Cardiol Young 2007; 17(Suppl. 2): vii–x

ISSN 1047-9511
doi: 10.1017/S1047951107001102

Introduction

Introduction – Part I: Heterotaxy and Isomerism of the Atrial Appendages

Robert H. Anderson,[1] Jeffrey P. Jacobs,[2] J. William Gaynor,[3] Gil Wernovsky[4]

[1]Cardiac Unit, Institute of Child Health, Great Ormond Street Hospital for Children, London, United Kingdom; [2]The Congenital Heart Institute of Florida, Division of Thoracic and Cardiovascular Surgery, All Children's Hospital/Children's Hospital of Tampa, University of South Florida College of Medicine, Cardiac Surgical Associates, St. Petersburg and Tampa, Florida, United States of America; [3]Cardiac Surgery, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States of America; [4]Division of Pediatric Cardiology, The Children's Hospital of Philadelphia, Pennsylvania, United States of America

In the section of the supplement that follows, we present three reviews that put into context the association between visceral heterotaxy and isomerism. The first review, coordinated by Jeff Jacobs, encapsulates the deliberations of the International Nomenclature Working Group concerning the relationship between visceral heterotaxy, the splenic syndromes, and isomerism as it can be seen within the body. The second review, expertly collated by Meryl Cohen, includes contributions from all those who presented in the closing symposium of the meeting organised by Children's Hospital of Philadelphia, and is dedicated to the memory of Stella Van Praagh (Fig. 1). The third review, orchestrated by Andy Atz, is based on data submitted from the 7 centres in North America that together constitute the Pediatric Heart Network. Taken together, the reviews will hopefully provide order relative to a topic that has oftentimes been considered ambiguous. During the course of the evolution of the various reviews, it is also the case that many of the authors, ourselves included, have become much more aware of the reasons why the topic has been controversial. It is our hope that the definitions provided at the end of the review by the International Working Group will resolve these controversies. To put them in context, we recapitulate here our understanding of the evolution of thought concerning situs ambiguus, heterotaxy, and isomerism.

Correspondence to: Professor Robert H. Anderson, Cardiac Unit, Institute of Child Health, University College, London WC1N 1EH, United Kingdom. Tel: +44 0 20 7905 2295; Fax: +44 0 20 7905 2324; E-mail: r.anderson@ich.ucl.ac.uk

Situs ambiguus

When Richard Van Praagh and his colleagues first introduced the segmental approach to nomenclature,[1] they based their analysis on examination of autopsied specimens, and on the aspects of the heart that, at that time, were visible to the clinician. In essence, from the clinical stance, this meant the morphological features that could be discerned from angiographic investigation. They stressed that the starting point for analysis was determination of the arrangement of the atrial segment of the heart, and suggested that there were 3 possibilities, situs solitus, the mirror-imaged variant termed situs inversus, and then a third variant which they dubbed situs ambiguus.

Isomerism within the body

Many of those working in the field of the congenitally malformed heart at the time of evolution of the segmental approach had already noted that, in the setting of situs ambiguus, certain structures within the body showed evidence for symmetrical development, as opposed to the lateralised features that were characteristic of situs solitus and situs inversus. Thus, already by the time that Van Praagh and his colleagues had emphasised the ambiguous nature of the atrial segment as the third variant of situs,[1] Van Mierop and colleagues[2]

Figure 1.
The late, and much lamented, Stella Van Praagh, shown in one of her characteristic situations, surrounded by students to whom she is imparting the mysteries of the congenitally malformed heart. The symposium that formed the basis for the second review in this section of the Supplement was dedicated to her memory.

had demonstrated that the atrial appendages and the sinus nodes were duplicated and symmetrical in patients with congenital asplenia, whilst shortly thereafter Moller and his colleagues[3] pointed to the presence of symmetrical arrangement of morphologically left-sided structures in those with congenital polysplenia. Despite this emphasis on bodily isomerism, confirmed by Landing and his colleagues[4] as being present also in the lungs and bronchial tree, cardiologists, for the most part, continued to stratify the ambiguous arrangement on the basis of absence of the spleen, or presence of multiple spleens. This approach was perceived as creating unnecessary difficulties by those working in Europe when, on occasion, it led to description of presence of the spleen in the setting of "asplenia syndrome". Stimulated by the promulgation of the so-called "Morphological method",[5] the Europeans argued that the ambiguity could be removed from "situs ambiguus" by describing the presence of either right isomerism or left isomerism.[6]

The Morphological Method

Introduced quite rightly by Van Praagh and his colleagues[5] as a justifiable criticism of the attempt made by the European nomenclaturists to define "univentricular" hearts of right ventricular type on the basis of absence of the valve of inlet to the morphologically left ventricle,[7] the morphological method stated that structures that were themselves variable should not be used as the basis of definition for other variable structures. Taking this criticism of their previous work to heart, the European school realised that the logic of the approach suggested by Van Praagh and his associates[5] applied particularly to the cardiac structure in the setting of so-called "situs ambiguous". At that time, it had been usual to use the termination of the inferior caval vein as the marker of the morphological right atrium, and the connection of the pulmonary veins as the criterion for the morphologically left atrium. Both of these features, of course, were known to be lacking in many hearts from patients with situs ambiguus, adding strength to the emphasis on the ambiguity of the situation. The Europeans, however, sought a marker of atrial differentiation that was present even in the setting of situs ambiguus, and believed that they had discovered this in the form of the atrial appendages. Unfortunately, rather than describing their findings in terms of isomerism of the atrial appendages, they chose to advertise their new approach on the basis of atrial isomerism,[6] attracting further criticism from those who argued that patients with left atrial isomerism would logically possess 8 pulmonary veins, whilst those with right atrial isomerism should logically be required to have 2 superior caval veins, 2 inferior caval veins, and 2 coronary sinuses. It was also pointed out by Van Praagh and colleagues,[8] in criticising the approach based on shape of the appendages, that shape could be modified by haemodynamics. Responding again to this justified criticism, the Europeans redoubled their efforts to find a morphological marker that differentiated the atrial appendages irrespective of shape and size, and discovered this in the extent of the pectinate muscles relative to the atrioventricular junctions.[9] By this time, they had also realised the inappropriateness of describing the findings in terms of "atrial isomerism", and henceforth argued that atrial arrangement should be described on the basis of the atrial appendages, with only 4 possibilities, namely the usual pattern, its mirror-image, and isomerism of the morphologically right or morphologically left atrial appendages.

Heterotaxy

In the meantime, whilst many in Europe were emphasising the need to commence cardiac analysis by describing the arrangement of the atrial appendages, and this approach was becoming accepted as the starting point of the European Paediatric Cardiac Code, many working elsewhere in the World popularised the use of heterotaxy, or visceral heterotaxy, to describe the arrangement previously known as "situs ambiguus". One problem with this approach is that, strictly speaking, heterotaxy accounts for anything other than the normal arrangement. It has become accepted,

https://doi.org/10.1017/S1047951107001102 Published online by Cambridge University Press

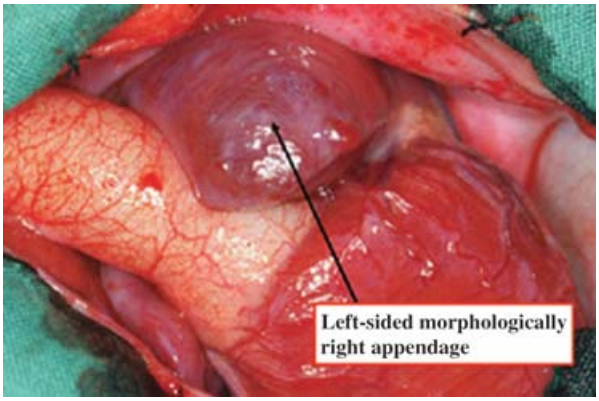

Figure 2.
This picture was taken in the operating room by Benson R. Wilcox, from the University of North Carolina, and is reproduced with his permission. It shows a left-sided atrial appendage with unequivocal right morphology. The right-sided appendage was also of right morphology. The patient also had all the features of asplenia syndrome.

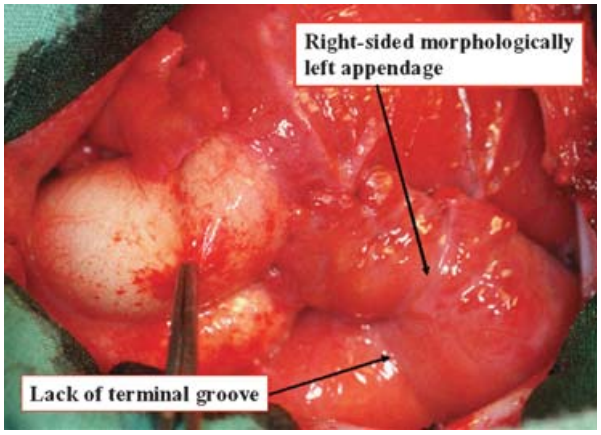

Figure 3.
This picture, also taken in the operating room by Benson R. Wilcox, and reproduced with his permission, shows unequivocal isomerism of the morphologically left appendages. The patient also had all the features of polysplenia syndrome.

nonetheless, that the term should be used as though synonymous with the splenic syndromes, and that it can then be stratified on the basis of division into the asplenia syndrome and the polysplenia syndrome. If we also accept that description of these groupings as "syndromes" means that it is possible to have "asplenia syndrome" in presence of a spleen, or "polysplenia syndrome" in absence of the spleen, then it does mean that cross-mapping becomes possible between the systems currently existing on the one hand as the European Paediatric Cardiac Code, and on the other hand as the system devised by the Society of Thoracic Surgeons working together with the European Association of Cardiothoracic Surgeons. This will require recognition by all parties of the fact that visceral heterotaxy should be considered synonymous with situs ambiguus, that this form of situs can be stratified into the asplenia syndrome and the polysplenia syndrome, and that the essence of the cardiac features of these syndromes is isomerism of either the morphologically right or the morphologically left atrial appendages (Figs 2 and 3). In terms of heterotaxy, recognition of the unequivocal similarities between the existing systems for coding shows that, irrespective of the words used for description, "situs ambiguus" can be stratified into 2 subsets, these being, on the one hand, the asplenia syndrome, with unequivocal features of right isomerism, and on the other hand, the polysplenia syndrome, with features of left isomerism. If we are to solve the genetic background to heterotaxy, it will be essential, in future, to recognise this stratification.[10] Once this basic stratification has been made, the features of these syndromes can be specified in any given individual by providing descriptions of all relevant structures, since it is also well recognised that one of the important aspects of heterotaxy is lack of harmony in the morphological arrangement of the various systems of organs and the atrial appendages.[10] Accounting for the given arrangement of each system, preferably combined with description of the morphology of the appendages in the individual case, serves to remove ambiguity, and to provide order in the place of previous chaos.

Acknowledgement

We are indebted to Benson R. Wilcox, retired Chief of Cardiothoracic Surgery from the University of North Carolina, Chapel Hill, for granting us permission to reproduce Figures 2 and 3. We also thank Amy Juraszek, Curator of the Van Praagh Archive at Boston Children's Hospital, for providing us with Figure 1.

References

1. Van Praagh R, Van Praagh S, Vlad P, Keith JD. Anatomic types of congenital dextrocardia. Diagnostic and embryologic implications. Am J Cardiol 1964; 13: 510–531.
2. Van Mierop LHS, Patterson PR, Reynolds RW. Two cases of congenital asplenia with isomerism of the cardiac atria and the sinoatrial nodes. Am J Cardiol 1964; 13: 407–412.
3. Moller JH, Nakib A, Anderson RC, Edwards JE. Congenital cardiac disease associated with polysplenia: a developmental complex of bilateral "left-sidedness". Circulation 1967; 36: 789–799.
4. Landing BH, Lawrence TY, Payne VC Jr, Wells TR. Bronchial anatomy in syndromes with abnormal visceral situs, abnormal spleen and congenital heart disease. Am J Cardiol 1971; 28: 456–462.
5. Van Praagh R, David I, Wright GB, Van Praagh S. Large RV plus small LV is not single LV. Circulation 1980; 61: 1057–1058.

6. Macartney FJ, Zuberbuhler JR, Anderson RH. Morphological considerations pertaining to recognition of atrial isomerism. Consequences for sequential chamber localisation. Br Heart J 1980; 44: 657–667.
7. Keeton BR, Macartney FJ, Hunter S, et al. Univentricular heart of right ventricular type with double or common inlet. Circulation 1979; 59: 403–411.
8. Van Praagh S, Kreutzer J, Van Praagh R. Systemic and pulmonary venous connections in visceral heterotaxy, with emphasis on the diagnosis of the atrial situs: a study of 109 postmortem cases. In: Clark EB, Takao A (eds). Developmental Cardiology: Morphogenesis and Function, 1st edn. Futura Publishing Co., Inc., Mount Kisco, NY; 1990, pp. 671–727.
9. Uemura H, Ho SY, Devine WA, Kilpatrick LL, Anderson RH. Atrial appendages and venoatrial connections in hearts with patients with visceral heterotaxy. Ann Thorac Surg 1995; 60: 561–569.
10. McElhinney DB. Searching for order amongst disorders of laterality. Cardiol Young 2007; 17: 264–267.

https://doi.org/10.1017/S1047951107001102 Published online by Cambridge University Press