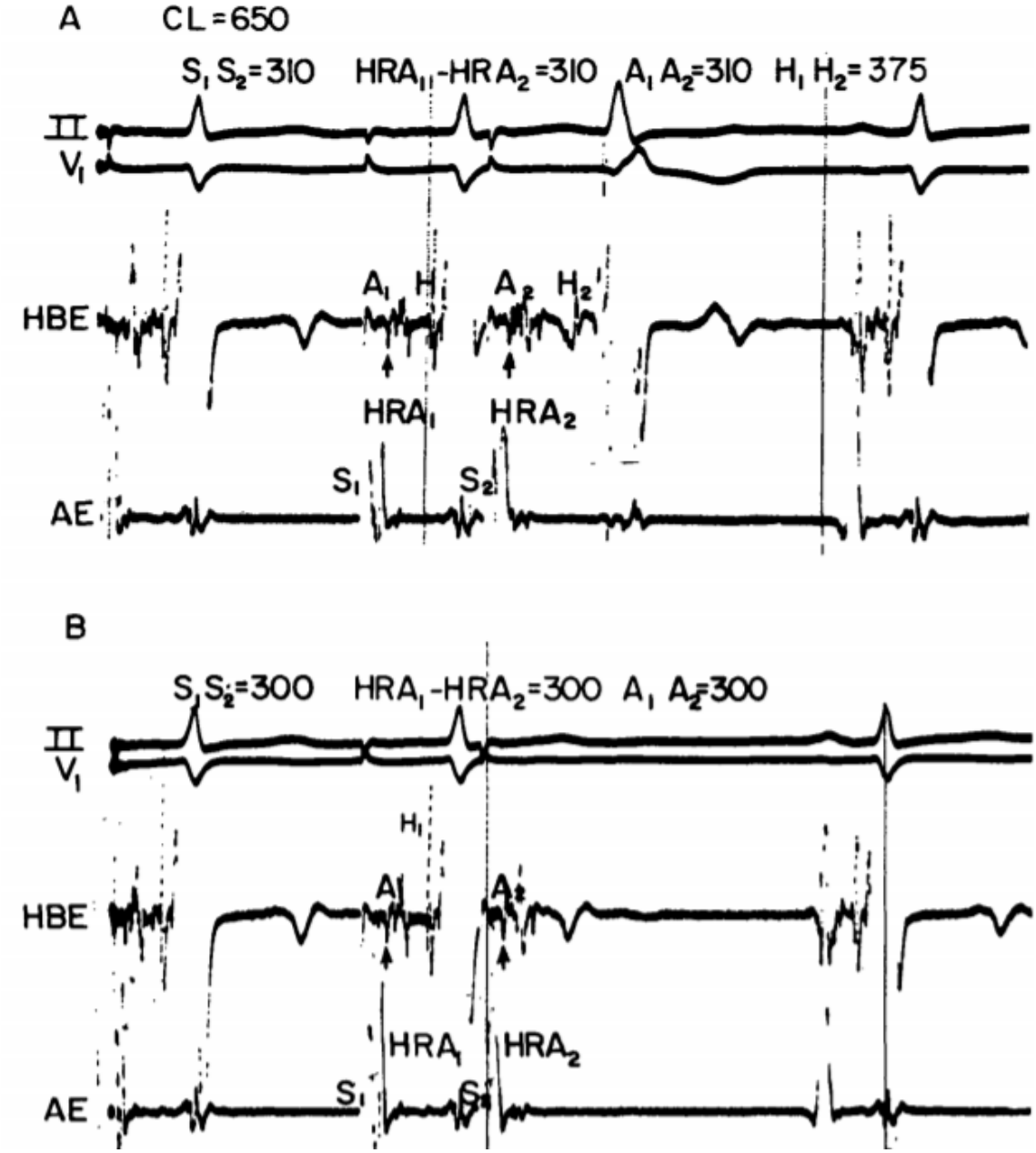
2) **Diastolic phase 4 depolarization**

The presence of diastolic depolarization (phase 4 depolarization) can also lead to apparent supernormal excitability and conduction, Premature beats that arrive early when the membrane potential is within the potential range of the supernormal period of excitability will conduct more rapidly than earlier or later premature beats.

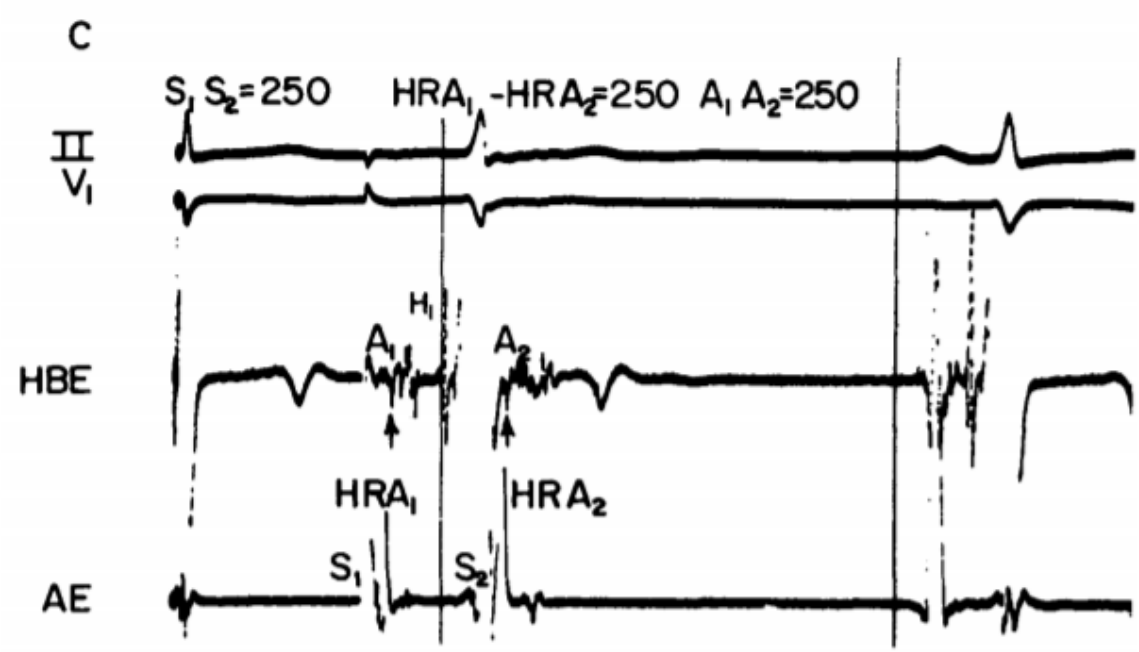
3) **The Gap phenomenon**

One type of supernormal conduction, i.e., the paradoxical propagation of closely coupled stimuli when stimuli at longer coupling intervals are blocked, reflects a gap phenomenon. This phenomenon occurs when the refractory period of a distal conduction site limits conduc- tion. With closely coupled stimuli, enough proximal delay occurs so that the impulse arrives at the distal conducting site late enough to be conducted. This term in A-V conduction was originally used by Moe et al experimentally in dogs (**Moe 1965**) and in humans (**Durrer 1968**) to define a zone in the cardiac cycle during which premature atrial contraction (PAC) failed to evoke ventricular responses, while PAC of greater and lesser prematurity conducted to the ventricles. The gap phenomenon was attributed to functional differences of conduction and/or refractoriness in two or more regions of the conduction system. The physiologic basis of gap phenomenon in most instances depended on a distal area with a shorter refractory period. During the gap phenomenon, initial block occurs distally. With earlier impulses, proximal delay is encountered which allows the distal site of early block to recover excitability and resume conduction. When the AV node is excited early by conduction from the PAC, prepotential occurs, preceding the all-or-none AV N AP. The AVN pre-potential results in a delay in conduction through the AV node, allowing the bundle branch (BB) AP to recover to a potential closer to the RMP. Accordingly, the BB can be excited and propagated response to the ventricles. Premature A response develops later, allowing conduction to reach the AV node when it is excitable. The all-or-none AVNAP results in conduction to BB fiber when the BB has not repolarized to a sufficient membrane potential to permit an all-or- none response, Conduction to the ventricles fails. It is the most accepted theory. The following figure shows the Gap phenomenon

Figure



Demonstration of the gap phenomenon between the AV node (distal) and the atrium (proximal). Records of the lead II ECG (II) and ventricular (V_1), His bundle (HBE), and high right atrial (AE) electrograms are shown. Paper speed is 100 mm/sec and time lines represent 1 second on this and all subsequent illustrations. The basic driving cycle length was 650 msec. Arrows indicate the first high-frequency atrial spikes of both driven and test beats recorded from the His bundle electrogram. A: At an S,-S2 interval of 310 msec, S2 was conducted to the ventricles with an A,-A2 interval of 310 msec.B



C: At an S_1-S_2 interval between 300 and 250 msec, S_2 was blocked in the AV node because the A_1- A_2 interval was less than the effective refractory period of the AV node (300 msec). The HR A_2 - A_2 interval was equal to the HRA,-A, interval.

The atrioventricular (AV) gap phenomenon occurs when the effective refractory period of a distal site is longer than the functional refractory period of a proximal site and when closely coupled stimuli are delayed enough at the proximal site to allow distal site recovery.

Gap in A-V conduction in man; types I and II.

The mechanism of the "gap" phenomenon in A-V conduction was studied in man during premature atrial stimulation studies using His bundle recordings. Relatively late premature atrial impulses are blocked within the His-Purkinje system, earlier premature atrial impulses may successfully propagate to the ventricle if they encounter sufficient A-V nodal delay to allow recovery of the distal area of refractoriness (Type I "gap"). Gallangher et al (**Gallagher JJ. 1973 A**) described an analogous mechanism of the "gap" is described which is due to delay within the His-Purkinje system (Type II "gap"). Relatively late premature atrial impulses were noted to block within the His-Purkinje system, similar to the findings in Type I. Conduction resumed in Type II, however, when earlier premature atrial impulses encountered delay in a relatively proximal area of the

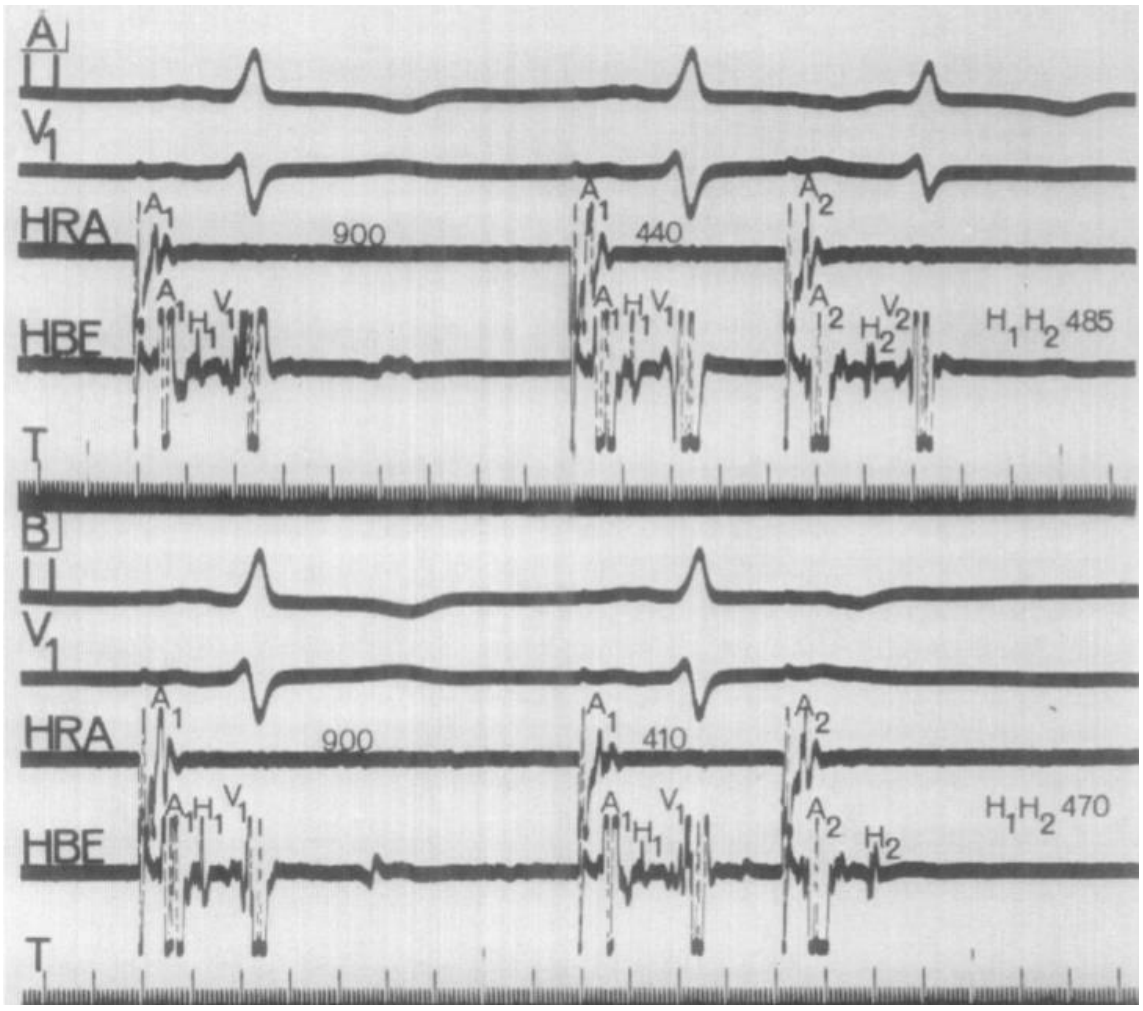
His-Purkinje system, allowing more complete recovery of the distal area of refractoriness. Both types of gap phenomena represent examples of apparent supernormal conduction.

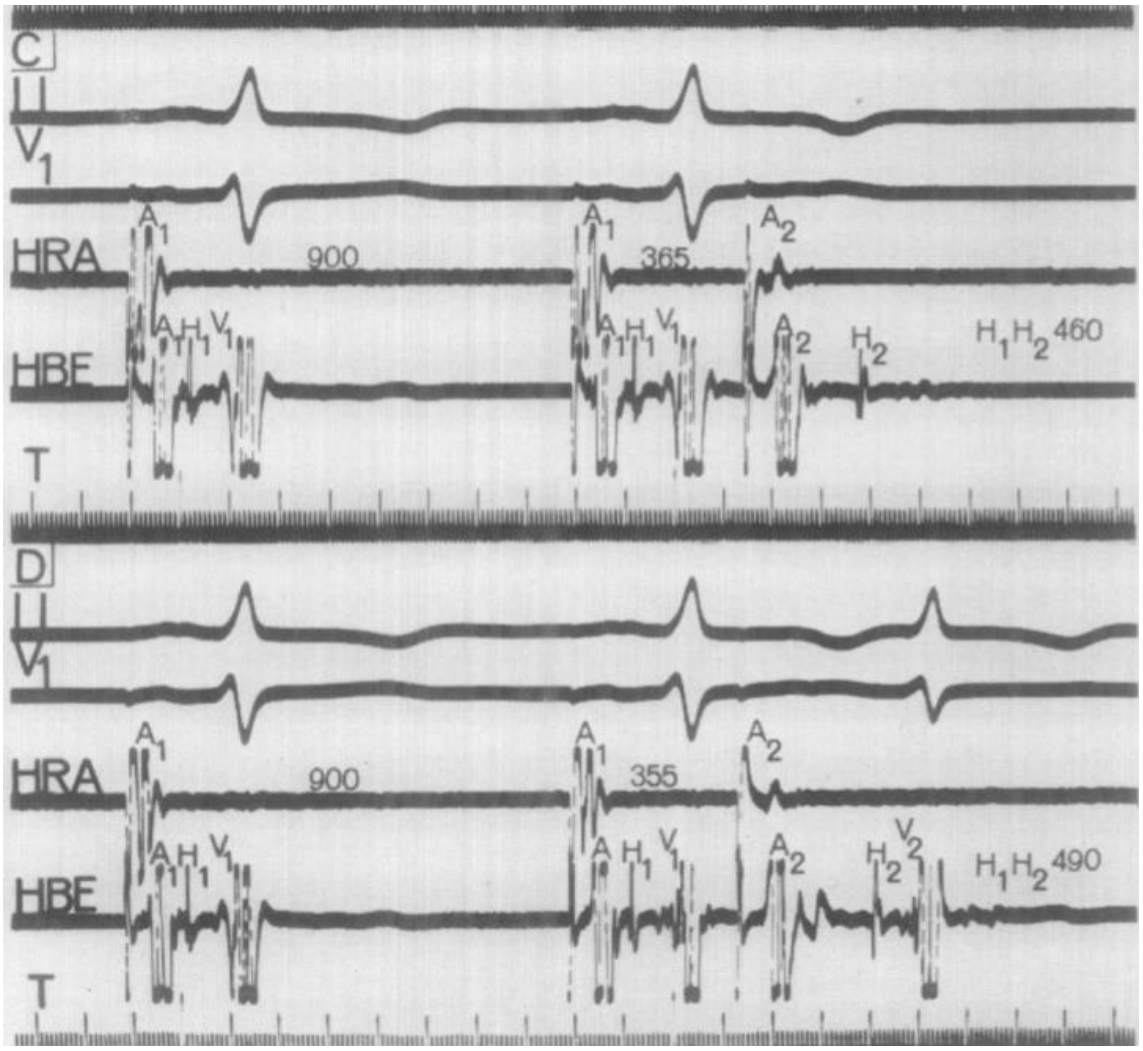
In summary:

Type I "gap"**:** the distal site of block is distal to the His bundle (ventricular specialized conduction system) and the proximal site of block is in the AV node.

Type II "gap"**:** both the proximal and the distal sites of conduction block are within the delay within the His-Purkinje system.

Using His bundle recordings and atrial extra-stimulus techniques in man, Wu et al observed three previously undescribed types of gaps between (1) The AV node (distal) and the atrium (proximal) or Type I "gap", (2) The His bundle (distal) and the AV node (proximal) or Type II "gap", and (3) the ventricular specialized conduction system or a bundle branch (distal) and the His bundle (proximal). The delays at the His bundle in the second and third types of gaps seen in this study were demonstrated as splitting of His bundle potentials. Gaps between the AV node or the His bundle and the ventricular specialized conduction system were more easily demonstrated at long cycle lengths, but gaps between the atrium and the AV node were more easily demonstrated at short cycle lengths. Therefore, the subdivision of gaps into two types is an oversimplification, because gaps can occur between multiple sites in the conduction system. The gap phenomenon may be potentiated by both long and short cycle lengths; long cycle lengths increase the effective refractory period of a distal site, e.g., the His bundle and the ventricular specialized conduction system, and the short cycle lengths decrease the functional refractory period of a proximal site, e.g., the atrium and the AV node. (**Wu D, 1974**) **Figure**


A
II
V1
HRA
HBE
T
A1
900
440
A2
H1
V1
H2
V2
H1H2 485
B
410
H1H2 470



A through D. “Gap” in A-V conduction (Type I). Recordings from top down in panels A through D are standard electrocardiographic Leads II and V_1, a high right atrial electrogram (HRA), a His bundle electrogram (HBE) and time lines (T) at 10 and 100 msec. intervals. In panels A through D, premature atria1 stimuli (Ax) are introduced at progressively shorter coupling intervals during a basic driving cycle length of 900 msec. (Al Al). The AI HI interval is 90 msec. and the HI VI interval is 60 msec. A = atria1 electrogram; H = His bundle electrogram; V = ventricular electrogram.

The ECG can be useful in differentiating these two mechanisms. When a sufficiently premature impulse is conducted to the ventricle with a normal QRS configuration, resulting in a “gap” phenomenon, this is most consistent with a Type I “gap.” When conduction resumes with an aberrant configuration, either Type I or Type II “gap” may be present. With the use of His bundle electrograms, the distinction can be readily made: in Type I “gap,” the HI HP interval at which conduction resumes is longer than that at which block below Hz initially occurs, while in Type II gap, the H1 Ht interval at which

conduction resumes is shorter than that at which block below Hz initially occurs. In both types of “gap,” early premature atria1 impulses are successfully propagated, while relatively late premature impulses

4) **Dual A-V nodal pathways**

Dual AV nodal pathways have been shown to be responsible for many clinical arrhythmia syndromes, most notably AV nodal reentrant tachycardia. It is the most common cause of *supraventricular tachycardia (SVT).* It is more common in women than in men and presents in all age groups. Patients with *AVNRT* have at least two pathways of tissue in their *AV node* that allows for an abnormal electrical circuit to perpetuate within their *AV node.* However, there are many individuals who have dual pathways of AV nodal tissue, but never have the electrical circuit perpetuate to develop sustained tachycardia. It is this spinning circuit that goes “round-and-round” enclosed in the *AV node* that allows for rapid stimulation of the ventricles through the normal *His bundle, bundle branches,* and ultimately *Purkinje fibers* to the ventricular muscle. Although there has been a considerable amount of research on this topic, the subject of dual AV nodal pathways physiology remains heavily debated and discussed. Despite advances in understanding arrhythmia mechanisms and the widespread use of invasive electrophysiologic studies, there is still disagreement on the anatomy and physiology of the AV node that is the basis of discontinuous antegrade AV conduction. Three hypotheses are postulate.

I) **The decremental driving force hypothesis** this hypothesis suggests that conduction along the AV node may change in such a way that the propagating "AP becomes progressively less effective as a stimulus to the unexcited portion of the fiber ahead of it" (**Hoffman BF 1960**).

II) **The electrotonic transmission hypothesis**, (**Janse 1977**) and states that the driving voltage is constant, but that inexcitable microscopic segments cause "stagnation" between different zones of the AV node.

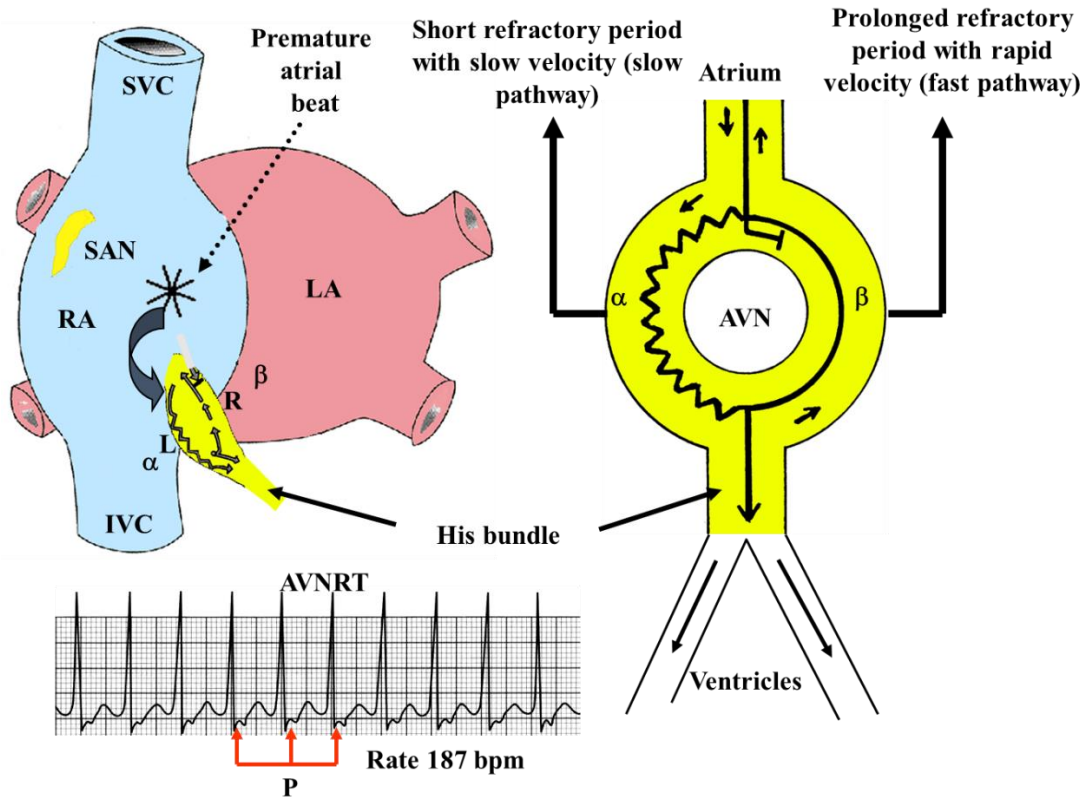
III) **The connexin hypothesis:** Cx43 was found in myocytes of the human AV junction, and its expression pattern delineates two separate continuous structures: one consists of the LE and CN with little Cx43, and the other consists of the His, leftward and rightward nodal extensions lower nodal

bundle, and leftward nodal extension expressing approximately half the Cx43 of the interatrial septum. The differential Cx43 expression may provide each structure with unique conduction properties, contributing to arrhythmias arising from the AV junction. (**Hucker WJ2008**).

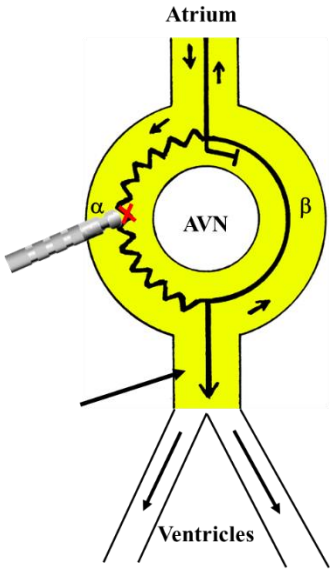
Dual AV pathways can allow earlier PAC to propagate over the slower AV pathway, resulting in early PAC being propagated to ventricles. Later PAC that propagate over the fast AV pathway are blocked since they reach the AV nodal cells when they are still refractory. This demonstration observed in nest figure of fast pathway conduction adds strong evidence for the existence of dual A-V nodal pathways.

Model of dual AV nodal pathways physiology in sinus rhythm, with a premature atrial contraction (PAC) which initiates typical "slow-fast" AVNRT,

Physiopathogenic mechanism of atrioventricular nodal reentrant tachycardia (AVNRT)

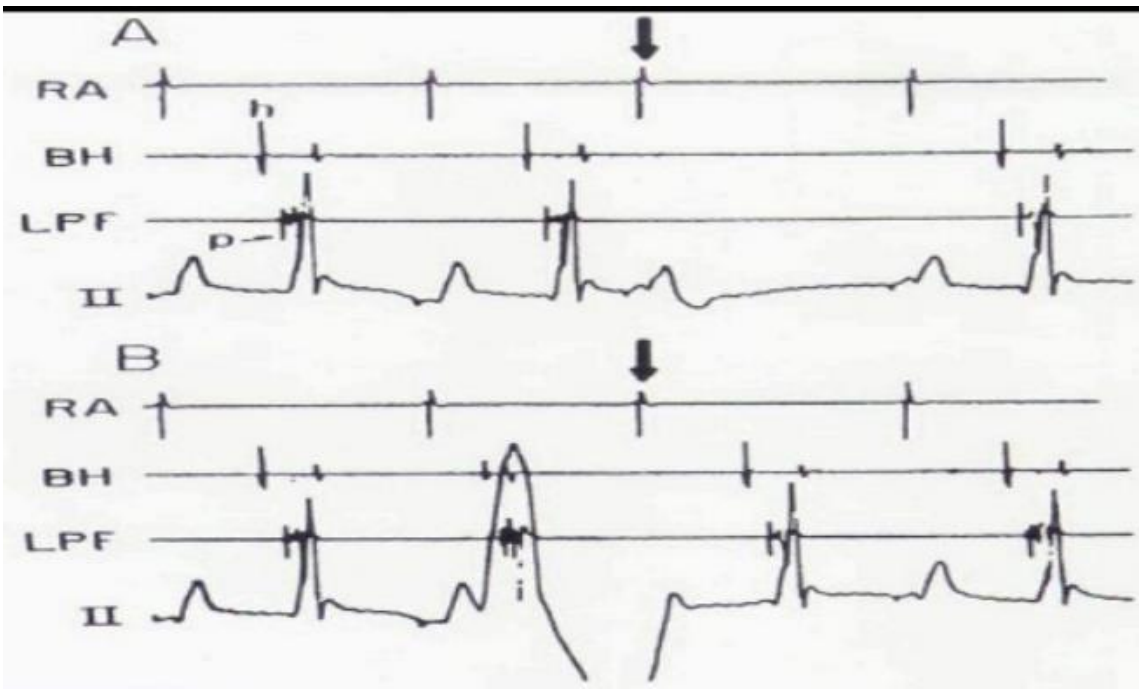


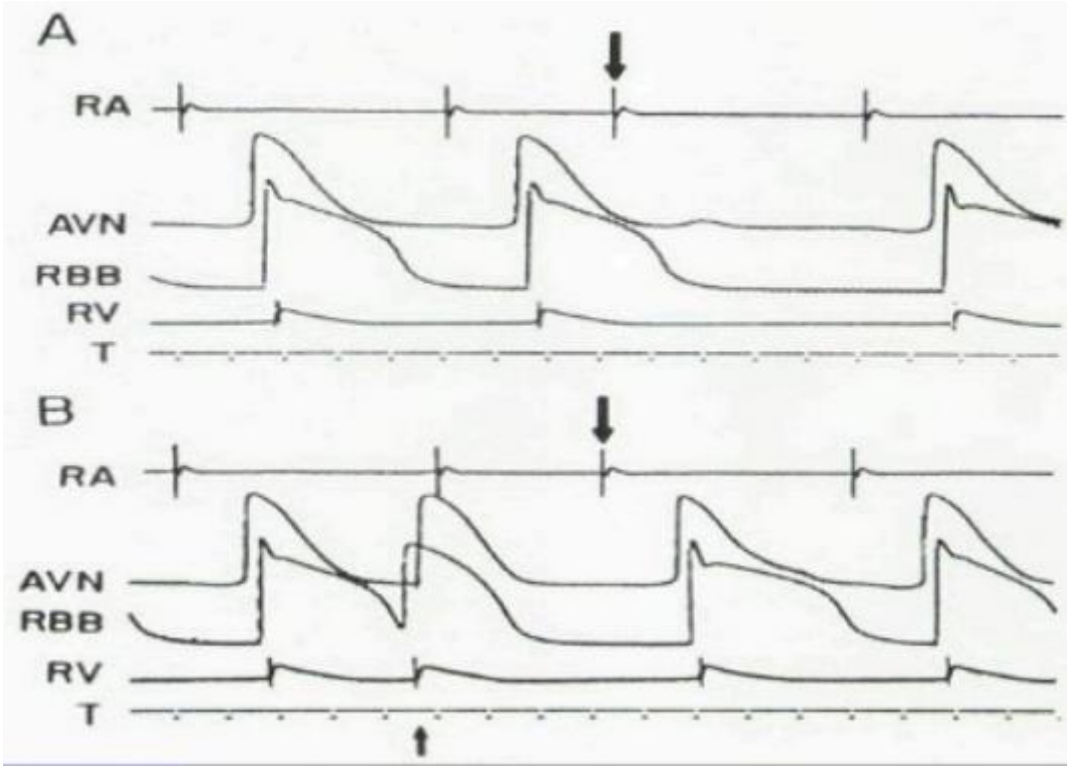
Schema of AVNRT which occurs when an atrial impulse self-perpetuates and revolves in the AV node in a pattern of circuit reentry. These AV nodal reentry beats stimulate both the atrium and the ventricles rapidly in typically a 1 to 1 fashion with a strip of the ECG shown at the bottom.



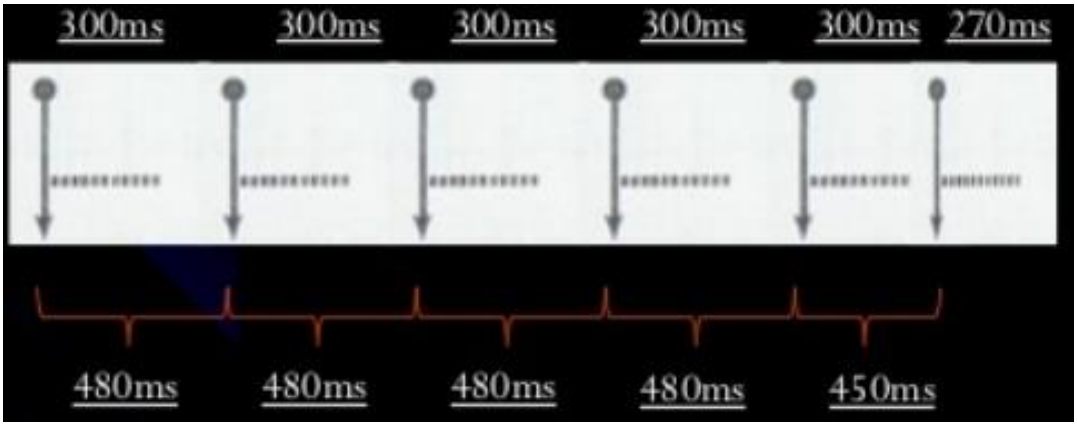
Schema of the AV node with radiofrequency energy delivered via an ablation catheter, typically at the site of the slow pathway to eradicate the circuit that initiates and perpetuates AVNRT.

6) **Peeling back refractoriness:** Pre-excitation of the AV node by a ventricular or junctional best shortens the absolute refractory period of the AV or the His-Purkinje system and allows conduction of a supraventricular impulse

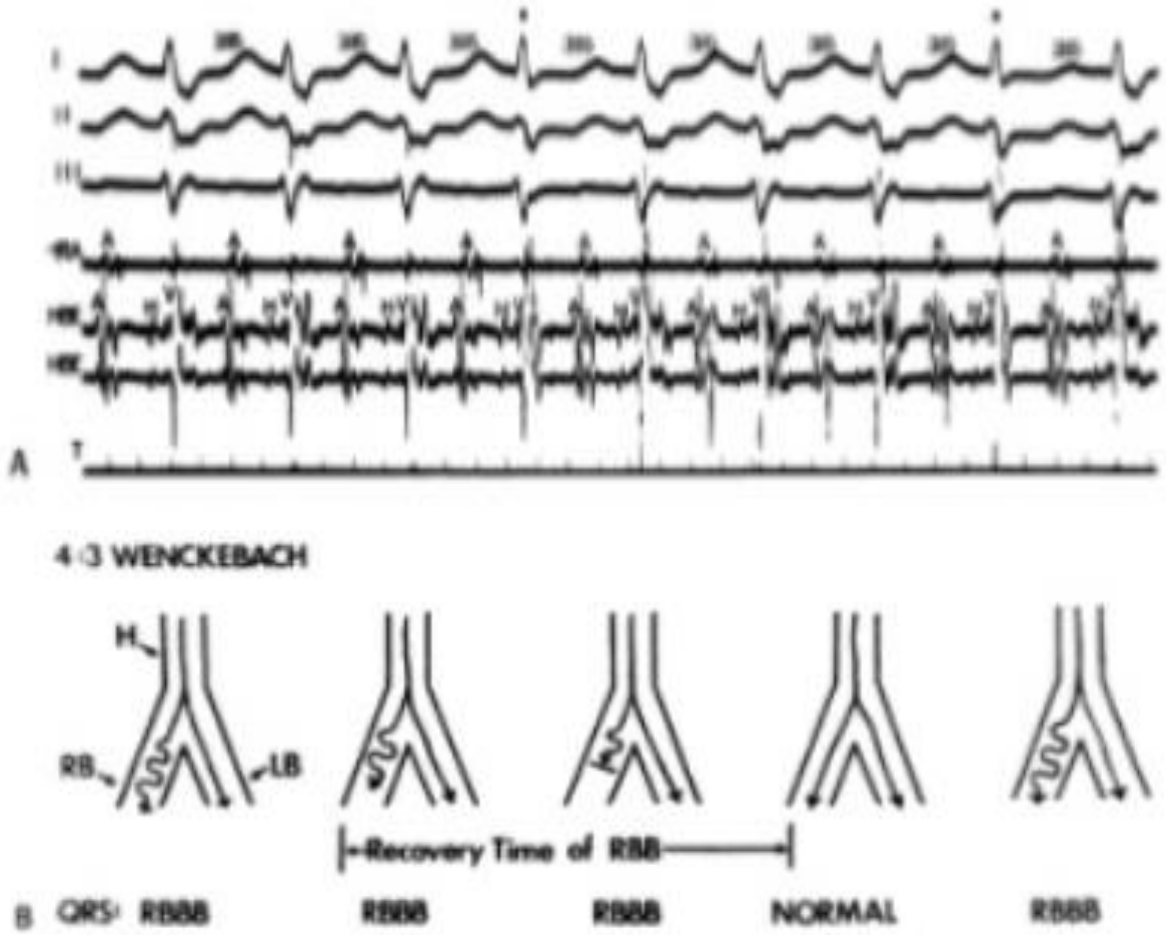




7) **The shortening of refractoriness by changing the preceding cycle:** The duration of refractory period is directly proportional to length of preceding R-R interval



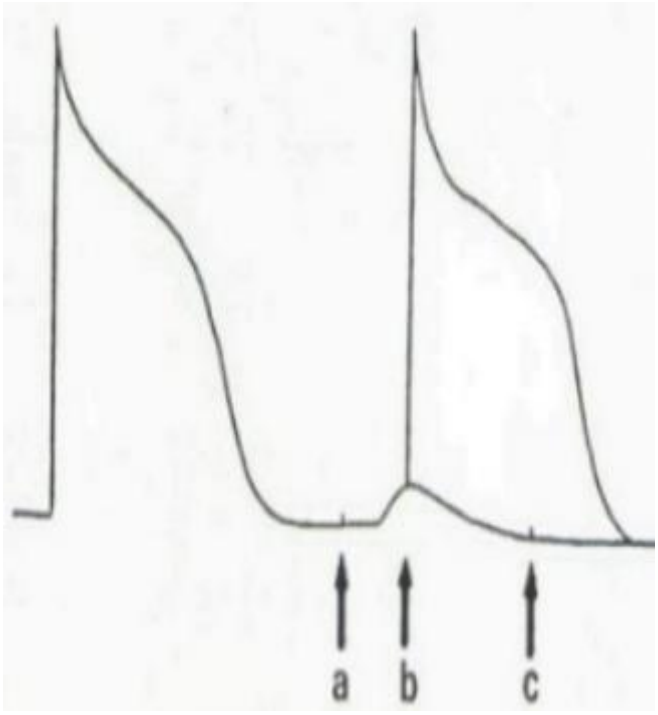
8) **The Wenckebach phenomenon in the bundle branches**



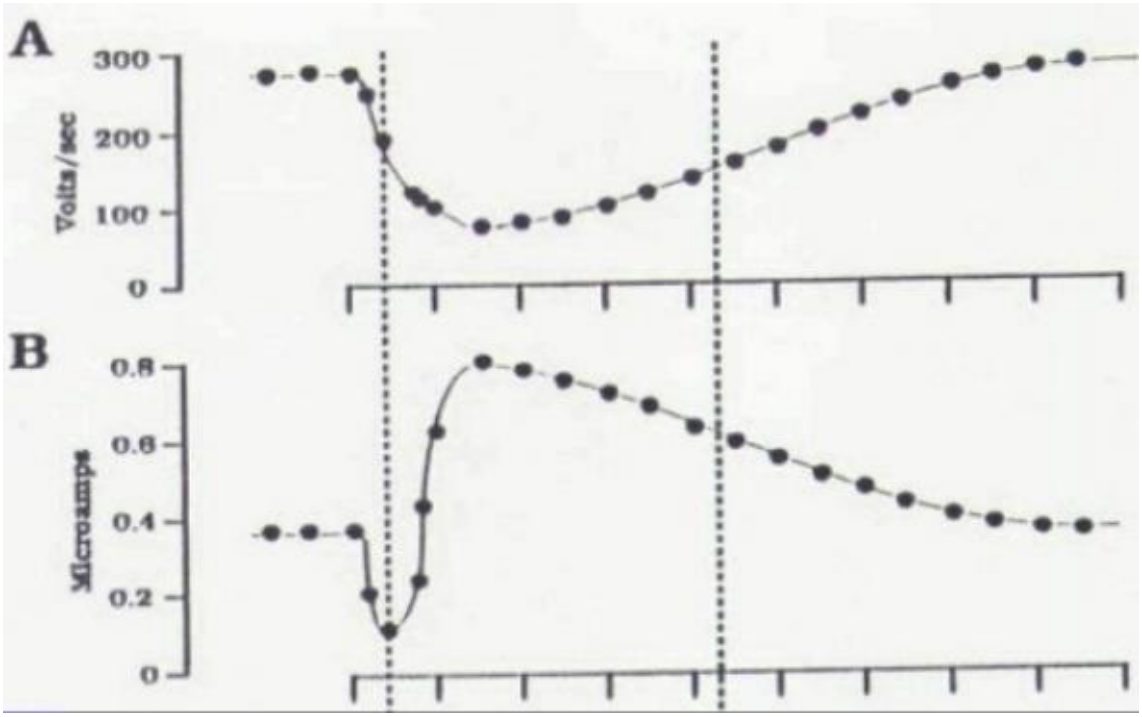
Pseudo-supernormal conduction that is due to type I Wenckebach second degree block in the right bundle branch (RBBB). A: Supraventricular tachycardia with RBB block (RBBB) shown at a cycle length of 385msec. The fourth and eight complexes (Asterix) manifest normal conduction. B: Repetitive normalization in this fashion can be explained by the Wenckebach type block in the RBBB, which is schematically presented. In A. the normal, constant AV interval (45msec) suggests normal conduction through the LBB. Conduction through the RBB is progressively impaired because of some areas prolonged refractoriness. The first two variably penetrate this area, while the third complex fails to engage the area. This effectively doubles the cycle length of the impulses that reach the critical area of delay., allowing time for recovery and subsequent normal conduction. (**Gallagher JJ, 1973 B**)

Observation: The term "true" supernormal conduction will be reserved to conditions under which conduction improves and occurs in relation to a true supernormal phase of excitability in a sick tissue.

9) **Summation of Subthreshold Responses**: If the controlled subthreshold stimulus is applied intracellularly at times A or B excitation did no cause depolarization. However, if that same stimulus was delivered at time B depolarization occurred,



The following experiments demonstrated that summation of two subthreshold events in Purkinje fibers can elicit propagated responses.



Gilmour et al using standard microelectrode techniques, the cellular electrophysiologic features of ventricular myocardium resected from eight patients with refractory arrhythmias were studied in vitro. APs from damaged myocardium compared with normal myocardium had reduced resting membrane potential, amplitude, and phase 0 maximal upstroke velocity. Tetrodotoxin (TTX), but not verapamil, suppressed 3 APs with resting APs between -60 to -64 mV and Vmax < 70 V/s. Verapamil, but not TTX, suppressed 4 APs with resting potentials of -44 to -57 mV and Vmax < 20 V/s. Unidirectional block, Wenckebach block, and summation occurred in damaged zones. Exit block from and frequency-dependent entrance block into an ectopic focus were observed. Subthreshold responses in the focal area induced by APs in the surrounding myocardium and by subthreshold current pulses injected through the recording microelectrode altered the spontaneous discharge rate of the focus, as previously described for modulated parasystole. Pulses early in the spontaneous cycle delayed the next expected discharge, and later pulses accelerated the subsequent discharge. Pulses injected at the singular point completely suppressed automaticity (annihilation). TTX and verapamil suppressed automaticity in some fibers. Single APs induced in quiescent fibers triggered and terminated sustained rhythmic activity. These observations suggest that depressed fast responses, slow responses, and subthreshold potentials can generate and modulate ectopic activity in damaged human ventricle and that fast- and slow-channel blocking agents and single premature stimuli can terminate such activity. (**Gilmour RF Jr 1983**.).

10) Wendensky facilitation:

Depressed segment of PF Mus fibers…. Keep the impulse reaching this site locked at this site…. block is overcome……. multiple stimuli reach the distal site…. Suprathreshold stimulus results…. conduction. (**Schamroth L1969**). Friedberg described a mechanism of the Wedensky phenomena in the left bundle branch (LBB) in a patient with acute myocardial infarction complicated with type I second degree AV block with the Wenckebach phenomenon. Paradoxically, only the first sequence beat showed left bundle branch block; beats conducted after shorter R-R intervals had normal intraventricular conduction. The explanation of this, is that Wedensky facilitation follows the beat that terminates a long R-R interval and allows the passage of the next descending impulse through the LBB; the Wedensky effect allows the conduction of any further impulses that

pass the A-V node to arrive at the depressed zone while the enhancing mechanism is still operative.

Electrotonic (physical) potentials spread through and beyond the depressed zone in the wake of the blocked, propagated (biologic) impulse. Further electrotonic potentials invade the depressed area from the antidromic invasion of the distal left bundle, and also from nearby fibers. These potentials summate to raise the resting potential of the zone of block nearer to threshold, and thus facilitate conduction. (**Friedberg HD 1971**)

11) Bradycardia-dependent conduction blocks

Occurrence of impaired intraventricular conduction after long pauses or slowing of the heart to a critical rate. Due to a gradual loss transmembrane resting potential during a prolonged diastole with excitation form a less negative take-of-potential. (**Jacobson 2014**). We present the case of a patient who showed electrocardiographic pattern consistent with intermittent Left Septal Fascicular Block, associated with left anterior superior fascicular block (left bifascicular block), incomplete right bundle branch block, electrically inactive anterior-apical area and Mobitz type I second degree atrioventricular block of variable degree. The intermittent presence of prominent anterior QRS forces as an expression of left septal fascicular block appeared related to decreased heart rate, thus representing the first case in the literature – as far as we know- of bradycardia-dependent fascicular block. (**Ibarrola 2014**)

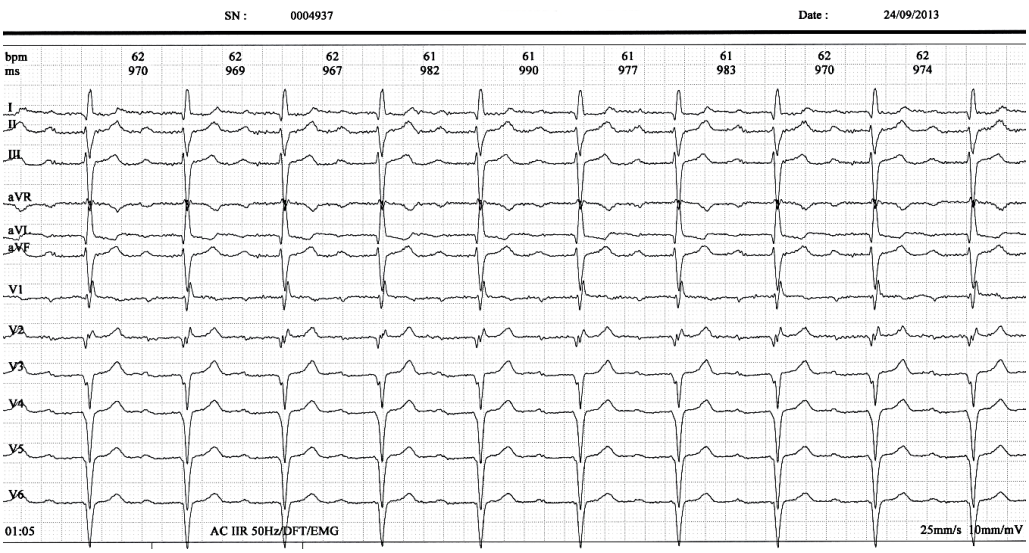
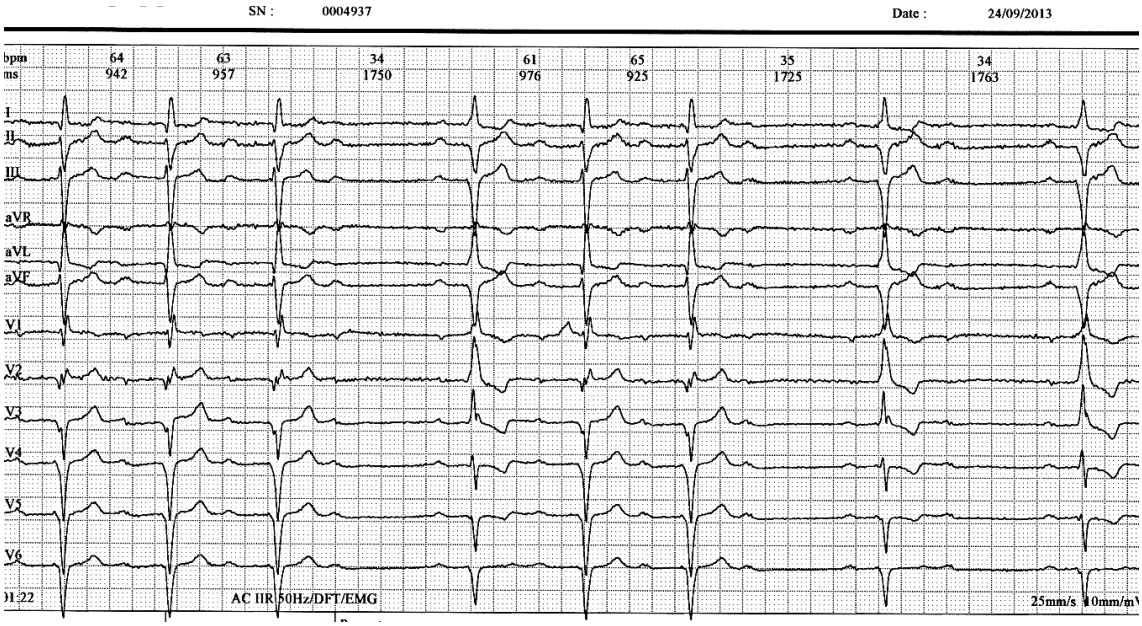


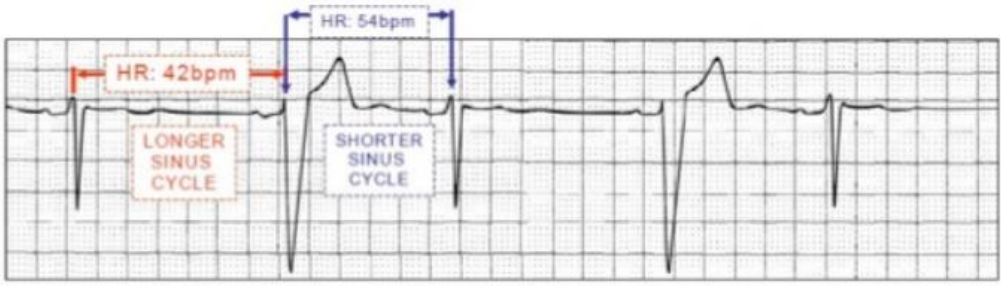
Figure 1. Basal electrocardiogram (ECG 1) sinus rhythm, prolonged PR interval of 308 ms (first degree atrioventricular block), extreme deviation of the QRS electrical axis to the left (-65°), rS in II , III and aVF with SIII > SII , qR in I and aVL: left anterior fascicular block, QR pattern in V1- V2 (BIRD complicated with septal infarction) and QS from V3 to V6, a manifestation of sequela of transmural anteroapical infarction.

Figure 2. Electrocardiogram showing left septal fascicular block with PAF



ECG diagnosis: Mobitz 1 second-degree AV block variable 3:1 and 2:1. The 3 initial conducted beats present a fixed prolonged PR interval (PR = 380 ms) and similar features to the ECG in Figure 1. In the fourth post- pause conducted beat, PR interval suffers a sharp shortening (270 ms), the electrical axis in the frontal plane becomes slightly more negative (-71°), initial q waves of DI and aVL and initial r waves of II , III and aVF disappear, an indication of the disappearance of the first vector, vector of the septum , or initial middle septal vector of the 1/3 of the left septal surface and in the right precordial lead we verify clear increased voltage of R and slight increase in the duration of QRS (of 100ms) followed by negative T wave; this is related to the decrease in heart rate (intermittent bradycardia-dependent left fascicular block). Absence of wide S waves in the left leads and final wide R wave in aVR as would be expected in case of RBBB.

Another example of transient phase 4 LBBB



Phase 4 aberration is observed in 2nd and 4th QRS complex. The longer sinus cycle end with LBBB pattern ant the shorter sinus cycle is followed by a narrow QRS complex.

In patients with bradycardia dependent aberrancy, th beat at the end of a lengthened cycle is aberrated. It is generally unexpected since there should be sufficient time for the bundles to recover and conduction to be normal after a long cycle. One explanation for its occurrence is that the bundles are severing as pacemaker tissue and manifests spontaneous phase 4 depolarization. This pacemaker tissue is no longer suppressed by stimuli form upper pacemakers when the cycle length is very prolonged, leading to generation of an impulse which be conducted via the bundle and hence aberrantly.

El-Sherif and Jalife (**El-Sherif N 2009**) suggests other possible mechanisms for bradycardia-dependent block in the setting of AV conduction disturbances: rapid pacing may produce an electrotonic effect across the ablation line that allows for generation of an AP in the isolated PV tissue (because of rate-related changes in slow inward current), or a decrease in AP amplitude can occur at slower rates leading to failure of propagation.

After the implantation of a cardiac implantable electronic device, a rise in the capture threshold is a common complication that requires early reintervention. Precise measurements of the sensing amplitude and capture threshold are important to estimate lead position and stability and to determine sensing and pacing settings. Although pacing rate is commonly thought not to significantly affect capture threshold. Kimata et al encountered three patients undergoing pacemaker implantation for sick sinus syndrome (SSS) in whom the pacing rate was a critical determinant of successful capture of the atrial myocardium because of a bradycardia-dependent rise in the atrial capture threshold **(Kimata A 2015**) . The bradycardia-dependent rise in the atrial capture threshold may be explained by “phase 4 block.” Phase 4 block can be responsible for atrioventricular block, bundle branch block, left septal fascicular block (**Ibarrola M 2014**) and accessory pathway (**Przybylski J 1987**.) conduction block in some cases. (**El-Sherif N 2009**)

(**Fujiki 1992**). Singer et al(**Singer DH1967**.)suggested that phase 4 depolarization in potentially automatic cells could explain the conduction abnormalities associated with prolongation of the cycle length.

Rosenbaum et al postulated that phase 4 block results from spontaneous diastolic depolarization by reducing AP amplitude and upstroke velocity in an attempt to activate the depolarized area (**Rosenbaum M.B 1973**)

Although the mechanism of the bradycardia-dependent rise in the atrial capture threshold is unclear, it is possible that pacemaker lead-induced inflammation, necrosis, and fibrosis of the atrial myocardium may cause spontaneous phase 4 depolarization.

Phenomenon	Mechanism
More rapid than normal conduction of premature impulse in a Purkinje fiber	Enhanced conduction due to supernormal excitability associated with late repolarization.
More rapid Purkinje fiber conduction with moderate hyperkalemia	Increased excitability associated with slight potassium- induced membrane depolarization
Conduction across a site of bidirectional block in a Purkinje strand following an appropriately timed impulse that blocked distally	Enhanced excitability at the site of block due to summation with a sub-threshold response (Wedensky facilitation)
AV conduction of early and late premature impulses with an intervening zone of block	The gap phenomenon where a proximal delay of a premature impulse allows time for recovery of excitability of a distal site of block
Conduction of previously blocked atrial impulse following an appropriate timed retrogradely concealed ventricular impulse	Peeling back of refractory barrier due to premature engagement and early recovery of excitability

12) Tachycardia-dependent bundle-branch block (phase 3 block) associated with supernormal conduction

Disturbance of bundle branch block (BBB) and fascicular block not infrequently, they appear and disappear with changes in heart rate. This may not even represent a pathological phenomenon, since sudden and consistent changes in cardiac cycle can result, even physiologically, in aberrant conduction. However, when a BBB appears intermittently for simple and progressive increments, or even deceleration, of the sinus rate, this is related to a true BBB pathology, i.e. tachycardia-dependent or phase 3 block or bradycardia-dependent or phase 4 block, respectively. Phase 3 block is believed to express a pathological increase in the duration of the recovery period of the bundle branch.

According to steadiness LBBB could be (**Pérez-Riera AR 2018**) 1. Permanent or definitive: most of the cases.

2. Intermittent, transient, episodic, or second-degree LBBB that could be:

• Rate-dependent intermittent LBBB

Tachycardia-dependent or "phase 3" LBBB: it occurs when an impulse arrives at tissues that are still refractory caused by incomplete repolarization. Transient LBBB is less common than transient RBBB (only 25% of phase 3 aberration is of the LBBB type).

Phase 4 block was best explained on the basis of enhanced phase 4 depolarization of the bundle branch system, with inability of excitation if the cardiac cycle is particularly prolonged. The two types of block, phase 3 and phase 4, often coexist. An intraventricular conduction disturbance that appears during increasing heart rate for a phase 3 block is maintained, if frequency slows down, even for cycles greater than those that brought about its appearance. This is due to retrograde activation of the bundle branch blocked in the antegrade direction, with delay of its AP inscription. Sometimes, in the presence of phase 3 BBB, very early PACs are paradoxically conducted in the normal way (supernormal conduction). Perhaps, this phenomenon is related to a possible "climb over" of the injured zone of the bundle branch by the blocked impulses that arise beyond the injured area as subliminal impulses, exciting the healthy tissues if catches them during their phase of supernormal excitability. In the presence of intermittent BBB it is not uncommon to observe long periods of sinus rhythm with regular PP interval, conducted with alternating (2:1) BBB. Intermittent left BBB is a clinical model of cardiac memory: in these cases, negative T waves in the antero-septal leads during normal conduction are

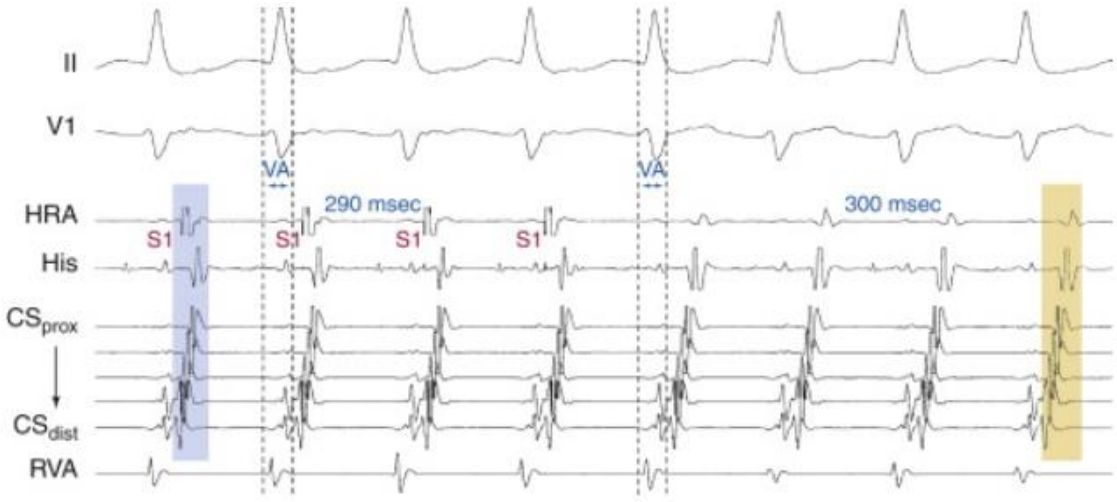
often evident. This negativity is an expression of cardiac memory, and not of ischemia as initially interpreted. Intermittent BBB is an excellent model to study in vivo the effects of antiarrhythmic drugs on the pathological bundle branches. Narrowing of the QRS complex in the presence of BBB is not always an expression of intermittent aberrancy: beware of late ectopic beats originating from the ipsilateral ventricle to the blocked branch, that merging with the antegrade beat conducted with BBB, restrict the QRS, simulating intermittent aberrancy. (**Costantini M. 2014**)

13) Worsening in conduction in the unaffected branch, leading to conduction times equalization in both branches

14) Fusion beat (hybrid QRS complexes)

Presence of *fusion beats*, which identify simultaneous depolarization of the ventricle by both the normal conduction system and an ectopic impulse originating in the ventricle. The presence of fusion beat during tachycardia is indicative of ventricular in origin.

During Orthodromic Atrioventricular Reentrant Tachycardia atrial pacing at a cycle length (CL) slightly shorter than the tachycardia CL generally can entrain orthodromic AVRT. If the P waves on the surface ECG can be seen, which usually is not the case, they may appear to be fusion beats resulting from intraatrial collision of the impulse propagating from the paced site with the one emerging from the BT. In general, when pacing is initiated orthodromically to the zone of slow conduction (the AVN in this case), conduction time within the area of slow conduction is long enough to allow a wide atrial antidromic wave front to generate surface ECG fusion



Atrial entrainment of orthodromic atrioventricular reentrant tachycardia (AVRT) using a left lateral bypass tract (BT). Atrial fusion (between the paced and tachycardia wavefronts; compare shaded areas) is observed during entrainment, which is consistent with AVRT and excludes both focal atrial tachycardia and atrioventricular nodal reentrant tachycardia. Note that the ventriculoatrial (VA) interval (dashed lines) of the return cycle after cessation of atrial pacing is similar to that of the supraventricular tachycardia (V-A linking), because retrograde VA conduction of the last entrained QRS is mediated by the BT.

The Wolff-Parkinson-White (WPW-S) is defined by the WPW pattern in addition to arrhythmias. The WPW-S pattern results from an AP, the Kent bundle, which directly links the atria to the ventricles, bypassing the atrioventricular (AV) node. The ventricular myocardium is activated early as a result of this AP, prior to activation via the normal AV node/His-Purkinje pathway. Thus, the QRS complex in WPW represents a fusion beat; the initial part results from slow ventricular activation via the accessory pathway, while the terminal portion of ventricular activation is via the normal conduction system. The ECG demonstrates a short PR interval (<120ms) and a delta (δ) wave (slurred and broad upstroke of the QRS complex), representing early ventricular activation via the abnormal accessory pathway. The QRS duration is wide (≥ 120ms) and bizarre appearing. This is due to myocardial activation directly through the ventricular myocardium fusing with myocardial activation using the His-Purkinje system: fusion or hybrid beat. Thus, the QRS complex in WPW represents a fusion beat; the initial part results from slow ventricular activation via the accessory pathway, while the terminal portion of ventricular activation is via the normal conduction system. Often there are associated ST segment and T wave abnormalities reflecting abnormal ventricular repolarization.

His bundle electrograms were recorded in a patient with WPW syndrome during atrial pacing studies and during the induction of premature atrial depolarization at varying coupling intervals. Early ventricular depolarization (preexcitation) occurred simultaneously with the His depolarization, suggesting that conduction occurred via both the Kent and the normal A-V nodal-His-Purkinje pathway during sinus rhythm. Atrial pacing at increasing rates showed progressive advance of the His spike into the QRS and increasing duration of the delta wave until the appearance of broad bizarre QRS complexes with prolonged P-J intervals, suggesting major, if not total, depolarization of the ventricle by the Kent pathway. PAD's induced at coupling intervals of 360, 330, and 300 msec caused progressive delay of the His bundle depolarization, with the His spike occurring after the QRS at S(1)-H intervals of 230, 265, and 325 msec, respectively, and Q-H intervals of 123, 160 and 220 msec, respectively. These findings suggest that during sinus rhythm the QRS was a fusion beat. With early premature atrial stimulation, conduction

occurred solely via the Kent pathway, with conduction via the normal A-V nodal pathway encountering increasing delay. The finding of His depolarization occurring after the QRS suggests retrograde myocardial-His block, and may explain the absence of paroxysmal supraventricular tachycardias in this patient. (**Gomes JA, 975**.)

Electrical fusion between left ventricular (LV) pacing and spontaneous right ventricular activation is considered the key to resynchronization in sinus rhythm patients treated with single-site LV pacing. Use of QRS morphology to optimize device programming in patients with heart failure (HF), sinus rhythm (SR), left bundle branch block (LBBB), treated with single-site LV pacing. Fusion band is defined as the range of AV intervals within which surface ECG showed an intermediate morphology between the native LBBB and the fully paced right bundle branch block patterns (**Gianfranchi L**)

Fusion beat (Gomes 1975)

15) Linking phenomenon

The linking phenomenon is an electrophysiological phenomenon of conduction between two different pathways, such as bundle branches, atrioventricular node and APs in macroreentrant circuits. (**Itagaki T 2001**). The term "linking" has been used specifically to describe the mechanism for perpetuation of functional anterograde BBB: namely, repetitive transseptal retrograde concealed penetration by impulses propagating along the contralateral bundle (**Lehmann MH1985**.). Theses authors presented 4 mechanisms:

1) Persistent retrograde functional conduction delays in the His-Purkinje system during right ventricular pacing;
2) Anterograde Kent bundle conduction at fast rates, dependent on prior block in the normal pathway;
3) Persistent anterograde functional infra-His block of atrial impulses during rapid ventricular pacing in the presence of a retrogradely conducting AP, and
4) Transient advancement of His activation with ventricular fusion complexes during overdrive ventricular pacing of bundle branch reentrant tachycardia.

Linking as a generalized electrophysiologic phenomenon in which each successive impulse entering a macroreentry circuit propagates preferentially along one limb because of functional block in the contralateral limb resulting from the effects of the prior impulse. It is proposed that such functional block may be dynamically maintained either by repetitive impulse interference, which perpetuates local refractoriness or by repetitive impulse collision.The general conceptual scheme outlined can be applied to

specific electrophysiologic phenomena associated with a wide variety of reentry circuits in man.

Occurrence of linking by collision during attempted overdrive pacing of reentrant tachycardias accounts for the entrainment phenomenon. (**Lehmann MH, 1988**).

16) Supernormal conduction period by a small window in the cardiac cycle:

During the initial stage of left bundle branch (LBB) recovery, at the end of the AP, a small window in the cardiac cycle may lead to a shift from the sick area in the blocked branch, where the tissue has a supernormal conduction capacity (the greater the heart rate, the earlier the window for supernormal conduction capacity). Because of the short period of this phase, only a very early atrial premature contraction of the second beat interrupts the functional LBBB, thus allowing conduction through both branches. After two sinus beats with normal intraventricular conduction (narrow QRS complexes), there is gradual slowing of conduction through the LBB, which causes return of the LBBB pattern. The atrial premature contraction necessarily must fall at relatively constant positions within the cardiac cycle close to the end of the T wave, known as supernormal period.

Conclusion

The supernormal conduction may be much more common than previously thought, particularly when the clinical conditions are present and the phenomenon is systematically searched in patients with advanced AV block or intermittent conduction in the His-Purkinje system or in the case of accessory pathways. One of the main still unresolved problems will be to elucidate the exact mechanism of this almost forgotten electrophysiologic curiousness, which, occasionally, plays a relevant role in dangerous arrhythmias.

References

1. Adrian ED, Lucas K: On the summation of propagated disturbances in the nerve and in the muscle. J Physiol 1912; 44:68- 124.
2. Costantini M. Intermittent bundle branch block: a clinical model for the study of electrophysiological phenomena.G Ital Cardiol (Rome). 2014 Jan;15(1):25-36.
3. Durrer D. Electrical aspects of human cardiac activity: a clinical-physiological approach to excitation and stimulation. Cardiovasc Res. 1968 Jan;2(1):1-18.

4. Elizari MV, Schmidberg J, Atienza A, Paredes DV, Chiale PA1.Clinical and experimental evidence of supernormal excitability and conduction. Curr Cardiol Rev. 2014 Aug;10(3):202-21.
5. El-Sherif N, Jalife J. Paroxysmal atrioventricular block: are phase 3 and phase 4 block mechanisms or misnomers? Heart Rhythm. 2009; 6:1514–1521.
6. Friedberg HD. Mechanism of the Wedensky phenomena in the left bundle branch.Am J Cardiol. 1971 Jun;27(6):698-702.
7. Fujiki A., Tani M., Mizumaki K., Yoshida S., Sasayama S. Rate-dependent accessory pathway conduction due to phase 3 and phase 4 block. Antegrade and retrograde conduction properties. J Electrocardiol. 1992;25:25–31.
8. Gallagher JJ, Damato AN, Caracta AR, Varghese PJ, Josephson ME, Lau SH. Gap in A-V conduction in man; types I and II. Am Heart J. 1973 Jan;85(1):78-82 A
9. Gallagher JJ, Damato AN, Varghese PJ, Caracta AR, Josephson ME, Lau SH.Alternative mechanisms of apparent supernormal atrioventricular conduction. Am J Cardiol. 1973 Mar;31(3):362-71. B DOI: https://doi.org/10.1016/0002-9149(73)90269-5
10. Gianfranchi L, Bettiol K, Sassone B, Verlato R, Corbucci G, Alboni P.Fusion beat in patients with heart failure treated with left ventricular pacing: may ECG morphology relate to mechanical synchrony? A pilot study. Cardiovasc Ultrasound. 2008 Jan 1; 6:1. doi: 10.1186/1476-7120-6-1
11. Gilmour RF Jr, Heger JJ, Prystowsky EN, Zipes DP. Cellular electrophysiologic abnormalities of diseased human ventricular myocardium. Am J Cardiol. 1983 Jan 1;51(1):137-44.
12. Gomes JA, Haft JI. Wolff-Parkinson-White syndrome type B with His depolarization occurring after the QRS. Further evidence that WPW-QRS is a fusion beat. Chest. 1975 Apr;67(4):445-9
13. Gouaux JL, Ashman R. Auricular fibrillation with aberration simulating ventricular paroxysmal tachycardia. Am Heart J. 1947 Sep;34(3):366-73.
14. Hoffman BF, et al. Electrophysiology of the heart. New York: McGraw-Hill; 1960.
15. Hucker WJ, McCain ML, Laughner JI, Iaizzo PA, Efimov IR.Connexin 43 expression delineates two discrete pathways in the human atrioventricular junction, Anat Rec (Hoboken). 2008 Feb;291(2):204-15.

16. Ibarrola M., Chiale P.A., Perez-Riera A.R., Baranchuk A. Phase 4 left septal fascicular block. Heart Rhythm. 2014;11:1655–1657
17. Itagaki T, Ohnishi Y, Inoue T, Yokoyama M. Linking phenomenon in dual atrioventricular nodal pathways. Jpn Circ J. 2001 Nov;65(11):937-40
18. Jacobson JT, Ciaccio EJ, Biviano AB, Whang W, Garan H.Bradycardia-dependent conduction block into pulmonary vein after isolation.Circ Arrhythm Electrophysiol. 2014 Aug;7(4):762-3. doi: 10.1161/CIRCEP.113.001304
19. Janse MJ, et al. Electrophysiology and structure of the atrioventricular node of the isolated rabbit heart. In: Wellens HJJ, et al., editors. The conduction system of the heart. Leiden, The Netherlands: Stenfert Kroese; 1976. p. 296.
20. Katoh T, Kinoshita S, Tsujimura Y, Sasaki Y, Oyama Y.Tachycardia-dependent right bundle-branch block with supernormal conduction. Clin Cardiol. 2000 Jan;23(1):59-62.
21. Kimata A, Yoshida K, Takeyasu N, Nakagami R, Osada J, Mitsuhashi T, Aonuma K, Nogami A.Bradycardia-dependent rise in the atrial capture threshold early after cardiac pacemaker implantation in patients with sick sinus syndrome.HeartRhythm Case Rep. 2015 Oct 3;2(1):27-31. doi: 10.1016/j.hrcr.2015.08.012
22. Lehman MH, Denker S, Mahmud R, Addas A, Akhtar M: Linking: A dynamic electrophysiologic phenomenon in macroreentry circuits. Circulation 1985; 1985 Feb;71(2):254-65.
23. Lehmann MH, Steinman RT. Linking by collision initiated in the absence of preexisting reentrant tachycardia. Am J Cardiol. 1988 Feb 1;61(4):354-60.
24. Lewis T, Master AM: Supernormal recovery phase, illustrated by two clinical cases of heart block. Heart 1924; 11:371- 87,
25. Moe GK, Mendez C, Han J. aberrant A-V impulse propagation in the dog heart: A study of functional bundle branch block. Circ Res. 1965 Mar;16:261-86.
26. Moe GK, Childers RW, Merideth J. An appraisal of “supernormal” AV conduction. Circulation. 1968 Jul;38(1):5-28.
27. Pérez-Riera AR, Barbosa-Barros R, de Rezende Barbosa MPC, Daminello-Raimundo R, de Abreu LC, Nikus K.Left bundle branch block: Epidemiology, etiology, anatomic features, electrovectorcardiography, and classification proposal.Ann Noninvasive Electrocardiol. 2018 Jun 22:e12572. doi: 10.1111/anec.12572

28. Przybylski J, Chiale PA, Sánchez RA, Pastori JD, Francos HG, Elizari MV, Rosenbaum MB. Supernormal conduction in the accessory pathway of patients with overt or concealed ventricular pre-excitation.
29. J Am Coll Cardiol. 1987 Jun;9(6):1269-78.
30. Rosenbaum M.B., Elizari M.V., Lazzari J.O., Halpern M.S., Nau G.J., Levi R.J. The mechanism of intermittent bundle branch block: Relationship to prolonged recovery, hypopolarization and spontaneous diastolic depolarization. Chest. 1973;63:666–677.
31. Schamroth L, Friedberg HD. Wedensky facilitation and the Wedensky effect during high grade A-V block in the human heart.Am J Cardiol. 1969 Jun;23(6):893-9.
32. Singer D.H., Lazzara R., Hoffman B.F. Interrelationship between automaticity and conduction in Purkinje fibers. Circ Res. 1967;21:537–558.
33. Weidmann S. Effects of calcium ions and local anesthetics on electrical properties of Purkinje fibers. J Physiol. 1955 Sep 28; 129(3):568-82.
34. Wu D, Denes P, Dhingra R, Rosen KM. Nature of the gap phenomenon in man.Circ Res. 1974 May;34(5):682-92.

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