HISTORY OF MEDICINE

A hitherto Unknown First of Jan Ev. Purkinje: Myocardial Sleeves of the Pulmonary Veins. A Contribution to the Pathogenesis of Atrial Fibrillation

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SUMMARY

According to recent electrophysiological discoveries, atrial fibrillation is triggered by ectopic beats, which in most cases originate in the pulmonary veins, in extensions of the left atrial myocardium upon these veins: the so-called myocardial sleeves. In the relevant literature it is stated that this anatomical structure was first described by Ferdinand Raeuschel in 1836 in the publication "De arteriarum et venarum structura". This publication appeared as Raeuschel's dissertation thesis at the faculty of medicine in Breslau (now Wroclaw in Poland) at the Department of Physiology under the leadership of Jan Ev. Purkinje. In the introduction, the author thanks his tutor for introducing him into the issue and for providing continuous help, stating that all new discoveries in the dissertation should be ascribed to Purkinje. Thus the description of myocardial sleeves of the pulmonary veins appears to be yet another first of this great Czech scientist.

Key words: myocardial sleeves, J. E. Purkinje, atrial fibrillation, firsts, pulmonary veins.

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The year 1998 saw the publication of a landmark paper by French authors (1), who, using electrophysiological studies, demonstrated that the impulse triggering atrial fibrillation, ectopic beat, originates in the majority of cases from the region of the pulmonary veins. In the above study, this was so in 94% of cases, most frequently from the left upper pulmonary vein. This revolutionized the concept of the pathogenesis of atrial fibrillation as the most frequent supraventricular arrhythmia. The consequences of the new discovery included novel methods of catheter-based treatment of sustained atrial fibrillation, i. e., ablation of the ectopic focus inside a pulmonary vein or complete electrical isolation of the pulmonary veins (2).

Needless to say, the new discovery led to a search for the morphological substrate of the electrical impulse in the pulmonary veins; a host of anatomical and pathological studies appeared, mapping the area of communication between the left atrium and pulmonary veins (e. g., 3-5). Today, the ectopic beat seems to have been clearly shown to originate in extensions of the left atrial myocardium upon the pulmonary veins as so-called myocardial sleeves. These sleeves are present in 70-90% of pulmonary veins; on average, they are 10 mm long (rarely as long as 30 mm) and 1 mm in thickness.

Over the past two years, we have been carrying out a grant research project addressing the pathology of these sleeves in relation to atrial fibrillation; results of the project are to be presented on another occasion.

When researching the literature relevant to the issue of myocardial sleeves, I repeatedly noted authors referring to F. Raeuschel as the first to describe this anatomical structure in 1836 (e. g., 6, 7). The name of F. Raeuschel rang a bell, and I later realized it was included in Volume 6 of the Collected Papers (Opera omnia) of Jan Evangelista Purkinje, about dissertation theses by Purkinjes students (8).

In the years 1823-1850 Purkinje served as Professor of Physiology at the Medical School of Breslau University in what was formerly Prussia (currently Wroclaw, Poland). In 1832 Purkinje received his long-awaited microscope and began to investigate a wide range of tissues in the human body as well as those of animals and plants. He would involve his students in these microscopic studies. At that time a requirement for graduating from a school at Wroclaw University was to present and publicly defend a dissertation thesis. A number of these dissertation theses, including that developed by Raeuschel, originated at Purkinje's institute and, not surprisingly, many of these theses addressed microscopic issues.

The student Ferdinand Raeuschel (born in 1809 in Silesia) defended his inaugural anatomic-physiological dissertation thesis called "De arteriarum et venarum structura" on 29 October 1836. He even published his dissertation thesis as a 24-page booklet with a single enclosure featuring anatomical and histological drawings. In his thesis Raeuschel addressed the microscopic structure of arteries, veins and arterioles while using original histological techniques for tissue fixation and processing.

On page 18 of the last chapter, Raeuschel addressed venous structure. Writing in Latin, Raeuschel says (translation by Prof. K. Žlábek) (10): "**Real muscle fibres** (i. e., myocardial fibres, K. Ž.) **are only found in the venae cavae superior and inferior close to the heart, whereby they create its central membrane ... The same**

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behaviour can be found with pulmonary veins, whose muscular central layer can be shown until the place where their branches further divide into separate branches ". This is in fact the very first description of pulmonary vein myocardial sleeves!

The introduction of Raeuschel's dissertation thesis is most interesting as regards the first description of this anatomical structure. Raeuschel, the author, dedicates his first scientific paper to "J. E. Purkinje, the most reputable, respected, and greatest man …… on grounds of his excellent education and learning, to the dearest tutor, deserving ultimate respect".

Still, it is the foreword to the thesis which is most eloquent: "…Purkinje readily persuaded me, as a scholar in the dark as regards the topic of my dissertation thesis, to investigate, under his guidance, the structure of walls of blood vessels and to present my observations in a modest dissertation thesis... The respected man provided me, a beginner, with not negligible assistance in those experiments, and I openly declare that, if the reader finds anything new or a more careful observation in my modest dissertation thesis, **the credit for this should not go so much to me but to the respected man..."**.

Therefore the situation resembles that of most scientific papers developed by students, whereby the idea and methods have been adopted from the tutor, the supervisor.

One can thus give the credit for the first description of pulmonary vein myocardial sleeves to the long series of discoveries of our great scholar. However, it took more than 160 years before the discovery made by Raeuschel-Purkinje was officially recognized and translated into clinical practice in the management of patients with atrial fibrillation.

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COMMENTARY

Comment on the Article by Prof. I. Šteiner "A hitherto Unknown First of Jan Ev. Purkinje: Myocardial Sleeves of the Pulmonary Veins. A Contribution to the Pathogenesis of Atrial Fibrillation"

One can only note with pleasure that the name of Jan Evangelista Purkinje (spelled Purkyně in Czech) is not merely a name engraved on the tomb of a prominent personality of the past, or simply a long-forgotten classic. The article by Prof. Šteiner discusses another - and by no means insignificant - primacy of perhaps the ultimate giant of Czech medical science. The fact that Purkinje eminence was already realized by his contemporaries is attested to, among other things, by the perhaps notorious sentence from a letter by J. W. Goethe to Purkinje, dated 18 March 1826: "It is not easy to master the wealth of experience you have drawn from Nature with such dogged effort and determination." It is also not exceptional for the ingenious ideas of Purkinje to form the basis of his disciples' dissertation theses. At the same time, Raeuschel's dissertation thesis has long been a well-known area, and the issue of structural differences among various arteries that it mostly addresses – which is of interest to researchers - continues to be quoted frequently. However, it is the earlier part of Raeuschel's dissertation thesis referring to the discovery of pulmonary vein myocardial sleeves that has clearly been long out of our focus. This is most likely due to the fact that the role of pulmonary vein myocardial sleeves in the pathogenesis of atrial fibrillation was only recently identified (1), so the discovery was not given adequate attention. Still, as clearly suggested in the editorial by Prof. Šteiner, it seems the chapter of mapping the

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investigational firsts from the exquisite mind of Purkinje has not been completed, and we may be well in for some puzzling surprises in this respect.

Let us now dwell briefly on the relevance of the above discovery of pulmonary vein myocardial sleeves, particularly from the perspective of the current concept of the pathogenesis of atrial fibrillation. Current theories of the mechanism of atrial fibrillation are based both on the existence and activity of one or several ectopic foci (initiation of atrial fibrillation) and the presence of one or several re-entry circuits (perpetuation – fixation of atrial fibrillation). According to these theories, atrial fibrillation is usually triggered by repeat impulses from ectopic foci, which seems to be most often located in the pulmonary vein ostial myocardium. The classical finding that the atrial myocardium shows structural alterations with increasing age can today be considered a well-established fact. The most obvious of these alterations seems to be patchy fibrotization of the atrial myocardium. Most recent studies (2) have revealed that these structural alterations are more appreciable in the hearts of patients with paroxysmal atrial fibrillation compared with age-matched patients with coronary heart disease who have not yet developed demonstrable supraventricular arrhythmias. Seen from the perspective of the work by Prof. Šteiner, it is of interest that these alterations involve just the pulmonary vein myocardial sleeves and, additionally, area with rapid impulse conduction in the atria, such as Bachman bundle. It is precisely these structural alterations which would be consistent with theories of potential substrates of initiation (e. g., pulmonary vein myocardial sleeves) and fixation (e. g., Bachman bundle) of atrial arrhythmias, and atrial fibrillation in particular. On the other hand, one still has to consider other potential mechanisms of initiation of atrial fibrillation. Quite recently, Chevalier et al. (3) pointed to the interesting fact that the left atrium also has several different gradients of innervation in various areas of the atrium. At the same time, the ostia of the four pulmonary veins have been shown to have a significantly higher nerve density compared with the more distal left atrial segments. One cannot rule out an association of this fact with the pathogenesis of atrial fibrillation or, at least, with successful outcomes of radiofrequency ablation as a therapeutic option in the management of atrial fibrillation. Whatever the case, this innervation is no doubt related to pulmonary vein myocardial sleeves, as innervation of other cardiac tissues, e. g., endocardium, differs substantially from this myocardial type of innervation in terms of morphology.

Whatever the pathogenesis of atrial fibrillation, a non-negligible role in the pathogenesis is clearly played by pulmonary vein myocardial sleeves, so knowledge of their existence, even from the perspective of current medical science, is an accomplishment with particular theoretical and clinical implications. Hence, there is no doubt we can be rightly proud of the fact this discovery (in addition to other discoveries) is among the legacy of firsts devised by Purkinje's ingenious mind.

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