

The Long Journey to Interatrial Block Discovery

A. Bayés de Luna

Fundació Investigació Cardiovascular, ICCV, Barcelona, Spain

Email: abayes@csic-iccc.org

1. Introduction

To begin, I feel it is important to point out that before our publications on interatrial block starting in the mid-1970s, a number of papers had already discussed, with isolated cases or short series, different aspects of so-called blocks at atrial levels and specifically of interatrial or intraatrial block (IAB) [1-8], that is the topic that we will comment in this paper. Although there is some discrepancy in different papers [1-4] about the significance of the concept of interatrial or intraatrial block, usually this represents an impaired propagation of the stimulus between two portions of the atria, with enlarged P waves greater than or equal to 110-120 ms, and normally accompanied by left atrial enlargement. In a few articles [5-8] written in Latin languages, also was considered that if the stimulus was completely blocked at the upper part of the Bachmann zone, the activation of the left atrium would take place retrogradely, originating a long P wave (≥ 120 ms) together with a \pm morphology in II, III and VF. However, there are many aspects that are not well explained or discussed in these publications, as outlined below.

1. In no publication did it state that these ECG patterns of interatrial (intraatrial) block (IAB) are in fact a pattern of block based on the presence of the following 3 conditions: a) the pattern may appear suddenly and may be transient, b) the pattern may exist without associated enlargement of involved chambers. In fact, the term “left atrial abnormality” was coined and widely used to encompass both “atrial enlargement” and “interatrial block” [9, 10] and c) the ECG pattern may be reproduced experimentally.
2. Furthermore, no paper discussed at any time any possible clinical implications of these ECG patterns. We, therefore, cannot know if these cases were associated with supraventricular tachyarrhythmias, mortality or other problems.
3. There was no clear definition and classification of block at the atrial level, specifically of interatrial block (IAB) this means block between two atria. There was no mention that IAB may be, as other types of block, of partial (first-degree block), transient (second-degree block) or advanced (third-degree block) types.
4. There were no data about the prevalence of these blocks, and its etiological aspects.
5. There were no clear ECG-VCG criteria for advanced IAB, based on long series of patients.
6. The concept of IAB is not frequently used in cardiology. The P wave still remains “The Cinderella of the ECG”. In a review of 76 books on ECG in English, Spanish, French and Italian languages, from the beginning of ECG study (Lewis’ books) to present day, we have only found a clear reference to interatrial block in our books since the first edition [11] and in Piccolo and Oreto’s book [12, 13]. For example, Te-Chuan Chou [14] states that “in P-wave changes, conduction defects may be present.” A less specific term such as *atrial abnormality* is found in other books. Macfarlane [15], while discussing the concept of intra-atrial block, only defines it following the criteria of WHO/ISFC [16] that corresponds to partial interatrial block (IAB). In terms of general cardiology, the textbook by Braunwald [17] includes “all anomalies of P wave” under the term “*atrial abnormalities*”, which is also the case in the chapter on ECG of the previous editions of the textbook “The heart”, by Fuster et al [18], except the last edition written by our group.

2. Our studies on interatrial block

Our dedication to the study of blocks at the atrial level, and especially to interatrial blocks (IAB), has been one of our favourite topics throughout the last 40 years. The following is a summary of the most important successive studies performed by our group.

Identification and classification of blocks at atrial level

We classified blocks at atrial level [19-22] in interatrial and other types of atrial blocks that includes right atrial block and atrial aberrancy. For the remainder of this paper we will focus on interatrial block (IAB). This is the block between the right and left atria in the zone of the Bachmann bundle and may be of first-degree (partial), when the stimulus pass through the Bachmann bundle but with delay the ECG criterion of which is P wave ≥ 120 ms (≥ 110 for others); third-degree (advanced), when the stimulus is blocked in the zone of Bachmann bundle, and left atrium is retrogradely conducted to left atrium (RCLA) (Fig.1-3); the ECG criteria of which are P wave ≥ 120 ms and \pm morphology in II, III and VF. Second-degree, IAB is a transient pattern of partial or advanced IAB, a form of atrial aberrancy (Fig.4).

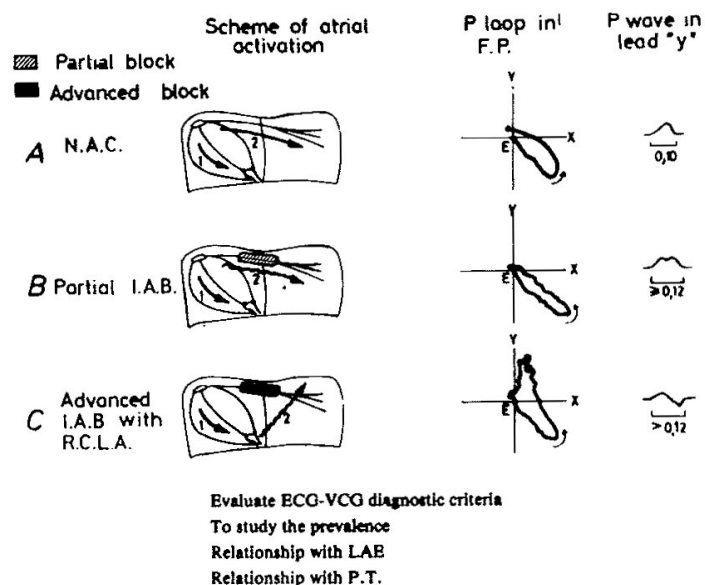


Fig. 1. Left: Scheme of atrial activation in a normal case (A), in presence of partial IAB (B), and of IAB with LARA (C). Right: Characteristics of the P loop and P wave in each case.

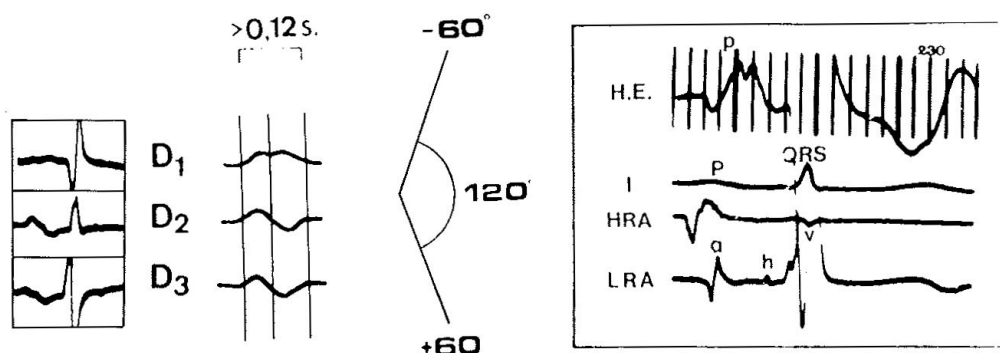


Fig. 2. Left: Characteristics of the P wave in the three bipolar limb leads. Note the existence of an open angle between the vector of the 1st part and of the 2nd. Right: Electrophysiological study that demonstrates the retrograde activation of the left atrium. HE: High esophageal lead. HRA: High right atrium. LRA: Low right atrium. In HE the morphology is +- because the electrode first face the tale of activation and later the head of the vector. The way of activation is HRA-LRA-Second part (positive) in HE.

Although we published this classification already in the 70's [19-22] and in all editions of our ECG books published since the mid 1970s, this concept has not become popular. Very recently, we published a consensus paper on IAB under the auspices of ISHNE in the Journal of Electrocardiology [23] and a new edition of my book [30], and we hope this will help to further disseminate all these concepts.

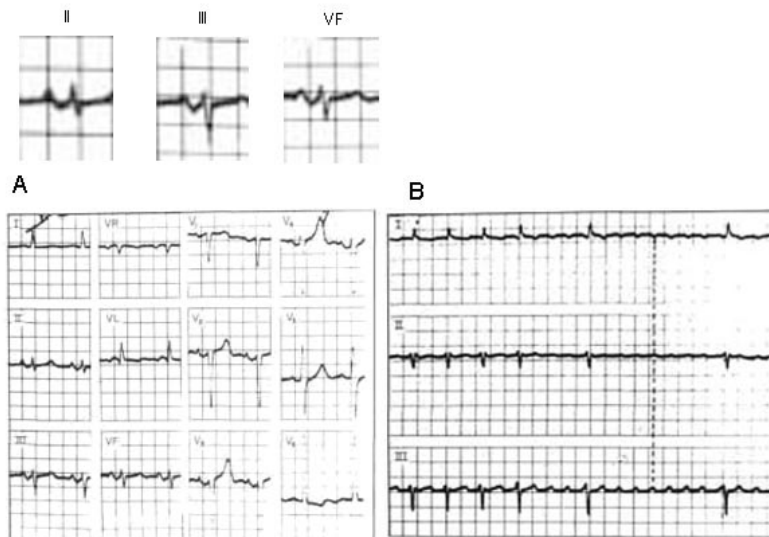


Fig. 3. A. Typical morphology of advanced interatrial conduction block and retrograde activation of the left atrium, in sinus rhythm. B. The polarity of the flutter wave indicates that the flutter is an atypical flutter.

These patterns may correspond to block.

Evidence consisted of the following: a) we found cases of partial and advanced IAB without LAE [21, 22]; b) we found cases of intermittent and progressive partial and advanced IAB [22]; and c) in the 1970s Waldo and others demonstrated that the pattern of advanced IAB may be reproduced experimentally [24] (Fig.5).

Definition of ECG-VCG diagnostic criteria

In 1976 and 1978 we published, our first abstract and paper on advanced interatrial block (19,20). Later, a larger series was published in 1985 (22) (Figs. 1-3) (Table 1).



Fig. 4. Two cases of atrial aberrancy. The first one **A** is a case of second degree interatrial block. This is a case of a patient with basal advanced interatrial block (P_{\pm} with first part isoelectric that mimics AV junction rhythm) that presents aberrant atrial conduction, ectopically induced by premature atrial complex, with a pattern, in this case, of first degree interatrial block (**x**). **B**. A patient with aberrant atrial conduction also ectopically induced by a premature atrial complex. After this premature complex, a transitory P wave with a different morphology, but not with a pattern of first or third interatrial block appear (**x**). The PR interval is equal to previous PR intervals. Other explanations to this change (atrial escape, artifact, etc.) are unlikely (see Bayés de Luna 2014 [30]).

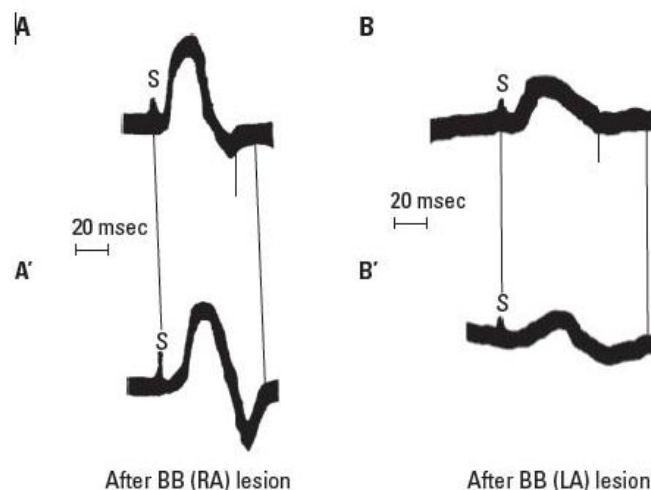


Fig. 5. Adapted from experimental Bachmann's bundle block (Waldo et al. 1971). (A) Control P wave recorded in ECG lead II when the atria were paced from the right atrium. See the change of morphology after Bachmann's bundle lesion in the right side. (B) P wave recorded in lead II after the creation of a lesion in the left atrial (LA) portion of Bachmann's bundle (BB). In both cases the changes in conduction time and morphology after block are shown.

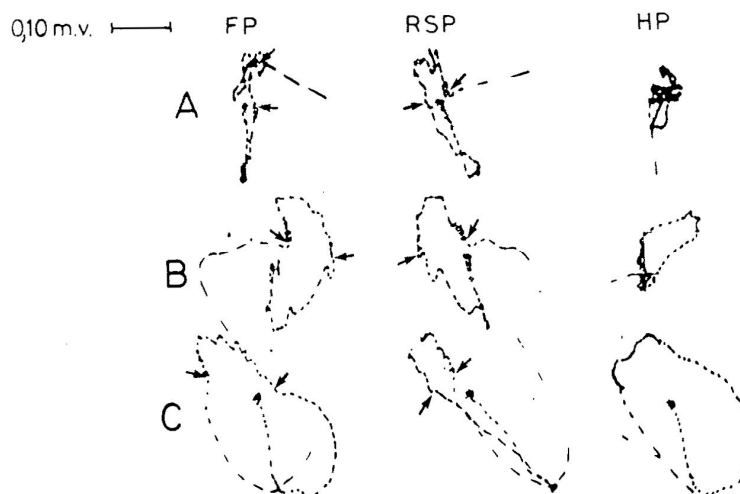


Fig. 6. Examples of the P loops in presence of advanced IAB. A) Closed loop. B) Open loop with a left final part. C) Open loop with a right final part.

Of the 81.000 ECGs, we collected, 83 cases that fulfilled the criteria of advanced IAB ($P \pm$ in II, III and VF with P width ≥ 120 ms.). We presented a detailed study of 35 cases with surface ECG and VCG and 29 cases with orthogonal ECG leads (Table I and fig. 2, 3, 6, 7). The results were then compared against 2 control groups: patients with heart disease (30 cases) and those without heart disease (25 cases). The prevalence of advanced IAB was nearly 1% in the global population, and 2% among patients with valvular heart disease.

The diagnostic criteria for advanced IAB included (Fig.6, 7 and Table I); 1) ECG: $P \pm$ in II, III and VF and $P \geq 120$ ms, with an open angle (usually $>90^\circ$) between the first and second parts of the P wave; 2) orthogonal ECG: $P \pm$ in the Y lead with a negative mode > 40 ms; 3) VCG: more than 50 ms above the X or Z axis, duration of the P loop ≥ 110 ms, with an open angle between the 2 parts of the P loop in both frontal ($131.3^\circ \pm 32.3^\circ$) and right saggital planes ($171.2^\circ \pm 15.1^\circ$), and the presence of notches and slurrings in the last part of the P loop.

TABLE I
Diagnostic Criteria of advanced IAB

-
- 1) Surface ECG:
 - P ± II, III, VF (in II can be only + with isodiphasic last part)
 - P ≥ 120 msec.
 - Open angle (usually >90°) between the 2 parts of the P wave
 - 2) Orthogonal ECG:
 - P ± in Y lead with a negative mode duration ≥ 40 msec.
 - 3) VCG:
 - More than 40 msec. above X or Z axis
 - P loop duration ≥ 110 msec.
 - Open angle in FP and RSP
 - Slurrings and delays in the last part of the loop
 - 4) Oesophageal ECG:
 - H.O.L. = P wave ∓ with delayed inscription
 - L.O.L. = P wave ±
 - 5) Interacavitary ECG:
 - C raneocaudal sequence in RA
 - C audocraneal sequence in LA (combined with oesophageal ECG)
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HOL: High oesophageal lead. LOL: Low oesophageal lead. RA: Right atrium. LA: Left atrium.

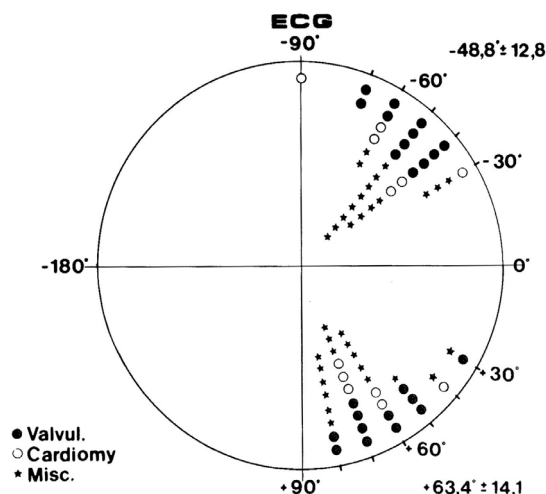


Fig. 7. Direction of the vectors of the first and second parts of the P wave in presence of advanced IAB in the three groups studied.

We have found that the pattern of interatrial block, not only may be transient (second degree) (Fig. 4A) but also may appear progressively (Fig. 8). In these papers [22, 23] we had already emphasized that the diagnosis of advanced IAB is not only of academic interest but may also have clinical implications due to the following:

- a) This is a very specific sign of LAE that is present in ≈ 90% of cases.
- b) In the absence of preventive treatment there is a high incidence of supraventricular paroxysmal arrhythmia (96 %) (flutter and fibrillation) within 1 year. Incidence is 100 % in valvular disease and cardiomyopathic groups.
- c) Paroxysmal arrhythmia appears to be due to IACD-LARA rather than atrial enlargement; in the control groups of valvular disease and cardiomyopathies with similar LAE the incidence of paroxysmal tachyarrhythmia is much lower (20 % vs 100 %).

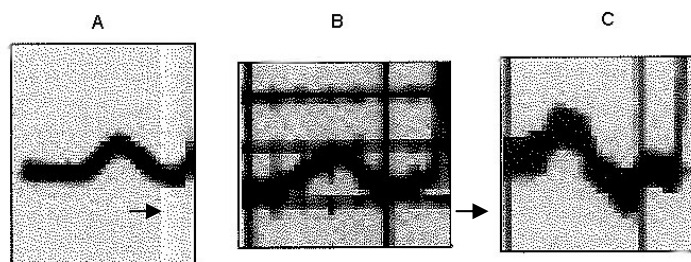


Fig. 8. Progressive interatrial block: P wave patterns in VF from a patient with mitro-aortic valve disease. (A) P wave with normal atrial duration (P = 105ms), (B) An intermediate morphology that corresponds to a first-degree interatrial block (P = 135ms). (C) Advanced interatrial block appearing after 5 years with P ± morphology in II, III, and VF (P = 145ms).

Identification of the syndrome [25]

We proceeded to study a series of patients with a long-term follow-up to better determine the true incidence of supraventricular arrhythmias in these groups of patients when compared with patients of the same clinical and echocardiographic characteristics. We studied 16 patients with electrocardiographic evidence of advanced IAB and retrograde activation of the left atrium ($P \geq 0.12$ s and dysphasic (\pm) P waves in leads II, III and VF). Eight patients had valvular heart disease, 4 had dilated cardiomyopathy and 4 had other forms of heart disease. Patients were compared with a control group of 22 patients with similar clinical and echocardiographic characteristics but who presented partial instead of advanced IAB.

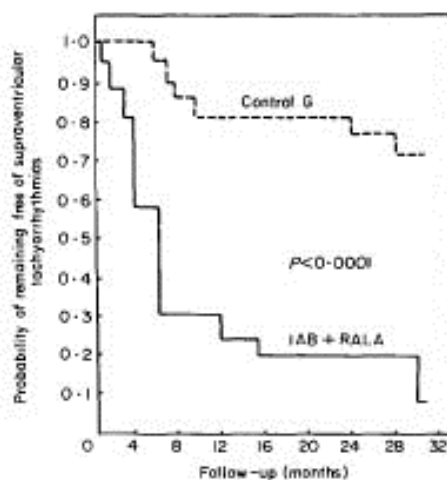


Fig. 9. Life table analysis of the probability of remaining free of supraventricular tachyarrhythmias in patients with advanced interatrial block (IAB) and controls. Taken from [26].

Patients with advanced IAB and retrograde activation of the left atrium had a much higher incidence of paroxysmal supraventricular tachyarrhythmias (93.7 %) during follow-up when compared to the control group with partial IAB, (27.7 %) ($P < 0.001$) (Fig.9). Eleven of the 16 patients (68.7 %) with advanced IAB and retrograde activation of left atrium had atrial flutter (atypical in 7 cases, typical in 2 cases, and with 2 or more morphologies in 2 cases). Six patients from the control group (27.7 %) had sustained atrial tachyarrhythmias (5 with atrial fibrillation and 1 with typical atrial flutter) (Fig.3 and Table II). The atrial tachyarrhythmias were due more to advanced IAB and retrograde activation of the left atrium with frequent atrial extrasystoles than to left atrial enlargement, because the control group of patients with a left atrium of the same size, but with partial IAB instead of advanced IAB and less incidence of atrial extrasystoles, had a much lower incidence of paroxysmal tachycardia.

Prevention of the syndrome and recurrences [26]

Having found a strong relationship between the presence of advanced IAB and the incidence of atrial flutter or atrial fibrillation when compared with a control group (93.7 % vs. 27.7 %), along with a high incidence of an uncommon type of atrial flutter (4), we decided to study the role of preventive antiarrhythmic treatment for this disorder.

Fifteen of the 16 consecutive patients we studied, who did not have preventive antiarrhythmic treatment (93.75 %), presented at least 1 crisis of paroxysmal supraventricular tachyarrhythmia requiring emergency treatment over a follow-up of 10 ± 6.1 months.

In view of the confirmation of high incidence of paroxysmal supraventricular tachyarrhythmias in this type of patient, and especially in valvular disease and cardiomyopathic patients, we decided to institute preventive antiarrhythmic treatment in subsequent patients.

With the use of preventive antiarrhythmic treatment in our 16 subsequent patients, once diagnosed of advanced IAB, the incidence of paroxysmal supraventricular tachyarrhythmia was greatly lowered (25 %) even with longer follow-up (18 ± 10.2 months) (Fig.10). Because of the high risk of embolism in valvular and cardiomyopathic disease, we now consider it advisable to start preventive antiarrhythmic treatment in such patients, prior to the onset of tachyarrhythmia.

It is extremely important to corroborate these results in a greater series of patients. We are therefore preparing a larger trial for this purpose.

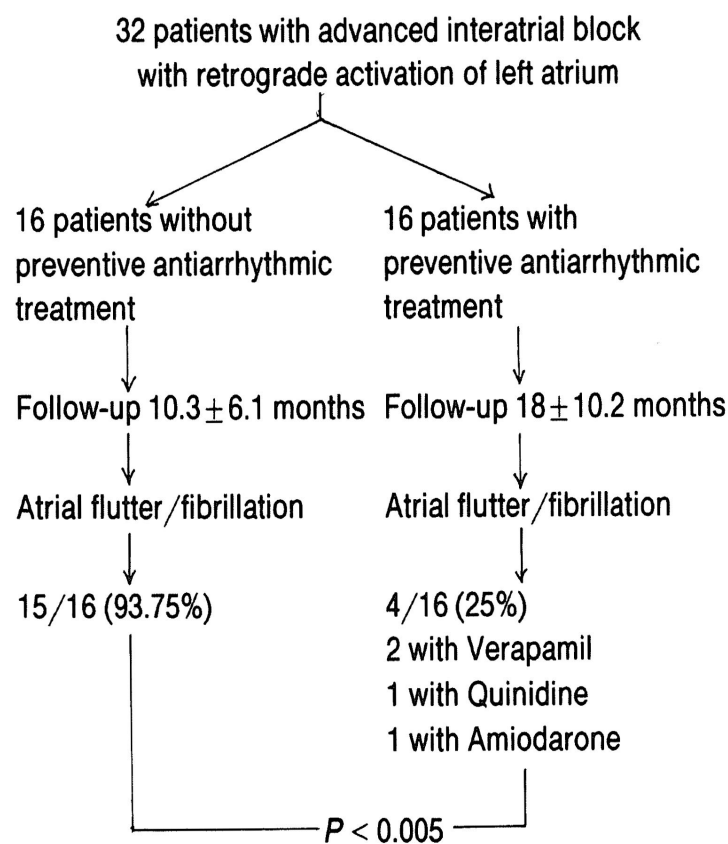


Fig. 10. Follow-up of 32 patients with advanced interatrial block with retrograde activation of left atrium with and without antiarrhythmic treatment

Table II. Characteristics of the sustained paroxysmal tachyarrhythmias

Group with interatrial block (16 patients; 15 with tachyarrhythmia during the follow-up) (93,7%)	
Atrial flutter	7 / 15 cases
Atrial fibrillation	4 / 15 cases
Atrial flutter with fibrillation	4 / 15 cases
MRV 133 ± 42 beats min^{-1}	
Characteristics of the atrial flutter (11 cases)	
Typical form (AR 276 ± 21 min ⁻¹)	2 cases
Atypical form (AR 252 ± 36 min ⁻¹)	7 cases
Two or more morphologies	2 cases
Control group (22 patients; 6 with tachyarrhythmia at follow-up) (27,7%)	
Typical atrial flutter (AR 270 min ⁻¹)	1 case
Atrial fibrillation	5 cases
MRV 127 ± 28 beats min^{-1}	

AR, atrial rate; MVR, mean ventricular rate during crises.

3. Our most recent papers

In 1999 we published [27] a review paper in *Europace* commenting “The syndrome of advanced interatrial block and supraventricular arrhythmia” in which we summarized all previous research by our group and confirmed our view that this association most certainly constituted a syndrome.

We also published a review paper on block at atrial level [21], including the possible diagnosis of right atrial block in case of clockwise rotation of P loop in FP. Also we publish several papers on atrial aberrancy [28, 29], concept that, if the change of P wave is a pattern of partial or advanced IAB, corresponds to a second degree IAB [30] (Fig.4).

We emphasized as we stated in papers and books on ECG [11, 22, 30] and in the latest consensus paper on IAB [23] that these ECG patterns described as patterns of partial and advanced IAB are due to a block, not to atrial enlargement because a) it may be transient and progressive (Fig.7) , b) it may exist without associated left atrial enlargement and c) it may be reproduced experimentally [24] (Fig.12).

4. Conclusion

- a) We have defined the ECG-VCG criteria of advanced IAB and its etiological aspects and prevalence.
- b) We have observed that supraventricular arrhythmias appear very often in a short follow-up in patients with ECG pattern of advanced IAB, if left untreated, and that when are in front of a patient with atypical flutter we can be nearly certain that in sinus rhythm the patient will have the ECG pattern of advanced IAB.
- c) We have demonstrated that if we treat with antiarrhythmic drugs the patients with advanced IAB, the incidence of supraventricular tachyarrhythmic in the future is much lower.
- d) Therefore, we may conclude that this association should be considered a syndrome.

5. The recognition and the future

Thanks to all this information, a select group of cardiologists have manifested their agreement by writing with our view and are convinced that the association of advanced IAB together with supraventricular arrhythmias is a syndrome. This includes Braunwald [31], Daubert [32], and Brugada [33]. Furthermore some groups especially the ones of Daubert [34], Spodick [35, 36], Platonov [37, 38] Garcia-Cossio [39] and Baranchuk and Conde [40-43] have also published different and important aspects on this topic. However, in all these decades it has never occurred to me that one might consider the name *Bayés syndrome*. Therefore, it was with great surprise that I learned of the generosity of Adrian Baranchuk, seconded by Diego Conde, and many other colleagues when I received the first paper on the proposed name for this syndrome, which appeared recently in *Revista Instituto de México* [40], and later other articles in *Revista Argentina Cardiología* [12], the *American Journal of Cardiology* [42], *ANE* [43], among others. What is truly important, however, is that the physicians have to be awarded that the association of advanced IAB plus supraventricular arrhythmias is a syndrome. Really the ECG pattern of advanced IAB is an extremely strong marker of supraventricular tachyarrhythmias in a short period of time, much more so than the presence of partial IAB (only $P \geq 120$ msec), which already presents a high incidence of arrhythmia [26, 28], although to a lesser degree when compared with advanced IAB pattern, as we have already shown. The other speakers of this symposium will explain other very important aspects of the electrophysiology of the atria, and Adrian Baranchuk, the father of this symposium will outline the many possibilities for research that still exist with this syndrome, whatever its name may be in the future.

I would like to express my gratitude to Dr. L. Bacharova President of the meeting (ICE-2014), and International Society of Electrocardiology (ISE) President Dr.C.Pastore, for giving to me the opportunity to explain this story to so many friends. It was extremely generous of her. My special thanks go to all other members of this round table for your friendship and for attending this symposium. I also have to thank the support and intellectual challenge provided by several cardiologists working in this field in different aspects, who have been exchanging ideas with me from the beginning: P. Puech, J.C. Daubert, D. Spodick, P. Platonov, A. Waldo, F. Garcia-Cossio, A. Baranchuk, D. Conde and the friendly support of B. Olson, E. Braunwald, P. Chiaie, M. Elizari, A. Perez-Riera, R. Barbosa, C. Pastore, Hnos. Brugada, X. Viñolas, W. Zareba, I. Cygankiewicz, R. Baranowski, R. Villuendas, A. Bayés Genís, and of course each and every member of my team. Thank you all so very much.

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