

Editorial

What if Ivemark had suggested the term “Syndrome of Visceral Symmetry with Asplenia” instead of “Asplenia, a Teratologic Syndrome of Visceral Heterotaxy”?

William A. Devine

As a novice dealing with congenital malformations of the heart, I was struck when, at an autopsy at which I assisted, the diagnosis was made of “asplenia syndrome with a spleen”. Then, last year, we performed an autopsy on a child who had the expected malformations of “asplenia syndrome” yet we discovered two spleens (Figures 1a & 1b). And recently, I conversed with a pathologist who had just performed an autopsy on a child who had the malformations of the organs consistent with “polysplenia syndrome”, but in whom a single spleen had been found. Such discrepancies between the state of the spleen, the arrangement of the other thoracoabdominal organs, and the combination of cardiac malformations anticipated for the “splenic syndromes” have been known for years.¹ Odd, therefore, to continue to argue for use of the state of the spleen to classify congenitally malformed hearts,² the more so since the spleen is an organ whose identification during life is neither easy nor inexpensive. Surely, as logical descriptions of congenitally malformed hearts become increasingly adopted worldwide, it should be accepted that the concept of “splenic syndromes” leaves something to be desired. For myself, I am convinced that classification of cardiac defects as found in these so-called cardioplenic syndromes should be based on the heart, using as the diagnostic criterion a component that can be accurately and reliably identified, namely, the atrial appendages. In this brief review, I will try to substantiate this argument.

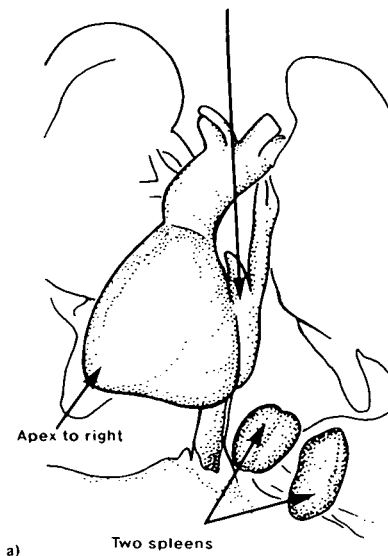
Background

It is long established³ that the “cardioplenic syndromes” are associated with complex cardiovascular malformations and a jumbled up arrangement of the abdominal organs (“heterotaxy”). Thus, atrioventricular septal defects, totally anomalous pulmonary venous connections, abnormal ventriculoarterial connections and

pulmonary arterial stenosis are known generally to be common findings with “asplenia syndrome”. Similarly, it is usual to find partially anomalous pulmonary venous return, bilateral superior caval veins, interruption of the inferior caval vein with azygos continuation, along with atrioventricular septal defects, in patients with “polysplenia syndrome”. Since the study of Van Mierop and Wigglesworth,⁴ however, it has also been established that cases with “asplenia syndrome” have thoracic organs (including the atrial appendages) which show isomerism of features normally found on the right side of the body, while Moller and his colleagues⁵ emphasized the isomerism of structures normally found on the left side of the body in “polysplenia syndrome”. I do not stand alone since then¹ in advocating the use of the morphology of the atrial appendages as the subsequent basis for sequential segmental analysis of hearts^{1,6} to characterize the conditions known historically as the splenic or heterotaxia syndromes. Studies to which I contributed have shown^{7,8} that classification according to the morphology of the atrial appendages is a better guide to the anticipated cardiac defects than is either the state of the spleen or the anomalous position of organs. It seems to me, therefore, that the cardiac manifestations of “asplenia syndrome” are best described from the stance of the heart and analyzed on the basis of right isomerism of the atrial appendages, while so-called “polysplenia syndrome” can, in terms of the heart, best be called left isomerism of the atrial appendages. I must then note, nonetheless, that the concept of using the morphological symmetry (isomerism) of the atrial appendages as an indicator and means of classifying these hearts has failed to find universal favor.^{2,9} If I understand the objections to the concept correctly, they stem from a different interpretation of the nature of isomerism in living systems, coupled with the belief that isomerism of the atria does not exist. Let us examine, therefore, both of these potential caveats.



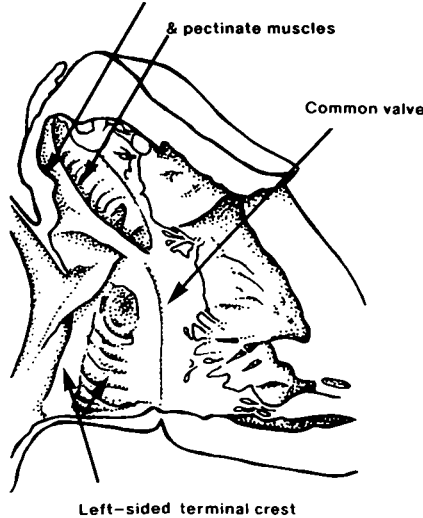
Left-sided morphologically right appendage



a)



Right-sided terminal crest



b)

Figure 1. These views of the thoracoabdominal organs are from a patient with bilateral superior caval veins, a common but stenotic pulmonary vein draining to the left superior caval vein, bilateral morphologically right trilobed lungs and a right-sided heart. This anterior view (a) shows the presence of two spleens. The internal aspect of the heart (b) reveals pectinate muscles and terminal crests present bilaterally, together with a common atrioventricular valve connected to a dominant left ventricle.

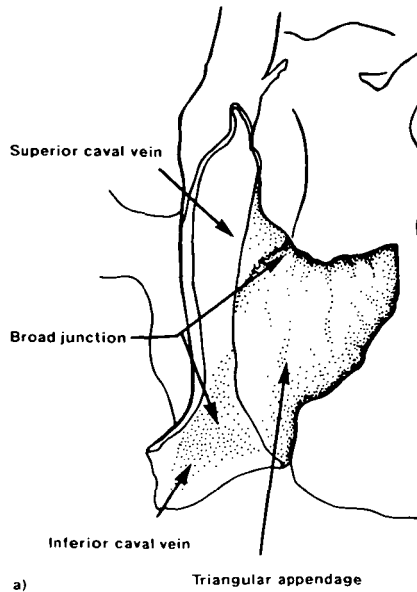
What is isomerism?

Dictionaries give several definitions for isomerism. A common means of illustrating isomerism is to use the stereoisomeric nature of D- and L-glucose. These compounds are, in overall structure, mirror-images of each other. Molecules in their environment, however, are not static structures as seen on the printed page. If it was possible to look closely, let us say, at the distribution of the electrons around each molecule, they would no longer be strict mirror-images. Gardner¹⁰ has made the statement “Chiral and achiral are sharp adjectives only in pure geometry ...and with reference to ensembles of

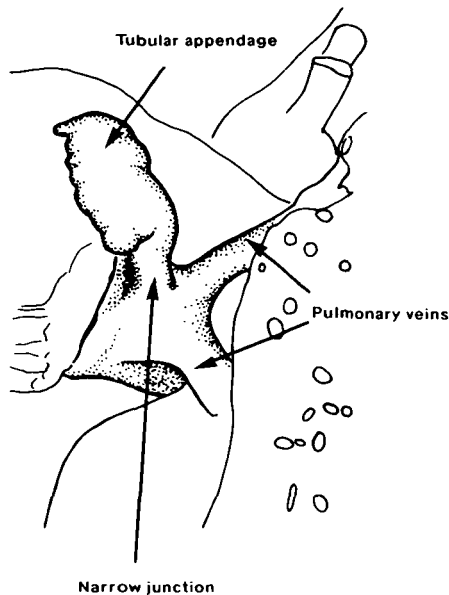
molecules, the adjectives become fuzzy... and lie on a spectrum of more or less”. Using the concept of isomerism of individual molecules as the yardstick for isomerism in a hominid, therefore, is unduly restrictive. The cardiologist, pathologist and surgeon are not examining individual, non-living molecules, but are studying a complex molecular system, a living organism (Homo sapiens) which belongs to the phylum Chordata, subphylum Vertebrata. A characteristic of this subphylum is overall bilateral symmetry, but with significant asymmetry of some organs. In respect of potential isomerism in this setting, however, it has also been argued² that differences in size, due, for example, to abnormal hemo-

dynamics, exclude biological structures from being isomeric. Evidence can be produced to show that this is not the case. The right and left halves of the cerebral hemispheres are morphologically very similar. According to Blinkov and Glezer,¹¹ nonetheless, the left cerebral hemisphere is generally longer than the right, yet the structures are morphologically isomeric. The third finger of my left hand measures 8.6 cm long, and the corresponding finger on my right hand measures only 8.3 cm in length. My hands, conceptually, remain isomers of each other. The average right arm of a right-handed person is larger than the left arm, and this

difference in size is more apparent in an avid right-handed tennis player. And so on. It is not unexpected, therefore, to find an enlarged atrium due to hemodynamics in the setting of right or left isomerism of the atrial appendages as a result of the associated congenital heart disease. Are these discrepancies in size sufficient reason not to describe the appendages as having bilateral morphological symmetry? Of course not. Symmetry (isomerism) in an organism cannot be used in the strict sense defined for description of chemical compounds. Isomerism in living systems means that the morphology of the left-sided structure is, conceptually, a mirror-image of its right-



a)



b)

Figure 2. These illustrations, from separate hearts, show the typical features of a) a morphologically right and b) a morphologically left appendage.

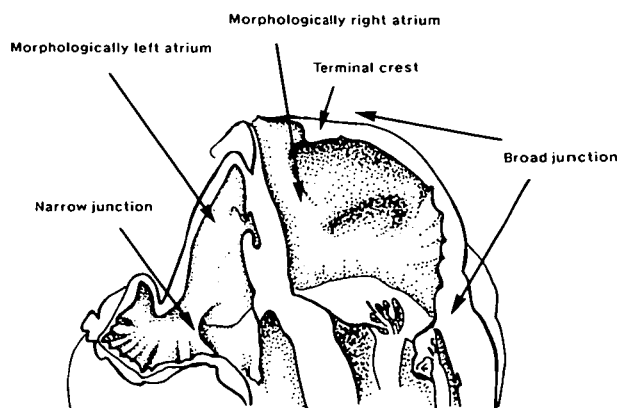


Figure 3. This specimen, viewed from behind, shows the typical internal features of the right and left appendages.

sided counterpart. Size is not a critical feature.

Can there be isomerism of the atrial appendages?

The arrangement of the appendages of the normal human heart is anatomically asymmetrical. The right appendage (Figure 2a), as viewed from the outside, has a triangular shape with a wide base. Internally (Figure 3), it has a broad junction with the systemic venous component of the atrium. A terminal crest is present at the junction, and the pectinate muscles arising from the crest surround the atrioventricular junction, extending to the post-Eustachian sinus.¹² In contrast, the morphologically left appendage as viewed externally (Figure 2b) is a tubular structure with a narrow base. Internally, there is no terminal crest between it and the pulmonary venous component, and only a few pectinate muscles lie outside the junction (Figure 3). As Van Mierop and his co-workers,^{3,4} along with other investigators,^{1,6} have pointed out, those cases with so-called splenic syndromes have morphological isomerism of the atrial appendages when assessed in terms of their junction with the venous components (Figures 1a & 3). Other authorities, in contrast, hold that the shape of the atrial appendages in hearts from patients with the “splenic syndromes” is due to hemodynamics in fetal life, and that the appearance of isomerism is spurious.^{2,9} This notion fails totally to account for the presence or absence of terminal crests; the distribution of pectinate muscles; the presence of bilateral sinus nodes in cases of “asplenia syndrome”; or in the existence of poorly-formed, small or virtually absent sinus nodes in hearts which carry the label “polysplenia syndrome”.¹³

It remains a morphological fact that the most constant feature of an atrium for determining the atrial arrangement is the appendage.¹² I should emphasize, in this respect, that no one believes that the entire atrial

chambers in patients with the “splenic syndromes”, including the venous connections, are isomeric. It is only the appendages, particularly their junctions with the venous components of the atriums, which show morphological isomerism. It is well established that, in hearts with isomerism of the appendages, the pulmonary and systemic venous connections are markedly variable; the coronary sinus may be absent (particularly in those with right isomerism); and that the atrial septum is usually deficient, if not entirely absent.^{1-3,7} The nature of the variability of these structures is crucially important and must be categorized. The recognition of such malformations, along with the condition of the spleen and the anomalous placement of the other abdominal organs, are all helpful in diagnosis. The most reliable feature for diagnosis of the cardiac lesions, nonetheless, remains the morphology of the atrial appendages.

Implications for classification

Some would divide atrial “situs” into three categories: situs solitus, situs inversus, and undiagnosed situs—with the last designation being employed simply because those using this approach do not recognize the existence of isomerism of the atrial appendages.^{2,9} In reaching this conclusion, the morphological evidence in favor of the isomeric nature of the atrial appendages seems to be ignored. Instead, the decision concerning rightness or leftness of an atrium is based on the identification of structures which are themselves variable (systemic venous connections, coronary sinus, or atrial septum). The atrial arrangement in these hearts, nonetheless, does not remain undiagnosed when viewed in the light of the morphology of the junction of the appendages with the venous components of the atriums. It is recognition of the isomeric appendages

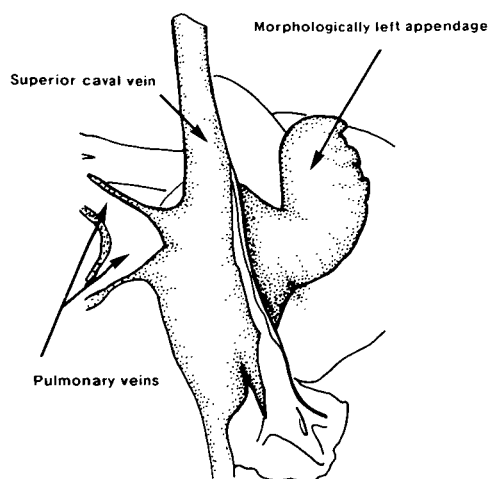


Figure 4. Illustration of a heart with isomerism of the morphologically left appendages showing a right-sided superior caval vein and partially anomalous pulmonary venous return with a right-sided, morphologically left appendage.

that permits the connections to the ventricular mass to be described appropriately as biventricular and ambiguous. The term "situs ambiguous" as applied to the atrial appendages alone, in contrast, can only lead to confusion since, when judged on the basis of the anatomy of their junctions, the appendages are either of morphologically right or left structure. It is the nature of the atrioventricular connections which is truly ambiguous, but even then only when biventricular, since double inlet ventricle or absence of one atrioventricular connection can still be described specifically in the presence of isomeric appendages.

As I have already discussed and emphasized, the condition of the spleen is not as reliable as the morphology of the appendages in predicting the cardiovascular malformations characteristic of the "splenic syndromes".^{1,5,7,8,14} I have also argued that splenic status is not easily determined in life. In this respect, it must be conceded that the arrangement of the atrial appendages can itself be difficult to assess accurately in life. It is fortunate, therefore, that there is a very high concordance between the arrangement of the appendages and the anatomy of the bronchial tree. A pattern of right bronchial morphology bilaterally (isomeric short main bronchi) is almost always associated with isomerism of the right atrial appendages ("asplenia syndrome"), while isomeric left bronchial pattern (bilateral long main bronchi) is almost uniform with isomerism of the left atrial appendages ("polysplenia syndrome").^{1,3,8,15} The bronchial arrangement can be easily determined using a plain chest radiograph.¹⁶ This is a very reliable method of inferring atrial arrangement, with only a few reported exceptions.^{8,17,18} The optimal method of using the mor-

phology of the atrial appendages, nonetheless, is coming ever closer, since it has been shown that this feature can now accurately be evaluated using transesophageal echocardiography.¹⁹

Conclusion

It has been widely demonstrated that the cardiac features of those children with complex congenital heart disease characteristic of the so-called "splenic" or "heterotaxia" syndromes are more accurately diagnosed and described using the morphology of the atrial appendages as the primary arbiter. By identifying the arrangement of the appendages as the first step in sequential segmental analysis of hearts, even the most complex hearts, such as those found in conjoined twins, can easily be described and diagnosed.²⁰ Let us move away, therefore, from calling these conditions splenic or heterotaxia syndromes. What are the alternatives? It would be just as easy, and more accurate, to call them syndromes of right or left bronchial isomerism, but that, again, would be less than perfect when describing the heart, and would still leave some exceptions. Ivemark himself,²¹ the father of the term "Asplenia Syndrome", observed that the hearts in his patients showed a symmetric pattern, although he did not discuss either the atrial appendages or the forms of symmetry he noted. In his section "A Note on Symmetry" he describes what he called "Asplenia Syndrome" as a "Syndrome of Visceral Symmetry". One can only speculate how these syndromes would have been described subsequently if Ivemark had suggested the diagnoses "Syndromes of Visceral Symmetry with Asplenia" instead of "Asplenia,

a Teratologic Syndrome of Visceral Symmetry"! If the heart is involved in the major pathology found in these syndromes, and if it is the condition of the heart that most interests the cardiologist, then surely the cardiac defects are best characterized on the basis of the heart, using as the major criterion the morphology of the isomeric appendages.

*Pathology Department
Children's Hospital of Pittsburgh
One Children's Place
Pittsburgh, PA 15213 USA
Tel. (412) 692 5647*

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