By definition, accessory atrioventricular pathways are aberrant muscle bundles that connect the atrium to a ventricle outside of the regular atrioventricular conduction system. Clinically, they may manifest as substrates for ventricular preexcitation. The first accessory pathway in a patient who suffered from Wolff-Parkinson-White syndrome was described in 1943 by Wood, Wolferth, and Geckler.\(^1\) Shortly after, Öhnell created a reconstruction of an accessory pathway that very elegantly showed the close proximity of the pathway to the fibrous attachment of the mitral valve and its relationship with the sulcus coronarius (Figure, A).\(^2\) Subsequent histological studies have demonstrated unequivocally that these pathways are the anatomic substrates for the classical Wolff-Parkinson-White variety of preexcitation.

Accessory atrioventricular pathways are found most often in the parietal atrioventricular junctional areas, including the paraseptal areas. They breach the insulation provided by the fibrofatty tissues of the atrioventricular groove (sulcus tissue) and the hingelines (fibrous annulus) of the valves. They are rarely found in the area of fibrous continuity between the aortic and mitral valves because in this area, there is usually a wide gap between the atrial myocardium and ventricular myocardium to accommodate the aortic outflow tract. On the left parietal side, the accessory pathways tend to pass close to the hingeline of the mitral valve (Figure, B). In the right atrioventricular junction, the atrioventricular groove is much deeper than on the left side, and the accessory muscle bundles can cross at any depth. Cardiac surgeons have suggested that the deep groove may itself allow the atrial wall to fold over the ventricular wall, thereby producing atrioventricular myocardial continuity.\(^3\) Most of the pathways identified through the use of microscopy have been working myocardium, with only a few reported to contain histologically specialized cells.\(^4\) Whether comprising working myocardium or abnormal myocytes, these pathways have normal gap junctions with a pattern suggestive of working ventricular myocardium.\(^5\) Morphologically, these threads of musculature are thicker at their atrial origins and they branch into finer strands at the ventricular insertions. They are up to 3 mm in width but may be 10 mm or more long.\(^2,4,6\)

Other types of accessory atrioventricular pathways found in certain circumstances are well recognized. One of the 7 pathways in the study conducted by Becker and colleagues\(^4\) was a specialized bundle that had its atrial insertion in a node of specialized tissues in the parietal margin of the tricuspid annulus, forming an atriofascicular tract.\(^7\) Multiple pathways can occur in the setting of so-called Purkinje cell tumors, often with additional tumors within the ventricles. Another type of pathway related to coronary veins is usually manifested in the form of extensive myocardial cuffs around the veins crossing the atrioventricular junction or expanded as diverticulums into the ventricular mass. Others are related to the atrial appendages overlying ventricular masses (Figure, C).

For several decades, accessory pathways have been avulsed successfully through surgery using conventional dissection or by cryothermy or radiofrequency ablation. In the past 2 decades, advancements in precision mapping and ablation of accessory pathways via the transcatheter route have made it possible for many patients to be cured. Although rare, sudden death may be the first presenting sign in patients with undiagnosed and/or asymptomatic preexcitation syndrome. This is particularly worrisome for families with an affected child. The majority of cases have no clear familial involvement, but a small number of patients have affected relatives. Recently, the transcatheter procedure has been deemed safe and effective in experienced hands, but whether it should be used as a prophylactic measure against life-threatening events remains controversial.\(^8,9\) Clearly, there is a need to know more about how these pathways develop so as to guide further therapeutic strategies.

In the embryonic human heart, a ring of musculature at the atrioventricular canal provides myocardial continuity between developing atrial and ventricular myocardium in the early stages. This canal myocardium was shown initially to have slow conduction properties in the chick.\(^10\) The canal myocardium is sandwiched by sulcus tissue on the outside and endocardial cushions on the inside. Kim and colleagues\(^11\) showed that the bulk of the canal myocardium was incorporated into the vestibules making up the atrial walls leading toward the valvar orifices, but it did not contribute to ventricular myocardium. A small part of the canal myocardium becomes the atrioventricular node, and normally this is the only site of myocardial continuity, with the developing ventricular conduction bundles at completion of cardiac septation. In their earlier study, however, Wessels and colleagues\(^12\) noted strands of myocardial continuity between...
atrial and ventricular tissues in all human fetal hearts and many normal neonatal hearts.

Pivotal to the understanding of accessory atrioventricular pathways is knowledge of how the insulating tissue plane at the sulcus and annulus came into being. Vessels and colleagues, among others, offered the explanation that sulcus tissue joins with endocardial cushion tissues at the ventricular margin of the canal. According to this study, the valvar leaflets were formed by cushion tissue, without contribution or real inward growth of sulcus tissue. Instead, the ventricular walls distal to the atrioventricular canal bulged like shoulders toward the atria. They suggested that accessory pathways resulted from incomplete fusion between sulcus and cushion tissues. It is not clear from their study, however, how myocardial discontinuity was effected so as to allow sulcus tissue to meet cushion tissue. In contrast, a simpler explanation was put forward by others who suggested that invagination of sulcus tissue like a wedge through the muscular canal wall was part of the process for development of valvar leaflets, with little contribution from the cushions. Be that as it may, there is consensus that the insulating tissues came from the epicardial side.

It was while studying the embryologic origins of the coronary vessels in chicken-quail chimeras that Gittenberger-de Groot and coworkers identified and traced the migration of a novel population of cells termed epicardial-derived cells (EPDCs) from the epicardial side. By way of comparison, fibrous insulation was complete in the adult quail. Coincidentally, they observed that MLC2a-positive pathways were also stained with peristin, a fibroblast marker that has a role in regulating fibroblast-myocyte interaction. In the present report, the small pathways in both wild-type and EPDC-inhibited hearts stained positive for both MLC2a and peristin. Broad pathways were only found in EPDC-inhibited hearts, but these were associated with local interruption of peristin staining. An important observation of the present study is the interplay between EPDCs, peristin, and accessory pathways. The investigators proposed the concept that impeded migration of EPDCs through the myocardium to the endocardial cushions delayed the development of the fibrous annulus. Although the study has given us a glimpse of pathways that are candidates for premature ventricular activation in the quail, the question of why some accessory pathways produce a functional effect, occasionally devastatingly so, whereas others do not, remains to be clarified. In his monograph, Öhnell considered that some may have been acquired, for instance after myocarditis, a view also put forward more recently by Basso and her colleagues.

Developmentally, the work of Kolditz and colleagues would appear to support the notion that accessory pathways resulted from incomplete interruption of canal myocardium resulting from late arrival of EPDCs. Although incomplete interruption due to sulcus tissue stopping short of the annulus can account for accessory atrioventricular pathways that pass close to the annulus, it is difficult to picture the same process being involved in pathways that are in peripheral locations or in other morphologies as described above. The conundrum of whether those develop later by growing through holes in the tissue plane remains. For those related to coronary veins, what causes the walls to become muscularized (or remain muscularized)? Do the multipotent EPDCs and peristin have a role in those, too? We await further insights into this intriguing area of study.
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